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Bradley Stoke
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Tel: +44 (0)1174 406489
E-mail: info@ese-hormones.org
Web site: http://www.ese-hormones.org

Conference Secretariat
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Bristol BS34 8YU, UK
Tel: +44 (0)1454 642240
Fax: +44 (0)1454 642222
E-mail: ece2023@endocrinology.org
Website: https://www.ese-hormones.org/ece2023

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Plenary Lectures

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The clinical importance of high resolution, automated, ambulatory measurement of tissue steroids
PL2

Stafford Lightman, University of Bristol, UK

Almost all hormonal systems are dynamic with hormones being secreted in various combinations of ultradian, circadian, monthly and even yearly patterns.These patterns have emerged as natural consequences of the multilevel regulation of the hormone axes themselves and in response to environmental conditions such as the light:dark cycle, food availability and temperature. The Hypothalamic-Pituitary-Adrenal (HPA) axis is critical for life and delivers a complex system of pulsed steroid release from the adrenal gland with an approximate hourly ultradian rhythm underlying a much better recognised circadian rhythm. Both of these rhythms have been shown to be critical for good health, and are an important aspect of the regulation of cognitive, appetitive,-metabolic, immunological and cardiovascular function. Since these oscillating levels of corticosteroids are so important for health, and so many disease processes from Cushings disease, hyperaldosteronism and Addisons disease to metabolic immunological and psychiatric disorders., are associated with HPA dysfunction, it is clearly important to be able to assess 24 hour hormone levels. As it is not feasible to take multiple blood samples from subjects going about their normal lives- including during normal sleep- we have designed a novel automated ambulatory sampling system that allows us to sample interstitial fluid hormone levels in normal ambulant subjects (www.u-rhythm.co.uk). Using our automated sampler the Horizon 2020 funded 'Ultradian' project between Bergen, The Karolinska, Athens and Bristol, has now published our first paper on 214 normal subjects to establish normal indices for the dynamic changes in the corticosteroidome across the day. I will be discussing the rich data set from these subjects and what it tells us about the heterogeneity of HPA activity between normal subjects, differences between blood and tissue for cortisol and cortisone levels,and the remarkable evidence for differences in aldosterone regulation between different subjects.The use of multiple sampling technology for the diagnosis and management of patients with adrenal disorders will be discussed by Dr Thomas Upton in his talk on Monday.

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The Silent Decline: Unlocking the Enigma of Dropping Sperm Counts and Fertility Rates
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From molecular biology to precision medicine in endocrine tumors: Are we there yet?
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Symposia

Craniopharyngioma: Pathogenesis and novel targeted treatments

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Thyroid hormones and development

S2.1

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Neural pathways controlling feeding behaviour: impact of circulating hormones

S3.1

Amylin – an anorexigenic pancreas-brain signal
Christelle Le Foll

Amylin is a pancreatic gut hormone co-released with insulin in response to a meal. Amylin signaling has drawn a large amount of interest these past years due to its potential as an anti-obesity treatment. Amylin binds to an heterodimeric receptor (AMY1-3) composed of the calcitonin receptor (CTR) and the receptor activity modifying proteins (RAMP1-3). These receptors are located in multiples brain areas involved in the homeostatic and hedonic control of energy homeostasis. The distribution and the localization of these receptors subtype may be important in mediating amylin's specific effects. Amylin's main binding site is located in the area postrema where its activates noradrenergic neurons to produce its anorectic effect by decreasing meal size. The signal is then propagated to the nucleus of the solitary tract and lateral parabrachial nucleus (LPBN) and transmitted to forebrain areas such as central amygdala and bed nucleus of the stria terminalis. In the LPBN, amylin signaling mainly activates non-aversive non-CGRP (calcitonin-gene related peptide) neurons while the AMY agonist salmon calcitonin, which also binds the CTR alone, activates CGRP neurons leading to malaise and nausea. Amylin also act in the mediobasal hypothalamus where it sensitize leptin action. Cagrilintide is a long acting, dual amylin and calcitonin receptor agonist (DACRA) that induces weight loss in people living with obesity. The combination of cagrilintide and the long-acting glucagon-like peptide 1 receptor (GLP-1R) agonist, semaglutide (CagriSema) is currently in clinical development for treatment of obesity and type-2-diabetes. Our current work aim to identify the exact neuronal pathways and molecular identity of the neurons activated by these drugs.
Key learning points
- Amylin is a pancreatic peptide secreted in response to a meal; it controls eating and energy homeostasis.
- Amylin acts through a variety of receptor composed of the calcitonin receptor and the receptor activity modifying protein 1-3.
- Amylin primary sites of action are located in the area postrema and the arcuate nucleus of the hypothalamus.
- Amylin receptor agonist promote an aversive through NTS-LPBN neuronal pathway.
- The amylin receptor agonist, cagrilintide, acts in concert with semaglutide to decrease body weight at lower dose than each compound alone.
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Osteoporosis Conundrums

S4.1

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Symposium: 'Does sclerostin inhibition increase cardiovascular risk?'

Elena Tsourdi

In the ARCH study[1], romosozumab was compared with an active comparator, alendronate. Unexpectedly, an imbalance in adjudicated serious cardiovascular AEs was observed during the first year of the study, triggering numerous discussions among experts and giving rise to hypotheses regarding the mechanism leading to such a difference. However, it should be noted that an even lower cardiovascular risk in high-dose romosozumab treatment as compared to placebo was reported in a meta-analysis[2]. In addition, a recent systematic review and meta-analysis showed no increase in cardiovascular risk with regard to stroke, atrial fibrillation, heart failure, coronary artery disease, and cardiovascular death individually while, however, increasing the risk for the composite of four-point major adverse cardiovascular events[3]. Given that these results were not completely conclusive[3], a comparative trial between romosozumab and antiresorptive agents is needed to shed further light on this question. In conclusion, he difference in rates of cardiovascular events between romosozumab and alendronate seen in ARCH could be attributable to a possible cardioprotective effect of alendronate or could also represent a chance finding[4]. However, a recent genome-wide association study meta-analysis using Mendelian randomization in 33.961 European individuals provided genetic evidence to suggest that lower levels of sclerostin may increase the risk of hypertension, type 2 diabetes mellitus, myocardial infarction, and the extent of cardiovascular disease[5]. Thus, there is a need to develop strategies to mitigate potential AEs associated with romosozumab treatment on atherosclerosis and its related risk factors.

Highlights

- The role of wnt signalling in atherogenesis raises the possibility that the wnt inhibitor, sclerostin, provides a natural defence to this process, and that anti-sclerostin antibodies might increase the risk of atherosclerosis and associated conditions such as CVD.
- Randomised controlled trials of treatment with the anti-sclerostin antibody, romosozumab, have yielded conflicting evidence with respect to possible adverse effects of sclerostin inhibition on CVD risk.
- Three Mendelian randomisation (MR) studies have examined effects of sclerostin lowering on CVD outcomes. Concordant findings were seen in two studies, comprising an effect of sclerostin lowering on increased risk of MI and type II diabetes mellitus. One study also suggested that sclerostin lowering increases coronary artery calcification.

Triangulation of evidence from different sources provides some suggestion that sclerostin lowering increases MI risk, supporting the need for CVD risk assessment when considering treatment with romosozumab.

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Emerging aspects of menopause

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New applications of Steroid Hormones

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S6.3

Novel forms of adrenal insufficiency

Christa E. Flück
Division of Pediatric Endocrinology, Diabetology and Metabolism, Department of Pediatrics, Bern University Hospital, University of Bern, Switzerland and Department of Biomedical Research, University of Bern, Switzerland. Christa.flueck@unibe.ch

Genetic variants causing adrenal insufficiency (AI) are either disrupting corticosteroid production exclusively leading to isolated AI or they are causing additional organ malfunctions as part of a syndromic form of AI. In **isolated AI**, genetic disorders may affect structure and function of the adrenal cortex or adrenal steroidogenesis specifically, but often also lead to overall disturbances of steroidogenesis affecting other steroid organs (mainly the gonads or the placenta). This can then result in a disorder of sex development (DSD, e.g. congenital adrenal hyperplasia (CAH)) as steroid hormone biosynthesis, regulation and metabolism rely on a common gene network. Nevertheless, cell- and tissue-specific expression and regulation of steroidogenic genes leads to organ-specific steroid production. Genetic variants in core genes of steroid hormone biosynthesis may therefore be recognized by characteristic clinical phenotypes and changes of steroid profiles. However, considerable overlap exists. Although **syndromic forms of AI** seem easier to recognize through their broader range of typically involved organ systems, this remains theory in many cases. Syndromes with primary AI can manifest similar, oligosymptomatic or atypical mainly because the typical spectrum may only develop over time or simply because the phenotype is only recognized when searched for. Molecular disease mechanisms causing genetic forms of primary AI are manifold and include disorders of steroidogenesis, adrenal dysgenesis (e.g. IMAGe, MIRAGE), familial glucocorticoid deficiency (e.g. *MC2R*/*MRAP*, OXPHOS system and ROS detoxification (*NNT*), metabolic (e.g. *SGPL1*) and autoimmune disorders (*AIRE*). Remarkably, only a few variants in genes critically involved in **adrenal development**, as revealed by basic research studies, have been identified in humans with dysgenetic, syndromic AI. It is highly likely that pathogenic variants of genes essential for adrenal development and beyond are embryonic lethal and thus go undetected. For instance, a homozygous mutation in *WNT4* has been found in three fetuses with SERKAL syndrome, characterized by female sex reversal and dysgenesis of kidneys, adrenals, and lungs. In a recent study, we reported a homozygous splice variant in the *LGR4* gene within a highly consanguineous family. Offspring with this variant either died in utero or at birth from adrenal salt-wasting crises. Only three affected children survived the neonatal period, and they required early steroid replacement therapy. These survivors manifested symptoms including adrenal insufficiency, hearing loss, nail anomalies, short stature, delayed puberty, and mental retardation. LGR4 is the R-spondin-dependent receptor that stimulates the WNT/β-catenin signaling in the adrenal cortex, playing a crucial role in adrenal cortex zona glomerulosa formation and function, thus aldosterone synthesis.
Key learning points
- Genetic forms of (primary) adrenal insufficiency may manifest isolated or as syndromic forms.
- Clinical characteristics may overlap that a genetic diagnosis is mostly necessary.
- Genotype-phenotype correlation is also variable.
- Genes and pathways involved in adrenal development are excellent candidates for explaining adrenal disorders, but seldom found in patients.
A variant in LGR4, an R-spondin stimulated receptor for activating WNT/β-catenin signaling, has been found in several members of a consanguineous family presenting with a novel syndromic form of isolated mineralocorticoid deficiency.

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What's new in metabolic-associated fatty liver disease?

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Novel pathological aspects of adipose tissue

S8.1

A macrophage-collagen fragment axis in the regulation of adipose tissue functionality

Milica Vujičić, Isabella Broderick, Pegah Salmantabar, Charlène Perian, Jonas Nilsson, Carina Sihlbom Wallem & Ingrid Wernstedt Asterholm
University of Gothenburg, Sweden

Efficient removal of fibrillar collagen is essential for adaptive expansion of subcutaneous adipose tissue (SAT); a process that protects against deleterious ectopic lipid deposition in the visceral compartment during weight gain. Fibrillar collagen degradation in adipose tissue is initiated by extracellular collagenases, and we recently found that SAT-resident M2-like macrophages remove the fragmented collagen via endocytosis and lysosomal degradation. Moreover, these macrophages' engagement in collagen endocytosis is diminished in obesity/insulin resistance associated with elevated levels of collagen fragments that exert fibroinflammatory changes in fibroblasts. Accordingly, we propose that collagen sequences that normally are hidden within the triple-helical structure of fibrillar collagen act as endogenous danger signals. Our new data within this area indicate that our findings translate to the clinic. We have also observed sex differences; female M2-like macrophages are more engaged in collagen endocytosis than those of males. In conclusion, our data delineate the importance of a macrophage-collagen fragment axis in physiological SAT expansion. Therapeutic targeting of this process may be a mean to improve adipose tissue function in obesity, which in turn may reduce the risk for metabolic disorders.

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Microscopic companions of the endocrine system

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Bone and muscle vitamin replacement

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Recent studies that changed my practice

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Senescence-mediated signalling in the pathogenesis of endocrine-related cancer: Pathogenesis and novel therapeutic opportunities

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From reproduction to male contraception

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The role of muscle in metabolic diseases

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S16.3

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DOI: 10.1530/endoabs.99.S16.3

Advances in the management of adrenocortical carcinoma

S17.1

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DOI: 10.1530/endoabs.99.S17.1

S17.2

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Joint Sessions

Joint Session 1: ESE and the European Society of Endocrine Surgeons

JS1.1

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DOI: 10.1530/endoabs.99.JS1.1

Joint Session 2: ESE and European Society of Paediatric Endocrinology

JS2.1

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DOI: 10.1530/endoabs.99.JS2.1

JS2.2

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DOI: 10.1530/endoabs.99.JS2.2

Joint Session 3: ESE and the Korean Endocrine Society – Mild autonomous cortisol secretion (MACS): new insights from European and Korean studies

JS3.1

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DOI: 10.1530/endoabs.99.JS3.1

JS3.2

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JS3.3

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DOI: 10.1530/endoabs.99.JS3.3

Joint Session 4: European Society of Endocrinology and the SBEM, FASEN, SMNE (Central/South America societies)

JS4.1

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JS4.3

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Joint Session 5: European Society of Endocrinology and the Androgen Excess and PCOS Society

JS5.1

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JS5.2

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DOI: 10.1530/endoabs.99.JS5.2

JS5.3

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DOI: 10.1530/endoabs.99.JS5.3

Eyes Symposium

EYES1

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DOI: 10.1530/endoabs.99.EYES1

Ecas Symposium

ECAS1

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DOI: 10.1530/endoabs.99.ECAS1

New Scientific Approaches

Insights into Endocrine Pathology: What Does the Endocrinologist Need to Know?
NSA1

Abstract unavailable
DOI: 10.1530/endoabs.99.NSA1

Methylomics in aggressive pituitary tumours
NSA2

Abstract unavailable
DOI: 10.1530/endoabs.99.NSA2

Artificial intelligence in Endocrinology
NSA3

Abstract unavailable
DOI: 10.1530/endoabs.99.NSA3

Debate Sessions

Bone biomarkers – helpful for decisions in osteoporosis patients?

D1.1

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DOI: 10.1530/endoabs.99.D1.1

D1.2

Abstract unavailable
DOI: 10.1530/endoabs.99.D1.2

Pituitary tumours: Should Cavernous sinus invasion be removed

D2.1

Abstract unavailable
DOI: 10.1530/endoabs.99.D2.1

D2.2

Abstract unavailable
DOI: 10.1530/endoabs.99.D2.2

Active surveillance of thyroid cancer FOR or AGAINST

D3.1

Abstract unavailable
DOI: 10.1530/endoabs.99.D3.1

D3.2

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Meet the Expert Basic Scientist Sessions

Human adrenal development
MTEBS1

Abstract unavailable
DOI: 10.1530/endoabs.99.MTEBS1

Identifying new receptors in the regulation of fertility
MTEBS2

Abstract unavailable
DOI: 10.1530/endoabs.99.MTEBS2

In vitro cellular reprogramming to model gonad development and its disorders
MTEBS3

Abstract unavailable
DOI: 10.1530/endoabs.99.MTEBS3

Meet the Expert Sessions

Osteoporosis in advanced chronic kidney disease
MTE1

Abstract unavailable
DOI: 10.1530/endoabs.99.MTE1

Radiotherapy/radiosurgery for pituitary tumours; long term outcome and consequences
MTE2

Abstract unavailable
DOI: 10.1530/endoabs.99.MTE2

Estogen & immune micro environment in tumour progression
MTE3

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DOI: 10.1530/endoabs.99.MTE3

The HPA axis response to critical illness
MTE4

The HPA axis response to critical illness
Prof. dr. Greet Van den Berghe
(adapted from Langouche, Téblick, Gunst, Van den Berghe, Endocrine Reviews 2023.44.1096-1106)

Based on insights obtained during the last decade, the classical concept of an activated hypothalamus-pituitary-adrenocortical (HPA) axis in response to critical illness is in need of revision. After a brief central HPA axis activation, the vital maintenance of increased systemic cortisol availability and action in response to critical illness is predominantly driven by peripheral adaptations rather than by an ongoing centrally-activated several-fold increased production and secretion of cortisol. Besides the known reduction of cortisol binding proteins that increases free cortisol, these peripheral responses comprise suppressed cortisol metabolism in liver and kidney, prolonging cortisol half-life, and local alterations in expression of 11βHSD1, GRα and FKBP51 that appear to titrate increased GRα-action in vital organs and tissues while reducing GRα-action in neutrophils possibly preventing immune-suppressive side effects of increased systemic cortisol availability. Peripherally increased cortisol can exert negative feed-back inhibition at the pituitary level impairing processing of POMC into ACTH and reducing ACTH-driven cortisol secretion, while ongoing central activation explains increased circulating POMC. These alterations are likely adaptive and beneficial for the host in the short term. However, as a consequence, patients with prolonged critical illness who require intensive care for weeks or longer may develop a form of central adrenal insufficiency. The new insights challenge the validity of earlier concepts such as "relative", as opposed to "absolute", adrenal insufficiency and generalized systemic glucocorticoid resistance in the critically ill. They also question the scientific basis for broad implementation of stress dose hydrocortisone treatment of patients suffering from acute septic shock solely based on assumption of cortisol insufficiency.
DOI: 10.1530/endoabs.99.MTE4

Paediatric concerns of endocrine disruptors
MTE5

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DOI: 10.1530/endoabs.99.MTE5

Female infertility
MTE6

Abstract unavailable
DOI: 10.1530/endoabs.99.MTE6

Management of Functional Pancreatic Neuroendocrine Neoplasms
MTE7

Abstract unavailable
DOI: 10.1530/endoabs.99.MTE7

Primary Hyperparathyroidism 2024: What's new and Further Perspectives
MTE8

Abstract unavailable
DOI: 10.1530/endoabs.99.MTE8

Update on the management of Graves Disease
MTE9

Abstract unavailable
DOI: 10.1530/endoabs.99.MTE9

How to prevent weight regain?
MTE10

Abstract unavailable
DOI: 10.1530/endoabs.99.MTE10

Management of malignant pheochromocytoma
MTE11

Abstract unavailable
DOI: 10.1530/endoabs.99.MTE11

Pre-Congress Course

Androgen Excess and PCOS Society (AEPCOS) Update Meeting

PCC1.1

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PCC1.2

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PCC1.3

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PCC1.4

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PCC1.5

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PCC1.6

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PCC1.7

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PCC1.8

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PCC1.9

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Growth Hormone Research Society (GRS) Congress (Day1)

PCC2.1

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PCC2.4

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DOI: 10.1530/endoabs.99.PCC2.4

PCC2.5

Growth hormone, mini-mice, football, dirty shorts, and a new drug
John J Kopchick

The growth hormone receptor antagonist was discovered via expression of mutated GH genes in transgenic mice. Although we were attempting to generate potent GH analogs, our mouse studies indicated that the compound was 'inhibiting' GH action. We subsequently showed that it was a GH receptor antagonist, the first of its type. Many hurdles needed to be 'jumped' in the development of this compound into a drug including protection of intellectual property; funding for purification, preclinical, and clinical trials; and registration to and approval by the various regulatory agencies. Ultimately the compound was approved in the mid-2000s for the treatment of patients with acromegaly. The name of the drug is Somavert (Pegvisomant for injection). Pegvisomant treatment in a dose dependent manner results in normalization of IGF-1 levels in most patients and has been found to be safe and efficacious. Since the GH/IGF-1 axis has been implicated in the progression of several types of cancers, many have suggested the use of Pegvisomant as an anti-cancer therapeutic. In this talk, I will describe experiments in which the GHA was discovered, review results of Pegvisomant's preclinical and clinical trials, and provide data suggesting Pegvisomant's value in selected types of cancer.
Key Learning Points
- Unexpected experimental findings can, at times, be very promising.
- Trials and tribulations of translating laboratory finding to the patient.
- Serendipity played an important role in our drug development process.

DOI: 10.1530/endoabs.99.PCC2.5

PCC2.6

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DOI: 10.1530/endoabs.99.PCC2.6

Growth Hormone Research Society (GRS) Congress (Day2)

PCC3.1

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PCC3.2

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PCC3.3

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DOI: 10.1530/endoabs.99.PCC3.3

PCC3.4

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DOI: 10.1530/endoabs.99.PCC3.4

Thyroid Ultrasound Practical Course

PCC4.1

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PCC4.2

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DOI: 10.1530/endoabs.99.PCC4.2

PCC4.3

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PCC4.4

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PCC4.5

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PCC4.6

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European Academy of Andrology (EAA) pre-congress course

PCC5.1

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PCC5.2

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PCC5.3

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PCC5.4

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PCC5.5

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Nurse Sessions

Precision Medicine: Thyroid Disorder

N1.1

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N1.2

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DOI: 10.1530/endoabs.99.N1.2

N1.3

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DOI: 10.1530/endoabs.99.N1.3

Precision Medicine: Craniopharyngioma

N2.1

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N2.2

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N2.3

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DOI: 10.1530/endoabs.99.N2.3

How to Workshop

N3.1

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DOI: 10.1530/endoabs.99.N3.1

N3.2

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N3.3

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Endocrine Nurse Achievement Session

N4.1

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N4.2

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DOI: 10.1530/endoabs.99.N4.2

N4.3

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DOI: 10.1530/endoabs.99.N4.3

Oral Communications

Oral Communications 1: Reproductive and Developmental Endocrinology

OC1.1

Hypospadias is linked to genetic susceptibility to the environment through oncogenes and its incidence is geographically correlated to that of cancers worldwide

Nicolas Kalfa[1], Anne Bergougnoux[1], Pascal Philibert[2], Nadège Servant Fauconnet[1], Alice Faure[3], Jean Breaud[4], Laura Gaspari[1], Charles Sultan[1] & Francoise Paris[1]
[1]Hospital Center University De Montpellier, Montpellier, France; [2]University Hospital of Nimes, Nîmes, France; [3]Hospitals Academics De Marseille, Marseille, France; [4]Hospital Pasteur, Nice, France

Background
The etiology of hypospadias may be at the crossroad of genetics and environment. The study of these factors taken individually failed to find an unequivocal explanation in most cases. But the interactions between exposure to endocrine disruptors chemicals (EDC) and genetic background have not yet been studied. We thus aimed to find a genetic susceptibility to the environment in hypospadias.
Methods
Through a multicenter prospective comparative study, we gathered environmental and genetic data from patients with isolated hypospadias to determine at-risk polymorphisms when combined to exposure to EDC compared to a control group. 300 boys with hypospadias and 300 controls were included and evaluated by: 1-Questionnaire QLK4-1999-01422 to detect personal, environmental, professional exposures to pollutants. 2-Next-generation-sequencing of 336 genes implicated in genital and gonadal development and hypospadias. The interaction between genetics and environment was studied using logistic regression analysis.
Results
We identified 4 variants at risk for hypospadias when combined to exposure to EDC in the following genes: BRAF (rs3789806), AKR1C3 (rs10508293), AHR (rs2074113) and CITED2 (rs4076025). Surprisingly, beside their role in steroidogenesis and sensitivity to chemicals, these genes are also identified as oncogenes. The in-silico predictions of these variants are to modify the transcription factor binding sites for proteins encoded by other oncogenes and genital development genes. We thus hypothesized a connection between hypospadias and cancers. To further evaluate this association, we used data from the International Birth-Defect Surveillance Systems and from the International Agency for Research on Cancer (WHO). We found a geographical correlation, across 17 countries, between the incidence of hypospadias and the overall incidence of cancers ($r=0.81$). This correlation was particularly observable for urological tumors and leukemias, two cancers highly suspected to be linked to pollutants.
Conclusions
Hypospadias is at the crossroad of genetics and environment. Susceptibility to EDC may be associated with genetic variants on genes both implicated in fetal development and oncogenesis. Moreover, the incidence of hypospadias is geographically correlated to that of cancers worldwide. Hypospadias may thus not be a simple defect of the urethra but a witness of the global health population and of EDC impregnation.
Source of funding
This work was supported by Programme Hospitalier de Rercherche Clinique PHRC UF 8270 and Public funding from the National Reference Network for Rare Disease, Genital Development DSD DevGen.

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OC1.2

Mortality among women with POI, nationwide register based case-control study

Hilla Haapakoski[1], Heidi Silvén[1,2], Paula Pesonen[1], Susanna Savukoski[1,2] & Maarit Niinimäki[1,2]
[1]University of Oulu; [2]Department of Obstetrics and gynecology, University Hospital of Oulu, Obstetrics and Gynecology

Introduction/Purpose
Despite some evidence that women with premature ovarian insufficiency (POI, loss of ovarian activity <40 years of age) are at risk for diminished life expectancy, large scale population-based studies are still scarce. The evidence on whether hormone replacement therapy (HRT) use decreases the mortality risk among women with POI are lacking. The aim of our study was to explore mortality among women with spontaneous POI and their controls in a large national cohort and whether HRT use modifies the mortality risk among them.
Methods
All spontaneous POI cases diagnosed in Finland between 1988-2017 were identified by their reimbursement right for HRT, from Social Insurance Institution medicine reimbursement registry. We explored mortality among women with spontaneous POI, compared to age and municipality matched controls (four/each POI case, $n=22859$). Cox regression analysis was used to compare mortality hazard ratio (HR) between women with POI and their controls in different causes of death. Women with cancer or cardiovascular morbidity before the index day were excluded from the analysis. Women with POI were classified as HRT users if they had purchased systemic HRT for ≥ 6 months. The data on mortality, causes of death and death ages were collected from Cause of Death Registry.
Results
The mean follow-up time for all groups was 17.5 years (standard deviation 8.5). At the end of the follow-up, 9.8% of women with spontaneous POI and 2.9% of controls were deceased. Compared to control women, age-standardized all-cause mortality was increased among women with spontaneous POI, among those without HRT (HR 1.60 95% Confidence Interval, CI 1.07-2.37) and those with HRT (HR 2.27 95% CI 1.46-3.5). Cancer mortality was also increased among spontaneous POI cases without HRT use, (HR 4.04 95% CI 3.04-5.37) and with HRT (HR 1.78 95%CI 1.27-2.48), as well as cardiovascular mortality (HR 2.30 95% CI 1.34-3.97) and (2.53 95% CI 1.58-4.06), respectively.
Conclusions
Women with spontaneous POI are at increased risk for all-cause, cardiovascular and cancer mortality, and HRT use of ≥ 6 months did not eliminate the risk. Future studies should focus on whether longer use of HRT associates with diminished mortality risk among women with POI. Specific attention should be paid to health of women with spontaneous POI to decrease excess mortality.
DOI: 10.1530/endoabs.99.OC1.2

OC1.3

Pregnancy loss in women with endocrine disorders – a nationwide registry-based cohort study of 366,548 Danish women

Pia Egerup[1], Sofie Bliddal[1,2], David Westergaard[1], Dorte Glintborg[3], Steen J. Bonnema[3], Ulla Feldt-Rasmussen[2], Mette Nyegaard[4,5], Laust Hvas Mortensen[6] & Henriette Svarre Nielsen[1]
[1]Copenhagen University Hospital Hvidovre, Department of Obstetrics and Gynecology, Hvidovre, Denmark; [2]Copenhagen University Hospital Rigshospitalet, Department of Endocrinology and Metabolism, Copenhagen, Denmark; [3]Odense University Hospital, Department of Endocrinology, Odense, Denmark; [4]Aalborg University, Department of Health Science and Technology, Aalborg, Denmark; [5]Statens Serum Institut, Department of Congenital Disorders, Copenhagen, Denmark; [6]Statistic Denmark, Copenhagen, Denmark

Background
Pregnancy loss affects approximately 25% of pregnancies, of which 40% have no detectable chromosome abnormalities and are suspected to be caused by maternal comorbidity. Pregnancy loss has been associated with specific endocrine disorders, e.g. autoimmune thyroid disease (AITD), polycystic ovarian syndrome (PCOS) or diabetes mellitus (DM). Because of the well-described overlap between these endocrine disorders, we hypothesized that pregnancy loss is associated with any endocrine disorder and that having more than one endocrine disorder constitutes a more severe phenotype with a higher risk of pregnancy loss.
Methods
Danish nationwide cohort based on the Danish Health Registries containing information on ICD-8/ICD-10-diagnoses, all redeemed medicine prescriptions, and pregnancy outcomes. We identified women born from 1977-1993 with ≥ 1 pregnancy. Cases had a diagnosis of a non-iatrogenic endocrine disorder and controls had none. Logistics regression models, with the number of pregnancy losses as the outcome, adjusted for birth year provided odds ratios for endocrine disorders. Results are given as odds ratio with 95% confidence interval.
Results
The cohort consisted of 366,548 women of which 54,394 (15%) had an endocrine disorder. There was a highly significant association between endocrine disorders and pregnancy loss increasing with the number of pregnancy losses; one loss 1.15 (1.12-1.17), two losses 1.31 (1.24-1.38) and three losses 1.81 (1.70-1.93), $P<0.001$. The risk of pregnancy loss was also increased by AITD (1.21, 1.17-1.25), PCOS (1.32, 1.26-1.38), DM1 (1.38, 1.25-1.53), and DM2 (1.22, 1.09-1.35) , respectively, and increased further with a higher number of pregnancy losses. When these disorders were included simultaneously in the model, the increased risk associated with each individual condition persisted, suggesting that each disorder contributes distinctly to the pregnancy loss risk. Lastly, compared to

individuals with no endocrine disorders, those with one disorder had a higher risk of pregnancy loss (1.23, 1.19-2.6). This risk was further amplified in individuals with two disorders (1.60, 1.44-1.78), indicating a progressive elevation in risk correlating with the number of comorbid endocrine conditions.
Conclusion
In this nationwide register-based cohort study, there was a highly significant association between endocrine disorders and pregnancy loss. This was especially the case with an increasing number of pregnancy losses, and in women having more than one endocrine disorder. The observed additive effects indicates that each endocrine condition independently elevates the risk of pregnancy loss. This underscores the critical need for personalized intervention strategies including monitoring of each endocrine disorder to reduce the cumulative risk of pregnancy loss.

DOI: 10.1530/endoabs.99.OC1.3

OC1.4

Kisspeptin as a test of hypothalamic function in women presenting with oligo / amenorrhoea

Bijal Patel[1], Ali Abbara[1], Arthur Yeung[1], Maria Phylactou[1], Jovanna Tsoutsouki[1], Kanyada Koysombat[1], Megan Young[1], Sandhi Nyunt[1], Ambreen Qayum[1], Aaran Patel[1], Agata Zielinska[1], Yusra Omar[1], Pei Eng[1], Edouard G Mills[1], Simon Hanassab[1], Lisa Webber[1,2], Channa Jayasena[1], Tricia Tan[1], Richard Quinton[3], Sophie Clarke[4], Alexander Comninos[1] & Waljit Dhillo[1]
[1]Imperial College London, United Kingdom; [2]Singapore General Hospital, Obstetrics and Gynaecology, Singapore, Singapore; [3]Newcastle upon Tyne, Newcastle upon Tyne, United Kingdom; [4]University College London Hospitals Nhs Foundation Trust, United Kingdom

Background
Polycystic Ovary Syndrome (PCOS) and Functional Hypothalamic Amenorrhoea (FHA) are the two commonest causes of menstrual disturbance in pre-menopausal women. In practice, differentiating these two common reproductive disorders can be challenging. A fundamental abnormality that underpins both conditions is altered gonadotrophin releasing hormone (GnRH) pulsatility, being increased in PCOS but reduced in FHA. Likewise, congenital (e.g. congenital hypogonadotropic hypogonadism; CHH) and functional causes of hypogonadotropic hypogonadism (e.g. FHA) both have decreased hypothalamic function and can exhibit similar hormonal profiles presenting a diagnostic dilemma. Kisspeptin is a potent stimulator of hypothalamic GnRH secretion, and thus could be a novel tool to interrogate hypothalamic function in women presenting with menstrual disturbance.
Methods
Healthy women ($n=33$), women with PCOS ($n=30$), FHA ($n=30$), or CHH ($n=8$) aged 18-35 yrs not currently taking hormonal treatments, underwent two study visits to assess the hypothalamic response to an intravenous bolus of kisspeptin-54 (9.6 nmol/kg), and the pituitary response to GnRH (100 mg). Serum luteinising hormone (LH) and follicle stimulating hormone (FSH) were measured every 15 mins for 8 hrs. The maximal rise in LH and FSH from baseline was compared between the groups using an unpaired t test or Mann Whitney U test according to the distribution of the data. Receiver Operator Characteristic (ROC) analysis was used to assess the discriminatory potential of the hormonal response to kisspeptin and GnRH.
Results
The mean (SD) of the maximal rise in LH (IU/l) after kisspeptin was 9.7 (11.4) in healthy women, 9.7 (8.3) in women with PCOS, 17.6 (10.8) in women with FHA, and 1.0 (1.1) in women with CHH. The mean (SD) of the maximal rise in FSH (IU/l) after kisspeptin was 4.2 (3.4) in healthy women, 2.8 (2.1) in women with PCOS, 9.2 (5.6) in women with FHA, and 0.7 (0.5) in women with CHH. The maximal rise in FSH after kisspeptin could differentiate women with lean PCOS (BMI <25 kg/m^2) from those with FHA (area under ROC 0.91, $P=0.0001$). The maximal rise in FSH after kisspeptin could differentiate women with FHA from women with CHH (auROC 1.00, $P<0.0001$), whereas the equivalent auROC for FSH rise after GnRH was 0.7 ($P=0.086$).
Conclusion
Kisspeptin offers a novel approach to assessing hypothalamic function in patients presenting with different reproductive disorders causing oligo/ amenorrhoea. Our data reveals for the first time that the hormonal response to kisspeptin has promising diagnostic potential to aid in the evaluation of women presenting with menstrual disturbance.

DOI: 10.1530/endoabs.99.OC1.4

OC1.5

Gender affirming treatment and employment rate in 3,812 Danish transgender persons and 38,120 controls. A nationwide register-based cohort study

Dorte Glintborg[1,2], Jens-Jakob Møller[1,3], Katrine Rubin[3,4], Øjvind Lidegaard[5], Guy T'Sjoen[6], Mie-Louise Larsen[5], Malene Hilden[5] & Marianne Andersen[1,2]
[1]Odense University Hospital, Odense, Denmark; [2]University of Southern Denmark, Klinisk Institut, Odense, Denmark; [3]Odense University Hospital, OPEN, Odense, Denmark; [4]University of Southern Denmark, Research unit OPEN, department of clinical research,, Odense, Denmark; [5]Copenhagen University, Københavns, Denmark; [6]Ghent University Hospital, Gent, Belgium

Objective
Transgender persons often experience low socioeconomic status. Gender affirming treatment aims to improve gender dysphoria. We assessed employment rates in transgender persons compared to controls and demographic, health and treatment-related factors associated with unemployment in transgender persons.
Methods
National register-based cohort study in Danish transgender persons with diagnosis code of gender identity disorder during year 2000-2021. Five age-matched controls of the same sex at birth and five age-matched controls of the other sex at birth were included. The date of study inclusion was the first date of transgender diagnosis. Employment was the primary study outcome.
Results
The cohort included 3812 transgender persons with median age (interquartile range) 19 (15; 24) years for persons assigned female at birth (AFAB, $n=1993$) and 23 (19; 33) years for persons assigned male at birth (AMAB, $n=1819$) and 38,120 controls. Mean (standard deviation) follow up was 4.7 (4.6) years. The proportion of employment the year before study inclusion was 78.1% in transgender persons AFAB vs 91.6% female controls, and 56.2% vs 85.5% were employed after 5 years follow up. In transgender persons AMAB vs male controls, 69.1% vs 88.0% were employed the year before study inclusion and 50.4% vs 85.5% were employed after 5 years follow up. In transgender persons AFAB compared to control women, the OR (95% confidence interval) for unemployment was 2.99 (2.63; 3.40) before study inclusion and 4.14 (3.42; 5.00) in the fifth calendar year after index. In transgender persons AMAB compared to control men, corresponding ORs were 3.30 (2.93; 3.72) and 4.77 (4.04; 5.64). Use of gender affirming hormone in persons AFAB decreased probability of unemployment at all time points with OR after 5 years 0.62 (0.41; 0.93), $P=0.02$ (odds ratio (95% confidence interval). In persons AMAB, use of hormone treatment was not associated with changed employment rates, 5 years OR: 0.77 (0.55; 1.07), $P=0.11$.
Conclusion
Unemployment was more prevalent in transgender persons compared to controls. Masculinizing hormone treatment was associated with lower probability of unemployment.

DOI: 10.1530/endoabs.99.OC1.5

OC1.6

Sertoli cell function and the dose of denosumab is critical for the response to RANKL inhibition in human testis cultures

Christine Hjorth Andreassen[1], Nadia Krarup Knudsen[1], John Erik Nielsen[2], Sam Kafai Yahyavi[1,2], Rune Holt[1], Anne Jørgensen[1] & Martin Blomberg Jensen[1]
[1]Copenhagen University Hospital-Herlev and Gentofte, Division of Translational Endocrinology, Department of Endocrinology and Internal Medicine, Herlev, Denmark; [2]Copenhagen University Hospital-Rigshospitalet, Department of Growth and Reproduction, Copenhagen OE, Denmark

Currently, no treatment options exist to improve semen quality for the majority of infertile men, but it is well known that the interaction between Sertoli- and germ cells is essential to ensure complete spermatogenesis. A recent study suggested that denosumab, an inhibitor of receptor activator of nuclear factor kappa-B ligand (RANKL) signaling, may decrease germ cell apoptosis in human *ex vivo* testis cultures and stimulate sperm production in some infertile men. Here, we propose that the level of osteoprotegerin (OPG) expression in Sertoli cells may be indicative of dysgenesis in human testis tissue cultured *ex vivo* and that the expression of the RANKL signaling system, in combination with the dose, is predictive for the testicular response to denosumab. Human testis from orchiectomies was cultured *ex vivo* for 48 hours (34°C, 5% CO$<$ce:sub$>$2$<$/ce:sub$>$) and treated with 1, 30, or 100 ng/ml denosumab or vehicle. Samples positive for D2-40, a marker of germ cell neoplasia *in situ* (the precursor cell for

testicular cancer), were excluded. Immunohistochemical staining for OPG was used to assess dysgenesis in Sertoli cells in each seminiferous tubule of testis cultures. Proliferation and apoptosis were assessed by quantification of poly(ADP-ribose) polymerase cleavage (cPARP) and Bromdeoxyuridin (BrdU) positive germ cells, respectively. Treatment with 100 ng/ml of denosumab increased germ cell proliferation and decreased apoptosis in testis cultures with low or moderate OPG expression in Sertoli cells, while lower doses of denosumab had no effect. In contrast, 100 ng/ml denosumab increased germ cell apoptosis in testis tissue with high OPG expression in Sertoli cells but did not affect germ cell proliferation. Lower doses of denosumab did not affect germ cell proliferation or apoptosis in testis tissue with high OPG expression. This study suggests that the effect of denosumab depends on the function of Sertoli cells, with high OPG expression being a marker of dysgenesis. In addition, the testicular effect of denosumab is determined by the dose, and future clinical trials in infertile men should aim for a dose resulting in an intratesticular concentration close to 100 ng/ml.

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Oral Communications 2: Calcium and Bone | Part I

OC2.1

Encaleret (CLTX-305) sustained normalization of mineral homeostasis in patients with autosomal dominant hypocalcemia type 1 over 18 months in a phase 2 study [NCT04581629]

Rachel Gafni[1], Iris Hartley[1], Kelly Roszko[1], Karen Pozo[1], Edward Nemeth[2], Arun Mathew[3], Mary Scott Roberts[3], Scott Adler[3] & Michael Collins[1]
[1]National Institutes of Health, National Institute of Dental and Craniofacial Research, Bethesda, United States; [2]MetisMedica, Toronto, Canada; [3]Calcilytix Therapeutics Inc., San Francisco, United States

Autosomal dominant hypocalcemia type 1 (ADH1), caused by gain-of-function calcium-sensing receptor gene (*CASR*) variants, is characterized by low parathyroid hormone (PTH) levels, hypocalcemia, hypercalciuria, hyperphosphatemia and hypomagnesemia. Conventional therapy (calcium and active vitamin D) can exacerbate hypercalciuria, which may result in renal complications. Calcilytics that act as negative allosteric modulators of the calcium-sensing receptor (CaSR), like encaleret, decrease the sensitivity of hyperactive receptors to extracellular calcium and normalize biochemical abnormalities in ADH1 rodent models. This Phase 2b open-label study of the oral investigational calcilytic encaleret was comprised of 3 periods followed by a long-term extension (LTE). Conventional therapy was discontinued prior to encaleret initiation. Periods 1&2 included dose-finding and safety/tolerability evaluation. Period 3 (P3) optimized dosing and assessed safety and efficacy over 24 outpatient weeks; participants were then allowed to continue in the LTE. Thirteen adults with ADH1 were enrolled and encaleret was individually titrated to normalize albumin-corrected calcium (cCa) and minimize hypercalciuria. Encaleret was well-tolerated with no serious adverse events reported. There were no treatment discontinuations or withdrawals prior to the LTE; one participant withdrew during the LTE for family planning. The mean $\pm$ SD encaleret sulfate dose at the end of P3, Week 24 (P3W24) was 86 $\pm$ 70 mg BID, remaining stable at LTE Month 12 (LTEM12) ($n=12$) (75 $\pm$ 66 mg BID). Mean $\pm$ SD values taken 4-hours post-dose for P3W24 and LTEM12 compared to baseline (BL) are presented. PTH levels were low at BL (6.3 $\pm$ 7.8 pg/ml [nl 10-65]), normal at P3W24 (35.3 $\pm$ 10.2 [$P<0.01$]) and remained consistent through LTEM12 (36.9 $\pm$ 15.2 [$P<0.01$]). Similarly, the hypocalcemia seen at BL (cCa = 7.1 $\pm$ 0.4 mg/dl [nl 8.4-10.2]) was corrected at P3W24 (9.2 $\pm$ 0.5 [$P<0.01$]); eucalcemia was maintained through LTEM12 (9.2 $\pm$ 0.4 [$P<0.01$]). BL hypercalciuria (395 $\pm$ 216 mg/d [nl < 250-300]) decreased to 202 $\pm$ 83 ($P<0.05$) at P3W24 and normalization was sustained through LTEM12 (177 $\pm$ 94 [$P<0.05$]). BL blood phosphate (4.5 $\pm$ 1.1 mg/dl [nl 2.3-4.7]) decreased by P3W24 (3.4 $\pm$ 0.4 [$P<0.05$]) and was maintained at LTEM12 (3.4 $\pm$ 0.5 [$P<0.01$]). Blood magnesium increased (BL 1.7 $\pm$ 0.2 mg/dl [nl 1.6-2.6]); P3W24 2.0 $\pm$ 0.2 [$P<0.01$]; LTEM12 2.1 $\pm$ 0.2 [$P<0.01$]). Bone turnover markers increased from BL ($n=7$) (CT_X = 253 $\pm$ 111 pg/ml; P1NP = 34 $\pm$ 10 mg/l) by P3W24 ($n=13$) (CT_X = 744 $\pm$ 565; P1NP = 104 $\pm$ 87) [$P<0.01$] and remained elevated at LTEM12 (CT_X = 988 $\pm$ 652; P1NP = 83 $\pm$ 49 [$P<0.01$]). This study represents a molecularly targeted, precision medicine approach to the treatment of ADH1. The consistent and sustained results from over 18 months of outpatient encaleret treatment are clinically meaningful and support Phase 3 evaluation of the efficacy and safety of encaleret as the first potential treatment indicated for ADH1.

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OC2.2

Sustained improvement in renal function with palopegteriparatide in adults with chronic hypoparathyroidism: 2-year results from the phase 3 PaTHway trial

Peter Schwarz[1], Lars Rejnmark[2], Elvira Gosmanova[3], Aliya Khan[4], Noriko Makita[5], Yasuo Imanishi[6], Yasuhiro Takeuchi[7,8], Stuart Sprague[9], Dolores M. Shoback[10,11], Lynn Kohlmeier[12], Mishaela Rubin[13], Andrea Palermo[14,15], Claudia Gagnon[16,17], Elena Tsourdi[18], Carol Zhao[19], Michael Makara[19], Michael Ominsky[19], Bryant Lai[19], Jenny Ukena[19], Christopher Sibley[19] & Aimee Shu[19]
[1]Rigshospitalet, Copenhagen, Denmark; [2]Aarhus University Hospital, Aarhus, Denmark; [3]Albany Medical College, Albany, United States; [4]McMaster University, Hamilton, Canada; [5]University of Tokyo Graduate School of Medicine, Tokyo, Japan; [6]Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan; [7]Toranomon Hospital, Tokyo, Japan; [8]Okinaka Memorial Institute for Medical Research, Tokyo, Japan; [9]NorthShore University Health System-University of Chicago Pritzker School of Medicine, Chicago, United States; [10]University of California, San Francisco, United States; [11]VA Medical Center, San Francisco, United States; [12]Endocrinology and Spokane Osteoporosis, Spokane, United States; [13]Columbia University, New York, United States; [14]Fondazione Policlinico Campus Bio-medico, Rome, Italy; [15]Unit of Endocrinology and Diabetes, Campus Bio-medico University, Rome, Italy; [16]CHU de Québec-Université Laval Research Centre, Québec, Canada; [17]Department of Medicine, Université Laval, Quebec City, Québec, Canada; [18]Technische Universität Dresden Medical Center, Dresden, Germany; [19]Ascendis Pharma Inc, Palo Alto, United States

Hypoparathyroidism is an endocrine disease caused by insufficient levels of parathyroid hormone (PTH). Individuals with chronic hypoparathyroidism managed with conventional therapy (active vitamin D and calcium) are at increased risk for renal complications and declines in renal function. In clinical trials, palopegteriparatide treatment enabled independence from conventional therapy (no active vitamin D and $\leq$600 mg/day elemental calcium) and maintained serum biochemistries within normal ranges. This analysis examines the impact of palopegteriparatide treatment on renal function in adults with chronic hypoparathyroidism through week 104 of the PaTHway trial. PaTHway is a phase 3 trial with a randomized, double-blind, placebo-controlled 26-week period and ongoing 156-week open-label extension. Estimated glomerular filtration rate (eGFR) $\geq$30 ml/min/1.73 m^2 was required for eligibility. In this post hoc analysis, changes in renal function were assessed using eGFR. Safety assessments included 24-hour urine calcium excretion and treatment-emergent adverse events (TEAEs). At week 104, 93% (76/82) of participants remained in the trial. Of those, 82% had normal albumin-adjusted serum calcium levels (2.07-2.64 mmol/l), 97% were independent from conventional therapy, and none required active vitamin D. Mean (SD) serum phosphate (1.1(0.2) mmol/l) and albumin-adjusted calcium $\times$ phosphate product (2.5(0.4) $mmol^2/l^2$) levels were also within normal ranges. At week 104, mean (SD) eGFR was 77.8 (14.8) ml/min/1.73 m^2. Palopegteriparatide treatment resulted in a mean (SD) increase in eGFR of 8.9 (11.0) ml/min/1.73 m^2 ($P<.0001$) from baseline to week 52, which was sustained through week 104 with a mean (SD) change from baseline of 9.0 (10.3) ml/min/1.73 m^2 ($P<.0001$). By week 104, 61% and 44% of participants had an increase in eGFR of $\geq$5 ml/min/1.73 m^2 and $\geq$10 ml/min/1.73 m^2 respectively. Among participants with baseline eGFR < 60 ml/min/1.73 m^2 ($n=23$), palopegteriparatide treatment resulted in a mean (SD) increase in eGFR of 13.8 (10.0) ml/min/1.73 m^2 from baseline to week 104, and 78% and 57% had an increase in eGFR of $\geq$5 ml/min/1.73 m^2 and $\geq$10 ml/min/1.73m^2 respectively. Palopegteriparatide treatment normalized mean 24-hour urine calcium within 26 weeks and maintained levels below 6.2 mmol/day through week 104 (4.0(2.3) mmol/day). No cases of nephrolithiasis were reported with palopegteriparatide treatment. Most TEAEs were mild or moderate; no new safety signals were reported. This post hoc analysis of the phase 3 PaTHway trial through week 104 demonstrates the sustained renal safety of palopegteriparatide and suggests that PTH replacement therapy with palopegteriparatide and independence from conventional therapy may not only preserve but improve renal function in adults with chronic hypoparathyroidism.

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OC2.3

A translational approach to investigate the mechanism whereby eneboparatide induces prolonged calcium normalization in patients with chronic hypoparathyroidism

Guillaume Ravel[1], Rakesh Datta[2], Stephane Milano[1], Michel Ovize[1], Soraya Allas[1], Myriam Aouadi[1] & Michael Culler[2]

[1]Amolyt Pharma, Écully, France; [2]Amolyt Pharma, Cambridge, United States

Maintaining normal serum and urinary calcium in patients with chronic hypoparathyroidism (cHP) remains a therapeutic challenge. Parathyroid hormone (PTH) replacement therapy is not ideal due to its short half-life and transient activation of the PTH 1 receptor (PTH1R). Eneboparatide is a hybrid analog of PTH and PTH-related peptide specifically designed to induce prolonged activation of the PTH1R. Despite a short half-life, eneboparatide is able to normalize serum and urinary calcium levels over a full 24 hours in cHP patients. To gain deeper insight into the mechanism whereby eneboparatide provides sustained calcium normalization, we analyzed tissue distribution and retention of eneboparatide in comparison to natural PTH(1-34) following subcutaneous injection in rats. Quantitative whole-body autoradiography in rats treated with radiolabeled eneboparatide and PTH(1-34) revealed similar rapid elimination from the circulation and accumulation of both compounds in tissues expressing PTH1R, with highest levels observed in renal cortex. However, 6 hours postdose, 38.6% of eneboparatide remained in renal cortex, while only 3.7% of PTH(1-34) was detectable. These results demonstrated a preferential retention of eneboparatide in the renal cortex, where the PTH1R regulates calcium reabsorption. We next assessed whether the eneboparatide tissue retention observed *in vivo* was due to prolonged binding to the PTH1R. Ligand binding to the PTH1R leads to conformational changes of the receptor from G protein-dependent (RG) to G protein-independent (R^0). Using a specific PTH1R binding assay, we confirmed high affinity of eneboparatide for the R^0 conformation compared to PTH(1-34) (1.5 nM vs 30.9 nM, respectively). We next investigated whether the strong affinity of eneboparatide for the R^0 conformation translated into prolonged receptor activation. To mimic the rapid elimination from the circulation *in vivo*, we treated HEK293 cells overexpressing the human PTH1R with both ligands for 15 min and, after washing, continued incubation with media alone. As expected, activation of the PTH1R by both PTH(1-34) and eneboparatide led to a rapid and similar increase in cAMP. After removal of PTH(1-34), cAMP production returned to baseline in less than 1 hour. However, following removal of eneboparatide, cAMP production decreased gradually, and residual signal remained strikingly constant and detectable through the last time point measured, 16 hours. Our translational approach demonstrates the potential therapeutic advantage of eneboparatide over PTH(1-34) due to its ability to be retained in renal cortex, to induce a prolonged activation of the PTH1R and to maintain normal serum and urinary calcium over 24 hours in cHP patients.

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OC2.4

Increased urinary excretion of calcium and nephrolithiasis: Real-life data from the epi-hypo cohort of hypoparathyroidism patients

Bertocchio Jean-Philippe[1], Nidercorn Christelle[2], Peter Kamenicky[3], Vantyghem Marie Christine[4], Maruani Gerard[5], Lionel Groussin[6], Michel Ovize[7], Agnès Linglart[3] & Pascal Houillier[5]
[1]APHP-Hopital Pitié Slapétrière, Service Thyroïde-Tumeurs endocrines, Paris, France; [2]Hypoparathyroidisme France, Annecy-le-Vieux, France; [3]APHP-Hopital du Kremlin Bicetre, Service Endocrinologie et Maladies de la Reproduction, Le Kremlin-Bicêtre, France; [4]CHU de Lille, Lille, France; [5]APHP Hopital Européen Georges Pompidou, Service de Physiologie Rénale, Paris, France; [6]APHP Hopital Cochin, Service d'Endocrinologie Adulte, Paris, France; [7]Amolyt Pharma, Clinical Development, Ecully, France

Introduction
In chronic hypoparathyroidism (cHP), hypercalciuria is frequent, the mechanism of which remains unclear. The repetition of episodes of urinary tract obstruction by lithiasis can play a key role in the progressive deterioration of renal function. Taking advantage of the prospective cohort Epi-Hypo, we examined the relationship between nephrolithiasis and hypercalciuria.
Methods
The Epi-Hypo cohort started in 2016 in France and is still actively recruiting. Inclusion criteria include i) chronic (i.e. $\geq$6 months) cHP, ii) patient followed in France, and iii) patient agreement to participate. Exclusion criteria include i) transient cHP and ii) pseudo-hypoparathyroidism. Both pediatric and adult participants are recruited by physicians. Data are collected online through a secure digital platform for: demographics, circumstances of diagnosis, and follow-up (clinical events such as nephrolithiasis, as well as biology including calciuria) and entered in the database by physicians.
Results
The database was frozen on March 1st, 2023. At that time, urinary excretion of calcium was available for 776 patients; 74% were female and the median [IQR] age at diagnosis was 43 [31;56] years. Neck surgery accounted for 73% of cases. Hypercalciuria (defined as urinary calcium excretion $>$7.5 mmol/d in men and $>$ 6.25 mmol/d in women) was present in 258 (33%) of study patients. The proportion of patients with nephrolithiasis was significantly higher in patients with than in patients without hypercalciuria (26 vs 17%, $P=0.023$). Age, gender, or cause of hypoparathyroidism did not differ between patients with or without nephrolithiasis. The percentage of patients with hypercalciuria treated by oral calcium or active vitamin D was significantly higher than that of patients without hypercalciuria (72% vs 52%; 78% vs 65%, respectively; $P<0.05$ for both). Alternatively, hypercalciuric patients received significantly less often 25(OH) vitamin D (28% vs 35%; $P=0.024$).
Discussion/Conclusion
These data indicate that nephrolithiasis is more prevalent in cHP patients with hypercalciuria. The follow-up of this population may allow to assess a causal relationship between hypercalciuria and nephrolithiasis. It further suggests that normalization of urinary calcium excretion is a key therapeutic objective in patients with cHP hypoparathyroidism. Its impact on renal function remains to be investigated.

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OC2.5

Remaining secretion of parathyroid hormone is associated with calcium excretion in chronic hypoparathyroidism

Bertocchio Jean-Philippe[1], Nidercorn Christelle[2], Peter Kamenicky[3], Vantyghem Marie Christine[4], Maruani Gerard[5], Lionel Groussin[6], Michel Ovize[7], Agnès Linglart[3] & Pascal Houillier[5]
[1]APHP-Hopital Pitié Slapétrière, Paris, France; [2]Hypoparathyroidisme France, Annecy-le-Vieux, France; [3]APHP-Hopital du Kremlin Bicetre, Le Kremlin-Bicêtre, France; [4]CHU de Lille, Lille, France; [5]APHP Hopital Européen Georges Pompidou, Paris, France; [6]APHP Hopital Cochin, Paris, France; [7]Amolyt Pharma, Ecully, France

Introduction
In Chronic hypoparathyroidism (cHP), secretion of parathyroid hormone (PTH) is insufficient to maintain blood calcium concentration (PCa) steady. More than 70% of cases result from neck surgery and therefore in insufficient secretion of PTH as in mutations of genes involved in PTH synthesis, while mutations of the calcium-sensing receptor (CaSR) and its signaling pathway may result in a remaining secretion of PTH. cHP can exert nephrocalcinosis and/or nephrolithiasis in which calciuria (CaU) may play a key role. If the relationship between PCa and CaU has been studied, very few is known about the determinants of CaU during cHP. Taking advantage of the prospective cohort Epi-Hypo, we designed a study to analyze the determinants of CaU during cHP.
Methods
Epi-Hypo started in 2016 in France and is still actively recruiting. Inclusion criteria are i) chronic (i.e. $\geq$6 months) hypoPT, ii) followed in France, and iii) agreement to participate. Exclusion criteria are i) transient hypoPT and ii) pseudo-hypoparathyroidism. Both pediatric and adult participants are recruited. Data collected online through a secure digital platform refer to: demographics, circumstances of diagnosis, and follow-up including biology (PCa, CaU, and PTH as its ratio (PTHr) to the upper level of the normal laboratory range).
Results
The database was frozen on March 1st, 2023. At that time, 1,249 patients were included: 893 (71%) were female with median[IQR] age at diagnosis 43[31;56] years. In 937 (73%) patients, the cause was surgery. Nephrolithiasis and/or nephrocalcinosis was diagnosed in 198 (15%) patients over a mean$\pm$SD period of 12$\pm$10 years of follow-up. We gathered a subpopulation of 768 patients in whom both PCa and CaU (collected in 24-h urine collection) were available at least once. Mean$\pm$SD PCa and CaU values were 2.08$\pm$0.28 mM and 5.5$\pm$4.2 mmol/day, respectively, 33% patients exhibiting hypercalciuria. A positive correlation between PCa and CaU ($r^2=0.29$, $P<0.001$) and a negative correlation between blood PTH level and CaU ($r^2=-0.30$, $P<0.001$) were identified. Neither age, gender, or etiology of hypoparathyroidism were significantly different among patients with or without a remaining secretion of PTHr (ie PTHr $\geq$0.10).
Discussion/Conclusion
Controlling CaU during cHP is a challenging task. For the first time in a large cohort of patients, we report that a remaining secretion of PTH is linked to a lower CaU. Further studies are required to decipher whether this secretion is stable over time and whether it has to be taken into account when treating patients suffering from cHP.

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OC2.6

CALIBRATE: A phase 3, randomized, open-label study evaluating the efficacy and safety of encaleret (CLTX-305) compared to standard of care in participants with autosomal dominant hypocalcemia type 1 [NCT05680818]

Lars Rejnmark[1], Michael Mannstadt[2], Maria Luisa Brandi[3], Keiichi Ozono[4], Peter Tebben[5], Arun Mathew[6], Mary Scott Roberts[6], Scott Adler[6] & Rachel Gafni[7]
[1]Aarhus University Hospital, Institute of Clinical Medicine, Aarhus, Denmark; [2]Massachusetts General Hospital and Harvard Medical School, Endocrine Unit, Boston, United States; [3]University of Florence, Florence, Italy; [4]Osaka University, Osaka, Japan; [5]Mayo Clinic, Division of Endocrinology, Rochester, United States; [6]Calcilytix Therapeutics, Inc., San Francisco, United States; [7]National Institutes of Health, National Institute of Dental and Craniofacial Research, Bethesda, United States

Autosomal dominant hypocalcemia type 1 (ADH1), caused by pathogenic gain-of-function calcium-sensing receptor gene (*CASR*) variants, is characterized by low parathyroid hormone (PTH) levels, hypocalcemia, hypercalciuria, hyperphosphatemia and hypomagnesemia. Current standard-of-care (SoC) (calcium and active vitamin D) can exacerbate hypercalciuria, which may result in renal complications. Encaleret is an investigational oral calcilytic, functioning as a negative allosteric modulator of the calcium-sensing receptor, that is being studied as a potential treatment for ADH1. A Phase 2b study [NCT04581629] in 13 adults with ADH1 showed that encaleret led to sustained normalization in mean blood levels of intact PTH, albumin-corrected calcium (cCa), phosphorus, magnesium and 24-hr urine calcium (UCa) excretion over 24 weeks compared with baseline. Encaleret was well-tolerated with no serious adverse events reported. CALIBRATE is a global Phase 3 study designed to evaluate the efficacy and safety of encaleret compared to SoC in approximately 60 participants ($\geq$18-years-old in Europe; $\geq$16-years in other sites) with ADH1. After a screening evaluation, eligible participants will undergo SoC optimization followed by a 4-week SoC maintenance period (Period 1 [P1]). Participants will then be randomized 2:1 (encaleret:SoC) into a 20-week dose titration period (Period 2). Doses of encaleret or SoC will be titrated to achieve target cCa concentrations while minimizing UCa excretion. Participants will then enter a 4-week maintenance period (Period 3 [P3]) where doses of encaleret or SoC are intended to be fixed. The primary efficacy endpoint is a composite endpoint: a) cCa within 8.3-10.7 mg/dl (2.1-2.7 mmol/l) AND b) 24-hr UCa within reference range (men: $<$300 mg/day [7.5 mmol/day]; women: $<$250 mg/day [6.25 mmol/day]). Participants who meet both criteria will be considered responders. The primary analysis will be a within-patient comparison of the proportion of responders in the encaleret group at the completion of P3 vs P1 (SoC). Key secondary endpoints include between-treatment arm comparisons (encaleret vs SoC at P3) as well as the evaluation of mineral homeostasis parameters, renal health, bone health, and patient-reported outcomes. Following completion of P3, eligible participants will have the option to enter a long-term extension (LTE) period with all participants having access to encaleret. CALIBRATE is actively recruiting study participants and has sites (active and planned) in 12 countries: USA, Canada, Brazil, Netherlands, Denmark, France, Italy, Czech Republic, Taiwan, Australia, United Kingdom, and Japan.

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Oral Communications 3: Adrenal and Cardiovascular Endocrinology | Part I

OC3.1

Long-term incidence of acute cardiovascular events in transgender people – a large cohort study with national registry data

Lieve van Zijverden[1], Abel Thijs[2], Jeske van Diemen[2], Annemieke Staphorsius[1], Martin den Heijer[1] & Chantal Wiepjes[1]
[1]Amsterdam University Medical Centre, Department of Endocrinology, Centre of Expertise on Gender Dysphoria, Amsterdam, Netherlands; [2]Amsterdam University Medical Centre, Department of Internal Medicine, Amsterdam, Netherlands

Background
Transgender people often use gender-affirming hormone therapy to obtain physical characteristics that comply with their experienced gender. Transgender women use estradiol, usually with anti-androgens. Transgender men use testosterone. It has been reported that gender-affirming hormone therapy is associated with increased risk of acute cardiovascular events, however, this data constitutes largely of low quality evidence. We aimed to investigate the long-term incidence of acute cardiovascular events (CVEs) in our large cohort of transgender people compared with incidence in cisgender men and women.

Methods
This retrospective cohort study includes all people who visited the gender identity clinic of the Amsterdam University Medical Centre in the Netherlands between 1972 and 2018. All people were linked to a nationwide data registry (Statistics Netherlands) to obtain data on medical diagnoses, which were registered from 2012 until 2021. The outcomes were myocardial infarction, stroke, thrombosis and overall acute CVE incidence. Exclusion criteria were not using hormones and death before 2012. Standardized incidence ratios (SIRs) for each outcome were calculated using general population incidence rates stratified by age, sex and calendar year.
Results
2983 transgender women (follow-up: 49440 person-years) and 2143 transgender men (follow-up: 25346 person-years) were included. Median age at hormone therapy initiation was 29 (IQR 22-40) and 21 (IQR 18-28) years, respectively. Transgender women experienced 142 acute CVEs, which was higher compared with cisgender women (SIR 1.5, 95%CI 1.3-1.8), but not cisgender men (SIR 1.1, 95%CI 0.9-1.3). Myocardial infarction incidence was higher compared with cisgender women (SIR 1.8, 95%CI 1.2-2.5), and lower compared with cisgender men (SIR 0.7, 95%CI 0.5-0.9). Thrombosis incidence was elevated compared with both cisgender groups (women: SIR 1.9 [95%CI 1.4-2.4], men: SIR 1.8 [95%CI 1.4-2.4]). Stroke SIR was 1.2 (95%CI 0.9-1.5) compared with cisgender women and 0.9 (95%CI 0.7-1.2) compared with cisgender men. Transgender men experienced 62 CVEs, which was higher compared with cisgender women (SIR 1.9, 95%CI 1.5-2.4) and men (SIR 1.5, 95%CI 1.1-1.9). Myocardial infarction SIRs were also higher than in cisgender women (4.8, 95%CI 3.1-6.9) and men (1.7, 95%CI 1.1-2.4). This was not the case for stroke SIRs (cisgender women: 1.5 [95%CI 0.9-2.1], men: 1.2 [95%CI 0.8-1.8]) and thrombosis SIRs (cisgender women: 1.2 [95%CI 0.7-1.9], men: 1.5 [95%CI 0.9-2.4]).
Conclusion
Transgender women have a higher overall CVE risk than cisgender women, particularly in thrombosis and myocardial infarction. For transgender men overall CVE risk is higher than in both cisgender groups, mostly affected by increased myocardial infarction risk.

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OC3.2

Copeptin and asymptomatic arterial disorder in patients with type 2 diabetes, a cross-sectional study

Lee Ti Davidson[1], Jan Engvall[2], Simona Chisalita[3], Carl Johan Östgren[4] & Fredrik Nyström[2]
[1]Linköping University, Department of Emergency Medicine and Department of Biomedical and Clinical Sciences, Linköping, Sweden; [2]Linköping University, Division of Diagnostics and Specialist Medicine, Department of Health, Medicine and Caring Sciences, Linköping, Sweden; [3]Linköping University, Department of Endocrinology and Department of Health, Medicine and Caring Sciences, Linköping University, Linköping, Sweden; [4]Linköping University, Division of Prevention, Rehabilitation and Community Medicine, Department of Health, Medicine and Caring Sciences, Linköping, Sweden

Background
Individuals with diabetes are at higher risk for developing arterial disorders. The toe-brachial index (TBI) is associated with peripheral vascular disease, and aortic pulse-wave velocity (aPWV) is currently the gold standard for assessing arterial stiffness. High concentrations of plasma arginine vasopressin (AVP) preferentially stimulate V1a receptors, which affect the vascular bed and may contribute to cardiovascular (CV) complications. Copeptin, a more stable peptide of AVP, is co-secreted from the pituitary gland in equimolar amounts to AVP upon hemodynamic, osmotic, and other stress-related stimuli. Elevated levels of copeptin are potentially linked to vascular dysfunction.
Objective
To analyze the association of copeptin to TBI and aPWV as a marker of arterial disorder in patients with type 2 diabetes mellitus (T2D).
Methods
A cross-sectional analysis was conducted on 681 patients from the epidemiological study CARDIPP (Cardiovascular Risk Factors in Patients with Diabetes – a Prospective Study in Primary Care; ClinicalTrials.gov identifier NCT01049737) with data on copeptin, TBI, and aPWV. The relationship between the conventional cardiovascular risk factors and copeptin with TBI and aPWV were examined, respectively. Pearson correlation analysis and linear regression analyses were used.
Results
Copeptin correlated to TBI (r=-0.086, P=0.027) and aPWV (r=0.143, $P<$0,001). Copeptin was also negatively associated with TBI (β=-0.093, P=0.027) and aPWV (β=0.121, P=0.004) independently of age, sex, diabetes

duration, BMI, smoking, previous cardiovascular diseases, HbA1c, HDL cholesterol, and estimated glomerular filtration rate.
Conclusion
Copeptin is independently associated with TBI and aPWV. Copeptin may play an important role in the development of arterial disorders. Measuring copeptin levels may be a simpler method and more efficient way to identify individuals at risk for arterial disorders compared to current methods such as TBI and aPWV.

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OC3.3

Inflammation-based scores in patients with pheochromocytoma

Chiara Parazzoli[1], Alessandro Prete[2,3,4,5], Vittoria Favero[1,6], Carmen Aresta[7], Valentina Pucino[8,9], John Ayuk[4], Miriam Asia[4], Yasir S Elhassan[2,3,4], Iacopo Chiodini[1,6] & Cristina L Ronchi[3,4,9]
[1]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy; [2]University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, United Kingdom; [3]Birmingham Health Partners, Centre for Endocrinology, Diabetes and Metabolism, Birmingham, United Kingdom; [4]Queen Elizabeth Hospital Birmingham, Department of Endocrinology, Birmingham, United Kingdom; [5]University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, National Institute for Health Research Birmingham Biomedical Research Centre, Birmingham, United Kingdom; [6]Ospedale Niguarda Cà Granda, Unit of Endocrinology, Milan, Italy; [7]IRCCS, Istituto Auxologico Italiano, Department of Endocrine and Metabolic Diseases, Milan, Italy; [8]University of Oxford, Kennedy Institute of Rheumatology, Birmingham, United Kingdom; [9]University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom

Background
Pheochromocytoma is associated with systemic inflammation, but the underlying mechanisms are unclear. Hypothesising a putative effect of catecholamines on immune cells, we investigated the relationship between plasma metanephrine levels and haematological parameters – as surrogates for systemic inflammation – in patients with pheochromocytoma. Moreover, we aimed to assess the influence of preoperative α-blockade treatment on the inflammation-based scores.
Design and Methods
We included a retrospective cohort of 68 patients with pheochromocytoma who underwent adrenalectomy (mean age 53 years, 64.7% female) and two control groups matched for age, sex and body mass index: 68 patients with non-functioning adrenocortical tumours (NFAT) and 53 with essential hypertension. The full blood count and various inflammation-based scores [neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), lymphocyte/monocyte ratio (LMR), Systemic Inflammation Index (SII), Prognostic-Nutrition Index (PNI)] were assessed in all patients at diagnosis and compared between the three groups. In addition, in a subgroup of pheochromocytomas, these parameters were compared before and after preoperative α-blockade treatment ($n=29$, median time 110 days, IQR 78.5-261.5) and before and after adrenalectomy ($n=26$, median time 15.6 months, IQR 5.7-42.3).
Results
A higher inflammatory state, as reflected by both full blood count and inflammation-based scores, was observed in patients with pheochromocytoma compared to NFAT and essential hypertension, whilst no differences were found between the two control groups. Notably, plasma metanephrine levels showed a positive correlation with NLR ($r=0.4631$), PLR ($r=0.3174$), SII ($r=0.3709$), and a negative correlation with LMR ($r=0.4368$) and PNI ($r=0.3741$), even after adjustment for age, sex, ethnicity, BMI, and tumor size, except for PLR. After adrenalectomy, we observed a significant increase in lymphocyte count ($P=0.01$) with corresponding changes in the relative inflammation-based scores. Specifically, a decrease in NLR ($P=0.001$), PLR ($P=0.003$), SII ($P=0.004$) and a concomitant increase in LMR ($P=0.0002$) were detected postoperatively. Similarly, α-blockade treatment led to a reduction in NLR ($P=0.007$) and SII ($P=0.03$).
Conclusions
The preoperative systemic inflammatory state observed in patients with pheochromocytoma, reflected by high NLR, PLR and SII, as well as low LMR and PNI, and ameliorated by adrenalectomy and α-blockade, is probably related to an excessive amount of secreted catecholamines. The impact of circulating catecholamines on the systemic inflammatory response may play a role in the cardio-metabolic comorbidities in patients with pheochromocytoma and may optimise treatment approaches.

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OC3.4

HHEX is required for maintaining circulating glucocorticoid levels through expression of steroid transporter ABCB1 and regulation of lipid droplet homeostasis in the adrenal cortex

Typhanie Dumontet[1], Katie Basham[2], Micah Foster[1], Kyle Heard[1], Christopher Lapensee[1], Christina Bothou[3], Felix Beuschlein[3], William Rainey[1], Adina F. Turcu[1], Antonio Lerario[1] & Gary Hammer[1]
[1]University of Michigan, Ann Arbor, United States; [2]Huntsman Cancer Institute, Salt Lake City, United States; [3]University Hospital of Zürich, Zürich, Switzerland

The adrenal cortex synthesizes glucocorticoids that are essential for metabolic homeostasis and modulation of immune responsiveness. Glucocorticoid-producing cells, located in the zona fasciculata (zF), constitute the critical effector of the HPA axis that serves to mediate the mammalian stress response. Dysregulation of glucocorticoid function results in significant morbidity with complete deficiency being incompatible with life. While the zF is composed of heterogenous cell populations exhibiting proliferative, remodeling, and differentiation capabilities, the mechanisms and physiological importance of such diversity remain unexplored. To define the functional significance of the cellular diversity of the zF, we first performed single-cell RNAseq of the steroidogenic lineage in the adult mouse adrenal. We identified the homeodomain protein, HHEX, as the top enriched transcription factor in zF cells. To determine its role in adrenal homeostasis, we generated adrenal-specific Hhex knockout mouse models. Importantly, *HHEX KO* mice exhibited a profound glucocorticoid deficiency at baseline. We then performed bulk RNAseq and identified *Abcb1b* as the top gene dysregulated in *HHEX KO* of both sexes. ABCB1 (also P-glycoprotein, multidrug resistance protein 1) is a steroid efflux pump that is enriched in an inner-most zF cluster of cells and centrifugally expands during chronic stress. In humans, ABCB1 polymorphisms are associated with altered HPA axis regulation suggesting a critical role in chronic stress adaptation. Using CUT&Tag technology to profile *in vivo* genomic binding, we provide evidence that HHEX directly occupies *Abcb1b* regulatory regions. By combining RNAscope for *in situ* localization, and chronic ACTH treatment, we observed that *HHEX KO* fail to increase *Abcb1b* expression. Taken together these results suggest a critical role for HHEX in *Abcb1b* expression and chronic stress adaptation in both sexes. We then proceeded to determine adrenocortical cholesterol content (steroid precursor), and a profound decrease was evident specifically in the inner zF of *KO* males. Temporal analyses of HHEX expression revealed an 8-fold higher level in males at puberty compared to female counterparts, and genomic binding studies confirmed AR binding to HHEX promoter region *in vivo*. These observations suggest a sexually dimorphic role of HHEX in lipid (cholesterol ester) homeostasis. To explore the possibility that the dimorphism was mediated in part by androgens, we gonadectomized males and observed a complete rescue of the lipid loss in *HHEX KO* adrenals. Taken together, our results provide evidence that HHEX orchestrates the function and identity of the zF to promote chronic stress adaptation and protect lipid droplet integrity in males.

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OC3.5

Hip fractures in patients with primary aldosteronism – A Swedish nationwide study

Eleftheria Gkaniatsa[1,2], Tatiana Zverkova Sandström[3], Annika Rosengren[4,5], Penelope Trimpou[1,2], Andreas Muth[6], Gudmundur Johannsson[1,2] & Oskar Ragnarsson[1,2,7]
[1]Institute of Medicine, Sahlgrenska Academy, Department of Internal Medicine & Clinical Nutrition, Gothenburg, Sweden; [2]Sahlgrenska University Hospital, Department of Endocrinology, Gothenburg, Sweden; [3]Sahlgrenska Academy, University of Gothenburg, Health Metrics Unit, Gothenburg, Sweden; [4]Institute of Medicine, Sahlgrenska Academy, Department of Molecular and Clinical Medicine, Gothenburg, Sweden; [5]Sahlgrenska University Hospital, Department of Medicine, Geriatrics and Emergency Medicine, Gothenburg, Sweden; [6]Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Department of Surgery, Sweden; [7]Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg

Objectives
Clinical studies indicate that primary aldosteronism (PA) is associated with dysregulated bone homeostasis. The aim of this study was to evaluate the incidence of hip fractures in patients with PA.
Methods
We studied a nationwide cohort of 2419 patients with PA (1997-2019) and 24 187 age and sex matched controls from the general population. Hip fractures were

identified by ICD codes in the Swedish National Patient Register. We estimated hazard ratios (HRs) for incident hip fractures, adjusted for socioeconomic factors, diabetes, cardiovascular disease (CVD), osteoporosis, hyperparathyroidism, and prior fractures. Pairwise subgroup comparisons were performed by age (18-56 and $\geq$56 years), sex, CVD at baseline, and treatment for PA.
Results
During a mean follow up of 8 ± 5 years, 64 (2.6%) patients had a hip fracture after being diagnosed with PA, compared to 401 (1.7%) controls. After adjustments, PA was associated with increased risk of hip fracture compared to controls (HR 1.55 [1.18-2.03]). HRs were increased in women (HR 1.76 [95% CI 1.24-2.52]), patients aged >56 years (HR 1.62 [95% CI 1.21-2.17]), and patients with CVD at diagnosis (HR 2.15 [95% CI 1.37-3.37]). PA patients treated with adrenalectomy did not have higher risk than controls (HR 0.84 [95% CI 0.35-2.0]), while patients treated with mineralocorticoid receptor antagonists (MRA) retained a greater risk (HR 1.84 [95% CI 1.20-2.83]).
Conclusions
PA is associated with increased hip fracture risk, especially in women, patients diagnosed after the age of 56 years and patients with established CVD at diagnosis. Also, patients treated with MRA seem to have an increased risk of hip fractures, while adrenalectomy may be protective.

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OC3.6

Multiple dosing of immediate-release hydrocortisone is associated with a greater risk of hypothalamic-pituitary-adrenal axis suppression when compared to low-dose prednisolone when weaning in steroid-induced adrenal insufficiency

Simon Mifsud[1], Emma Louise Mifsud[1], John Newell-Price[1,2], Richard Ross[1] & Miguel Debono[1,2]
[1]The University of Sheffield, United Kingdom; [2]Sheffield Teaching Hospitals NHS Foundation Trust, United Kingdom

Background
Long-term glucocorticoids can result in iatrogenic Cushing's syndrome with adrenal suppression. Most patients reactivate their hypothalamic-pituitary-adrenal axis once they're weaned off glucocorticoids. During glucocorticoid withdrawal, many clinicians switch patients to hydrocortisone to benefit from its short half-life[1]. However, in some patients, hypothalamic-pituitary-adrenal axis recovery is delayed despite the above. It is unclear whether this could be related to persistent ongoing hydrocortisone overexposure. To investigate, we measured waking salivary cortisone (WSC), ACTH levels, blood pressure (BP), and body mass index (BMI) in patients on physiological doses of prednisolone and hydrocortisone with and without adrenal suppression after being weaned off high-dose glucocorticoids.
Method
A total of 99 patients on low-dose oral glucocorticoids (prednisolone $\leq$5 mg/day, or immediate-release hydrocortisone $\leq$25 mg/day) were assessed in a cross-sectional study. All patients were on glucocorticoids for more than 12 months. Patients with WSC levels >17 nmol/l were considered adrenal-sufficient, whereas those with levels <7 nmol/l, were adrenal-insufficient (AI). Patients with levels >7 nmol/l and <17 nmol/l had an ACTH-stimulation test, with a 30-minute post-Synacthen cortisol level >430 nmol/l confirming adrenal sufficiency. ACTH, BP, and BMI were measured on the day WSC was done.
Results
58.6% ($n=58$) of this cohort had AI. 22% ($n=13$) of the AI cohort had a suppressed ACTH (<5 ng/l). In contrast, no adrenal-sufficient patients had a suppressed ACTH(<5 ng/l) ($P=0.0006$). Systolic BP ($P=0.226$), diastolic BP ($P=0.968$), and BMI ($P=0.133$) did not differ significantly between patients with AI and adrenal sufficiency. 48.3% ($n=28$) of patients with AI and 31.7%($n=13$) with adrenal sufficiency were on hydrocortisone whilst the remaining were on prednisolone($P=0.146$). Patients on hydrocortisone with AI had a significantly lower WSC than patients on prednisolone (median WSC:3.68 nmol/l [IQR:0.74-4.43] vs median WSC:6.94 nmol/l [IQR:1.40-8.34], respectively; $P=0.0164$) and 84.6%($n=11$) of AI patients with a suppressed ACTH(<5 ng/l), were on hydrocortisone thrice daily($P=0.0046$).
Conclusion
Our study suggests that overall adrenal suppression in patients on physiological glucocorticoid doses is unlikely to be related to continuing steroid overexposure as only 22% of the AI cohort had a suppressed ACTH(<5 ng/l) and steroid biomarkers were not raised. Conversely, patients on multiple immediate-release hydrocortisone doses were more likely to have adrenal suppression, as evidenced by a fully suppressed ACTH (<5 ng/l) and a lower WSC level when compared to patients on prednisolone, indicating a greater risk of overexposure which could delay adrenal recovery.

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Oral Communications 4: Diabetes, Obesity, Metabolism and Nutrition | Part I

OC4.1

Glucose-loaded dopamine transporter is associated with mood altering effect of sweet foods and control over eating sweets

Kyoungjune Pak[1], Jihyun Kim[1], Keunyoung Kim[1], Seongho Seo[2] & Myung Jun Lee[1]
[1]Pusan National University Hospital; [2]Pai Chai University

Introduction
Craving for sweet taste is innate, and spans all ages in humans. The hedonic response to sweet taste predicts the future weight gain in humans. In this study, we investigated the association of sweet taste questionnaires (STQ) with dopamine transporter and brain glucose uptake.
Methods
Thirty-five healthy, nonobese male subjects were enrolled in this study. Each subject visited the institution three times, on separate days, for three brain PET scans (two^{18} F-FP-CIT PET scans and one^{18} F-FDG PET scan). Dynamic^{18} F-FP-CIT PET scans were acquired 10 mins after injection of either glucose (300 mg/kg) or placebo. Static ^{18} F-FDG PET scans were acquired 60 mins after injection of^{18} F-FDG. For^{18} F-FP-CIT PET, dopamine transporter (DAT) availability, expressed in terms of binding potential (BP_{ND}), were measured by analyzing time-activity curve via the simplified reference tissue method. For^{18} F-FDG PET, the mean uptake of each striatal region-of-interest was scaled to the mean of global cortical uptake of each individual, and defined as standardized uptake value ratio (SUVR). Also, subjects were assessed with 12-item self-reporting Sweet Taste Questionnaire (STQ) with 2 factors; STQ 1: sensitivity to the mood altering effect of sweets, and STQ 2: impaired control over eating sweet foods. The effects of STQ on striatal $BP_{ND}$and SUVR were investigated using Bayesian hierarchical modelling. We created models separately with STQ 1, and STQ 2 as predictors, with striatal BP_{ND} and SUVR as a dependent variable, adjusting for age.
Results
Thirty-five subjects (age 24.4 ± 2.7 years, BMI 23.8 ± 3.4 kg/m^2) underwent two^{18} F-FP-CIT brain PET scans, and twenty-four underwent additional^{18} F-FDG brain PET scans. STQ 1 (sensitivity to the mood altering effect of sweets) ranged from 7 to 28 with the mean of 14.9 ± 5.9. STQ 2 (impaired control over eating sweet foods) ranged from 5 to 19 with the mean of 9.1 ± 4.3. Glucose-loaded DAT availability was negatively associated with STQ 1 (sensitivity to the mood altering effect of sweets), and positively with STQ 2 (impaired control over eating sweet foods). However, the effects of STQ 1 and STQ 2 on placebo-loaded DAT availability and brain glucose uptake markedly overlapped with zero.
Conclusion
Glucose-loaded dopamine transporter is associated with mood altering effect of sweet foods and control over eating sweets. The change of dopamine transporter after glucose loading may be the key role for the craving for the sweet foods.

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OC4.2

Glucose at gestational diabetes diagnosis predicts neonatal hypoglycaemia, large-for-gestational age and post-partum abnormal maternal glucose homeostasis

Catarina Cidade-Rodrigues[1], Bruna Silva[1], Catarina Chaves[1], Vania Benido Silva[1], Ana Saavedra[1], Alexandra Araujo[1], Claudia Machado[1], Catarina Pereira[1], Vania Gomes[1], Odete Figueiredo[2], Anabela Melo[2], Anabela Ferreira[2], Mariana Martinho[3], Ana Morgado[2], Margarida Almeida[1], M Ceu Almeida[4] & Filipe Cunha[1]
[1]Centro Hospitalar do Tâmega e Sousa, Endocrinology, Guilhufe, Portugal; [2]Centro Hospitalar do Tâmega e Sousa, Gynecology and Obstetrics, Guilhufe, Portugal; [3]Centro Hospitalar Vila Nova de Gaia / Espinho-Unit 1, Endocrinology, Vila Nova de Gaia, Portugal; [4]Centro Hospitalar e Universitário de Coimbra, Gynecology and Obstetrics, Coimbra, Portugal

Introduction
Hyperglycaemia has been associated with worse maternal and foetal outcomes as well as higher risk for future type 2 diabetes (T2D).

Objectives
We study the association between glucose above diagnostic threshold (GADT) at gestational diabetes (GD) diagnosis and risk of perinatal complications and maternal glucose abnormalities at post-partum.
Materials and Methods
Retrospective study based on the national register of GD. Included women with live-born singleton pregnancies followed between 2012 and 2017. Excluded women without data on variables of interest. GADT defined as higher difference between measured glucose and diagnostic threshold at first trimester fasting glucose or 24-28th week OGTT. Primary endpoint: hypertensive disorders of pregnancy (HDP) – preeclampsia or gestational hypertension; preterm labour (PTL), caesarean section (CS), hypoglycaemia, large-for-gestational-age (LGA), and abnormal maternal glucose homeostasis (AMGH) at 4-12 weeks postpartum. Multivariate logistic regression models were built to test the association between GADT and the primary outcomes: adjustments for age, body mass index (BMI), family history of T2D, previous GD or macrosomia, insulin therapy, HbA1c, chronic hypertension, maternal excess weight gain during pregnancy, and time of GD diagnosis plus variables known to be associated with the primary outcome.
Results
We studied 6927 women with a median age of 34 (30-37) years and BMI of 25.8 (22.8-30.4) kg/m^2. Median GADT was 5 (2-11) mg/dl. HDP was found in 336 (4.9%) of women, PTL in 406 (5.9%), CS in 2704 (39.0%), neonatal hypoglycaemia in 262 (3.8%), LGA in 728 (10.5%), and AMGH in 486 (7.0%) – T2D in 56 (0.8%). In the univariate analysis, GADT, per 5 mg/dl increase, was associated with HDP, CS, neonatal hypoglycaemia, LGA, and AMGH, but not PTL with an OR (95% CI) of 1.07 (1.00-1.14), $P=0.04$; 1.06 (1.03-1.09), $P<0.001$; 1.08 (1.01-1.16), $P=0.03$; 1.08 (1.03-1.13, $P<0.001$); 1.32 (1.27-1.38), $P<0.001$, and 1.03 (0.97-1.09), $P=0.33$. After multivariate adjustments, GADT, per 5 mg/dl, remained associated with neonatal hypoglycaemia [1.09 (1.01-1.18), $P=0.03$], LGA [1.06 (1.00-1.11), $P=0.03$], and AMGH [1.31 (1.25-1.38), $P<0.001$] but not with HDP [1.04 (0.97-1.11), $P=0.30$] and CS [1.00 (1.00-1.01), $P=0.21$].
Conclusions
GADT is associated with worse neonatal outcomes and with AMGH but not with obstetric outcomes. Per 5 mg/dl increase of GADT, there is a 9% higher risk of neonatal hypoglycaemia, 6% higher risk of LGA newborns and 31% higher risk of AGMH at postpartum reclassification.

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OC4.3

Nitrate-mediated dilation is impaired in people with type 1 diabetes and co-existent metabolic dysfunction-associated steatotic liver disease

Jonathan Mertens[1,2], Tibor Stoop[2], Sven Francque[1,2], Christophe De Block[1,2] & Hilde Heuten[2]
[1]University of Antwerp-Faculty of Medicine, Antwerpen, Belgium; [2]Antwerp University Hospital, Edegem, Belgium

Introduction
The risk of cardiovascular disease (CVD) is increased in type 1 diabetes (T1D). Metabolic dysfunction-associated steatotic liver disease (MASLD) is linked to CVD, but evidence hereof is limited in people with T1D. Endothelial dysfunction is currently considered a key early event in the atherosclerotic process, but is never determined in people with T1D and co-existent MASLD.
Methods
We measured flow-mediated dilation (FMD) and nitrate-mediated dilation (NMD) in non-smoking adults without prior CVD with T1D. MASLD was diagnosed using ultrasound and presence of minimally one cardiometabolic risk factor. FMD was evaluated by longitudinal ultrasonographic imaging of the right brachial artery at rest and during reactive hyperaemia after inflating and deflating a forearm blood pressure cuff distal to the ultrasound probe (200 mmHg or $\geq$50 mm Hg above peak systolic blood pressure for 5 minutes) using high-resolution B-mode ultrasound. Wall-tracking software and continuous ECG registration were used to measure the end-diastolic diameter, coincident with the R-wave. Following FMD, NMD was evaluated by administering 25 µg of nitro-glycerine.
Results
Ninety-two adults were included, of whom 23 had MASLD. Diabetes duration was 30$\pm$14 years, median HbA1c was 7.0% (IQR 6.6-7.6). People with MASLD had a higher BMI compared to those without (31.6 [29.0-34.0] (MASLD) vs 23.9 [22.5-26.7]kg/m^2 (no MASLD), $P<0.001$). There were no differences in age, diabetes duration, blood pressure, presence of arterial hypertension, kidney function, or low-density lipoprotein cholesterol between groups. Cohort FMD was 5.47$\pm$2.89%, while NMD measured 19.7$\pm$7.1%. There was no significant difference in FMD between groups (5.58$\pm$3.12 (MASLD) vs 5.43$\pm$2.83% (non MASLD), $P=0.836$), but NMD was lower in those with MASLD (16.8$\pm$5.0 (MASLD) vs 20.8$\pm$7.5% (non MASLD), $P=0.009$).
Conclusion
Endothelial-independent vasodilation (NMD) is compromised in people with T1D and co-existent MASLD. However we could not notice a difference in endothelial-dependent dilation (FMD) between groups.

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OC4.4

Sphinganine increases GLP-1 secretion and causes weight loss in mice

Mark Smits[1], Anna Drzazga[1], Katrine Galsgaard[1], Jarkko Lackman[1], Victor Gerdes[2,3], Arnold van de Laar[3], Sjoerd Bruin[3], Mette Rosenkilde[1] & Jens J. Holst[1]
[1]University of Copenhagen, Department of Biomedical Sciences, København, Denmark; [2]Amsterdam UMC, locatie AMC, Amsterdam, Netherlands; [3]Spaarne Gasthuis, Hoofddorp, Netherlands

Recent years have demonstrated increasing focus on augmenting secretion of glucagon-like peptide (GLP)-1 from intestinal L cells, to improve the treatment and/or prevention of obesity and type 2 diabetes. However, finding strong stimuli and identifying novel compounds has proven difficult. To discover new GLP-1 secretagogues, we gave 49 individuals (76% female, BMI 28.3$\pm$4.8 kg/m^2) a high-fat liquid mixed meal (250 mL Nutridrink, Nutricia®). Plasma samples, taken before and repeatedly after the meal, were analysed for total GLP-1 (using radioimmunoassay) and subjected to untargeted metabolomics (LC-MS/MS, Metabolon). Using machine learning statistical techniques, we identified that among over 900 metabolites, the meal-induced increase in sphinganine was the strongest predictor of a strong GLP-1 response. In those subjects with high GLP-1 secretion, the increase in sphinganine was significantly higher ($P=0.027$). When murine GLUTag cells were exposed to sphinganine for 2 h, a dose-dependent increase in GLP-1 was seen (10 µM=28% [95%-CI 8–48]; 100 µM=[55% [37–73]). Moreover, sphinganine increased intracellular calcium mobilization (10 µM=3.9% [1.1–6.7]), as assessed using Fluo-4. This effect was reduced by concomitant exposure to 2-APB (IP-3 blocker, reduction 46%) and nifedipine (calcium-channel blocker, reduction 59%), suggesting a Gq-mediated pathway. Antagonists of GPR40, GPR55, GPR119 and S1PR1 reduced the effects of sphinganine by 30-59%. Next, we studied isolated intestinal and, separately, colon perfusion models in Wistar rats. In male rats, luminal perfusion with 100 µM sphinganine increased intestinal GLP-1 secretion (26% [1–52]) and tended to increase colonic GLP-1 secretion (18% [0-37]). Vascular administration did not affect GLP-1 secretion. In female rats, there were no significant effects. Single-dose sphinganine (20 mg/kg) given via oral gavage to male and female C57Bl6/JRj mice did not increase GLP-1 levels (measured with ELISA) compared to saline. Finally, male C57Bl6/JRj were fed a high-fat diet with or without sphinganine (dose of 0.05% w/w). After 21 days, sphinganine-fed mice had gained less weight compared to control diet (7% vs 13%, $P=0.045$). Sphinganine had no effect on food intake. No significant differences were seen during an insulin tolerance test and oral glucose tolerance test (OGTT), and sphinganine did not increase GLP-1 levels during the OGTT. In conclusion, sphinganine increases GLP-1 secretion *in vitro* and in perfusion studies in male rats. In mice, the effect of sphinganine on GLP-1 secretion is not evident, yet it reduces weight gain during high-fat feeding. As such, further studies for metabolic benefits of sphingolipids are warranted.

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OC4.5

Characteristics of presentation and management of people admitted with severe hypoglycaemia highlight the need for targeted educational interventions to mitigate occurrences-Pilot data from DEKODE Hypoglycaemia study

Sam Sherratt-Mayhew[1], Aashritha Buchipudi[1], Aditya Bal[1], Alexandra Lubina Solomon[2], Amanda Ling Jie Yee[1], Kalyaani Persad[1], Mariam Idrissi[1], Pratik Choudhary[3], Punith Kempegowda[4] & Team Dekode[4]
[1]University of Birmingham Medical School, United Kingdom; [2]Dudley Group NHS Foundation Trust, United Kingdom; [3]University of Leicester, United Kingdom; [4]Institute of Applied Health Research, United Kingdom

Background
Severe hypoglycemia, marked by blood glucose levels below 3 mmol/l (level 2) or necessitating third-party assistance (level 3), poses a significant risk leading to unplanned hospital admissions in individuals with diabetes. However, there is a paucity of information on admitted patients' characteristics, management, and outcomes.

Objective
To explore the characteristics of the population, precipitating factors and outcomes of people admitted with either level 2 or 3 hypoglycemia.
Methods
This retrospective study was conducted from October 2023 to January 2024 across five hospitals in the UK. All adults aged > 18 years admitted to hospitals with either level 2 or level 3 hypoglycaemia from November 2022 to October 2023 were included in the study. Various data on sociodemographics, precipitating factors, management and outcomes were collected. Data was analysed on SPSS 29.0.
Results
We identified 222 episodes of severe hypoglycemia, with 160 occurrences in individuals with type 2 diabetes and 62 in those with type 1 diabetes. Among these episodes, 158 were classified as level 2 (110 in type 2 and 48 in type 1), while 64 were categorised as level 3 (50 in type 2 and 14 in type 1). 22.5% of individuals with type 2 diabetes had received insulin treatment before admission. The median (interquartile) age was 44.5 (40.0-64.3) and 80.0 (70.0-83.0) years for people with type 1 and type 2 diabetes, respectively. Their Charlson comorbidity index was 4 (2-6) and 7 (6-8) respectively. The primary precipitating factor for hypoglycemia was a missed meal, accounting for 58.8% of type 2 and 45.2% of type 1 diabetes cases. Furthermore, 17.7% of people with type 1 diabetes and 12.5% with type 2 diabetes received glucagon either at home, in an ambulance, or upon admission. However, only 2.7% (6/222) of individuals (6.5% (4/62) with type 1 diabetes and 1.3% (2/160) with type 2 diabetes) were prescribed glucagon upon discharge. Insulin dose reduction emerged as the most common therapeutic adjustment on discharge, with 111 cases overall (31 in type 1 and 80 in type 2). Additionally, 11.3% of type 1 and 2.5% of type 2 diabetes cases commenced continuous glucose monitoring (CGM) upon discharge for timely alerts and prevention of further hypoglycemic events.
Conclusion
Individuals requiring hospitalisation for severe hypoglycemia were typically elderly and frail, often due to missed meals. Despite glucagon needs during episodes, prescriptions upon discharge were infrequent. These findings underscore the need for targeted educational interventions to mitigate such occurrences.

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OC4.6

GSDME Deficiency Sensitizes Mice to Diet-Induced Obesity by suppressing Lipolysis

Yuanyuan Wei[1,2], Yue Wu[2], Zuyi Yuan[2], Jian'an Wang[1] & De Ling Yin[1]
[1]Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Department of Cardiology, Hangzhou, China; [2]The First Affiliated Hospital of Xi'an Jiaotong University, Department of Cardiology, Xi'An, China

Background
Obesity, as a worldwide healthcare problem, has been attracting more and more attention. Chronic low-grade inflammation is regarded as an inducer of adipocyte cell death. Pyroptosis,a kind of inflammatory cell death,is involved in various inflammatory diseases.Gasdermin E(GSDME) is a mediator of pyroptosis via the cleavage of caspase-3. However, whether GSDME is involved in the regulation of adipose tissue function remains unknown. In the present study, we aim to investigate the role of GSDME in the development of obesity.
Methods and results
To investigate the role of adipose GSDME, we generate GSDME knockout ($GSDME^{-/-}$) mice. As compared with control mice, GSDME-/- mice show obesity when induced with a high-fat diet(HFD), along with hepatic steatosis, insulin resistance, glucose intolerance, and hypercholesterolemia. The effect of GSDME ablation on basic metabolic activity was also evaluated. Under the HFD condition, $GSDME^{-/-}$ mice showed significantly increased respiratory exchange rate (RER) and reduced oxygen consumption as compared with the controls. Gene array assay of control and GSDME-deficient adipose tissue revealed that lipolysis-associated genes including ATGL were significantly decreased with GSDME ablation in adipose tissues. Furthermore,the epiWAT from HFD-fed control and $GSDME^{-/-}$ mice was isolated and treated with isoproterenol (ISO). ISO-stimulated glycerol and FFA release were decreased in $GSDME^{-/-}$ explants.In vivo,the serum FFA and glycerol levels were measured after stimulated lipolysis by CL316243. Serum FFA as well as glycerol levels were significantly lower in $GSDME^{-/-}$ than control mice 15 min after CL316243 stimulation.
Conclusions
This study reveals that GSDME functions as a positive regulator of lipolysis by the ATGL expression regulation. Deletion of GSDME promoted HFD-induced obesity, impaired adipose function and deteriorated glucose intolerance and insulin resistance. GSDME may be a potential therapeutic target for ameliorating obesity and obesity related metabolic disorders.

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Oral Communications 5: Pituitary and Neuroendocrinology | Part I

OC5.1

Effects of Glucagon-like Peptide-1 Receptor Agonists on Copeptin in healthy volunteers and patients with primary polydipsia-A secondary analysis of the randomized, double-blind, placebo-controlled, crossover GOLD & GATE trials

Svenja Leibnitz[1,2], Mirjam Christ-Crain[1] & Bettina Winzeler[1]
[1]University Hospital Basel, Endocrinology, Diabetes and Metabolism, Basel, Switzerland; [2]University Hospital Basel, Clinical Research, Basel, Switzerland

Background/Introduction
Today, GLP-1 receptor agonists have great clinical importance in the treatment of type 2 diabetes and obesity. Beside their known mechanisms to lower blood sugar and enhance satiety signals, GLP-1 also seems to play a significant role in sodium and water balance. This can be supported by the finding of GLP-1 receptor expression in various locations of the kidney, the enteric system and key brain structures. Recent findings investigating long-term effects of treatment with GLP-1 receptor agonists showed a significant reduction of fluid intake and 24-h-urine volume compared to placebo. There were no changes in serum sodium, urinary sodium excretion or in hormones of the RAAS system as a possible physiological explanation. To our knowledge data are inconclusive regarding physiological mechanisms that could explain these observations. Furthermore, no direct effect of GLP-1 on Vasopressin has been observed to date. The aim of this secondary analysis was to investigate changes of Copeptin levels in euvolemic participants treated with dulaglutide vs placebo. We hypothesize that dulaglutide effects a stimulation in Vasopressin due to reduced water intake, lowered blood pressure and nausea which are known side effects of GLP-1 receptor agonists.
Methods
A secondary analysis of randomized, double-blind, placebo-controlled, cross-over-trials in 20 healthy participants (GATE trial) and 34 patients with primary polydipsia (GOLD trial) was performed at the University Hospital of Basel between 2016 and 2019. In both studies participants received either Dulaglutide (Trulicity®) 1.5 mg or placebo, in random order, subcutaneously once weekly over a three-week treatment phase and attended an 8-hour evaluation visit during the last treatment week. After a wash-out period of at least three weeks, patients received the complementary intervention.
Results
All 54 participants of the two cross-over trials were included. Median age was 27 (IQR 24 to 37) years and 63% were female. Median plasma sodium concentration, plasma osmolality and GFR were all in the mid-normal range. To estimate the treatment effect of Dulaglutide, we derived the absolute within-subject differences of Copeptin between Dulaglutide and placebo and used the wilcoxon rank test for statistical analysis. After a three-week treatment phase, Dulaglutide showed a significant suppression of Copeptin in both trials ($P = 0.04$) compared to placebo [GOLD: treatment effect: -0.67 pmol/l vs GATE: treatment effect: -1 pmol/l].
Conclusion
This analysis provides further insights into the direct effects of GLP-1 on Vasopressin and reveals physiological mechanisms that could explain the role of GLP-1 in sodium and water balance.

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OC5.2

Molecular and functional characterization of RNA metabolism machineries in pituitary tumours

Álvaro Flores-Martínez[1,2,3,4], Miguel E. G-García[1,2,3,4], Ana S. De la Rosa-Herencia[1,2,3,4], María Ortega Bellido[1,2,3,4], Ignacio Gil-Duque[1,2,3,4], David Cano Gonzales[5], Manuel D. Gahete[1,2,3,4], Justo P. Castaño[1,2,3,4], María Ángeles Gálvez-Moreno[1,4,6], Alfonso Soto-Moreno[5], Antonio C. Fuentes-Fayos[1,2,3,4] & Raul M Luque[1,2,3,4]
[1]Maimónides Biomedical Research Institute (IMIBIC), Córdoba, Spain; [2]University of Cordoba, Department of Cell Biology, Physiology and Immunology, Córdoba, Spain; [3]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Córdoba, Spain; [4]Reina Sofia University Hospital

(HURS), Córdoba, Spain; [5]Hospital Universitario Virgen del Rocío (HUVR), Department of Endocrinology and Nutrition, Institute of Biomedicine of Sevilla (IBiS), Sevilla, Spain; [6]Service of Endocrinology & Nutrition, HURS, Córdoba, Spain

Pituitary tumours (PTs) constitute approximately 15% of all brain tumours, affecting up to 5% of the general population. The majority of PTs are hormonally active tumours (approximately 70%), resulting in significant comorbidities associated with hormone release. Furthermore, clinically non-functioning PTs (NFPTs, around 30%) exhibit mass effect-related comorbidities due to delayed diagnosis, despite lacking a link to hormone excess. Recent studies indicate that aberrant alternative splicing is a prevalent characteristic observed in various endocrine and tumour pathologies, including PTs. In this context, other machineries involved in mRNA metabolism, such as RNA-Exosome and Nonsense-Mediated-Decay (NMD), have also been associated with several endocrine-related cancers. Therefore, our objective was to characterize the presence of components belonging to the RNA-Exosome and NMD machineries, and to determine their putative pathophysiological role in PTs. Specifically, we evaluated the expression levels of 28 and 24 genes involved in RNA-Exosome and NMD machineries, respectively, using 73 NFPTs, 50 somatotropinomas and 10 normal-pituitaries (as control-tissues) and a microfluidic-array based on qPCR-technology. The main results were consistently validated across various human external cohorts. Additionally, diverse functional and molecular approaches were performed in GH3 cell-line and primary patient-derived tumour cells using available pharmacological inhibitors of the RNA-Exosome (isoginkgetin) and NMD (NMDi) machineries, and specific candidate-genes siRNAs. Bioinformatic analysis revealed a heterogeneous dysregulation in both cellular machineries in PTs, highlighting the overexpression of EXOSC5 and CBP80 (from RNA-Exosome and NMD, respectively), as the most discriminating factors between tumour and non-tumour samples. Moreover, expression levels of these two genes were associated with different aggressiveness parameters, suggesting a potential oncogenic role in both GHomas and NFPTs. Additionally, *in vitro* silencing of CBP80 and EXOSC5 expression through specific siRNAs reduced several endocrine and tumour parameters (i.e., proliferation, colony-formation, secretion) in GH3 cells, as well as NFPT and GHoma primary patient-derived cells. We also observed a modulation of several molecular markers related to the cell-cycle and other key pro-oncogenic features in response to CBP80 and/or EXOSC5 silencing. Finally, pharmacological inhibition of the NMD but not of the RNA-Exosome resulted in a significant dose-response alteration of several functional parameters, including a reduction in the proliferation rate and other aggressiveness features. Altogether, we provide solid evidence indicating a drastic alteration of mRNA metabolism machineries (such as RNA-Exosome and NMD) in PTs, wherein CBP80 and EXOSC5 could represent novel diagnostic/prognostic biomarkers and therapeutic targets in GHomas and NFPTs.

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OC5.3

Transcriptomics analysis confirms WHO classification of PitNETs and reveals distinct patterns related to invasiveness

Jelena Jotanovic[1,2], Abdellah Tebani[3,4], Neda Hekmati[1], Åsa Sivertsson[3], Cecilia Lindskog[1], Mathias Uhlèn[3], Olafur Gudjonsson[5], Erika Tsatsaris[6], Britt Eden Engstrom[6], Johan Wikström[7], Fredrik Pontén[1] & Olivera Casar-Borota[1,2]
[1]Uppsala University, Department of Immunology, Genetics and Pathology, Rudbeck Laboratory, Uppsala, Sweden; [2]Uppsala University Hospital, Department of Clinical Pathology, Uppsala, Sweden; [3]KTH Royal Institute of Technology, Science for Life Laboratory, Department of Protein Science, Stockholm, Sweden; [4]Normandie University, Department of Metabolic Biochemistry, UNIROUEN, INSERM U1245, CHU Rouen, Rouen, France; [5]Uppsala University, Department of Neuroscience, Uppsala, Sweden; [6]Uppsala University, Department of Medical Sciences, Endocrinology and Mineral Metabolism, Uppsala, Sweden; [7]Uppsala University, Department of Surgical Sciences, Neuroradiology, Uppsala, Sweden

Pituitary neuroendocrine tumors (PitNETs) are typically benign tumors presenting with symptoms related to hormone hypersecretion and/or intracranial mass. Current classification of PitNETs is based on the immunohistochemical expression of adenohypophysial hormones and three main pituitary-specific transcriptions factors PIT1, TPIT and SF1. PitNETs usually remain intrasellar, however, 20-40% of tumors show invasiveness into cavernous sinus and 6–8% infiltrate into the bones, affecting the prognosis. There is an unmet need to detect reliable biomarkers that can predict the parasellar and bone invasiveness of PitNETs as well as the factors related to tumor vascularization. We validated the current PitNETs classification by exploring gene expression patterns in a well-characterized cohort of 51 PitNETs of different histological and clinical types. The gene expression signatures were compared with clinical and immunohistochemically based classification. Next, we extended the cohort to acquire a higher fraction of invasive tumors. Applying the same transcriptomics analysis in this expanded cohort of 77 patients we studied the gene expression differences between invasive and non-invasive tumors regarding parasellar and bone-invasiveness. Moreover, we explored the genes that correlated to the contrast enhancement quotient, a radiological proxy of tumor vascularization. Our results revealed three main transcriptomics clusters of PitNETs, supporting the current immunohistochemical PitNETs classification. A few "null cell adenomas" clustered as either gonadotroph or corticotroph tumors, further questioning this controversial entity. Our results did not demonstrate clear clustering regarding the invasiveness. However, differentially expressed genes related to parasellar growth were genes with previously established role in tumor invasiveness, and the differentially expressed genes regarding bone invasiveness were those involved in anti-tumoral immune response and NF-κB pathway. Several genes involved in tumor biology and vascularization correlated significantly with the contrast enhancement quotient. In conclusion, we demonstrated that the current WHO classification of PitNETs based on the immunohistochemical expression of PIT1, TPIT and SF1 is in concordance with the three PitNETs subtypes with distinct gene expression patterns. The transcriptomic analysis also revealed differences in the molecular landscape between invasive and non-invasive PitNETs. However, a clear clustering was not demonstrated, which may, at least partly, be explained by the strong influence of the genes that drive the cell lineage differentiation in our diverse cohort of PitNETs. The contrast enhancement quotient appears as a novel potential radiological parameter of tumor vascularization. Several detected tumor-driving genes and genes related to the invasiveness and vascularization of PitNETs are potential therapeutic targets and prognostic biomarkers, thus warranting further research.

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OC5.4

Mast cells, a new actor in gonadotroph tumors

Mirela Diana Ilie[1], Maxime Lepetit[2], Marie Chanal[1], Alexandre Vasiljevic[1], Emmanuel Jouanneau[1], Olivier Gandrillon[2], Franck Picard[2], Gérald Raverot[1] & Philippe Bertolino[1]
[1]Inserm U1052, CNRS UMR5286, Cancer Research Center of Lyon, Lyon 1 University, Lyon, France; [2]École Normale Supérieure de Lyon, Lyon, France

Background
While gonadotroph tumors are lacking both medical treatment options and prognostic markers, the tumor microenvironment represents a promising tool. The aim of this study was to 1) identify new tumor microenvironment actors in gonadotroph tumors, 2) gain insight into the tumorigenesis mechanisms driven by these tumor microenvironment cells, and 3) identify new tumor microenvironment-related prognostic markers, as well as new therapeutic targets.
Methods
Single-cell transcriptomics of six gonadotroph tumors, spatial transcriptomics of three gonadotroph tumors, followed by immunohistological validation on 49 gonadotroph tumors.
Results
24,471 cells from the six tumors passed the quality control. Clustering analysis revealed expected tumor and tumor microenvironment cell types, as well as mast cells as a new population in pituitary tumors. Regarding mast cells' phenotype, 132/133 mast cells expressed tryptase, of which three co-expressed chymase; no mast cell expressed only chymase. Immunohistochemistry for tryptase, followed by analysis of whole slides, confirmed mast cells were present in all 49 gonadotroph tumors (0.01-4.33%). Next, we investigated the ligand-receptor networks. Using CellPhoneDB, bilateral crosstalk was identified between mast and endothelial cells. The top ranked secreted ligand from mast cells signaling towards endothelial cells was VEGFA, suggesting mast cells have a pro-angiogenic role in gonadotroph tumors. In line with this hypothesis, there was a very strong and positive correlation between the percentages of endothelial cells and of mast cells in the 6 tumors (rho = 0.94, $P = 0.01$). In addition, analysis of spatial transcriptomics data showed mast cells were usually found in the vicinity of endothelial cells, which we confirmed with double immunofluorescence staining (tryptase/CD34). Furthermore, mast cells expressed more frequently *VEGFA* than *TNF*, suggesting a pro-tumorigenic role for mast cells in gonadotroph tumors. Indeed, mast cells were associated with a bad prognosis in the clinical cohort, notably tumors that progressed/relapsed more rapidly after surgery had more abundant mast cells ($P = 0.002$). Moreover, for a same patient, recurrent tumors had more mast cells than the initial tumor ($P = 0.007$). Finally, Nichenet analysis identified KITLG (acting via KIT) as one of the probable up-

regulators of *VEGFA* expression in mast cells. Interestingly, the top ranked interaction identified between endothelial and mast cells was also KITLG-KIT.
Conclusion
We identified mast cells as a new population in gonadotroph tumors. In these tumors, mast cells appear to have pro-angiogenic and pro-tumorigenic roles. Moreover, mast cells were associated with a bad prognosis in the clinical cohort, suggesting that KIT targeting might be beneficial for the treatment of gonadotroph tumors.

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OC5.5

B-RAF and MEK inhibitor argeted therapy in papillary craniopharyngiomas: results from the French national multicenter study

Dario De Alcubierre[1], Grigorios Gkasdaris[2], Claire Briet[3], Fabien Almairac[4], Julien Boetto[5], Celine Mouly[6], Delphine Larrieu-Ciron[7], Anthony Joncour[8], Margaux Mordrel[9], Alexandre Vasiljevic[10], Chiara Villa[11], Camille Sergeant[12], Francois Ducray[13], Loic Feuvret[14], Bertrand Baussart[15], Gerald Raverot[2] & Emmanuel Jouanneau[2]
[1]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy; [2]Groupement Hospitalier Est, Hospices Civils de Lyon, Department of Neurosurgery, Bron, France; [3]CHU d'Angers, Angers, France; [4]Hôpital Pasteur II, University Hospital of Nice, Nice, France; [5]Gui de Chauliac Hospital, Montpellier University Medical Center, Montpellier, France; [6]CHU Toulouse, Toulouse, France; [7]Institut Universitaire du Cancer Toulouse Oncopole, Institut Claudius Re-gaud, Department of Medical Oncology, Toulpouse, France; [8]Poitiers University Hospital, Oncology Department, Poitiers, France; [9]Université de Poitiers, CHU de Poitiers, ProDiCeT, Poitiers, France; [10]Centre de Pathologie Est, Groupement Hospitalier Est, Hospices Civils de Lyon, Bron, France; [11]Hôpital Universitaire Pitié-Salpêtrière, APHP, Sorbonne Université, Department of Neuropathology, Paris, France; [12]Groupement Hospitalier Est, Hospices Civils de Lyon, Endocrinology Department, Bron, France; [13]Groupement Hospitalier Est, Hospices Civils de Lyon, Department of Neuro-Oncology, Bron, France; [14]Groupement Hospitalier Est, Hospices Civils de Lyon, Department of Radiation Oncology, Bron, France; [15]La Pitié-Salpêtrière Hospital, AP-HP, Sorbonne University, Department of Neurosurgery, Paris, France

Background
Papillary craniopharyngiomas (PCPs) are driven by V600E BRAF mutations in 95% of cases. Recently, combined anti-BRAF/MEK targeted therapy (TT) has emerged as a potential treatment in aggressive PCPs. However, standardized data on large cohorts are still lacking. Our study aimed to assess the real-life efficacy and safety of TT in patients with PCPs.
Methods
This was a retrospective national multicenter study involving patients with V600E BRAF-mutated PCPs treated with anti-BRAF/MEK TT in France up to July 2023. Volumetric magnetic resonance imaging analysis, clinical and hormonal assessments were performed before TT, after 3 months, and at the last available follow-up during treatment. Radiological response was classified as either complete (lesion disappearance), subtotal (volume reduction $>80\%$), partial (volume decrease 30-80%), stable disease (volume decrease $<30\%$ or increase $<20\%$), or progressive disease (volume increase $>20\%$).
Results
Sixteen patients (8 females, mean age 50.5 ± 15.75 years) were included. Patients received either neoadjuvant therapy (NEO) for non-resectable tumors ($n=6$), adjuvant therapy (ADJ) post-surgery ($n=8$), or palliative therapy (PAL) after multimodal treatment ($n=2$).Before TT, symptoms included headache (5 patients), endocrine dysfunction (14), visual impairment (9), weight gain (3), and cognitive dysfunction (2). Mean tumor volume was 7429 ± 2483 mm^3. After 3 months of TT, mean volume reduction was $82.2\pm16.9\%$, $52.9\pm21.9\%$, and $60.8\pm17.3\%$ [43.5-78.1] in the NEO, ADJ, and PAL groups, respectively. At the last follow-up (mean 7.6 ± 5.3 months), 12 patients (6 NEO, 4 ADJ, 2 PAL) showed subtotal response, 3 ADJ patients exhibited partial response, and one ADJ patient maintained stable disease. Mean volume reduction was $88.9\pm4.4\%$, $73.3\pm23.4\%$, and $91.8\pm4.3\%$ in the NEO, ADJ, and PAL groups, respectively.Clinically, TT resolved headaches in all patients and visual impairment in 6. Two patients had improved neurological symptoms, one presented weight loss, and two recovered endocrine function. Five patients stopped treatment due to adverse events. Two developed hepatic cytolysis, leading to temporary TT discontinuation and later reintroduction. One patient permanently discontinued TT due to peripheral oedema, another due to febrile pneumopathy, and the remaining one due to vomiting, skin rash, urinary tract infections, and hyperthermia.
Conclusions
Targeted therapy in PCP patients can induce impressive tumor volume reduction and clinical improvement within a few months from treatment initiation. Adverse events warrant careful monitoring. Further research is needed to establish standardized protocols, but present results advocate for reframing usual strategies.

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OC5.6

Digital voice analysis as a biomarker for acromegaly

Konstantina Vouzouneraki[1], Fredrik Nylén[2], Jenny Holmberg[2], Tommy Olsson[3], Katarina Berinder[4,5], Charlotte Höybye[4,5], Sophie Bensing[4,5], Maria Petersson[4,5], Anna-Karin Åkerman[6,7], Henrik Borg[8,9], Bertil Ekman[10,11], Jonas Robért[10], Britt Edén Engström[12,13], Oskar Ragnarsson[14,15,16], Pia Burman[8,9] & Per Dahlqvist[1]
[1]Umeå University, Department of Public Health and Clinical Medicine, Umeå, Sweden; [2]Umeå University, Department of Clinical Sciences, Umeå, Sweden; [3]Umeå Unversitty, Department of Public Health and Clinical Medicine, Umeå, Sweden; [4]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [5]Karolinska University Hospital, Department of Endocrinology, Stockholm, Sweden; [6]Örebro University Hospital, Department of Internal Medicine, Örebro; [7]Örebro University, Faculty of Health and Medical Sciences, Örebro, Sweden; [8]Lund University, Department of Endocrinology, Malmö, Sweden; [9]Skåne University Hospital, Department of Endocrinology, Malmö, Sweden; [10]Linköping University, Department of Health, Medicine and Caring Sciences, Linköping, Sweden; [11]Linköping University Hospital, Departments of Endocrinology in Linköping and Norrköping, Linköping, Sweden; [12]Uppsala University, Department of Medical Sciences, Endocrinology and Mineral Metabolism, Uppsala, Sweden; [13]Uppsala University hospital, Department of Medical Sciences, Endocrinology and Mineral Metabolism, Uppsala, Sweden; [14]Institute of Medicine at Sahlgrenska Academy, University of Gothenburg, Department of Internal Medicine and Clinical Nutrition, Gothenburg, Sweden; [15]Sahlgrenska University Hospital, Department of Endocrinology, Gothenburg, Sweden; [16]Wallenberg Centre for Molecular and Translational Medicine, Institute of Medicine, Gothenburg, Sweden

Background
Due to the rarity and the slow progress of the disease, there is a considerable diagnostic delay in acromegaly, contributing to increased morbidity and mortality. Voice analysis may decrease this delay as patients with acromegaly often develop a dark voice and unclear speech due to macroglossia, enlarged lips and edema in the pharynx and larynx. Modern technology offers higher speed and power of voice analysis and increased the interest in voice as a biomarker to identify several diseases. The aim of this study was to develop an algorithm identifying patients with acromegaly using a wide range of acoustic parameters and machine learning.
Method
Voice recordings from patients with acromegaly and from matched controls were collected using a mobile phone with a sound recording application (Voice Record Pro) at all University hospitals in Sweden. The recordings included a sustained "aaaaa". Anthropometric and clinical data and self-reported voice handicap index (VHI) were assessed. The voice analysis of the sustained "aaaaa" included 3274 parameters, used for training of three different models (Support Vector Machines, Random forests and k-Nearest Neighbor) to classify the speaker as "acromegaly" or "control". The models were combined into a model ensemble, a machine learning approach to combine models in the prediction process to increase the accuracy of classification. The model was trained with 75% of available data and its performance was assessed using the remaining 25% of the data set.
Results
We included 151 (39% women) Swedish patients with acromegaly, 77% in biochemical remission, 10% biochemically active despite treatment and 13% recently diagnosed and treatment naive. For comparison 139 matched controls (41% women) were included. The model ensemble could identify patients with acromegaly with a sensitivity of 71% and a specificity of 77% (diagnostic accuracy 74%, ROC AUC 84%) based on voice classification of the sustained "aaaaa". Self-reported voice problems (VHI) were significantly higher in patients with acromegaly compared to controls (median VHI 6 vs 2, $P<0.01$). The proportion of individuals with VHI >20, representing a clinically significant voice impairment was higher in the acromegaly group than the control group (22.5% vs 3.6%).
Conclusions
Modern voice analysis can identify patients with acromegaly from short voice recordings with a reasonable accuracy. Patients with acromegaly have an

increased prevalence of self-reported speech and voice disturbances even after biochemical control of acromegaly.

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Oral Communications 6: Environmental Endocrinology

OC6.1

Higher PFOS exposure associated with higher SHBG in third trimester. The odense child cohort

Richard Christian Jensen[1,2], Dorte Glintborg[1], Flemming Nielsen[2], Henriette Boye[3], Anne Schmedes[4], Tina Jensen[2,3] & Marianne Andersen[1]
[1]Odense University Hospital, Department of Medical Endocrinology, Odense C, Denmark; [2]University of Southern Denmark, Clinical Pharmacology, Pharmacy and Environmental Medicine, Odense C, Denmark; [3]Odense University Hospital, Odense Child Cohort, Odense C, Denmark; [4]Lillebaelt Hospital, Department of Biochemistry and Immunology, Vejle, Denmark

Background
Perfluoroalkyl substances (PFAS) are endocrine disrupting chemicals, with elimination half-lives ranging from four to eight years. Experimental studies indicate that PFAS may disrupt androgenic and estrogenic pathways, potentially affecting fetal development. During 1st trimester, concentrations of sex hormone-binding globulin (SHBG) increase due to higher estrogen levels from the placenta. The increment of SHBG concentration results in a compensatory increase in total testosterone (TT) in women at 1st and 2nd trimester, but levels of free testosterone (Free-T) remain within the range of non-pregnant women. Circulating Free-T increases significantly in women during 3rd trimester. To our knowledge, no previous study has investigated associations between PFAS exposure and concentrations of both SHBG and androgens in pregnant women.
Objective
To investigate associations between maternal PFAS concentrations and levels of SHBG and androgens in pregnancy.
Methods
In Odense Child Cohort (OCC), a single-center study, pregnancy serum concentrations of five PFAS: perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorodecanoic acid (PFDA) were measured in 1,609 eligible women at median gestational week (GW) 12 (25th, 75th percentile: 10, 15). Among these, concentrations of SHBG, calculated Free-T, and TT were assessed in 1,048 pregnant women at median GW 29 (25th, 75th percentile: 28, 30). Multivariate linear regression models were performed to estimate associations between PFAS concentrations and levels of SHBG and androgens.
Results
Included women had a mean age of 30.2 ($\pm$4.5 SD) years and median pre-pregnancy BMI of 23.5 (5th, 95th percentiles: 19.2, 32.6) kg/m^2 and 57.8% were nulliparous. A doubling in PFOS concentration was associated with an increment in SHBG concentration by 2.29% (95% CI: 0.04%, 4.59%) in adjusted analyses. PFOS exposure in the third tertile, as compared to the first tertile, significantly increased SHBG concentrations by 4.60% (95% CI: 0.46%, 8.26%). A significant dose-response relationship was observed across exposure tertiles for PFOS in the association with SHBG. A non-significant inverse association was found between PFAS and Free-T. No significant association was demonstrated between PFAS and TT.
Conclusion and perspectives
Our data suggested that PFOS exposure was associated with higher SHBG concentrations in pregnant women. This increase in SHBG may indirectly be through a PFOS-mediated aromatase induction. Possibly, the increase in SHBG without a compensatory TT increment may result in the non-significant decrease in Free-T. The findings underscore the necessity of the follow-up of children in terms of assessing putative long-term associations with PFAS during childhood.

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OC6.2

Thyroid Cancer and Endocrine Disruptive Chemicals: A Case-Control Study on Persistent Organic Pollutants (POPs)

Marina Lugaresi[1], Catherine Pirard[2,3], Claudia Moneta[1], Patrice Dufour[2,3], Erika Carbone[4], Alessandro Manzo[1,4], Carla Colombo[4,5], Laura Fugazzola[4,5], Corinne Charlier[2,3] & Valentina Cirello[4,5]
[1]University of Milan, Department of Biotechnology and Translational Medicine, Milan, Italy; [2]University Hospital of Liege (CHU Liège), Department of Clinical, Forensic and Environmental Toxicology, Liège, Belgium; [3]University of Liege (ULiège), Center for Interdisciplinary Research on Medicines (C.I.R.M.), Liège, Belgium; [4]Istituto Auxologico Italiano IRCCS, Department of Endocrine and Metabolic Diseases, Milan, Italy; [5]University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy

Objectives
Recent evidence suggest that environmental pollution may be involved in the worldwide increase of thyroid cancer (TC) incidence occurred over the last few decades. Indeed, some environmental pollutants, namely endocrine disruptive chemicals (EDCs), have been linked to endocrine system disruption, including thyroid dysfunction, and increased risk of TC. Several EDCs are known to be Persistent Organic Pollutants (POPs) due to their long half-life in the environment, such as Per-Fluoroalkyl Substances (PFAS), poly-chlorinated biphenyls (PCBs), and the pesticide dichlorodiphenyltrichloroethane (4,4'-DDT, and its metabolite 4,4'-DDE). Threatening ecosystems and human health, POPs have raised global concern, but to date few studies explored their association with TC and none considered the possible correlation with TC clinical and molecular features. The present case-control study aimed to evaluate the possible association between serum PFAS, PCBs and 4,4'-DDE concentrations, TC, and its clinical and molecular characteristics.
Materials and methods
We recruited 224 participants, of which 112 patients with a diagnosis of TC in the last five years and 112 sex and age-matched controls with no known history of thyroid diseases, primitive gonadic diseases, or other malignancies. Blood samples were taken from all participants and serum concentrations of some PFAS and PCBs, and 4,4'-DDE were measured using liquid chromatography or gas chromatography coupled to mass spectrometry. *BRAF* V600E mutation was assessed by standard methods. Logistic regression models were used to evaluate the association between TC, its clinical and molecular features, and POPs serums levels.
Results
The detection of perfluorodecanoic acid (PFDA) was positively correlated to TC (OR = 2.03), while a negative association was found with perfluorohexanesulfonic acid (PFHxS) levels (OR = 0.63). Worthy, perfluorononanoic acid (PFNA) was positively associated with the presence of thyroiditis, while PFHxS and perfluorooctane sulfonic acid (PFOS) with higher levels of pre-surgical TSH. PFHxS, PFOS, PFNA and PFDA were associated with less aggressive TC, while two poly-chlorinated biphenyls (PCB-105 and PCB-118) with larger and more aggressive tumours. Lastly, the presence of *BRAF* V600E mutation resulted associated with PCB-153, PCB-138 and PCB-180.
Conclusions
Our case-control study evaluate the impact of some POPs on TC, and it is the first to investigate their association with clinical and molecular features of the tumour. Beside the already known association between TC and PFDA, we found interesting correlations between some POPs and tumour aggressiveness, and between *BRAF* V600E mutation and PCBs. On the other hand, an inverse association was found with PFHxS, already reported in TC, but the underlying biochemical mechanisms are still unclear.

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OC6.3

NRF2 genetic polymorphisms modify the longitudinal association of serum polychlorinated biphenyls with glucose homeostasis damage: A gene-environment interaction analysis among Chinese general adults

Qiyou Tan[1], Min Zhou[1], Linling Yu[1], Bin Wang[1], Mengyi Wang[1] & Weihong Chen[1]
[1]Huazhong University of Science and Technology, School of Public Health, Wuhan, China

Background
As persistant organic pollutants, polychlorinated biphenyls (PCBs) are widespread in environment worldwide. Serum PCBs and nuclear factor erythroid 2-related factor 2 (NRF2) are associated with glucose homeostasis damage in the general population. However, there is a lack of epidemiological evidence on the interaction between serum PCBs and *NRF2* gene in relation to glucose homeostasis damage.
Objectives
We aimed to explore the interaction effects of PCB exposure and *NRF2* genetic polymorphisms on glucose homeostasis through a longitudinal epidemiological study.
Methods
A total of 1705 participants with 6 years follow-up from the Wuhan-Zhuhai prospective cohort was included. Repeated fasting plasma glucose (FPG) and

insulin (FPI), and serum PCBs were measured for each participant. The genotypes were determined using the Infinium OmniZhongHua-8 BeadChip and 39 single nucleotide polymorphisms within the *NRF2* gene were included. Generalized linear models were used to analyze the relationships of serum PCBs and *NRF2* genetic polymorphisms with glucose homeostasis indices over 6 years.

Results

NRF2 genetic polymorphisms (rs1806649, rs62173695, rs34468415, rs117045674, rs141429955, and rs117263449) were significantly associated with changes in glucose homeostasis indices over 6 years. Furthermore, we observed significant interactions between *NRF2* genetic polymorphisms and PCBs on changes in glucose homeostasis indices over 6 years (P interaction <0.05), especially rs117263449 and rs141429955. Each 1-unit increase in ln-transformed PCB-118 was associated with a 0.472 increment of FPG over 6 years among rs117263449 TT/TC genotype; and a 1.898 mmol/l, 47.894 mU/l, and 20.571 increment of FPG, FPI, and homeostasis model assessment of insulin resistance (HOMA-IR) over 6 years among rs141429955 AG genotype, respectively. Each 1-unit increase in ln-transformed PCB-52 and PCB-101 was associated with a 5.862 and 15.325 mU/l increment of FPI, and a 2.634 and 6.518 increment of HOMA-IR among rs117263449 TT/TC genotype, respectively. Each 1-unit increase in ln-transformed PCB-52 and PCB-101 was associated with a 27.386 and 60.361 mU/l increment of FPI, and a 11.849 and 25.636 increment of HOMA-IR among rs141429955 AG genotype, respectively.

Conclusions

The *NRF2* gene might modify the longitudinal relationships between PCB exposure and glucose homeostasis damage among Chinese general adults. Our results suggested that redox-related *NRF2* gene should be more considered to prevent glucose homeostasis damage, especially among individuals with high PCB exposure. More mechanistic studies are warranted.

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OC6.4

1,25-Dihydroxyvitamin D3 reduces adipogenesis and mitigates the bisphenol-A-induced pro-adipogenic effect in mouse 3T3-L1 cell line and human adipose-derived mesenchymal stem cells through miR-27-3p regulation

Donatella Provvisiero[1], Mariarosaria Negri[2], Feliciana Amatrudo[2], Roberta Patalano[1], Tatiana Montò[1], Gabriella Pugliese[1], Giulia de Alteriis[1], Chiara Graziadio[1], Annamaria Colao[1], Rosario Pivonello[1], Silvia Savastano[1] & Claudia Pivonello[3]

[1]Federico II University of Naples, Department of Clinical Medicine and Surgery, Naples, Italy; [2]Università Telematica Pegaso, Dipartimento di Scienze Umanistiche, Naples, Italy; [3]Federico II University of Naples, Department of Public Health, Naples, Italy

Endocrine-disrupting chemicals, including bisphenol A (BPA) may promote obesity. The role of 1,25-Dihydroxyvitamin D3 (VitD) in counteracting adipogenesis is still a matter of question. Thus, the current study aims to investigate whether and how VitD exposure during adipogenesis could prevent the BPA pro-adipogenic effect in adipocyte models: the mouse pre-adipocytes 3T3-L1 and the human adipose-derived mesenchymal stem cells (hAMSC). 3T3-L1 and hAMSC were treated with VitD (10^{-7} M) and BPA (10^{-8} M and 10^{-9} M), alone or in combination, throughout the differentiation in mature white adipocytes. Lipid droplet accumulation was assessed by RedOilO staining, mRNA and protein expression of key adipogenic markers were investigated by RT-qPCR and WB, respectively. miRNAs involved in the regulation of adipogenic transcription factors were evaluated by RT-qPCR and miRNA inhibitors were used to modulate miRNAs expression. RedOilO staining quantification evidenced a significant VitD anti-adipogenic outcome (~54%, $P=0.0022$) and a significant BPA pro-adipogenic outcome (~29%, $P=0.047$ BPA10^{-8} M and ~42%, $P=0.047$ BPA10^{-9} M) compared to 3T3-L1 control cells, and a significant VitD anti-adipogenic outcome (~27%, $P<0.0001$) and a significant BPA pro-adipogenic outcome (~8%, $P=0.0007$ BPA10^{-9} M) compared to hAMSC control cells. In both cell models VitD counterbalanced BPA pro-adipogenic effect by reducing lipid accumulation, with a maximum effect of ~76%, $P=0.0022$ (BPA10^{-9} M vs VitD+BPA10^{-9} M) and 34.9%, $P=0.0022$ (control vs VitD+BPA10^{-9} M)) compared with untreated 3T3-L1 cells and ~12%, $P=0.0003$ (BPA10^{-9} M vs VitD+BPA10^{-9} M) in hAMSC. In both 3T3-L1 and hAMSC, BPA significantly induced while VitD significantly inhibited mRNA and protein expression of the main adipogenic markers such as PPARγ, C/EBPα, leptin, adiponectin, and LPL. MiR-27a-3p and miR-27b-3p are known regulators of PPARγ. RedOilO staining revealed that miR-27a-3p and miR-27b-3p blocking prevents the anti-adipogenic effect of VitD in both cell models: in 3T3-L1 VitD significantly reduced lipid accumulation compared to untreated cells (58.5%, $P=0.0002$) whereas miR-27a-3p and miR-27b-3p inhibitors reverted the VitD anti-adipogenic effect (+35.8%, $P=0.013$ and +87.0%, $P<0.0001$ compared to VitD, respectively) and in hAMSC VitD significantly reduced lipid accumulation compared to untreated cells (32.9%, $P<0.0001$) whereas miR-27a-3p and miR-27b-3p inhibitors reverted the VitD anti-adipogenic effect (30.1%, $P<0.0001$ and 30.4%, $P<0.0001$ compared to VitD, respectively). In 3T3-L1 and hAMSC, VitD treatment reduced PPARγ, C/EBPα, adiponectin and leptin protein expression. This effect was reverted when miR-27a-3p and miR-27b-3p were blocked by inhibitors. These results suggest that VitD induces an anti-adipogenic effect and prevents BPA pro-adipogenic effect through the activation of miR-27a-3p and miR-27b-3p effectors in mature white adipocytes derived from 3T3-L1 and hAMSC.

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OC6.5

Assessing the interaction of styrene/ethylbenzene exposure with genetic susceptibility in type 2 diabetes mellitus: insights from a cohort study

Linling Yu[1,†], Qiyou Tan[1], Yongfang Zhang[1], Bin Wang[1] & Weihong Chen[1]

[1]School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Department of Occupational and Environmental Health, Wuhan

Background

Styrene and ethylbenzene (S/EB), the monomers found in polystyrene (PS) and polyethylene (PE), are known to continuously leach into the environment and food products. The prevalent use of hand sanitizers containing S/EB during the COVID-19 pandemic has heightened concerns about the health implications of S/EB exposure. Notably, the impact of S/EB exposure on the risk of type 2 diabetes mellitus (T2DM) and its interaction with genetic factors in the general population is not well understood. Additionally, the role of oxidative stress in the S/EB-T2DM link warrants further investigation to clarify the biological mechanisms involved.

Methods

In this prospective cohort study of 2219 Chinese adults followed for 6 years, we evaluated the association between S/EB exposure and T2DM incidence. We constructed a Genetic Risk Score (GRS) based on 205 T2DM-related SNPs to assess cumulative genetic effects and examined the interaction between S/EB exposure and GRS using both multiplicative and additive models. We also measured oxidative stress markers (8-hydroxy-2'-deoxyguanosine, 8-iso-prostaglandin F2α, and protein carbonyl) and developed an Oxidative Stress Score (OSS) to explore the potential mediating role of oxidative stress in the S/EB-T2DM association.

Results

A dose-dependent positive correlation was observed between S/EB exposure and T2DM incidence. High levels of S/EB exposure (RR = 1.930, 95% CI: 1.157-3.309) and GRS (RR = 1.943, 95% CI: 1.110-3.462) were significantly associated with an increased risk of T2DM. Notably, a substantial additive interaction between S/EB exposure and GRS was identified, with a relative excess risk due to interaction of 0.178 (95% CI: 0.065-0.292). Individuals with high S/EB and GRS levels had a markedly elevated risk of T2DM (RR = 2.602, 95% CI: 1.238-6.140) compared to those with low levels of both. Oxidative stress was found to partially mediate the relationship between S/EB exposure and T2DM, contributing to 5.98% of the association.

Discussion

This study provides the first clear evidence that S/EB exposure significantly increases the risk of T2DM, with this risk further exacerbated by genetic susceptibility. The role of oxidative stress in this association suggests potential pathways for intervention. These findings could lead to novel strategies for managing S/EB pollution and personalized approaches for T2DM prevention, emphasizing the importance of addressing both environmental and genetic factors in disease risk management.

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OC6.6

Active smoking is associated with hypercortisolism in adrenal tumors: A large cross-sectional study

Francesca Donnarumma[1,2], Lorenzo Tucci[1,2], Kimberly Coscia[1,2], Giacomo Colombin[1,2], Greta Muggioli[1], Cristina Mosconi[3], Caterina Balacchi[3], Uberto Pagotto[1,2], Valentina Vicennati[1,2] & Guido Di Dalmazi[1,2]

[1]Alma Mater Studiorum – Bologna University, Bologna, Italy, Endocrinology and Diabetes Care and Prevention Unit, IRCCS Sant'Orsola-Malpighi

Polyclinic, Bologna, Italy, Bologna, Italy; [2]Endocrinology and Diabetes Care and Prevention Unit, IRCCS Sant'Orsola-Malpighi Polyclinic, Bologna, Italy; [3]Radiology Unit, Department of Specialized, Diagnostic and Experimental Medicine (DIMES), Alma Mater Studiorum University of Bologna, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, Bologna, Italy

Background
Active smoking has been associated with alterations of the hypothalamic-pituitary-adrenal axis. A role in the pathogenesis of adrenal tumors has also been proposed previously. No data investigating the relationship between smoking and hormonal secretion of adrenal tumors are yet available.
Aim
To investigate the association between smoking habit with morphology and hormonal pattern of adrenal tumors.
Methods
We retrospectively evaluated 1346 patients with adrenal adenomas, hyperplasia, or adrenocortical carcinoma (ACC). We enrolled 1024 patients (wome $n=646$) fulfilling the inclusion criteria (adrenocortical tumors with data on hormonal secretion and smoking status): non-functioning tumors (NF, $n=572$), mild autonomous cortisol secretion (MACS, $n=310$), ACTH-independent Cushing Syndrome (CS, $n=33$), ACC ($n=34$), primary aldosteronism (PA, $n=75$). We analyzed the prevalence of active, former, and non-smokers among groups and the association with cortisol levels by regression analysis.
Results
Prevalence of active smokers was significantly different among groups (overall $P<0.001$): 28.1% ($n=161$) in NS, 39.4% ($n=122$) in MACS, 60.6% ($n=20$) in CS, 35.3% ($n=12$) in ACC, and 22.7% ($n=17$) in PA. Paired test revealed significant differences between NF vs MACS and CS, with no differences between MACS vs CS. Prevalence of former smokers was not significantly different among groups. The significant differences in active smokers among groups was confirmed in males ($P=0.002$) and females ($P<0.001$). Prevalence of smokers was significantly higher in female MACS (43.6%, $n=85/195$) and CS (53.8%, $n=14/26$) vs NF (28.5%, $n=102/358$), whereas it was not significantly different in MACS vs CS. In males, the proportion of smoker was higher in CS (85.7%, $n=6/7$) vs NF (27.6%, $n=59/214$) and MACS (32.2%, $n=37/115$), with no significant differences in MACS vs NF. Prevalence of former smokers was not significantly different in either sex. Logistic regression analysis revealed a significant association between cortisol after 1 mg-dexamethasone suppression test (DST) with active smoking (odds ratio [OR] = 1.03 each 10 nmol/l increase, 95% confidence interval [CI] = 1.01-1.04, $P=0.001$). This significant association was confirmed when sex (P for sex not significant) and age (P for age = 0.001, OR = 0.98, 95%CI = 0.97-0.99) where added to the model. When adrenal tumor morphology was analyzed, the prevalence of active smokers was significantly higher in patients with adrenal hyperplasia and MACS, when compared to NF adenomas and hyperplasia and adenomas with MACS.
Conclusion
The prevalence of active smokers is significantly higher in cortisol-producing lesions vs NF tumors, with some differences according to sex. Increasing post-DST cortisol is significantly associated with active smoking, independently of sex and age.

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Oral Communications 7: Endocrine-related Cancer

OC7.1

CRISPR/Cas9-mediated glucocorticoid receptor knockout effectively enhances antitumor efficacy of ROR1 specific CAR-T cells in advanced adrenocortical carcinoma

Marc Philipp Schauer[1,2], Justus Weber[2], Laura-Sophie Landwehr[1], Peter Spieler[2], Barbara Altieri[1], Tanja Maier[3], Matthias Kroiss[1,3,4], Stefan Kircher[5], Max Kurlbaum[1], Liz Tony[2], Silviu Sbiera[1], Martin Fassnacht[1,4] & Michael Hudecek[2]
[1]University Hospital Würzburg, Department of Internal Medicine I, Division of Endocrinology & Diabetes, Germany; [2]University Hospital Würzburg, Department of Internal Medicine II, Chair for Cellular Immunotherapy, Germany; [3]LMU Hospital Munich, Department of Internal Medicine IV, Division of Endocrinology & Diabetes, Germany; [4]Comprehensive Cancer Center Mainfranken, University of Würzburg, Germany; [5]University Hospital Würzburg, Institute of Pathology, Germany

Background
Adrenocortical carcinoma (ACC) is a rare and aggressive endocrine malignancy with poor prognosis and very limited treatment options in advanced disease. The only curative approach is complete surgical resection. Additionally, 60% of patients show endogenous glucocorticoid (GC) excess with clinical apparent hypercortisolism and low to no immune cell infiltration. To date, no therapeutically relevant surface markers are known for ACC, which is why it has not been considered for cell therapeutic interventions like CAR-T cell therapy.
Methods
In this study, we identified the receptor tyrosine kinase-like orphan receptor-1 (ROR1) as new promising target antigen for CAR-T cell therapy in a representative cohort of 197 ACC patientś samples using RNA-sequencing, qRT-PCR ($n=62$) and IHC ($n=135$). We further evaluated ROR1 expression in five human ACC cell lines using qRT-PCR, qFACS, super high resolution single molecule microscopy (dSTORM) and RNAscope single cell analysis. Lastly, we assessed immunotherapeutic performance of different next-generation ROR1 CAR-T cell modifications in different preclinical models of ACC.
Results
We demonstrate ROR1 to be highly upregulated in in 92.7% of human ACC specimen ($n=197$) as compared to healthy tissue and as clinically relevant prognostic marker for GC excess and disease progression in ACC. All five ACC cell lines were expressing ROR1 in different levels. ROR1 CAR-T cells were generated and functionally tested using preclinical models of ACC. Considering the GC-enriched inhibitory tumor microenvironment, we recapitulated these modalities using steroidogenic ACC cell lines, exogenous supplementation of dexamethasone, 3D cell culture and a novel difficult-to-treat steroidogenic ACC xenograft mouse model. We observed a considerable decrease in antitumor efficacy elicited by ROR1 CAR-T cells in vitro and in vivo. Pharmaceutical inhibition of GC effector functions induced significant mitigation of CAR-T cell potency and antitumor killing due to a corticosteroid inhibitor-related down-regulation of ROR1 on ACC tumor cells. This effect could be attributed to the inhibition of activated hGR/Stat3 tethered proximal transcription factor signaling. To maintain immunotherapeutic efficacy, we therefore desensitized ROR1 CAR-T cells by CRISPR/Cas9-mediated genome editing of the GC receptor (hGR) locus enabling (^{hGRKO} ROR1 CAR-T cells to completely eradicate all ACC xenografts while persisting in vivo, keeping periodic tumor regressions stable and inducing complete and sustained remission in 30% of all mice without toxicity.
Conclusions
Our results demonstrate ROR1 as promising target antigen for CAR-T cell therapy in ACC, while hGRKOROR1-CAR-T cells have been superior to a combined therapy using pharmaceutical blockade of GC effector functions in preclinical models of ACC.

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OC7.2

[177Lu]Lu-DOTA-TATE in newly diagnosed patients with advanced grade 2 and grade 3, well-differentiated gastroenteropancreatic neuroendocrine tumors: Primary analysis of the phase 3 randomized NETTER-2 study

Diego Ferone[1], Daniel Halperin[2], Sten Myrehaug[3], Ken Herrmann[4,5], Marianne Pavel[6], Pamela Kunz[7], Beth Chasen[2], Jaume Capdevila[8], Salvatore Tafuto[9], Do-Youn Oh[10], Changhoon Yoo[11], Stephen Falk[12], Thorvardur R Halfdanarson[13], Ilya Folitar[14], Yufen Zhang[15], Paola Santoro[15], Paola Aimone[14], Wouter W de Herder[16] & Simron Singh[3]
[1]IRCCS Policlinico San Martino and DiMI, University of Genova, Endocrinology, Genova, Italy; [2]MD Anderson Cancer Center, Houston, United States; [3]University of Toronto, Toronto, Canada; [4]National Center for Tumor Diseases (NCT), Heidelberg, Germany; [5]University of Duisburg-Essen and German Cancer Consortium (DKTK)-University Hospital Essen, Department of Nuclear Medicine, Essen, Germany; [6]Uniklinikum Erlangen, Friedrich Alexander University Erlangen-Nuernberg, Erlangen, Germany; [7]Yale School of Medicine, Yale University, New Haven, United States; [8]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [9]Oncologia Clinica e Sperimentale Sarcomi e Tumori Rari, Istituto Nazionale Tumori IRCCS, Naples, Italy; [10]Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea, Rep. of South; [11]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Rep. of South; [12]Bristol Haematology and Oncology Centre, University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom; [13]Mayo Clinic, Rochester, United States; [14]Novartis Pharma AG, Basel, Switzerland; [15]Novartis Pharmaceuticals Corp, East Hanover, United States; [16]Erasmus MC, Rotterdam, Netherlands

Background
There is no universally accepted first-line (1L) therapy for higher grade, well-differentiated gastroenteropancreatic neuroendocrine tumors (GEP-NETs). The Phase 3 NETTER-2 study (NCT03972488) evaluated [^{177} Lu]Lu-DOTA-TATE

(hereafter ^{177} Lu-DOTATATE) as 1L treatment in patients with grade (G)2 and G3 advanced GEP-NETs. This is the first trial to assess 1L radioligand therapy (RLT) in any solid tumor.

Methods

Eligible patients were newly diagnosed with somatostatin receptor-positive high G2 or G3 (Ki-67 $\geq$10% and $\leq$55%) advanced GEP-NETs within the last 6 months prior to enrollment. Patients were randomized (2:1) to receive 4 cycles of ^{177} Lu-DOTATATE (4 $\times$ 7.4 GBq) plus 30 mg octreotide long-acting release (LAR) at 8-weekly intervals during ^{177} Lu-DOTATATE treatment then every 4 weeks (^{177} Lu-DOTATATE arm), or 60 mg octreotide LAR every 4 weeks (control arm), stratified by grade (G2 vs G3) and tumor origin (pancreas vs other). The primary endpoint was progression-free survival (PFS), centrally assessed using RECIST 1.1. Objective response rate (ORR) was a key secondary endpoint.

Results

Overall, 226 patients were randomized to ^{177} Lu-DOTATATE (n=151) or control (n=75). Most tumors originated in the pancreas (54.4%) or small intestine (29.2%); G3 tumors were reported in 35.0% of patients. Median cumulative dose of ^{177} Lu-DOTATATE was 29.2 GBq, with 87.8% of patients receiving all 4 doses. Median PFS (95% confidence interval [CI]) was significantly prolonged by ~14.3 months from 8.5 months (7.7, 13.8) in the control arm to 22.8 months (19.4, not estimable) in the ^{177} Lu-DOTATATE arm; stratified hazard ratio 0.276 (95% CI: 0.182, 0.418; $P<0.0001$). The ORR was significantly higher in the ^{177} Lu-DOTATATE arm (43.0%) vs the control arm (9.3%); stratified odds ratio 7.81 (95% CI: 3.32, 18.4; $P<0.0001$). PFS and ORR results were consistent across all pre-specified demographic and prognostic subgroups. Among adverse events of special interest to RLT, G3/4 leukopenia, anemia and thrombocytopenia occurred in $\leq$3 patients each in the ^{177} Lu-DOTATATE arm. One case of myelodysplastic syndrome was reported (^{177} Lu-DOTATATE arm).

Conclusion

^{177} Lu-DOTATATE significantly prolonged PFS and demonstrated a clinically meaningful ORR, vs high-dose octreotide LAR, in patients with newly diagnosed advanced G2 and G3 GEP-NETs. Safety was in line with the established profile of ^{177} Lu-DOTATATE. This is the first randomized study to demonstrate efficacy of RLT as first-line treatment in any solid tumor and will change clinical practice.

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OC7.3

How close we are to optimise the assessment of SSTR status in NEN with a radiolabelled SSTR antagonist-final results of the TECANT clinical trial: Novel 99mTc-labelled somatostatin antagonists in the diagnostic algorithm of neuroendocrine neoplasms

Alicja Hubalewska-Dydejczyk, Luka Ležaić[2], Clemens Decristoforo[3], Renata Mikolajczak[4], Irene Virgolini[3], Petra Kolenc[2], Andrej Suden[5], Urban Simoncic[5], Marta Opalinska, Malgorzata Trofimiuk-Muldner, Piotr Garnuszek[4], Gianpaolo di Santo[3], Doroteja Novak[2], Christine Rangger[3], Marko Kroselj[2], Konrad Skorkiewicz[6], Melpomeni Fani[7], Barbara Janota[4], Boguslaw Glowa[6] & Agnieszka Sawicka[4]

[1]Jagiellonian University Medical College, Department of Endocrinology, Kraków, Poland; [2]University Medical Centre Ljubljana, Department of Nuclear Medicine, Ljubljana, Slovenia; [3]Medical University Innsbruck, Department of Nuclear Medicine,, Innsbruck, Austria; [4]National Centre For Nuclear Research Radioisotope Centre POLATOM, National Centre For Nuclear Research Radioisotope Centre POLATOM, Otwock, Poland; [5]University of Ljubljana, Faculty of Mathematics and Physics, Ljubljana, Slovenia; [6]SP ZOZ Szpital Uniwersytecki w Krakowie, Kraków, Poland; [7]Universitätsspital Basel, Basel, Switzerland

Introduction/Aim

Within the past two decades, the imaging and treatment of patients with neuroendocrine neoplasms (NEN) has been redefined by the successful introduction of radiolabelled somatostatin receptor (SSTR)-agonists targeting SSTR-subtype2 ($SSTR_2$) overexpressed in NEN cells. Reliable assessment of the SSTR status of the primary focus/metastasis in different NEN locations is a cornerstone of NEN management and enables a personalised/precise therapeutic approach. Recently, novel molecular probes based on antagonists have been shown to recognise more binding sites compared to commonly used agonists, which should lead to improved diagnostic/treatment outcomes for NEN patients, especially at lower SSTR expression. The aim of the multicenter phase 0/1 TECANT study was to develop a ^{99m} Tc-labelled $SSTR_2$-antagonist, a new sensitive diagnostic tool for a reliable SSTR status assessment on tumour cells and to initiate a clinical feasibility study.

Material/Methods

Within the preclinical study, two radiolabelled $SSTR_2$-antagonists: N4-LM-3(TECANT1) and N4-p-Cl-BASS(TECANT2), were tested in cell lines and animal studies assessing receptor affinity, internalisation status, toxicity, biodistribution and SSTR targeting properties. [^{99m} Tc]Tc-TECANT1 showed better targeting properties/lower toxicity, and was ultimately selected for clinical trial. Ten patients with advanced NEN and SSTR-positivity confirmed by routinely performed [^{68} Ga]Ga-DOTA-TATE/TOC-PET/CT were enrolled in clinical study (EudraCT no:2019-003379-20). Safety, tolerability, human pharmacokinetics, dosimetry, and NEN targeting properties of the TECANT1 were assessed. Clinical and imaging data collected at each clinical center were stored in a centralized secured database to standardize image analysis and integrate statistical tools.

Results

[^{99m} Tc]Tc-TECANT1 SPECT/CT was performed in all patients and no radiopharmaceutical-related side effects were observed. Tumour uptake was visible as early as 5 minutes after administration and retained 24 hours p.i. In all patients, rapid distribution with predominant renal excretion with a typical pattern for SSTR-analogues was observed. An excellent visualization of NEN lesions was obtained; in most cases with tumour-to-background ratio(TBR) superior to ^{68} Ga-SSTR-agonists, with the highest values of TBR at 4 hours p.i.

Conclusions

Images obtained with [^{99m} Tc]Tc-TECANT1 appear to be of great clinical importance and may be a step toward a more reliable assessment of SSTR status. Detailed quantitative analysis will be reported to support the initial highly comparable diagnostic performance to [^{68} Ga] Ga-DOTA-TATE PET/CT. Using a ^{99m} Tc-labeled SSTR antagonist may provide a widely available method for SPECT imaging, which should lead to further improvements in personalised NEN management.

This research is a part of the project "Novel ^{99m} Tc-labelled somatostatin receptor antagonists in the diagnostic algorithm of neuroendocrine neoplasms-a feasibility study" (TECANT), funded by ERA PerMed (ERAPERMED2018-125).

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OC7.4

Single-nucleus atlas of adrenocortical carcinoma reveals tumor ecotypes associated with outcome

Guillaume Assié[1,2], Anne Jouinot[1,2], Yoann Martin, Thomas Foulonneau, Yanis Bendjelal, Florian Violon[1,3], Philip Calvet, Brigitte Izac, Franck Letourneur, Celine Bertholle, Muriel Andrieu, Rachel Onifarasoaniaina, Maryline Favier, Charlene De Guitaut, Archibald Fraikin, Daniel De Murat, Roberta Armignacco, Nesrine Benanteur, Mathilde Sibony[1,3], Karine Perlemoine, Fideline Bonnet[1,4], Martin Gaillard[1,5], Bertrand Dousset[1,5], Eric Pasmant[1,6], Maxime Barat[1,7], Anthony Dohan[1,7], Magalie Haissaguerre[8], Antoine Tabarin[8], Rossella Libe[1,2], Laurence Guignat[2], Lionel Groussin[1,2], Annabel Berthon, Bruno Ragazzon, Jérôme Bertherat[1,2] & Guillaume Assié[1,2]

[1]Université Paris Cité, Institut Cochin, Inserm, CNRS, Paris, France; [2]AP-HP, Hôpital Cochin, Endocrinology, Paris, France; [3]AP-HP, Hôpital Cochin, Pathology, Paris, France; [4]AP-HP, Hôpital Cochin, Hormonology, Paris, France; [5]AP-HP, Hôpital Cochin, Digestive and Endocrine Surgery, Paris, France; [6]AP-HP, Hôpital Cochin, Genetics, Paris, France; [7]AP-HP, Hôpital Cochin, Radiology, Paris, France; [8]Bordeaux University Hospital, Endocrinology, France

Background

Bulk genomic studies have identified distinct molecular classes of adrenocortical tumors (ACT). Transcriptome profiles separate benign ACT ("C2" cluster) from carcinomas (ACC) and identify two groups of ACC, "C1A" ("steroid" and "proliferation" signatures) and "C1B" ("immune" signature), of poor and better prognosis respectively. However, these signatures were characterized at the tissue level ("bulk") and our knowledge of the cell composition of ACT is limited.

Aim

This study aims at providing a single-nucleus atlas of human normal adrenal cortex and ACT.

Methods

We performed single-nucleus RNA-sequencing (10$\times$) of ~170,000 cells from normal adrenal (n=4), benign ACT (n=14) and ACC (n=20). Cell Ranger and

Seurat pipelines were used for deciphering the cellular heterogeneity of steroid and microenvironment cells. Steroid and microenvironment signatures were then scored (ssGSEA and CIBERSORTx) in "bulk" transcriptomes of 201 ACC patients (ENSAT 2014 ($n=33$), TCGA 2016 ($n=79$) and ENSAT 2022 ($n=89$)), to define tumor ecotypes (consensus clustering) and to test their association with outcome.

Results

In steroid tumor cells, 8 variable expression programs were identified, including 4 related to steroidogenesis, mirroring normal adrenal functional zonation, and 4 related to oncogenic processes. Microenvironment of steroid cells was scarce, mainly composed of fibroblasts (4.7% of total cells), endothelial cells (5.1%), macrophages (9.9%) and T cells (1.2%). ACC microenvironment was characterized by cancer-associated signatures, including cancer-associated fibroblasts (CAF, expressing *PDGFRB* and *FN1*), tumor-associated endothelial cells (expressing *ANGPT2* and *VWF*) and tumor-associated macrophages (expressing *CD163* and *F13A1*). Compared to "C1A", "C1B" ACC were enriched in inflammatory "M1-like" macrophages. Deconvolution in ACC bulk transcriptomes identified 3 tumor ecotypes associated with outcome. A first ecotype combined cancer-associated fibroblasts and tumor-associated endothelial cells, with hypoxia and mitosis signatures in steroid cells. A second ecotype combined exhausted T cells, with zona fasciculata steroid signature. These ecotypes were associated with "C1A" and poor survival (log-rank $P<10^{-6}$ and $<10^{-9}$ respectively). Conversely, a third ecotype combined inflammatory macrophages, with zona reticularis steroid signature, and was associated with "C1B" and better outcome (log-rank $P<10^{-7}$).

Conclusion

Single-cell steroid and microenvironment signatures combine into tumor ecotypes associated with outcome, participating in the understanding of ACC heterogeneity and the C1A/C1B partition that we previously reported.

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OC7.5

Characterization and targeting of serpins alteration in chronic liver disease and hepatocellular carcinoma

Natalia Hermán- Sánchez[1,2,3,4], María Serrano-Jiménez[1,2,3,4], Victor Amado[1,5,6], Manuel Rodriguez-Peralvarez[1,5,6], Raul M Luque[1,2,3,4], Juan L. López-Cánovas[1,2,3,4] & Manuel D. Gahete[1,2,3,4]

[1]Maimónides Institute of Biomedical Research of Córdoba (IMIBIC), Córdoba, Spain; [2]University of Córdoba, Department of Cell Biology, Physiology and Immunology, Córdoba, Spain; [3]Reina Sofía University Hospital (HURS), Córdoba, Spain; [4]CIBER Pathophysiology of Obesity and Nutrition (CIBERobn), Córdoba, Spain; [5]Reina Sofía University Hospital, Department of Hepatology and Liver Transplantation, Córdoba, Spain; [6]CIBER Hepatic and Digestive Diseases (CIBERehd), Córdoba, Spain

Hepatocellular carcinoma (HCC) is an aggressive tumour frequently associated to an underlying chronic liver disease. In this sense, metabolic dysfunction-associated steatotic liver disease (MASLD) is considered as a growing cause of HCC development. Considering the need of novel therapeutic approaches, and the promising data about targeting the tumour microenvironment in cancer, we performed quantitative proteomics on HCC samples to characterize the components and regulators of the extracellular matrix (the matrisome). The cytosolic and nuclear proteomes of hepatic tissues of HCC patients [$n=42$; HCC vs non-tumour adjacent tissue (NTAT)] were determined using SWATH-MS. The abundance of matrisome proteins was evaluated in the proteomic HCC cohort, two retrospective HCC mRNA cohorts ($n=151$), and different *in silico* cohorts (8 HCC, 10 MASLD and cirrhosis; mRNA and protein). Functional assays (proliferation, migration, colony/tumorspheres formation) were performed in 2 HCC cell lines (Hep3B, SNU-387) after silencing/overexpressing *SERPINF2*. Finally, *in silico* scRNAseq cohorts of MASLD and non-MASLD-derived HCC were analysed. Through quantitative proteomics we identified 34 (cytosol) and 61 (nucleus) differentially expressed matrisome proteins (HCC vs NTAT). A broad dysregulation of the serpins family of protease inhibitors was corroborated in most MASLD, cirrhosis and HCC *in silico* cohorts, confirming their dysregulation in advanced stages of chronic liver disease and in HCC, wherein they were associated with aggressiveness and altered metabolic status. SERPINF2 was consistently dysregulated in most cohorts and associated to metabolic alterations (BMI, leptin/adiponectin ratio) and aggressiveness (survival, microinvasion). *SERPINF2* silencing in HCC cell lines reduced all the functional parameters evaluated, while SERPINF2 overexpression had the opposite effect. Interestingly, the supernatant of SERPINF2-overexpressing cell lines did not affect proliferation, suggesting different roles of intracellular and extracellular SERPINF2. Finally, the analysis of HCC single-cell-RNAseq *in silico* cohorts revealed a decreased expression of *SERPINF2* in tumour-associated endothelial cells and an increased expression in tumour cells. The comparison of cell populations with high or low *SERPINF2* expression also pointed to an alteration of cell-to-cell signalling including angiogenic (i.e. VEGF) and immune-associated (i.e. MIF) factors, consistently with the associations observed in *in silico* RNAseq and with the positive correlation between *SERPINF2* expression and the infiltration score in HCC patients. Taken together, we propose a potential role of serpins in the clinical management of chronic liver disease. Specially, SERPINF2 could represent a relevant tool for targeting HCC tumour cells and their microenvironment.

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OC7.6

Whole-exome sequencing of atypical parathyroid tumors identifies novel genes and mutations in common with benign and malignant parathyroid tumors

Elena Pardi, Marcello Poma[2], Liborio Torregrossa[2], Laura Pierotti, Simona Borsari, Simone Della Valentina, Claudio Marcocci & Filomena Cetani[3]

[1]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University of Pisa, Department of Surgical, Medical, Molecular Pathology and Critical Area,, Pisa, Italy; [3]Pisa University Hospital, Unit of Endocrinology 2, Pisa, Italy

Atypical parathyroid tumors (APT) represent parathyroid neoplasms characterized by an uncertain malignant potential due to the presence of histological features typical of parathyroid carcinomas (PC), without infiltration of surrounding tissues. The diagnosis of APT can be very challenging. Surgery is often curative but patients with APT may experience recurrence. Although the molecular landscape of benign parathyroid adenoma (PA) and PC has been explored, only few cases of APT have been included in low-throughput genomic analyses. We performed the first study investigating the whole exome sequencing (WES) of APT cases to characterize molecular signatures and deregulated pathways. Tumor specimens having a histopathological diagnosis of APT were collected from 16 Italian patients treated surgically for sporadic PHPT. DNA from tumors and matched peripheral blood were analyzed by WES on an Illumina HiSeq3000 instrument. A total of 192 somatic nonsynonymous variants were found. The median number of protein-altering mutations in APT was 9, lower than previously found in PC and higher than PA. No genes altered in more than 2 samples were observed. The most frequently mutated genes were *BCOR*, *CLMN*, *EZH1*, *JAM2*, *KRTAP13-3*, *MUC16*, *MUC19*, *OR1S1*. Seventeen mutated genes are reported in the Cancer Gene Census (*ATM*, *BCOR*, *CDC73*, *DNM2*, *EZH2*, *GPC3*, *MED12*, *MEN1*, *MTOR*, *PIK3CA*, *PIK3CB*, *RANBP2*, *RNF213*, *UBR5*, *ZNF521*, *FAT3*, *MUC16*). The gene network created with STRING had significantly more interactions than expected by chance ($P=0.001$). The most consistent hub genes were *ATM*, *COL4A5*, *EZH2*, *MED12*, *MEN1*, *MTOR*, *PI3*, *PIK3CA*, *PIK3CB* and *UBR5*. The PI3K/AKT/mTOR and Wnt signaling as well as the extracellular matrix organization were the main deregulated pathways. Interestingly, the study revealed variants in genes (*MEN1*, *CDC73*, *EZH2*, *PIK3CA*, *MTOR*) previously reported as established or putative/candidate driver genes in PA and/or PC. Only the APT sample *CDC73* mutation-positive was significantly enriched in APOBEC mutations. In conclusion, we provide evidence that APT might represent an intermediate entity between PA and PC even from a genomic point of view. It should be clarified if the rare occurrence of somatic *CDC73* mutations in APT is associated with higher risk of recurrence, although all patients of our series were cured after >6 years of average follow-up. This study also pinpointed the role of key epigenetic modifier genes (*BCOR*, *KDM2A*, *CHD4*, *MBD4*, *EZH2*) involved in chromatin remodeling, DNA and histone methylation. These mechanisms take on a role of growing interest in cancer development and offer promise for the development of novel epigenome-targeted therapies.

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Oral Communications 8: Thyroid

OC8.1

Autonomous AI-based diagnostic system for predicting malignancy in thyroid nodules

Saturnino Domínguez Cárdenas[1,2]
[1]Hospital Santa Fe, General Surgery, Panama, Panama; [2]Hospital Panamericano, General Surgery, Panama Oeste, Panama

Introduction
The present study investigates the efficacy of an autonomous diagnostic system that employs artificial intelligence (AI) for the prediction of malignancy in thyroid nodules. The study focuses on evaluating the performance of this AI-based system in detecting malignant thyroid nodules, with the aim of improving diagnostic accuracy and patient outcomes. AI, with its ability to analyze large amounts of complex data and identify patterns that may be difficult for humans to detect, can potentially improve the accuracy and speed of thyroid carcinoma diagnosis.
Materials and methods
A retrospective single-center study was carried out, where 1104 patients who required surgical management of thyroid nodules were included. We collected a new clinical dataset of 1104 clinical health records with their respective nodule histopathology; after that, we trained ten machine learning models on this dataset and estimated their prediction performance by cross-validation. The data is optimized, and each artificial intelligence algorithm is evaluated independently and through cross-validation to obtain the lowest possible error, the highest accuracy, and the highest precision with the shortest response time. Also, we conducted a variable importance analysis to examine the relevance of nodule characteristics on the model performance.
Results
In this study, 1104 subjects were enrolled, and 925 (83.78%) were women. The mean age was 47.7 years (24-82 y); the histopathology analysis diagnosed 753 (68.21%) nodules with malignancy. The accuracy of the recurrent neural network model after hyperparameter turning was as high as 99.06%, and the F1-Score was 0.971, whereas its sensitivity and specificity varied significantly in detecting malignancy with different algorithms. The sensitivity-specificity to detect any malignant nodule for the three most accurate algorithms was: Recurrent neural network (RNN) 95.06%-99.19%, Support Vector Machine (SVM) 88.17%-94.33%, and Random Forest (RF) 78.86%-93.28%. Also, our analysis of variable importance helps us identify three key variables in diagnosing malignant thyroid nodules. The variables that have been recognized are the existence of calcification, the cyst's composition, and the nodule's size. Each of these factors is a powerful indicator of malignancy in nodules and aligns with the findings of clinical research and prior modeling studies.
Conclusion
After conducting cross-validation, we've successfully created an AI model that accurately detects the potential risk of thyroid carcinoma. Nonetheless, since the models were trained based on a small dataset, more patient data would be required, and external validation through prospective studies is necessary.

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OC8.2

Antigen-specific peptide immunotherapy attenuates the pathogenic response in a murine model of Graves' disease

Yi-Li Cho, Clara Wenhart, Silvia Göbel, Andreas Reimann, Zhongmin Li & Götz Münch
advanceCOR, Munich, Germany

Background
Graves' disease (GD) is an autoimmune disease caused by autoantibody targeting the thyrotropin receptor (TSHR) in the thyroid gland, resulting in hyperthyroidism with an annual incidence of 15 to 80/100,000 people worldwide. Current mainstream treatments for GD include aggressive treatment with radioiodine and thyroidectomy or unspecific immune-modulating therapy with glucocorticoids, antithyroid medications or anti-CD20 antibodies like Rituximab. Therefore, our current focus is on the application of an antigen-specific immune modulation, namely peptide therapy using altered peptide ligands, which potentially reduce inflammatory responses via induction of immune tolerance in GD patients.
Methods
A mouse model that mimics symptoms of human GD was established by monthly immunization of adenovirus that produces TSHR A subunit protein (Ad-TSHR) and Ad-GFP adenovirus as control for 35 weeks. Herein, the therapeutic peptide P19 which was selected from potential antigens via *in silico* and *in vitro* evaluation was applied monthly in the diseased mice starting from 11 weeks after the first Ad-TSHR immunization to investigate its therapeutic effect. The study was achieved by conduction of typical clinical examinations including macro- and microscopic observation of affected organs i.e. thyroid, eye and heart, along with determination of thyroxine (T4) and anti-TSHR autoantibody level.
Results
Macroscopic examination revealed clearly enlarged thyroid glands in mice that had received nine immunizations of Ad-TSHR compared to the native and Ad-GFP mouse groups. On the contrary, diseased mice receiving P19 treatment had a significant decrease in thyroid size ($P>0.05$). Moreover, scalloped colloid and collapsed follicles were prominent in the Ad-TSHR mouse group under microscopic investigation, yet the histological presentation was markedly improved in the P19-treated group. Further analysis showed a remarkable reduction on T4 after two administrations of P19 ($P>0.05$) and the reduction was well maintained by means of P19 till the end of experiment. It indicated a significant amelioration of hyperthyroidism through application with P19. Autoantibody against TSHR as an essential clinical parameter was also tested and the result showed a concurrent decline of T4 and anti-TSHR autoantibody in a well correlated fashion with P19 treatment ($P>0.05$). Subsequently, the P19 application also represented a mild improvement on both orbital fibrosis and heart function in the diseased mice.
Conclusion
The therapeutic peptide P19 we identified revealed an anticipated benefit in the mouse model of Graves' disease with relevant clinical improvement. Thus, the results encourage further insightful exploration of this therapeutic application as a potential treatment for Graves' disease.

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OC8.3

Magnetic resonance imaging characteristics of Graves orbitopathy with elevated IgG4 serum concentration

Michał Olejarz[1], Marika Martelus[2], Ewelina Szczepanek-Parulska[1], Elżbieta Wrotkowska[1], Katarzyna Katulska[2] & Marek Ruchala[1]
[1]Poznan University of Medical Sciences, Department of Endocrinology, Metabolism and Internal Medicine, Poznan, Poland; [2]Poznan University of Medical Sciences, Department of General Radiology and Neuroradiology, Poznan, Poland

Background
Graves disease with elevated Immunoglobulin G4 serum concentration is a novel subtype of Graves disease (GD), which seems to be particularly associated with Graves orbitopathy (GO). It occurs in 17.6% of patients with GO and 5.4% of patients with GD without GO. In this study, we compare multiple magnetic resonance imaging (MRI) features of GO with elevated IgG4 serum concentration (IgG4-GO) with the classic GO subtype without IgG4 elevation. No such research has been performed to date.
Methods
We recruited 39 patients with GO. An unenhanced MRI of the orbits was performed on a 3T scanner. T1 weighted (T1WI) and short tau inversion recovery (STIR) sequences were obtained. The dimensions of orbital structures, extraocular muscles (EOM), and the presence of fatty infiltration were assessed on T1WI. The signal intensity (SI) was evaluated on the STIR sequence. Two assessors evaluated all images. IgG4 serum values were measured. Patients with IgG4 values >135 mg/dl were placed in the IgG4-GO group.
Results
There were 11 patients with elevated and 27 with normal IgG4 serum concentration. Patients with IgG4-GO had a larger diameter of the lateral rectus (5.25 [4.73; 5.88] vs 3.98 [3.49; 4.45], $P=0.004$), medial rectus (7.85 [5.68; 8.58] vs 5.08 [4.15; 5.45], $P=0.027$), and superior rectus muscle (5.75 [4.4; 6.78] vs 4.03 [3.14; 5.05], $P=0.022$). There was no significant difference in the diameter of the inferior rectus, inferior oblique, and superior oblique muscle. Patients with IgG4-GO had higher mean EOM to white matter SI ratio (SIR) (2.24 ± 0.39 vs 1.79 ± 0.32, $P>0.001$) and higher maximal EOM to white matter (3.03 [2.72; 3.34] vs 2.43 [2.24; 2.69], $P>0.001$). There was a lower prevalence of EOM fatty infiltration in IgG4-GO patients (9.09% vs 57.14%, $P=0.011$). The IgG4-GO group had a larger diameter of the lacrimal gland in the long axis (19.5 ± 3.1 vs 17.03 ± 3.44, $P=0.046$) but not short axis (6.25 [5.43; 7.15] vs 5.35 [4.6; 6.4] mm, $P=0.089$). IgG4-GO patients had a greater horizontal Barret's Index (51.88 [41.98; 57.55] vs 41.93 [37.04; 47.84]%, $P=0.048$) but not vertical Barret's index. No patient in the IgG4-GO group and only one in the normal IgG4 group had infraorbital nerve enlargement. All patients but one in the normal IgG4 group presented tendon sparing.
Conclusions
Graves orbitopathy with elevated serum IgG4 concentration is characterized by larger diameters of several EOMs, higher EOM mean and maximal signal intensity ratio on STIR, larger lacrimal gland size, and a lower prevalence of EOM fatty infiltration.

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OC8.4

The significance of 3-nitrotyrosine quantification in angioinvasive papillary thyroid carcinoma

Angelika Buczyńska[1], Maria Kościuszko[2], Aleksandra Wiatr[1], Agnieszka Adamska[2], Katarzyna Siewko[2], Janusz Dzieciol[3], Anna Popławska-Kita[2] & Adam Krętowski[2]
[1]Medical University of Bialystok, Clinical Reserch Centre, Bialystok, Poland; [2]Medical University of Bialystok, Department of Endocrinology, Diabetology and Internal Medicine, Bialystok, Poland; [3]Medical University of Bialystok, Department of Human Anatomy, Bialystok, Poland

Angioinvasion in papillary thyroid cancer (PTC) is a crucial determinant of patient prognosis. 3-Nitrotyrosine (3-NT) is a byproduct resulting from the interaction between nitric oxide and tyrosine, serving as a discernible marker indicative of oxidative stress. Within the context of PTC, oxidative stress plays a pivotal role in carcinogenic processes, particularly concerning angioinvasion. Patients with elevated levels of oxidative stress are correlated with an unfavorable clinical prognosis. Oxidative stress is intricately linked to the modulation of molecular pathways governing tumor progression, influencing the invasive potential of PTC. Hence, the quantitative assessment of 3-NT holds promise as a prognostic indicator for angioinvasion, providing valuable insights for the clinical management of PTC patients. This study aims to elucidate the potential of 3-NT quantification as a discerning marker of oxidative stress for stratifying patients at risk of angioinvasion in PTC. For the purpose of this study, 80 patients diagnosed with PTC participated in the study, with 55 exhibiting angioinvasion and 25 without. 3-NT levels were assessed using the enzyme-linked immunosorbent assay (ELISA). Robust statistical analyses, incorporating logistic regression, assessed the correlation between 3-NT levels and angioinvasion. Receiver Operating Characteristic (ROC) curves were meticulously constructed, unveiling Area Under the Curve (AUC) values. Significant differences in 3-NT levels were observed between patients with PTC with and without angioinvasion. Elevated concentrations of 3-NT were identified in the angioinvasion group, indicating a potential association between the angioinvasion process and elevated oxidative stress ($P<0.001$). The validation of these findings, particularly through logistic regression analysis with an odds ratio of 1.16 ($P=0.0006$), and ROC curves with an AUC of 0.963 ($P<0.0001$), carries substantial clinical implications. The quantification of 3-NT levels emerges as a promising tool for identifying a high-risk cohort of patients with angioinvasion in PTC. This approach facilitates personalized therapeutic strategies, potentially improving prognoses for individuals affected by PTC.

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OC8.5

"Epithelial and stromal landscape heterogeneity at spatial resolution in autoimmune thyroid diseases"

Pablo Sacristán- Gómez, Nuria Sánchez de la Blanca, Ana Serrano Somavilla, José Luis Muñoz de Nova, Miguel Sampedro Núñez, Mónica Marazuela & Rebeca Martínez Hernández
Hospital Universitario de la Princesa, Endocrinology, Madrid, Spain
Title: Epithelial and stromal landscape heterogeneity at spatial resolution in autoimmune thyroid diseases
Authors: Pablo Sacristán-Gómez[1], Nuria Sánchez de la Blanca[1], Ana Serrano-Somavilla[1], José Luis Muþoz de Nova[2], Miguel Sampedro-Núñez[1], Mónica Marazuela[1] and Rebeca Martínez-Hernández[1].
Affiliation: [1]Department of Endocrinology and Nutrition and Centro de Investigación BiomÔdica en Red de Enfermedades Raras (CIBERER GCV14/ER/12), Madrid, Spain.
[2]Department of General and Digestive Surgery, Hospital Universitario de la Princesa, Instituto de Investigacioen Sanitaria Princesa, Universidad Autœnoma de Madrid, Madrid, Spain.

Introduction
Autoimmune thyroid diseases (AITD) such as Graves' disease (GD) or Hashimoto's thyroiditis (HT) are autoimmune, organ-specific diseases probably related to a complex and multifactorial interplay of specific susceptibility genes and environmental exposures. T lymphocytes and their secretory cytokines play indispensable roles in disrupting tolerance. However, their roles are often complex and full of interactions among distinct components of the thyroid ecosystem. Novel technologies such as spatial transcriptomics (ST), allow us to explore the molecular architecture and the heterogeneity and landscape of the different cell-states within tissues.
Methodology
We profiled 8 human thyroid samples (3 HT, 3 GD and 2 controls) samples by ST using the Visium Spatial Gene Expression platform (10× Genomics). We spatially localized and histologically annotated thyroid folicular cells (TFCs), connective tissue and vessel areas to be independently studied. Furthermore, we defined and mapped into the space disease-associated subpopulations of cells. These markers have been validated using public single cell data and by protein in situ detection with immunofluorescence (IF) and/or immunohistochemistry (IHC).
Results
We revealed damaged antigen-presenting TFCs located close to the immune infiltration that contributed to the autoperpetuation of the immune response in AITD. Interestingly, we reported the participation of different fibroblasts subpopulations in HT and GD patients. Specifically, GD-associated ADIRF+ myofibroblasts surrounding TFCs and inflammation-associated fibroblasts (IAFs) within the connective tissue of HT patients. Furthermore, the presence of fenestrated PLVAP+ vessels in AITD, especially in GD, was highlighted.
Conclusions
Our data provides the molecular and cellular heterogeneity of AITD microenvironment and points toward the importance of different novel markers associated to cell subpopulations in the stroma and thyroid epithelium that could be essential to understand the pathogenesis of AITD.

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OC8.6

Filamin A is required for RET expression and signaling in medullary thyroid carcinoma (MTC) cells

Giusy Marra[1], Rosa Catalano, Emma Nozza[1,2], Gianluca Lopez[3,4], Andrea Contarino[1], Alessia Dolci[5], Elisabetta Iofrida[6], Giovanna Mantovani[1,5] & Erika Peverelli[1,5]
[1]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy, Milan, Italy; [2]PhD Programme in Experimental Medicine, University of Milan, Milan, Italy, Milan, Italy; [3]Department of Biomedical, Surgical and Dental Sciences, University of Milan, Italy, Milan, Italy; [4]Division of Pathology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, Milan, Italy; [5]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, milan, Italy; [6]Otolaryngology and Head and Neck Surgery Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, milan, Italy

Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor originating from parafollicular thyroid C cells that produce calcitonin, accounting for 5%-10% of thyroid cancers. In all inherited cases of MTC, and in about 40% of sporadic cases, activating mutations of the receptor tyrosine kinase proto-oncogene RET are found. Signaling pathways involved in cell proliferation, survival and motility are triggered by constitutively active RET, but the mechanisms underlying malignant transformation of C cells have been only partially elucidated. Neck surgery is the mainstay of treatment. New modalities of target treatments, including cabozantinib and vandetanib, two tyrosine kinase inhibitors, and selpercatinib and pralsetanib, two selective ret inhibitors have shown to be promising in advanced and recurrent disease. However, patients with unresectable MTC are difficult to treat and the prognosis remains unfavorable. The cytoskeletal protein filamin A (FLNA) is involved in the regulation of different signaling pathways mediated by various tyrosine kinase receptors, but there are no data on the role of FLNA in the RET-mediated pathway. Aim of this study was to test the role of FLNA in regulating RET expression, RET and ERK1/2 phosphorylation and cell proliferation, in human TT cell line, harboring the RET mutation C634W, and primary cultures cells deriving from surgically removed MTC. Our data showed that genetic silencing of FLNA in TT cell line significantly reduced RET expression (-18.54 (30.79)% vs control cells, P value<0.01) and its phosphorylation (-35.9 (37.4)% vs control cells, P value<0.01); moreover, it inhibited ERK1/2 phosphorylation (-40.73 (33.33)% vs control cells, P value<0.01) in accordance with cell proliferation reduction (-33 (21.08)% vs control cells, P value<0.01). Furthermore, we found a decrease in calcitonin secretion (-19.78 (17.57)% vs control cells, P value<0.05) in FLNA silenced cells. In primary cultured cells derived from MTC ($n=4$ RET wild type and $n=1$ C634S RET), FLNA knockdown reduced cell proliferation, regardless of RET mutational status. In conclusion, these data demonstrated that FLNA is required for RET expression and signaling and promotes cell growth in MTC cells, suggesting FLNA may represent as a novel possible target for effective treatment of MTC.

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Oral Communications 9: Pituitary and Neuroendocrinology | Part II

OC9.1

Differential gene expression in dopamine agonist sensitive and resistant human prolactinomas

Etienne Delgrange, Jacqueline Trouillas[2] & Anne Wierinckx[3]
[1]Université catholique de Louvain, CHU UCL Namur, Yvoir, Belgium; [2]Faculté de Médecine Lyon-Est, Lyon, France; [3]Institut Universitaire de Technologie, Université Lyon 1, Lyon, France

Dopamine agonists (DAs) are usually used as first line treatment in prolactinomas. Some tumors do not normalize prolactin levels under treatment and demonstrate a more aggressive course. The mechanisms underlying this chemoresistance are poorly understood. Previous gene expression studies have focused on candidate genes such as the DA receptor 2 (DRD2) or the nerve growth factor (NGF), but transcriptome analyses comparing tumors resistant and responsive to DA are still lacking. We compared gene expression, by microarray, in lactotroph pituitary tumors from male patients either resistant to DA ($n=5$) or demonstrating postoperative normalization of serum prolactin levels under conventional doses of DA ($n=11$). A fold change (FC) of at least 1.3 with a p value <0.05 was considered significant. The expression of the top 30 deregulated genes either with the highest FC or the most significant p values was correlated to proliferation markers and tumor grade. Among candidate genes, DRD2 was in the top list of genes with the most significant differential expression ($P=0.001$; FC -1.3), confirming its low expression in DA resistant tumors. Moreover, we identified molecules interacting with DRD2 or implicated in its pathway: a down regulation of GPR37, a G protein-coupled receptor (GPCR), interacting with DRD2; and, using Gene Set Enrichment Analysis and Ingenuity pathway analysis, a significant loss of expression of DA uptake and of DA signaling cascade. We observed also an under expression of a cell adhesion molecule, close homolog of L1 (CHL1), coding for a protein interfering with the trafficking of the DRD2 and an overexpression of fibronectin type III domain-containing protein 1 (FNDC1), which is known to modulate the PI3K/Akt signaling pathway. Overlapping in the top 30 lists for both p value and FC, was centrosomal protein 55 (CEP55), considered as an oncogene, which was overexpressed in case of DA resistance (FC +2.5; $P=0.005$) and correlated positively with mitoses ($r=0.63$; $P=0.01$) and tumor grade ($r=0.69$; $P=0.01$). Interestingly, the only pathways and functions significantly activated in resistant vs DA sensitive tumors are the pathways known to induce drug resistance of cancer cells. Our findings precise the deregulation of the DRD2 pathway in resistant lactotroph tumors and show that other GPCR possibly interacting with DRD2 could be implicated. They shed light on putative new players, such as an adhesion molecule (CHL1) and an oncogene (CEP55), in the DA chemoresistance.

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OC9.2

Successful breastfeeding in a parturient with panhypopituitarism: A case report and literature review with implications for endocrine practice

Yael Derdikman Ofir[1], Anne Eglash[2], Kerstin Moberg[3] & Irit Hochberg[4]
[1]Rambam Health Care Campus, Department of Anesthesiology, Haifa, Israel; [2]University of Wisconsin School of Medicine and Public Health, Department of Family and Community Medicine, Madison, Wisconsin, United States; [3]Swedish University Agriculture, Department of Animal Health and Welfare, Skara, Sweden; [4]Rambam Health Care Campus, Institute of Endocrinology, Diabetes and Metabolism, Haifa, Israel

Panhypopituitarism is a complex endocrine condition often thought to preclude breastfeeding due to its inherent hormonal deficiencies. Breastfeeding, however, is an important health behavior that reduces maternal morbidity and mortality. Breastfeeding reverses cardiometabolic risk factors acquired during pregnancy by reducing visceral fat and cholesterol, lowering risks of type 2 diabetes, cardiovascular and neurovascular comorbidity, and breast and ovarian cancer. We report on the management and outcome of a 34-year-old parturient with panhypopituitarism secondary to craniopharyngioma treatment who desired to breastfeed. The patient, with endocrine and lactation specialist support, prepared prenatally for lactation. Post-delivery, she used intranasal oxytocin to stimulate milk ejection and was treated with galactagogues. Despite her prolactin levels remaining below typical lactogenic ranges and the need for formula supplementation, she established a partial breastfeeding routine. Key to this success was the use of a supplemental nursing system, combined with regular milk expression and multidisciplinary support. We also reviewed published cases of women with hypopituitarism or panhypopituitarism who gave birth, where there was mention of attempted breastfeeding with successful or unsuccessful results. Our literature review, encompassing 33 articles and detailing 85 live births, found that a minority of these women succeeded in breastfeeding, with 96% of unsuccessful cases lacking documentation of lactation support. Our analysis also suggests a correlation between low prolactin levels or inadequate prolactin response to TRH-stimulation testing with the absence of spontaneous lactation post-delivery. These findings suggest that recombinant prolactin may be of benefit in the management of lactation in women with panhypopituitarism. Following these results, our case challenges the assumption that achieving successful breastfeeding is unfeasible in women with panhypopituitarism. The innovative application of intranasal oxytocin with a lactation plan of care that involves multispecialty involvement demonstrates a novel approach to managing such cases. This report emphasizes the importance of reassessing the lactation potential in women with endocrine disorders and encourages proactive, multidisciplinary support in their care.

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OC9.3

Loss of heterozygosity predicts treatment-refractory behavior in pituitary neuroendocrine tumors

Andrew Lin[1], Vasilisa Rudneva[1], Allison Richards[1], Yanming Zhang[2], Marc Rosenblum[1], Mark Donoghue[1], Viviane Tabar[1] & Eliza Geer[1]
[1]Memorial Sloan Kettering Cancer Center New York, New York, United States; [2]Memorial Sloan Kettering Cancer Center New York, Department of Pathology and Laboratory Medicine, New York, United States

Background
Pituitary neuroendocrine tumors (PitNETs) exhibiting treatment-refractory behavior are the rare subset that progress after radiation and are characterized by unrelenting growth and metastatic dissemination.
Methods
To identify biomarkers of treatment-refractory behavior, two groups of patients with PitNETs were consented to matched tumor-normal whole exome and targeted next-generation DNA sequencing on a clinical protocol: a prospective group ($n=66$) that was enrolled prior to surgery and a retrospective group ($n=26$) comprised of aggressive PitNETs.
Results
Across the cohort, treatment-refractory behavior, defined by progression following standard treatments including radiation, was associated with a higher mutational burden, $P=1.3\times10^{-10}$. Common genetic alterations in the treatment-refractory corticotroph PitNETs include mutations in *TP53*, *ATRX*, *DAXX*, and potentially targetable mutations in *TSC2* and mismatch repair genes (*MSH2*, *MSH6*, and *MLH1* with corresponding loss of protein expression on mismatch repair immunohistochemistry); only *TP53* was recurrently mutated in treatment-refractory lactotroph tumors. Treatment-refractory behavior was associated with increased fraction of loss of heterozygosity (LOH), $P=8.5\times10^{-9}$, and a higher fraction of LOH was associated with *TP53* mutations, $P=3.3\times10^{-8}$. Within the corticotroph lineage, treatment-refractoriness correlated with a characteristic pattern of recurrent chromosomal LOH, $P=1.7\times10^{-4}$. A machine learning approach confirmed that LOH is the most predictive variable tested for treatment-refractory behavior, outperforming the most common gene-level alteration. A fraction of LOH-based classifier identified treatment-refractory behavior with an accuracy of 0.88 (95% CI:0.70-0.96), sensitivity of 0.83, and specficity of 0.90.
Conclusion
Treatment-refractory PitNETs are genomically distinct from their benign counterparts; LOH predicts treatment-refractory behavior with high sensitivity and specificity.

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OC9.4

Kisspeptin administration does not alter anxiety or circulating cortisol levels in humans

Edouard G Mills[1,2], Layla Thurston, Lisa Yang, Sofiya Suladze[1], Tia Hunjan[1], Maria Phylactou[1,2], Bijal Patel[1], Sophie A. Clarke[1,2], Amar J. Shah[1], Chioma Izzi-Engbeaya[1,2], Jovanna Tsoutsouki[1], Paul Bech[1], Natalie Ertl[1,3], Lysia Demetriou[1,3], Matthew B. Wall[1,3], David Goldmeier[4], Ali Abbara[1,2], Alexander N. Comninos[1,2] & Waljit S. Dhillo[1,2]
[1]Imperial College London, Section of Endocrinology and Investigative Medicine, London, United Kingdom; [2]Imperial College Healthcare NHS Trust, Department of Endocrinology, London, United Kingdom; [3]Invicro London, London, United Kingdom; [4]Imperial College Healthcare NHS Trust, Jane Wadsworth Sexual Function Clinic, London, United Kingdom

Background
The neuropeptide kisspeptin is a key endogenous activator of the reproductive system. Due to its crucial role in modulating reproductive and behavioural processes, there has been accelerating interest in targeting kisspeptin-pathways to treat reproductive and psychosexual disorders. However, contradictory pre-clinical data from animal models suggests that kisspeptin can have an anxiolytic, anxiogenic or have no effects on anxiety. Given the rapid development of kisspeptin-based therapeutics, it is imperative to elucidate kisspeptin's effects on anxiety in humans. Herein, we report the largest study investigating the effects of kisspeptin on psychometric measures of anxiety and circulating cortisol levels.
Methods
Ninety-three eugonadal participants ($n=29$ healthy men, $n=32$ men with low sexual desire, $n=32$ women with low sexual desire) completed a double-blind, randomised, placebo-controlled, crossover study. Participants attended twice: once for intravenous infusion of kisspeptin-54 (1 nmol/kg/h) over 75 mins and for rate-matched placebo. Blood was sampled at 15 min intervals from -30 to 75 mins to measure circulating kisspeptin, LH, testosterone and cortisol [in men] and oestradiol [in women]. The validated 'State-Trait Anxiety Inventory (STAI) Y2-Trait' was completed prior to infusions to exclude abnormal anxiety traits, with all scores within normal limits. Subsequently, participants completed the 'STAI Y1-State' before and at the end of the infusions to assess for any dynamic effects on anxiety.
Results
Ninety-three participants (mean age $\pm$ SD 30.9 $\pm$ 8.7 yrs, BMI 24.0 $\pm$ 3.7 kg/m^2) completed the study. Baseline state anxiety and circulating cortisol levels were equivalent at the beginning of the kisspeptin and placebo visits. Intravenous kisspeptin potently increased serum LH to levels previously described using this administration protocol, confirming that the dose was biologically active ($P>0.001$). Importantly, state anxiety was unaltered by kisspeptin, compared to placebo (mean difference in 'STAI Y1-State' scores during the infusions: kisspeptin -0.03 $\pm$ 8.11, placebo 0.77 $\pm$ 8.08, $P=0.43$). Furthermore, kisspeptin had no effect on circulating cortisol compared to placebo during the 75 min study period ($P=0.92$). As expected, kisspeptin had no significant effects on downstream sex-steroid levels during the 75 min study period, thereby removing these as possible confounders.
Discussion
This is the largest study demonstrating that a biologically active dose of kisspeptin to healthy participants and patients with psychosexual disorders does not affect psychometric measures of anxiety and associated circulating cortisol levels. Given that animal studies have yielded inconsistent results, this provides key clinical data and reassurance that kisspeptin administration in humans does not induce anxiety and so informs safety for the rapid development of kisspeptin-based therapeutics for reproductive and psychosexual disorders.

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OC9.5

Defining the role of androgen signalling in GABA neurons in the development of PCOS-like traits

Christopher Coyle[1], Melanie Prescott[2], Kyoko Potapov[1] & Rebecca Campbell[2]
[1]University of Edinburgh, Centre for Discovery of Brain Sciences, Edinburgh, United Kingdom; [2]University of Otago, Centre for Neuroendocrinology and Department of Physiology, Dunedin, New Zealand

Androgen excess is a hallmark feature of polycystic ovary syndrome (PCOS), the most common form of anovulatory infertility. Clinical and preclinical evidence links developmental exposure to hyperandrogenism with programming the reproductive traits of PCOS. While the critical androgen targets remain to be determined, GABAergic neurons in the brain are postulated to be involved. GABA levels are elevated in the cerebrospinal fluid of PCOS patients, and both GABA transmission and innervation to gonadotrophin relseasing hormone (GnRH) neurons are elevated in prenatally androgenised models of PCOS. Here, we tested the hypothesis that androgen signalling in GABAergic neurons is critical in PCOS pathogenesis in a well-characterised, hyperandrogenic mouse model of PCOS. To generate mice with GABA neuron-specific knockout of androgen receptors (referred to as GABARKO), vesicular GABA transporter (VGAT)-ires-Cre (VGAT-Cre$^{\pm}$) mice were crossed with androgen receptor flox (AR$^{fl/fl}$) mice. Experimental animals were produced by crossing heterozygous VGAT-Cre$^{\pm}$; AR$^{fl/wt}$ females with homozygous AR$^{fl/Y}$ males. To generate experimental animals with fluorescent GnRH neurons, VGAT-Cre$^{\pm}$;AR$^{fl/wt}$ females were bred with AR$^{fl/Y}$;GnRH-GFP$^{+/+}$ males. VGAT-Cre$^{-/-}$; AR$^{fl/fl}$ females were used as controls (referred to as wildtype). Prenatally androgenized (PNA) PCOS-like mice and vehicle controls (VEH) were generated by injecting pregnant dams s.c. with 100 µl of either dihydrotestosterone (250 µg) dissolved in sesame oil or an oil vehicle alone on gestational days 16, 17 and 18. Female offspring were phenotyped for PCOS-like reproductive features and fixed brain sections were subsequently assessed for elevated GABAergic input to GnRH neurons using immunofluorescence and confocal microscopy. GABARKO did not impact the timing of pubertal onset, estrous cyclicity or ovarian morphology in VEH mice. As expected, wildtype PNA mice exhibited delayed pubertal onset and complete acyclicity compared to VEH mice. The majority of GABARKO PNA mice remained acyclic and ovarian morphology was unaffected across groups. However, while PNA predictably increased the density of putative GABAergic synapses to gonadotropin-releasing hormone (GnRH) neurons in adult WT mice, this PNA-induced plasticity in GABAergic innervation to the GnRH neurons was absent in GABARKO mice. Together, these findings suggest that while direct androgen signalling in GABA neurons is largely not required for the development of the reproductive PCOS-like traits in androgenised models of PCOS, developmental programming of GnRH neuron innervation is dependent upon androgen signalling in GABA neurons.

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OC9.6

Antiproliferative role of the vasopressin V2 receptor antagonist tolvaptan in a murine xenograft model of small cell lung cancer

Giada Marroncini, Laura Naldi, Simone Polvani, Francesca Pasella, Chiara Cirillo, Benedetta Fibbi & Alessandro Peri
[1]University of Florence, Experimental and Clinical Biomedical Sciences "Mario Serio", Florence, Italy

Vaptans are nonpeptide vasopressin receptors antagonists, developed for the treatment of euvolemic or hypervolemic hyponatremia. Among them, tolvaptan, a selective V_2receptors antagonist, approved for the treatment of hyponatremia secondary to the syndrome of inappropriate antidiuresis, was also approved for the treatment of polycystic kidney disease. Here, tolvaptan is able to reduce the growth of renal cysts and the rate of estimated glomerular filtration decrease. This unpredicted antiproliferative effect has been related to its inhibitory effect on the intracellular cAMP/PKA pathway in kidney epithelial cells. Noteworthy, there is *in vitro* evidence showing that tolvaptan reduces cell proliferation and invasion, and triggers apoptosis in different human cancer cell lines. To study this effect *in vivo*, a xenograft model of small cell lung cancer in Fox1$^{nu/nu}$ nude mice ($n=10$) was developed through subcutaneous inoculation of H69 cells transfected with a plasmid containing the luciferase gene. When masses of about 100 mm^3 were formed, mice were divided into two groups, a control group and a treatment group, which received tolvaptan at 0.15% daily. During the 60-day experimental period (T0-T60), tumor volume was assessed at different time points, both by using a digital caliper and by the IVIS Lumina system, which exploits the bioluminescence emitted by transfected cells. Through these observations, the size of the lesions appeared significantly greater in the control group compared with the treatment group at T60 (4271 $\pm$ 1915 mm^3 and 2307 $\pm$ 463 mm^3,respectively, $P\leq0.05$). Interestingly, there was a trend toward a longer survival in the treatment group compared to the control group (59 + 1 vs 50.4 + 4.7 days, mean + SE, respectively). The expression of PCNA, a proliferative marker, and of caspase 3, a marker of apoptosis, were evaluated on explanted tumors. The level of expression of PCNA was significantly lower in the masses of tolvaptan-treated mice compared to control ones, whereas caspase 3 was more abundantly expressed in the treatment group. In conclusion, these findings confirm also *in vivo* an effective role of tolvaptan in counteracting tumor progression. Overall, these results suggest a possible dual role of this drug in cancer patients with hyponatremia, which is a frequent finding in this condition and is most often related to the syndrome of inappropriate antidiuresis.

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Oral Communications 10: Calcium and Bone | Part II

OC10.1

Time to severe chronic kidney disease and nephrolithiasis in hypoparathyroidism: results from a large longitudinal retrospective study

Anna Piazza, Nicolò Bisceglia, Matteo Malagrinò, Paola Altieri, Andrea Repaci, Uberto Pagotto & Guido Zavatta
Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Italy

Introduction
Hypoparathyroidism (Hypo) is associated with a higher risk of chronic kidney disease (CKD) and renal stones, although the time to onset of these complications in the disease's natural history has never been explored. Calcium-Phosphate product (CaxP) has been shown to be a risk factor for moderate renal disease in Hypo in a limited number of cross-sectional or case-control studies.
Objective
To determine the time of onset of incident severe CKD and nephrolithiasis and their biochemical predictors in a cohort of Hypo patients treated with conventional therapy.
Design
Longitudinal retrospective study with review of paper and electronic medical records over 40 years.
Setting
Single academic medical center.
Patients
203 patients with chronic hypoparathyroidism who were regularly followed between 1980 and 2023 in an outpatient setting.
Main outcome measures
Demographic and biochemistries, time to first incident GFR <30 ml/min and time to first incident nephrolithiasis diagnosed clinically or radiologically.
Results
Mean age at last follow-up was 61 years [range, 20-93], with most patients having post-surgical Hypo (94.1%), predominantly women (79.3%), with a median disease duration of 11 years (range 0-50 years). The time-weighted average (TWA) of serum calcium was 8.4 ± 0.8 mg/dl, TWA serum phosphate was 4.4 ± 0.8 and the TWA CaxP was 38.2 [range, 23-47] mg^2/dl^2, while TWA urinary calcium was normal at 126 mg/day [range, 118-233]. Twenty-five (12.3%) patients experienced a GFR decline to less than 30 ml/min. In a Kaplan-Meier analysis, mean time from diagnosis to first GFR <30 ml/min was 38.6 years [33.9-43.3]95%CI. A shorter time to CKD was associated with greater CaxP (HR 45, $P=0.043$) and longer duration of Hypo (HR 16.9, $P>0.001$) in a Cox-regression model ($P>0.001$) independent of hypertension, TWA calcitriol dosage and TWA calcium supplements doses. Thirty-two (15.8%) patients experienced asymptomatic incident kidney stones. Mean time to first incident nephrolithiasis was estimated to be 36.6 years [31.7-41.7] 95%CI in a Kaplan-Meier analysis. In a Cox-regression model ($P>0.001$) adjusted for TWA urinary calcium, TWA calcitriol dosage, sex and TWA calcium supplements doses, a higher CaxP (HR 1.76, $P=0.048$) and longer duration of Hypo (HR 4.26, $P>0.001$) were the only significant predictors of early kidney stones.
Conclusions
In a predominantly post-surgical cohort of Hypo, a higher CaxP product accelerates the onset of severe CKD and nephrolithiasis despite averagely well biochemical control. A lower CaxP target than 55 mg^2/dl^2 might be considered to delay future renal disease in chronic hypoparathyroidism.

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OC10.2

The effect of gender affirming hormone therapy on calcium-phosphate homeostasis in transgender persons

Raya Geels[1,2], Renate de Jongh, Daan van Velzen[1,2], Mariska Vlot[3], Chantal Wiepjes[1,2], Guy T' Sjoen[4], Marc Vervloet[5], Annemieke C Heijboer[6] & Martin den Heijer[1,2]
[1]Amsterdam UMC, Department of Endocrinology, Amsterdam, Netherlands; [2]Amsterdam UMC, Center of Expertise on Gender Dysphoria, Amsterdam, Netherlands; [3]St. Jansdal Hospital, Department of Endocrinology, Harderwijk, Netherlands; [4]Ghent University Hopsital, Center for Sexology and Gender, Ghent, Belgium; [5]Amsterdam UMC, Department of Nephrology, Amsterdam, Netherlands; [6]Amsterdam UMC, Department of Clinical Chemistry Endocrinology, Amsterdam, Netherlands

Objective
The aim of the current study is to examine the effects of gender affirming hormone therapy in transgender persons on calcium and phosphate concentrations and their regulatory hormones.
Design
A prospective cohort study
Methods
This study investigated changes in calcium and phosphate concentrations and their regulatory hormones in trans women and trans men during the first year of hormone therapy. Trans women received estradiol and anti-androgens, while trans men received testosterone. Calcium, phosphate, PTH, FGF23 and 1,25diOHD were measured at baseline and after 1 year of hormone therapy. Calcium concentrations were corrected for serum albumin. Correlations between change in gonadal hormones and change in calcium- and phosphate and related hormone concentrations were studied.
Results
In 40 trans women [median age 29.1 years, 95% CI 25.7 to 45.4] calcium decreased with 1.7% [95% CI -2.8 to -0.6] and phosphate increased with 6.1% [95% CI 0.9 to 11.3]. PTH decreased with 8.9% [95% CI -17.2 to -0.6], whereas FGF23 and 1,25diOHD did not change in trans woman. In 40 trans man [median age 25.5 years, 95% CI 24.1 to 29.1] calcium increased with 1.2% [95% CI 0.1 to 2.3] and phosphate decreased with 9.7% [95% CI -14.9 to -4.5]. PTH decreased with 10.5% [95% CI -19.5 to -1.5] and FGF23 increased with 31.8% [95% CI 18.2-45.3], while 1,25diOHD concentrations did not change in trans man. In a pooled analysis, 1 SD change in testosterone concentrations [32.7 nmol/l] was related to an increase in calcium of 0.02 mmol/l [95% CI 0.01 to 0.04], a decrease in phosphate concentration of 0.06 mmol/l [95% CI -0.09 to -0.03] an increase of FGF23 concentrations of 18 U/ml [95% CI 6 to 31]. Changes in estradiol or LH concentrations were not related to any of the outcomes.
Conclusions
1 year of hormone therapy resulted in a decrease in phosphate concentrations in trans men and an increase in trans women. For calcium only a subtle change was observed in an opposite manner as phosphate changes. The increase in testosterone levels correlated with the decrease in phosphate concentrations. Increased phosphate excretion through FGF23 secretion or increased bone formation, may mediate the effects of testosterone.

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OC10.3

Calcium to magnesium ratio can be a new marker for predicting nephrolithiasis in patients with primary hyperparathyroidism

Ekin Yiğit Köroğlu[1], Abbas Ali Tam[2], Sevgül Fakı[1], Belma Tural Balsak[1], Fatma Ayça Edis Özdemir[3], Didem Özdemir[2], Oya Topaloğlu[2], Reyhan Ersoy[2] & Bekir Çakır[2]
[1]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara; [2]Ankara Yıldırım Beyazıt University Faculty Of Medicine, Endocrinology and Metabolism, Ankara; [3]Ankara Bilkent City Hospital, Radiology, Ankara

Purpose
In previous studies, magnesium (Mg) was found to be lower in cases with more severe primary hyperparathyroidism (PHPT) and higher calcium (Ca) levels. This study evaluated the relationship between serum Mg and serum Ca and phosphorus (P) levels in PHPT and their utility in discriminating osteoporosis and nephrolithiasis.
Methods
Patients who were followed up with PHPT between March 2019 and March 2023 were analyzed retrospectively. Biochemical data, renal ultrasonography results, dual-energy x-ray absorptiometry reports, and technetium 99m sestamibi parathyroid scintigraphy reports were obtained. MgxP, Mg/P, Ca/P, and corrected Ca (cCa)/P values were calculated. The relationships between biochemical parameters and clinical outcomes were evaluated statistically.
Results
A total of 543 patients were included in the study. For Ca/Mg, a cut-off value of 5.47 had a sensitivity of 74% and a specificity of 73% for the presence of nephrolithiasis. The cut-off value for cCa/Mg that can be used to predict nephrolithiasis was 5.24, with a sensitivity of 73.3% and a specificity of 73%. No statistically significant correlation existed between the Mg/P, MgxP, cCa/Mg, Ca/Mg values, and DEXA results.
Conclusion
Ca/Mg and cCa/Mg ratios especially seem more valuable in discriminating nephrolithiasis than the currently used 24-hour urine Ca measurement. Unlike urinary Ca measurements, they are cheaper, more practical, and more accessible.

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OC10.4

Morning urinary Calcium/Creatinine Ratio as screening tool for hypercalciuria in patients with hypoparathyroidism

Christina Berr[1], Carmina Teresa Fuss[2], Karen Gronemeyer[2], Christian Pfob[3], Thomas Pusl[1] & Stefanie Hahner[2]
[1]Augsburg, Department of Endocrinology, I. Medical Clinic, University Hospital Augsburg, Augsburg, Germany; [2]Würzburg, Endocrinology and Diabetes Unit, Department of Medicine I, University Hospital Würzburg, Würzburg, Germany; [3]Augsburg, Nuclear Medicine, Faculty of Medicine, University of Augsburg, Augsburg, Germany

Background
Hypercalciuria is a relevant complication in patients with treated hypoparathyroidism. Hypercalciuria is usually estimated by 24 h urinary calcium excretion (24 hUCa). In contrast, in pediatric endocrinology the calcium-creatinine-ratio (CaCrR) is more often used due to feasibility. This study aims to compare these two approaches in adult patients with hypoparathyroidism.
Methods
In 181 systematically evaluated patients with primary hypoparathyroidism (93% postoperative, 73% female), the 24 hUCa was compared with the CaCrR of a fasting morning spot urine. All patients were evaluated at two University hospitals.
Results
60% of patients met the sex-specific targets of 24 hUCa ($<$6.23 mmol/d for female, $<$7.51 mmol/d for men). CaCrR of spot urine correlated significantly with 24 hUCa ($n=181$, $r=0.583$, $P<0.001$). Although there were no significant differences between sexes in serum Calcium and 24 hUCa, females showed significant higher CaCrRs than men (0.41 vs 0.28; $P=0.02$) due to lower creatinine levels ($P=0.001$). In an ROC-analysis of the CaCrR the cutoff of 0.31 mmol/mmol correctly identified hypercalciuria in men with a sensitivity of 83.3% and a specificity of 86.7% (AUROC 0.88). By contrast, in females the optimal cutoff of 0.31 mmol/mmol only discriminated hypercalciuria from normocalciuria with a sensitivity of 83.3% and a specificity of 64.6% (AUROC 0.82). The negative predictive value for males was 86%. For females it was 64% (cutoff 0.3 mmol/mmol) or 85% (cutoff 0.45 mmol/mmol), respectively.
Conclusion
There are sex-specific differences in CaCrRs between female and male patients with hypoparathyroidism. Only in male patients a cutoff of 0.31 mmol/mmol discriminated well between normocalciuria and hypercalciuria. Highlight: To our knowledge, this is the largest cohort of patients with hypoparathyroidism in which urinary calcium excretion has been systematically investigated under standardized conditions.

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OC10.5

The utility of contrast-enhanced ultrasound (CEUS) in the preoperative localization of parathyroid gland adenomas

Agnieszka Żyłka[1], Katarzyna Dobruch-Sobczak[2], Elwira Bakuła-Zalewska[3], Hanna Piotrzkowska-Wróblewska[4], Piotr Góralski[1], Jacek Gałczyński[1] & Marek Dedecjus[1]
[1]Maria Sklodowska-Curie National Research Institute of Oncology, Department of Endocrine Oncology and Nuclear Medicine, Warsaw, Poland; [2]Maria Sklodowska-Curie National Research Institute of Oncology, Radiology Department II, Warsaw, Poland; [3]Maria Sklodowska-Curie National Research Institute of Oncology, Department of Pathology, Warsaw, Poland; [4]Institute of Fundamental Technological Research, Polish Academy of Sciences, Department of Ultrasound, Warsaw, Poland

Objectives
Preoperative detection of parathyroid gland adenomas in patients diagnosed with primary hyperparathyroidism (pHPT) represents a diagnostic challenge. The aim of the study was to assess the utility of contrast-enhanced ultrasound (CEUS) as the diagnostic tool for preoperative localization of parathyroid gland adenomas in conjuction with a conventional ultrasonography.
Methods
Between the years 2021 and 2022, 33 adult patients (30 women and 3 men, aged 37-79) diagnosed with pHPT, underwent high-resolution ultrasound (US) and CEUS of parathyroid gland adenomas preoperatively. During CEUS examination 1.5 ml of SonoVue contrast was administered intravenously. All patients were qualified to surgical treatment according to laboratory and imaging findings in a combination with clinical symptoms and underwent parathyroidectomy with histopathologic confirmation of parathyroid adenomas. Analysis of the B-mode features involved size, echogenicity, calcifications, cystic components and vascularity patterns assessed in color Doppler and superb microvascular imaging. Secondly contrast distribution in CEUS examination was evaluated in real-time and retrospectively. Qualitative contrast patterns assessed in CEUS involved: homo- or heterogenous enhancement; hyper- or hypoenhancement; distribution of contrast in wash-in phase (centripetal, centrifugal or combined) and in wash-out phase (centrally, peripherally or combined).
Results
Histopathologic results included 33 parathyroid adenomas (involved two cases of atypic adenomas) in 30 women and 3 men, the medium size 11.6 mm ($\pm$6.9) and volume 2.1 mm^3 ($\pm$2.3). In conventional US examination the majority of lesions were assessed as hypoechoic ($n=36$; 100%) with dominant inhomogenous echostructure ($n=18$; 54.5%), mixed vascularity ($n=22$; 66.6%) and polar vessel observed in 14 lesions (42.4%). Dominated qualitative features assessed in CEUS involved homogenous ($n=22$; 66.6%) and hyperenhancement ($n=25$; 75.7%), with centripetal distribution of contrast in wash-in phase ($n=24$; 72.7%) and dominant centrally wash-out of the contrast ($n=19$; 57.5%).
Conclusions
The study indicates that CEUS examinations in conjuction with the high-resolution ultrasonography facilitated the detection of parathyroid adenomas. The use of CEUS qualitative features is advised to improve the localization of suspected parathyroid lesions preoperatively. Further studies should be performed to introduce CEUS patterns in the diagnostic algorithm of primary hyperparathyroidism.

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OC10.6

Efficacy of a computerized therapeutic decision-making algorithm in a Fracture Liaison Service targeting hip fracture patients

Rachel Chava Rosenblum, Arthur Kogan, Dana Herzberg, Maysara Najjar, Oded Hershkovich, Orit Twito & Raphael Lotan
Wolfson Medical Center, Holon, Israel

Background
Osteoporotic fracture risk is doubled in patients with recent fracture; however, post-fracture treatment rates remain dismal. Fracture Liaison Services (FLS) aim to close the secondary prevention 'gap' and reduce fracture risk. This study evaluates the efficacy of a computer algorithm-supported, Nurse Practitioner-managed FLS developed in Wolfson Medical Center (WMC).
Methods
A computerized decision-making algorithm was developed using zoledronic acid as the default medication, and recommending endocrinology consultation for patients younger than 65 years, with estimated glomerular filtration rate (eGFR) $<$35 or prior osteoporosis therapy. The algorithm is performed by a Nurse Practitioner. Patients with vitamin D deficiency/insufficiency are given a loading dose. This retrospective study assesses utility of the algorithm in hip fracture patients hospitalized in WMC between 01/04/2023-31/10/2023.
Results
Two-hundred and eight hip fractures were identified. The cohort was predominantly female (137/208,65.9%); mean age was 79.9$\pm$9.6 years. Nurse practitioner evaluation was performed in 200/208 patients (96.2%). The algorithm provided a treatment recommendation in 140/200 (70.0%), while 60/200 (30.0%) required endocrinology consultation due to prior therapy)31/60,51.7%), low eGFR (20/60,33.3%), and/or age below 65 years (12/60,20.0%). Patients requiring endocrinology consultation were more likely to be female. Vitamin D deficiency/insufficiency was present in 161/202 (79.7%), and loading dose given in 89/99 (89.9%) deficiency and 44/62 (71.0%) insufficiency cases.
Discussion
This streamlined algorithm-based, FLS model was practical and functional; the algorithm provided therapeutic recommendations in 70% of cases without need for physician intervention. Simplified FLS interventions requiring minimal healthcare worker loads are feasible and hold promise for resource-poor healthcare settings.

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Oral Communications 11: Adrenal and Cardiovascular Endocrinology | Part II

OC11.1

Germline DNA methylation analysis reveals distinct alterations in a large cohort of patients with germline SDHB pathogenic variant

Reut Halperin[1,2,3], Roi Horwitz[4], Amna Jabarin & Amit Tirosh[1,2,3]
[1]Sheba, Endocrinology, diabetes and metabolism, Ramat Gan, Israel; [2]Sheba, ENTIRE Endocrine Neoplasia Translational Research Center, Ramat Gan, Israel; [3]Tel Aviv University, Medicine, Tel Aviv-Yafo, Israel; [4]Technion-Israel Institute of Technology, Medicine, Haifa, Israel

Patients with germline pathogenic variant (PV) in the *SDHB* gene (Paraganglioma syndrome type 4, PPGL4) have a high-risk of developing paragangliomas and pheochromocytomas. PPGL4 has increased risk for aggressive and metastatic abdominal-thoracic paragangliomas compared with other paraganglioma syndromes.
Aims
To assess possible germline DNA epigenetic alterations in patients harboring the *SDHB* PV.

Materials and Methods
Patients with PPGL4 were characterized clinically in our clinic and genetically via germline DNA sequencing for the familial variant (*SDHB* c.640C>T p.Q214Ter, $n=144$) and whole genome methylation analysis compared 19 patients vs 129 controls. The control group consisted of four *SDHB* PV-negative family members and 125 samples retrieved from a public database (GSE224359). Analysis was performed on Rstudio, using the ChAMP suite for normalization, imputation, differentially methylated probes (DMP), and regions (DMR) analyses. Pathway analysis and visualization were executed using the clusterprofiler and enrichplot packages. Promoter regions were defined by the transcription start site (TSS1500).
Results
The cohort includes three kindreds, presenting independently with an index patient: Index patient in <ce:bold>kindred A</ce:bold>, a 12-year-old boy, with thoracic paraspinal and testicular paragangliomas. Index patient in <ce:bold>kindred B</ce:bold>, a 26-year-old woman with abdominal paraganglioma, metastatic to the lungs and spine. Index patient in <ce:bold>kindred C</ce:bold>, a 41-year-old man with a locally aggressive abdominal paraganglioma, metastatic to the skull and spine. A total of 114 (44.2% females) patients underwent genetic evaluation (45/50, 16/28, and 25/36 in kindreds A, B and C, respectively). Of those, 50 (58.1%) harbored the familial *SDHB* PV (68.9%, 56.2%, and 40.0%, respectively). Twenty-six patients underwent at least partial clinical evaluation: eight had paraganglioma (4/8 had metastatic disease), three had pheochromocytoma, and two patients had neck masses that are currently being evaluated. Based on germline DNA promoter methylation data, *SDHB* PV carriers clustered separately from controls, including the *SDHB* PV non-carriers from the same kindred. No separation was demonstrated between patients that developed vs not developed PPGL at the time of the data collection. CpGs annotated to multiple genes were found differentially methylated between the groups. Of special interest are *MGMT* (encoding methyl guanine O-methyl transferase), and *ARID1B* (encoding AT-rich interactive domain-containing protein 1B) in the *SDHB* PV positive group.
Conclusions
We report one of the largest cohorts of PPGL4, showing typical low penetrance and aggressive phenotype. Genomic analysis shows distinct germline DNA methylation in *SDHB* PV-positive compared with the control group. Future studies may reveal an association between specific epigenetic alterations and penetrance/phenotypic patterns.

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OC11.2

Characterization of the interplay between the neuroendocrine stress axes and metabolic diseases

Diana Cozma[1,2], Panagiota Siatra[1,2], Ioannis Oikonomakos[1,2], Ulrike Friedrich[1,2,3], Stefan Bornstein[1,2,4], Cynthia Andoniadou[1,2,4] & Charlotte Steenblock[1,2]
[1]University Hospital Carl Gustav Carus Dresden, Medizinische Klinik 3, Dresden, Germany; [2]Technical University of Dresden Medical School, Dresden, Germany; [3]DRESDEN-concept Genome Center, Dresden, Germany; [4]King's College London Guy's Campus, United Kingdom

Metabolic syndrome is characterized by the hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to increased steroidogenesis and altered cortisol secretion. The molecular signaling mechanisms underlying HPA axis alterations in metabolic diseases remain poorly understood. In this study, our objective is to investigate how changes in signaling molecules within both plasma and adipose tissue contribute to the regulation of adrenal steroidogenesis in metabolic diseases and to elucidate the modified response of adrenocortical cells. Using a mouse model of obesity induced by a high-fat diet, we aim to pinpoint the onset of changes in steroid hormone response, correlating these changes with the metabolic status of the mice. We observed increased leptin and insulin concentrations in the mouse plasma as early as 8 weeks of high-fat diet feeding. Further, our findings revealed increased expression of *Lep* (leptin), and decreased expression of *Adipoq* (adiponectin) in the adipose tissue surrounding the adrenal upon 16 weeks of high-fat diet. These changes coincided with a rise in adrenal gland weight and elevated levels of steroid hormones, suggesting that increased steroidogenesis could directly be caused by interactions between adipokines and adrenocortical cells. To explore the direct impact on adrenocortical cells, we treated primary adrenocortical cell-derived spheroids with insulin and adiponectin. We observed that insulin induced an increase in diameter, indicating enhanced cell expansion and steroidogenesis, while adiponectin decreased the spheroid diameter, indicating an inhibitory effect on steroidogenesis. Bulk RNA sequencing of these *in vitro* primary spheroid cultures with and without insulin stimulation revealed differential expression of steroidogenic genes. Gene Set Enrichment Analysis indicated upregulation of gene sets associated with steroid biosynthesis among the top 5, suggesting a direct induction of adrenal steroidogenesis by insulin. Hyperinsulinemia together with a decreased expression of *Adipoq* in the peri-adrenal adipose tissue could be a cause of increased steroidogenesis observed in metabolic diseases *in vivo*. Our results underscore the crucial role of insulin and adipose tissue in regulating adrenal gland function in metabolic diseases contributing to a comprehensive understanding of HPA axis activity in these conditions.

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OC11.3

Prediction of adrenal masses nature through texture analysis and deep learning: Preliminary results from ENS@T RADIO-AI multicentric study

Lorenzo Tucci[1,2], Giulio Vara[3,4], Valentina Morelli[5], Edelmiro Luis Menendez Torre[6], Ulrich Dischinger[7], Athina Markou[8], Massimo Terzolo[9,10], Ariadni Spyroglou[11], Chiara Parazzoli[12], Aresta Carmen[5], Iacopo Chiodini[12,13], Diego Rivas[6], Alba Gutiérrez[6], Wiebke Schlötelburg[14], Krystallenia Alexandraki[11], Soraya Puglisi[9,10], Ilaria Improta[1,2], Antonio De Leo[1,15], Saverio Selva[16], Laura Alberici[16], Andrea De Giglio[1,17], Maria Abbondanza Pantaleo[1,17], Caterina Balacchi[18], Cristina Mosconi[1,18], Valentina Vicennati[1,2], Uberto Pagotto[1,2] & Guido Di Dalmazi[1,2]
[1]Alma Mater Studiorum-Bologna University, Medical and Surgical Sciences Department, Bologna, Italy; [2]IRCCS S. Orsola-Malpighi Polyclinic, Endocrinology and Diabetes care and Prevention Unit, Bologna, Italy; [3]Alma Mater Studiorum-Bologna University, Biomedical and Neuromotor Sciences Department, Bologna, Italy; [4]Civil Hospital "Umberto I", Diagnostic and interventional radiology Unit, Lugo (RA), Italy; [5]IRCCS Auxologico, Endocrinology and Metabolism Disease Unit, Milan, Italy; [6]Asturias Central University Hospital, Endocrinology and Nutrition Service, Oviedo, Spain; [7]University Hospital Würzburg, Department of Endocrinology and Diabetes, Würzburg, Germany; [8]G. Gennimatas General Hospital, Endocrinology Department, Athens, Greece; [9]Turin University, Biological and Clinical Sciences Department, Turin, Italy; [10]San Luigi Gonzaga University Hospital, Endocrine Internal Medicine, Turin, Italy; [11]Aretaieio Hospital, National and Kapodistrian University of Athens, 2nd Department of Surgery, Athens, Greece; [12]University of Milan, Department of Biotechnology and Translational Medicine, Milan, Italy; [13]Niguarda Cà Granda Hospital, Unit of Endocrinology, Milan, Italy; [14]Würzburg University Hospital, Department of Nuclear Medicine, Würzburg, Germany; [15]IRCCS S. Orsola-Malpighi Polyclinic, Anatomic Pathology Unit, Bologna, Italy; [16]IRCCS S. Orsola-Malpighi Polyclinic, Division of Pancreatic and Endocrine Surgery, Bologna, Italy; [17]IRCCS S. Orsola-Malpighi Polyclinic, Medical Oncology Unit, Bologna, Italy; [18]IRCCS S. Orsola-Malpighi Polyclinic, Diagnostic and interventional abdominal-pelvic radiology Unit, Bologna, Italy

Background
Current parameters of conventional radiology have several limitations in defining the nature of adrenal masses. Radiomics, or texture analysis, has shown high diagnostic performance in recent pilot studies, although confirmatory studies are needed. Moreover, the effect of combination of radiomics with hormonal secretion on diagnostic performance is poorly explored.
Aim
To evaluate the accuracy of radiomics in predicting adrenal masses nature in a large cohort of patients.
Methods
In 7 European Centres, we retrospectively analyzed 794 adrenal masses from 2006 to 2023: 472 lipid-rich adenomas (LRA), 178 benign indeterminate adrenal masses (BIAM, with histological confirmation or radiologic stability at 6-12 months), 33 adrenocortical carcinomas (ACC), 45 pheochromocytomas, 48 adrenal metastases, and 18 adrenal cysts (confirmed by nuclear magnetic resonance or histology). Adrenal masses were also divided by hormonal secretion: 354 non secreting, 261 with mild autonomous cortisol secretion, 42 with Cushing's syndrome, 45 pheochromocytomas and 94 with unknown secretion. ACC, pheochromocytomas and adrenal metastases were grouped together and labeled as malignant. Texture analysis was performed on unenhanced computerized tomography scan with LifeX software (version 7.2.0, ©LITO, France). We employed Deep Learning (DL) with 10-fold validation with hormonal secretion as factor and radiomic features as covariates.
Results
DL algorithms with radiomic parameters predicted the presence of malignant masses with average area under the receiver operating characteristic curve (AUROCC)=0.974, F1-score=0.801, sensitivity=92.7%, specificity=92.8%. Diagnostic accuracy was also high for subtyping adrenal masses: LRA with average AUROCC=0.979, F1-score=0.944, sensitivity=91.3%, specificity=96.8%, BIAM with average AUROCC=0.936, F1-score=0.746, sensitivity=93.1%, specificity=

83.8%, ACC with average AUROCC = 0.973, F1-score = 0.405, sensitivity = 100%, specificity = 88%, pheochromocytoma with average AUROCC = 0.908, F1-score = 0.341, sensitivity = 93.3%, specificity = 78.6%, adrenal metastasis with average AUROCC = 0.902, F1-score = 0.367, sensitivity = 97.9%, specificity = 78.3%, and adrenal cysts with average AUROCC = 0.899, F1-score = 0.123, sensitivity = 100%, specificity = 67.1%. When hormonal secretion was added as a factor, the prediction of malignant adrenal masses by DL algorithms was even higher, with average AUROCC = 0.999, F1-score 0.988, sensitivity 98.4%, specificity 99.9%. DL with radiomics and hormonal secretion predicted LRA with average AUROCC = 0.983, F1-score = 0.953, sensitivity = 92.7%, specificity = 97.3%, BIAM with average AUROCC = 0.968, F1-score = 0.816, sensitivity = 96.3%, specificity = 89.1%, ACC with average AUROCC = 0.933, F1-score = 0.318, sensitivity = 96.4%, specificity = 83.9%, pheochromocytoma with average AUROCC = 0.941, F1-score = 0.542, sensitivity = 100%, specificity = 89.2%, adrenal metastasis with average AUROCC = 0.951, F1-score = 0.599, sensitivity = 97.9%, specificity = 91.2%, and adrenal cysts with average AUROCC = 0.848, F1-score = 0.1, sensitivity = 100%, specificity = 63.4%.

Conclusion

Radiomic-based DL algorithm showed a high accuracy in predicting the presence of malignant adrenal masses and a heterogenous performance in predicting specific subtypes. The performance of the model was increased by adding the hormonal secretion to the models.

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OC11.4

Machine learning-based differentiation of uni- and bilateral primary aldosteronism using circulating microRNA combinations

Bálint Vékony[1,2], Gábor Nyirő[1,2,3], Zoltán Herold, János Fekete[4], Filiipo Ceccato[5], Sven Gruber[6], Lydia Kürzinger[7], Mirko Parasiliti-Caprino[8], Nikolette Szücs[1,2], Bálint Szeredás[1,2], Siti Khadija Syed Mohammed Nazri[9], Vanessa Fell[10], Mohamed Bassiony[10], Elena A B Aisha Azizan[9], Irina Bancos[10], Felix Beuschlein[6] & Péter Igaz[1,2]

[1]Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary; [2]Semmelweis University, Department of Endocrinology, Budapest, Hungary; [3]Semmelweis University, Department of Laboratory Medicine, Budapest, Hungary; [4]Semmelweis University, Department of Bioinformatics, Budapest, Hungary; [5]University of Padova, Endocrinology Unit, Department of Medicine, Padova, Italy; [6]University Hospital and University of Zurich, Department of Endocrinology, Diabetology and Clinical Nutrition, Zurich, Switzerland; [7]University of Würzburg, Department of Internal Medicine I, Division of Endocrinology and Diabetes, Würzburg, Germany; [8]University of Turin, Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, Turin, Italy; [9]The National University of Malaysia, Endocrine Unit, Department of Medicine, Kuala Lumpur, Malaysia; [10]Mayo Clinic, Division of Endocrinology, Diabetes, Metabolism and Nutrition, Department of Internal Medicine, Rochester, United States

Background

Primary aldosteronism (PA) is the most prevalent cause of secondary hypertension. Its two main clinical forms are unilateral adenoma (APA) and bilateral hyperplasia (BAH), which require markedly different medical treatments, so differentiating between the two is of utmost clinical importance. The current gold standard method for this is adrenal vein sampling (AVS), the application of which is hindered by limited availability and high skill requirements.

Aim

Our goal was to identify circulating microRNAs – or their combinations – which enable differentiation between the two most prevalent aetiologies of PA from a peripheral blood sample.

Methods

MicroRNA specific sequencing was performed on an Illumina platform, using EDTA coagulated blood samples taken during AVS, from 18 patients (10 uni-, and 8 bilateral). First, plasma samples from both adrenal veins were evaluated. Bioinformatical analysis applying the DeSeq2 algorithm was used to evaluate the differences in expression; and a neural network model, tasked to identify the most fit individual and groups of microRNAs for differentiation was used. The microRNAs comprising the five best performing models were then validated using reverse transcription real-time PCR, on 90 samples, including right and left AVS and peripheral plasma samples from 30 patients (15 uni-, and 15 bilateral). The qPCR results were then re-analysed using the same neural network. Finally, the model was validated on an independent peripheral plasma sample group from 84 patients (42 uni-, and 42 bilateral).

Results

Based on the qPCR results, miRNA abundance shows a non-significant decrease on the periphery compared to the adrenal vein samples. 10 neural network models comprised of 4 to 10 microRNAs were able to differentiate BAH and APA using peripheral plasma samples with an accuracy above 85%, with the best model consisting of 6 miRNAs having a specificity of 87.91%, a sensitivity of 86.3%, and an AUC value of 87.1%. The inclusion of clinical parameters into the models, such as imaging results, aldosterone, renin and potassium plasma levels and BMI did not meaningfully alter the performance of the model.

Conclusion

Circulating microRNA-based differentiation between uni-, and bilateral PA could prove to be a reliable diagnostic method. Should the diagnosis of BAH be established, medical treatment may begin immediately, with no further tests required to establish localization. This could prove highly beneficial for decreasing the health and financial costs of patients and providers alike.

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OC11.5

Results of systematic KDM1A genotyping in a large series of Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH) patients and analysis of the genotype/phenotype correlation

Lucas Bouys[1,2], Anna Vaczlavik[1], Patricia Vaduva[2], Anne Jouinot[2], Florian Violon[2], Annabel Berthon[2], Peter Kamenicky[3], Fanny Chasseloup[3], Stéphanie Espiard[4], Marie-Christine Vantyghem[4], Antoine Tabarin[5], Magalie Haissaguerre[5], Gerald Raverot[6], Francoise Borson-Chazot[6], Maria Candida Barisson Villares Fragoso[7], Charchar Helaine[7], Martin Reincke[8], Kroiss Matthias[8], Constantine A. Stratakis[9], Crystal Kamilaris[9], Karine Perlemoine[2], Lionel Groussin, Igor Tauveron[10], Maxime Barat[1], Laurence Guignat[1], Guillaume Assié[1], Eric Pasmant[1], Bruno Ragazzon[2] & Jerome Bertherat[1]

[1]Cochin Hospital, Paris, France; [2]Cochin Institute, Paris, France; [3]Bicetre Hospital, Le Kremlin-Bicêtre, France; [4]Hospital Center University De Lille, Lille, France; [5]Hospital Center University De Bordeaux, Bordeaux, France; [6]Hospices Civils de Lyon-HCL, Lyon, France; [7]University of São Paulo, Brazil; [8]Klinikum der Universität München, München, Germany; [9]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, United States; [10]CHU Gabriel-Montpied, Clermont-Ferrand, France

Introduction

Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH) is a rare disease responsible for variable levels of cortisol excess. Constitutional pathogenic variants of the tumor suppressor gene *ARMC5* are its most frequent molecular cause (20% of index cases). Recently, *KDM1A* has been identified as the causing gene for PBMAH associated with food-dependent Cushing's syndrome (FDCS), consecutive to the illegitimate expression of the GIP receptor (GIPR) in adrenocortical nodules. *KDM1A* has also been associated with multiple myeloma. This work aimed to assess the prevalence of *KDM1A* mutations in a large series of PBMAH index cases.

Methods

The constitutional genotyping of *KDM1A* and *ARMC5* genes has been performed by targeted NGS in 301 PBMAH index cases (67% female) from 8 centers (Cochin, Bicêtre, Lille, Lyon, Bordeaux, Sao Paulo, NIH, Munich), presenting with bilateral adrenal nodules and evidence for autonomous cortisol secretion (plasma cortisol after 1 mg dexamethasone suppression test >50 nmol/l and/or elevated 24 h urinary cortisol and/or high midnight plasma cortisol and/or suppressed plasma ACTH).

Results

Among the 301 index cases, 10 (3.3%) had a *KDM1A* and 60 (19.9%) an *ARMC5* pathogenic or likely pathogenic constitutional variant. *KDM1A* patients are all women with FDCS. Their median 24 h cortisoluria was 3.0N (0.7-6.6) vs 1.23N in *ARMC5* patients (0.2-10.7) and 0.66N in wild-type patients (0.1-10.1), $P<0.001$. Morning plasma cortisol was significantly lower: 192 nmol/l (86-672) vs 407 (111-1166) vs 428 (170-859), respectively, $P<0.001$; and their midnight cortisol significantly higher: 487 nmol/l (275-634) vs 262 (64-1178) vs 173 (39-867), respectively, $P<0.001$. A morning/midnight cortisol ratio <0.7 holds a sensitivity of 100% and a specificity of 99% for detecting of FDCS in PBMAH. Of the ten *KDM1A* patients, one had a monoclonal gammopathy of unknown significance (MGUS) and one had a familial history of multiple myeloma.

Conclusion

Constitutional *KDM1A* pathogenic variants are rare, occurring in less than 5% of PBMAH index cases, mutually exclusive with *ARMC5* variants, and always associated with FDCS. Conversely, all patients with FDCS were diagnosed with a germline *KDM1A* pathogenic variant. *KDM1A* genotyping should be considered in every patients with PBMAH and a morning/midnight cortisol ratio <0.7 and in all first-degree relatives of known *KDM1A* pathogenic/likely pathogenic variant carriers. Considering the association with myeloma, we

suggest a regular screening by serum protein electrophoresis in pathogenic/likely pathogenic variant carriers. Moreover, gender may play a role in the adrenal effect of *KDM1A* inactivation, since all *KDM1A* patients identified in this series were female.

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OC11.6

FKBP5 methylation in adrenal insufficiency: New insights into assessing the quality of glucocorticoid replacement

Irina Chifu[1], Anna-Lena Richter[1], Juliane Lippert[1], Mario Detomas[1], Carolin Scheuermann[1], Sabine Herterich[2], Janik Freytag[1], Barbara Altieri[1] & Stefanie Hahner[1]
[1]University Hospital of Würzburg, Endocrinology and Diabetes, Würzburg; [2]University Hospital of Würzburg, Clinical Chemistry and Laboratory Medicine, Würzburg

Introduction
Methylation of FKBP5, a glucocorticoid(GC)-receptor co-chaperone, negatively correlates with cortisol levels in both healthy and hypercortisolaemic individuals, and may serve as an indicator of GC exposure. We explored whether GC replacement correlates with FKBP5 methylation levels in patients with adrenal insufficiency (AI), aiming to assess the adequacy of substitution therapy.
Methods
In 122 patients with chronic primary ($n=73$) and secondary ($n=49$) AI on hydrocortisone replacement, we analyzed FKBP5 gene methylation at 54 CpG sites in introns, promoters, and proximal enhancers using bisulfite pyrosequencing. Results were correlated with GC replacement, salivary cortisol, 24-hour urinary cortisol, FKBP5 polymorphisms, physician-guided therapy adjustments, and a predefined clinical score for assessment of GC exposure. Methylation levels were further compared between AI patients, patients with cortisol-producing adenomas (CPA, $n=64$) and patients with non-functioning adrenal adenomas (NFA, $n=46$).
Results
Significant negative correlations were found between FKBP5 methylation levels in various regions and GC dose, clinical GC-replacement score, salivary/urinary cortisol levels, persisting after adjusting for sex and FKBP5 polymorphisms. Patients advised to increase their GC dose showed higher methylation levels than those recommended to reduce or maintain their dose. AI patients exhibited similar or lower methylation levels compared to those with CPA and NFA.
Conclusion
Findings suggest a dose-dependent impact of GC replacement on FKBP5 methylation. The alignment between methylation and clinical evaluation encourages further investigations with regard to an additional benefit in the assessment of replacement therapy. The unexpected observation of partially lower methylation in patients with AI compared to CPA and NFA raises the hypothesis that cortisol peaks in AI patients under conventional treatment have a relevant impact on FKBP5-methylation.

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Oral Communications 12: Diabetes, Obesity, Metabolism and Nutrition | Part II

OC12.1

Loss of murine Gpr45 leads to significant obesity due to hyperphagia and hypoactivity

Iqra Mumal, Soo Min, Diana Lee, Jacob Trenish, Dwaine Pryce, Daniel Gomez, Erqian Na, Parnian Bigdelou, Judith Altarejos, Mark Sleeman & Jason Mastaitis
Regeneron Pharmaceuticals, Inc., Tarrytown, United States

Monogenic obesity in humans is caused by loss-of-function mutations in several genes, all of which reside in the CNS, and many of which are involved in either leptin signaling or the downstream melanocortin pathway. Ablation of the CNS-specific orphan GPCR Gpr45 in mice is associated with significant monogenic obesity. However, to date, there are no associations between the loss of GPR45 and obesity in human genetics. To that end, we made our own line of Gpr45-/- mice and found, similar to published findings, that Gpr45-/- mice are obese, with significantly increased adiposity. In addition, these mice are hypoactive and have reduced energy expenditure compared to their wildtype counterparts. Interestingly, we also found there were phenotypic differences between the male and female knockout mice, which has not been previously shown. Specifically, we found male Gpr45-/- mice preferentially store fat in their livers, while the female knockouts have large subcutaneous and visceral adipose depots. Accordingly, the male knockouts have significantly increased serum levels of enzymes indicative of liver damage and are significantly more hyperglycemic and insulin-resistant compared to the females. Contrary to prior findings, we discovered that all Gpr45-/- mice exhibit hyperphagia, suggesting both a food intake and metabolic role in their obesity phenotype. Gpr45-/- mice have levels of leptin consistent with their adiposity, suggesting it is not leptin deficiency driving the obesity. Accordingly, administration of setmelanotide, which acts as a melanocortin 4 receptor agonist was effective at reducing food intake in Gpr45-/- mice indicating intact melanocortin signaling downstream of leptin. These results reveal that in mice, Gpr45 is a critical regulator of appetite and metabolism as well as a modulator of lipid storage in peripheral tissues.

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OC12.2

Intestinimonas butyriciproducens as a new preventive therapy for type 2 diabetes: a proof of concept randomized controlled trial

Valentina Antoniotti[1], Marina Caputo[2,3], Edoardo Luigi Maria Mollero[2], Alessandro Antonioli[3], Sabrina Tlni[3], Marcello Manfredi[4,5], Elisa Bona[6], Marco Pane[7], Angela Amoruso[7], Annachiara De Prisco[7], Sahin Gul[8], Nam Bui[8], Jos Seegers[8], Willem M De Vos[9], Gianluca Aimaretti[2] & Flavia Prodam[2,3]
[1]University of Piemonte Orientale, SCDU of Pediatrics, Department of Health Sciences, Novara, Italy; [2]University of Piemonte Orientale, SCDU of Endocrinology, Department of Translational Medicine, Novara, Italy; [3]University of Piemonte Orientale, Department of Health Sciences, Novara, Italy; [4]University of Piemonte Orientale, Department of Translational Medicine, Novara, Italy; [5]University of Piemonte Orientale, Center for Translational Research on Allergic and Autoimmune Diseases (CAAD), Novara, Italy; [6]University of Piemonte Orientale, Department of Sciences and Technological Innovation, Novara, Italy; [7]Probiotical Research Srl, Research & Development, Novara, Italy; [8]Caelus Health, Amsterdam, Netherlands; [9]Wageningen University, Wageningen, Netherlands

Background
The incidence of type 2 Diabetes Mellitus (T2D) is increasing worldwide. Prevention is possible by changing lifestyle but it's not effective alone in real life, due to poor compliance over time. New strategies are necessary, mostly for high-risk individuals. Therapeutic microbiology is a further proposed target, and butyrate-producing bacteria can improve metabolic parameters in obese patients. Our study aims to evaluate the effect of *Intestinimonas butyriciproducens* as a preventive therapy for T2D in prediabetes thanks to its effects in decreasing Advanced Glycation End Products (AGEs), converting sugars and proteins in butyrate, and increasing insulin sensitivity.
Methods
The trial is a double-blind, randomized, placebo-controlled (phase 1) and open-label pilot study with two different doses (phase 2) of 26 weeks. *I. butyriciproducens* (10^5 CFU/day) or placebo were given for 12 weeks, then subjects in placebo will start the treatment (10^5 CFU/day), and the other group will increase the dose (10^8 CFU/day) for 14 weeks. Overweight or obese patients with impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) were included. Patients were assessed for clinical, biochemical, and microbiota parameters at the time of recruitment (V1), after phase 1 (V7) and phase 2 (V10), during which the eating and lifestyle habits were also evaluated. No dietary advice was given.
Results
Nineteen have completed the study. Treated patients during the first phase had a significant improvement in glucose-insulin metabolism demonstrated through the HOMA Disposition Index ($P=0.0075$). Lipid profile also ameliorates in patients treated at a low dose and then at a high dose, particularly decreasing triglycerides (phase 1: $P=0.0212$; phase 2: $P=0.0261$). The weight and BMI of patients were stable throughout the period of study. Data from Flash glucose Monitoring (FGM) show a more stable glucose, mainly at the end of the study. Serum AGE concentrations showed a trend towards a decrease in treated patients, whereas IL-10 slowly increased without changes in IL-6 and IL-17. Lastly, 10 out of 19 patients after 26 weeks of treatment had a remission in IFG or IGT (52.6%).
Conclusions
Intestinimonas butyriciproducens seems to improve insulin sensitivity and triglycerides in treated patients. *Intestinimonas butyriciproducens* could be a new strategy in the work-up of T2D prevention.

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OC12.3

Growth hormone promotes in-vivo hepatic triglyceride export in humans

Clemens Baumgartner[1,2], Matthaeus Metz[1], Lorenz Pfleger[1], Anna Tosin[1], Marianna Beghini[1], Hannes Beiglboeck[1], Paul Fellinger[1], Franziska Schnait[1], Greisa Vila[1], Anton Luger[1], Alexandra Kautzky-Willer[1], Angelika Freudenthaler[1], Sabina Baumgartner-Parzer[1], Herbert Stangl[3], Martin Krssak[1,4], Thomas Scherer[1], Michael Krebs[1] & Peter Wolf[1]
[1]Medical University of Vienna, Department of Endocrinology and Metabolism, Wien, Austria; [2]Medical University of Vienna, Clinical Department of Nephrology and Dialysis, Wien, Austria; [3]Medical University of Vienna, Institute of Medical Chemistry, Center for Pathobiochemistry and Genetics, Wien, Austria; [4]Medical University of Vienna, High-Field MR Centre, Department of Biomedical Imaging and Image-Guided Therapy, Wien, Austria

Overview
Non-alcoholic fatty liver disease (NAFLD) is defined as a chronic increase in intrahepatic lipids (IHL). A surplus of IHL can be compensated through increased lipid export via very-low density lipoprotein (VLDL) particles. Growth hormone (GH) is known to reduce visceral and ectopic fat. However, the main pathways responsible for the in-vivo decrease of IHL under the influence of GH are yet to be determined.
Methods
We assessed hepatic lipid metabolism of 10 healthy, male volunteers (26 ± 5 years; BMI $=23\pm3$ kg/m^2) before and after one week of daily subcutaneous treatment with either 2 mg Genotropin® or the GH-antagonist Somavert® (20 mg/day, loading dose of 40 mg at the first day) in a single blinded, crossover balanced study design. After a washout period of ≥6 weeks (116 ± 67 days), the study protocol was repeated with the respective other drug. Experiments comprised IHL measurement withH-magnetic resonance spectroscopy, fasting blood analysis and the quantification of VLDL1-triglyceride (VLDL-TG) secretion via an intralipid infusion protocol.
Results
After GH treatment, IHL slightly increased in 8 of 10 cases, but drastically decreased in two participants with IHL $>10\%$ at baseline (11.2 and 12%, respectively). With respect to other participants ($n=8$), the increase in IHL reached statistical significance ($0.9\pm0.5\%$ vs 1.6 ± 0.9, $P=0.005$). Secretion of VLDL1-TG was available for nine subjects and showed an overall increase of 26.1% (590.5 ± 282.3 mg/h vs 738.8 ± 424.9 mg/h, $P=0.035$). After Somavert®, IHL also tended to increase in all ten participants compared to baseline (no significance), whereby no trends were observed regarding VLDL1-TG secretion. Marked and divergent changes in serum concentrations of IGF-1, insulin, and c-peptide during both conditions indicated a sufficient impact of individual treatment.
Conclusion
Our findings demonstrate a GH mediated increase in hepatic VLDL1-TG secretion. The promoted efflux of hepatic lipids may in the long term even be responsible for an overall decrease in IHL. We further report increases in IHL after both short-term GH excess and suppression. However, a slight increase in IHL due to GH-mediated lipolysis in white adipose tissue appears reasonable. We conclude that promoted VLDL1-TG secretion in response to short term GH therapy may be beneficial for hepatic lipid turnover and might lay the foundation of novel therapeutic strategies against NAFLD.

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OC12.4

Characteristics and outcomes of DKA in people taking SGLT2 inhibitors: DEKODE study

Nitish Mathur[1], Angelica Sharma[2], Nevil Philip[3], Lakshmi Rengarajan[3,4], Lucy Bomphrey[5], Anu Abraham[3], Sanjay Saraf[6], Ketan Dhatariya[2,7], Punith Kempegowda[3,4] & Dekode Working Group[4]
[1]The Royal Wolverhampton NHS Trust, Diabetes and Endocrinology, Wolverhampton, United Kingdom; [2]Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom; [3]The University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [4]Institute of Applied Health Research, Clinical Trials Unit College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; [5]Walsall Manor Hospital, Walsall, United Kingdom; [6]Good Hope Hospital, Birmingham, United Kingdom; [7]University of East Anglia, Norwich, United Kingdom

Background
Although SGLT2 inhibitors (SGLT2-i) have revolutionised the management of diabetes, they are associated with an increased risk of developing diabetic ketoacidosis (DKA). However, there remains a paucity of evidence about the risk factors, management, and outcomes of DKA episodes associated with SGLT2-i therapy. Improved understanding of these factors in order to optimise education, minimise risk, and improve outcomes of DKA episodes in individuals receiving SGLT2-i therapy is important.
Objective
To study the characteristics, causes and complications associated with the management of DKA in patients who were on SGLT2-i therapy vs those who were not.
Methods
We retrospectively analysed all DKA episodes across six hospitals participating in the DEKODE (Digital Evaluation of Ketosis and Other Diabetes-related Emergencies) initiative between January 2020-December 2022. Parameters including demographics, DKA precipitants, laboratory values, duration of DKA (hours), length of hospital stay (days), and mortality were collated and compared among individuals who developed a DKA episode on SGLT2-i vs those who did not. Statistical analyses were performed using SPSS 29.0.
Results
Of 1398 DKA episodes, 6% ($n=84$) developed DKA whilst on SGLT2-i therapy. Of these, 19% ($n=16/84$) were directly attributable to SGLT2-i therapy. SGLT2-i users were older (58 years vs 41 years, $P<.001$) and more commonly of Afro-Caribbean ethnicity (15.5% vs 6.2%). At presentation, SGLT2-i users had a lower pH (7.17 vs 7.20, $P=.024$), bicarbonate (10.7 vs 12.0 mmol/l, $P=.039$), glucose (18.4 vs 27.6 mmol/l, $P<.001$) and ketone (5.5 vs 6.0 mmol/l, $P=.018$) concentrations. COVID infections (13.1% vs 3.9%, $P=.00007$) accounted for a greater proportion of DKA episodes amongst SGLT2-i users. SGLT2-i users developed more episodes of hypokalaemia during DKA management (46.4% vs 33.9%, $P=.024$). However, the development of hyperglycaemia and hyperkalaemia during DKA management were comparable in patients with or without SGLT2-i therapy. DKA episodes whilst on SGLT2-i therapy had a longer duration (19.6 hrs vs 14.9 hrs, $P=.001$), prolonged hospital admission (5.4 days vs 3.4 days, $P<.001$) and higher mortality (7.1% vs 2.7%, $P=.048$).
Conclusion
DKA episodes in individuals receiving SGLT2-i therapy presented with lower glucose and ketone concentrations but more severe acidosis. These episodes were associated with more adverse outcomes compared to DKA in individuals not treated with SGLT2-i therapy.

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OC12.5

The effects of semaglutide vs testosterone replacement therapy on functional hypogonadism and sperm quality in men with type 2 diabetes mellitus and obesity

Nadan Gregoric[1], Jaka Sikonja[1], Andrej Janez[1] & Mojca Jensterle[1,2]
[1]University Medical Centre Ljubljana, Department of Endocrinology, Diabetes and Metabolic Diseases, Ljubljana, Slovenia; [2]University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

Objective
Diabetes and obesity cause functional hypogonadism (FH) and impair sperm quality. Testosterone replacement therapy (TRT) improves the signs and symptoms of FH but it further deteriorates sperm quality by inhibiting the endogenous gonadal axis. The effect of glucagon-like peptide-1 receptor agonists (GLP-1-RAs) on FH is suggested to be beneficial due to weight loss. However, the effect of GLP-1 RAs on sperm quality in patients with type 2 diabetes mellitus and obesity has not been sufficiently investigated.
Aim
We compared the effects of semaglutide and TRT on parameters of FH and semen quality in men with type 2 diabetes mellitus and obesity.
Design
We designed a randomized open-label trial that included 26 men with type 2 diabetes (aged 50 [46 to 60] years, BMI 35.9 [32.8 to 38.7] kg/m^2) and FH, characterized as the presence of at least 2 symptoms consistent with hypogonadism, two values of total testosterone below 11 nmol/l measured at least four weeks apart and exclusion of other causes of hypogonadism. Participants were randomized to semaglutide 1 mg/week or intramuscular testosterone undecanoate 1000 mg for a period of 24 weeks by following the standard titration protocols.
Methods
We measured anthropometric parameters and parameters of FH. Participants completed questionnaires of the International Index of Erectile Function-15 (IIEF-15) and the Aging Symptoms in Men (AMS). Seminal fluid analysis included measurements of ejaculate volume, sperm count, concentration, morphology and total number of motile sperm. All assessments were performed at baseline and after 24 weeks of treatment.
Results
Both groups experienced a significant increase in total testosterone and an improvement in AMS score, whereas IIEF-15 score was significantly improved

only in the TRT group. Seminal fluid volume, total mobile sperm cell concentration, and sperm normal morphology did not significantly change compared to baseline and did not differ between the groups at the end of the study. However, there was a significant difference between the groups in sperm cell concentration (semaglutide 16.7 [-2.6 to 70.5]% vs TRT -60.6 [-80.2 to -13.2]%; $P=0.039$). Significant weight loss (baseline 115 [102 to 120] kg vs 24-week 99 [96 to 118] kg; $P=0.004$) and visceral adipose tissue reduction as assessed by dual x-ray absorptiometry were achieved in semaglutide group ($P>0.05$ for between-treatment effect).
Conclusion
Semaglutide was superior to TRT in improving body composition and comparably increased testosterone along with improved AMS score. As opposed to TRT, semaglutide maintained sperm quality.

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OC12.6

Efficacy and safety of postbiotic supplementation for type 2 diabetes patients: Randomized clinical Ttrial (DELI Diab study)

Maryana Savytska[1], Olena Baka[2], Elina Manzhalii[3], Dmytro Kyriienko[3,4], Tetyana Falalyeyeva[5,6], Liubov Sichel[7] & Nazarii Kobyliak[6,8]
[1]Danylo Halytsky Lviv National Medical University, Lviv, Ukraine; [2]Center for Innovative Medical Technologies of the National Academy of Sciences of Ukraine, Kyiv, Ukraine; [3]Bogomolets National Medical University, Kyiv, Ukraine; [4]Kyiv City Clinical Endocrinology Center, Kyiv, Ukraine; [5]Taras Shevchenko National University of Kyiv, Kyiv, Ukraine; [6]Medical Laboratory CSD, Scientific, Kyiv, Ukraine; [7]Stellar Biotics, United States; [8]Bogomolets National Medical University, Endocrinology, Kyiv, Ukraine

Background
Probiotics have beneficial effect on obesity/type 2 diabetes (T2D) related disorders in both animal models and clinical trials, at the same time, some scientific papers question the effectiveness and the safety of probiotics. In turn, postbiotics are preparations of inanimate microorganisms and / or their components, which are directly identified with the safety of their use and the health benefits of the host.
Aim
To conduct placebo-controlled randomize clinical trial (RCT) to assess the short-term efficacy and safety of postbiotics as an adjunction to the standard anti-diabetic therapy on glycemic control parameters, insulin resistance, β-cells functional activity and anthropometric parameters in T2D patients.
Method
A total of 55 patients met the criteria for inclusion. The study includes 3 periods. Screening period of up to 1 week to assess the eligibility to inclusion/exclusion criteria. Treatment and follow-up periods for 3 months each. The participants receive a twice daily oral dose of postbiotics « Del-Immune V® Extra» (cell lysate and DNA fragments of the probiotic strain *L. rhamnosus DV*-NRRLB-68023) at the assigned dose of 100 mg or placebo in capsules. The primary main outcomes were the change of HbA1c and fasting plasma glucose (FPG). Secondary outcomes were the changes in HOMA-IR, insulin sensitivity (%S) and β-cells functional activity (%B) as assessed by HOMA-2 model and anthropomorphic variables. Trial registration: NCT05770076.
Results
Supplementation with postbiotic for 3 month was associated with significant reduction of HbA1c (7.88 ± 1.07 to 7.25 ± 0.92%; $P=0.001$) and FPG (7.99 ± 3.89 to 6.67 ± 2.01 mmol/l; $P=0.030$) mainly due to improvement of β-cells functional activity (%B-78.77 ± 41.26 to 91.17 ± 38.99; $P=0.011$). Also in postbiotic group insignificant improvement of insulin sensitivity was found (%S-60.69 ± 26.09 to 64.45 ± 28.04; $P=0.235$). In placebo group significant worsening of glycemic conrol in intra-group analysis was observed: HbA1C and FPG decreased on 6.85% ($P=0.05$) and 1.6% ($P=0.696$) respectively as compared to baseline value. In both groups we observed the reduction of anthropometric parameters. However, only in postbiotic group it was significant. After intervention discontinuation, at follow up visit worsening of endpoints was found as compared to end of treatment visit However, parameters did not achieve the baseline level.
Conclusion
To our knowledge its first RCT which demonstrate that postbiotic supplementation can improve glycemic-related parameters and β-cells functional activity in patients with T2D. Modulation of the gut microbiota represents a new treatment for T2D/obesity and should be tested in larger studies.

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Oral Communications 13: Late Breaking

OC13.1

BCL2 expression is enriched in androgen receptor-negative advanced prostate cancer:

Juan M Jiménez-Vacas[1], Daniel Westaby[1,2], Ines Figueiredo[1], Jan Rekowski[1], Claire Pettinger[2], Bora Gurel[1], Denisa Bogdan[1], Lorenzo Buroni[1], Antje Neeb[1], Ana Padilha[1], Joe Taylor[1], Wanting Zeng[1], Souvik Das[1], Emily Hobern[1], Ruth Riisnaes[1], Mateus Crespo[1], Susana Miranda[1], Ana Ferreira[1], Brian Hanratty[3], Daniel Nava Rodrigues[1], Claudia Bertan[1], George Seed[1], Maria de Los Dolores Fenor de La Maza[1,2], Christina Guo[1,2], Juliet Carmichael[1,2], Rafael Grochot[1,2], Khobe Chandran[1,2], Anastasia Stavridi[4], Andreas Varkaris[4], Nataly Stylianou[5], Brett Hollier[5], Nina Tunariu[1,2], Steven Balk[4], Suzanne Carreira[1], Wei Yuan[1], Peter Nelson[3,6], Eva Corey[6], Michael Haffner[3,6], Johann de Bono[1,2] & Adam Sharp[1,2]
[1]The Institute of Cancer Research, London, United Kingdom; [2]The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom; [3]Fred Hutchinson Cancer Center, Seattle, United States; [4]Beth Israel Deaconess Medical Center, Boston, United States; [5]Australian Prostate Cancer Research Centre-Queensland, Queensland University of Technology, Brisbane, Australia; [6]University of Washington, Seattle, United States

Background
Treatment resistance in prostate cancer can be the result of multiple different tumour cell adaptations generating castration-resistant prostate cancer (CRPC). Despite advancements in treatment, CRPC remains a highly lethal disease. Some CRPCs become AR independent with loss of AR expression and lineage plasticity, urgently requiring novel therapeutic strategies. BCL2 can be upregulated in some CRPCs and may be a therapeutic target for this disease subset.
Objective
To characterise BCL2 expression in late stage CRPC, determine its association with AR expression, uncover its mechanisms of regulation, elucidate their clinical significance, and evaluate BCL2 as a therapeutic target and/or biomarker with clinical utility.
Methods
AR and BCL2 protein expression were determined by immunohistochemistry (IHC) in two separate CRPC cohorts. IHC data were correlated with clinical outcomes. IHC for neuroendocrine markers was performed in a subset of tumours. Whole genome bisulfite sequencing (WGBS), RNA sequencing, and chromatin immunoprecipitation (ChIP) data from multiple independent CRPC cohorts were analysed. Finally, PC cell lines and patient-derived xenograft (PDX) models were characterised and treated with BH3-mimetics *in vitro*.
Results
AR protein loss emerged with castration resistance and was detected in 4.8% of metastatic CRPC (mCRPC), associating with shorter overall survival (OS). BCL2 expression was primarily detected in AR-negative mCRPC, and associated with shorter OS, and with resistance to AR-signalling inhibitors (ARSIs) but not docetaxel. High BCL2 expression associated with lineage plasticity features and neuroendocrine marker positivity. BCL2 expression was regulated by DNA methylation and increased by Snail and the neuronal transcription factor ASCL1. BCL2 inhibition has anti-tumour activity in some, but not all, BCL2-positive PC models. Simultaneously targeting other antiapoptotic proteins, including BCLXL and MCL1, resulted in rapid apoptotic cell death.
Conclusions
BCL2 expression is enriched in AR-negative mCRPC with features of lineage plasticity, and associated with worse clinical outcomes, with BCL2-positive mCRPC appearing more sensitive to docetaxel than ARSI. BCL2 expression is regulated by DNA methylation and driven by Snail and ASCL1. BCL2 inhibition has anti-tumour activity in some, but not all, BCL2-positive PC models identifying the need for combination strategies that selectively target tumour cell apoptosis to enhance response to therapy.

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OC13.2

Assessment of mitochondrial peptide humanin in women with polycystic ovary syndrome: Serum and skeletal muscle profile

Irem Sonmezoglu Kutuk[1], Senay Akı[2], Ali Haydar Demirel[3], Sezcan Mumusoglu[4], Turkmen Turan Ciftci[5] & Bulent Yildiz[6]
[1]Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey; [2]Division of Exercise and Sport Physiology, Faculty of Sport Sciences, Hacettepe University, Ankara, Turkey; [3]Faculty of Sport Sciences, Near East University, Lefkosa, Cyprus; [4]Department of Obstetrics and Gynecology, Hacettepe University School of Medicine,

Ankara, Turkey; [5]Department of Radiology, Hacettepe University School of Medicine, Ankara, Turkey; [6]Division of Endocrinology and Metabolism, Hacettepe University School of Medicine, Ankara, Turkey

Background and Aim
Humanin is a mitochondria-derived peptide (MDP) secreted in response to oxidative stress and linked to diverse cellular processes including inflammation and insulin resistance. Humanin has been shown to be downregulated in polycystic ovaries and exogenous humanin supplementation has attenuated insulin resistance and ovarian morphological abnormalities in a PCOS rat model. The aim of this study was to investigate the role of humanin in the pathophysiology of PCOS by comparing serum and skeletal muscle tissue profile of humanin in women with PCOS and healthy women.
Subjects and Methods
Forty women with PCOS [(mean ± SD) age:21.8 ± 2.3 years, BMI:25.0 ± 4.8 kg/m^2] and 40 age- and BMI-matched healthy controls were included. Anthropometric, hormonal, biochemical measurements and body composition analyses were carried out in all participants. Vastus lateralis muscle biopsies were analyzed for humanin expression on 6 PCOS and 6 age- and BMI-matched healthy controls within the study group.
Results
Women with PCOS showed significantly increased waist circumference, total testosterone, FAI, LDL, triglycerides, 120 min insulin during 75 gr OGTT compared to controls. Serum humanin levels were significantly lower in the PCOS group than those in controls [Median (IQR):474.9 (313.0 – 633.5) pg/ml vs 672.3 (481.7-764.6) pg/ml $P<0.001$)]. Humanin showed negative correlations with total testosterone, 120 min insulin during OGTT, total cholesterol, LDL, non-HDL cholesterol and triglycerides [(r=-0.275, P=0.013), (r=-0.266, P=0.017), (r=-0.306, P=0.006), (r=-0.292, P=0.009), (r=-0.241, P=0.032), (r=-0.261, P=0.02)]. Western blot analysis showed no significant difference in skeletal muscle humanin levels between PCOS and control groups (P=0.71).
Conclusion
Serum humanin levels are decreased in PCOS suggesting mitochondrial dysfunction that is associated with androgen excess, insulin resistance and dyslipidemia. Reduction of circulating humanin is not linked to an alteration of this MDP in the skeletal muscle which constitutes the majority of the mitochondrial reserve in the body. A better understanding of potential roles of humanin and other MDPs in the pathophysiology of PCOS may enable development of new treatment options for mitochondrial dysfunction in the future.

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OC13.3

Circulating CircRNAs for early diagnosis and prediction of gdm and their impact on trophoblast cell function

Shuo Ma & Guoqiu Wu
Zhongda Hospital, Medical School of Southeast University, Center of Clinical Laboratory Medicine, Nanjing, China

Background
Gestational diabetes mellitus (GDM) is one of the most common complications during pregnancy, with a globally increasing incidence that significantly affects maternal and infant health. Currently, there is a lack of effective early diagnostic markers for GDM. Therefore, it is necessary to identify diagnostic biomarkers for early screening of GDM during pregnancy. Circular RNA (CircRNA) has been found to be a structurally unique non-coding RNA, more stable than linear RNA, and can be encapsulated in exosomes, playing a role in the pathogenesis of various diseases, making it a promising candidate biomarker for various diseases.
Methods
We compared the expression profiles of circRNAs in the serum samples of three GDM patients and three matched controls using high-throughput sequencing technology. The specificity of circRNAs was validated using Sanger sequencing and agarose gel electrophoresis. The stability of circRNAs was assessed through RNase R and actinomycin D experiments. The relative expression levels of circRNAs in serum samples were measured using RT-qPCR. A logistic regression model was constructed for early prediction of GDM using circRNAs. The overall performance of circRNAs and the constructed model for early prediction and diagnosis of GDM was evaluated using ROC curves. The correlation between circRNAs and OGTT levels was assessed using Pearson correlation analysis. The effects of circRNAs on proliferation, migration, invasion, apoptosis, and cell cycle of human trophoblast cells were investigated using CCK-8 assays, EdU staining, Transwell assays, and flow cytometry.
Results
Hsa_circ_0031560 and hsa_circ_0000793 were highly expressed in the serum of GDM patients, and their expression levels were also high in the early stages of GDM development. Both circRNAs were positively correlated with OGTT expression. Hsa_circ_0031560 and hsa_circ_0000793 effectively diagnosed GDM in different cohorts. Furthermore, the model constructed using these two circRNAs effectively differentiated between GDM and non-GDM groups, with an AUC value of 0.852 in the overall cohort. In subsequent in vitro functional experiments, knockdown of hsa_circ_0031560 and hsa_circ_0000793 promoted proliferation, migration, and invasion of human trophoblast cells (HTR-8), increased the proportion of cells in the S phase, and suppressed cell apoptosis. Finally, knockdown of hsa_circ_0031560 and hsa_circ_0000793 was found to inhibit IL-8 expression.
Conclusion
Our study revealed high expression of hsa_circ_0031560 and hsa_circ_0000793 in the serum of GDM patients and their impact on trophoblast cells, suggesting their potential as candidate biomarkers for early diagnosis of GDM.

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OC13.4

Protective effect of growth hormone-releasing hormone (GHRH) and its agonistic analog MR-409 in Alzheimer's disease

Francesca Pedrolli[1], Giulia Morello[2], Iacopo Gesmundo[1], Renzhi Cai[3,4], Wei Sha[4], Andrew V. Schally[3,4,5], Ezio Ghigo[1], Elena Tamagno[2], Michela Guglielmotto[2] & Riccarda Granata[1]
[1]Division of Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [2]Department of Neuroscience and Neuroscience Institute Cavalieri Ottolenghi Foundation (NICO), University of Turin, Turin, Italy; [3]Endocrine, Polypeptide, and Cancer Institute, Veterans Affairs Medical Center, Miami, FL, United States; [4]South Florida VA Foundation for Research and Education, Veterans Affairs Medical Center, Miami, FL, United States; [5]Department of Medicine, Divisions of Medical/Oncology and Endocrinology, and Department of Pathology, Miller School of Medicine, University of Miami, Miami, FL, United States

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by the formation of amyloid-β (Aβ) plaques and Tau neurofibrillary tangles, leading to neuronal loss, inflammation, reduced neurogenesis, and cognitive impairment. Currently, there is no effective cure for AD, highlighting the urgent need for novel therapeutic strategies. Growth hormone-releasing hormone (GHRH), besides promoting the release of pituitary growth hormone (GH), exerts many peripheral functions, such as the stimulation of cell survival and proliferation. Notably, both GHRH and its agonistic analog MR-409 exert antinflammatory, cardioprotective, and neuroprotective effects, and protect against skeletal muscle atrophy. However, the role of GHRH in AD remains to be elucidated. Thus, in the present study we explored the neuroprotective functions of GHRH *in vitro*, in rat hippocampal neural stem cells (NSCs) and human neuroblastoma SH-SY5Y cell line, and *in vivo*, in transgenic 5xFAD mouse model of AD. *In vitro*, GHRH(1-44)NH_2increased cell survival and proliferation, and reduced apoptosis in NSCs and SH-SY5Y cells, under both growth factor deprivation and exposure to amyoid-β 1-42 ($A\beta_{1-42}$) peptide. The underlying mechanisms included stimulation of $G\beta_{\alpha s\beta}$/cAMP/PKA/CREB pathway, as well as ERK1/2 and PI3K/Akt, and inactivation of GSK-3β. Furthermore, GHRH showed neurogenic effects by promoting the differentiation of NSCs into neurons and astrocytes, and SH-SY5Y cells into neurons. Importantly, GHRH counteracted the $A\beta_{1-42}$-induced phosphorylation of Tau and activation of GSK-3β while suppressing the expression of inflammatory cytokines and phosphorylation of NF-κB. *In vivo*, 3-month-old male mice were assigned to the following groups: wild type (WT)-vehicle (VH) (n=7); WT-MR-409 (n=7); 5xFAD-VH (n=10); 5xFAD-MR-409 (n=10). Mice were subcutaneously treated daily with 0.8 mg/kg MR-409 or VH for 3 months. Compared with untreated, 5xFAD-MR-409 mice showed increased body weight. Importantly, we observed that treatment with MR-409 strongly reduced brain amyloid-β deposits and astrogliosis, as well as mRNA expression of inflammatory cytokines and phosphorylation of NF-κB in brain tissues of 5xFAD mice. Moreover, MR-409 reduced neuron loss, evaluated by neuronal marker NeuN, and increased brain-derived neurotrophic factor (BDNF) expression in brain lysates of 5xFAD mice. MR-409 also reduced the phosphorylation of Tau protein and inhibited the activation of GSK-3β in brain tissues of AD mice. Finally, AD mice treated with MR-409 showed attenuated expression of the atrophy-related markers atrogin and MurF1 in the skeletal muscle. Overall, these results, combined with our previous *in vitro* findings, suggest a protective role for MR-409 in AD.

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OC13.5

Use of thiazide diuretics in hypoparathyroidism: indication and effects

Marie Helene Schernthaner-Reiter, Claudius Looser, Anna Nagel, Alexandra Kautzky-Willer, Anton Luger & Greisa Vila
Medical University of Vienna, Clinical Division of Endocrinology and Metabolism, Department of Internal Medicine III, Vienna, Austria

Introduction
Hypoparathyroidism can occur post-surgically after thyroid or parathyroid surgery or in autoimmune or genetic diseases. Over several decades, the management of hypoparathyroidism included only supplementation with calcium, vitamin D3 (cholecaliferol), as well as active 1,25-dihydroxyvitamin D (calcitriol). In cases with severe hypoparathyroidism, this treatment can be limited by hypercalciuria, and these patients often need substitution with recombinant parathyroid hormone. In daily clinical practice, thiazide diuretics may also be administered to reduce calciuria, however few data are available on the effects of thiazide use in hypoparathyroidism.
Methods
In this observational study, we retrospectively analyzed patients with hypoparathyroidism in routine medical treatment at our endocrine outpatient clinic. Clinical and biochemical parameters were collected at the time of first presentation, before the initiation of thiazide treatment, and at the time of last check-up.
Results
Our cohort includes 103 patients (m/f $n=21/82$) with hypoparathyroidism who were observed for a median of 2.1 ($\pm$ 6.6) years. 81 of those patients had prior thyroid or parathyroid surgery (26 due to thyroid nodules, 14 due to thyroid cancer, 17 due to Graves' disease, 4 due to primary hyperparathyroidism and 2 due to primary hyperparathyroidism and thyroid nodules), while hypoparathyroidism was not surgery-related in 19 patients.A therapy with thiazide diuretics (hydrochlorothiazide with a median dose of 12.5 mg $\pm$ 12.5 mg) was established in 40 of those patients. During treatment with thiazides, while parathyroid hormone measurements significantly decreased (7.9 to 4.8 pg/ml, $P=0.011$), albumin-adjusted serum calcium (2.0 and 2.1 mmol/l, respectively), estimated glomerular filtration rate (81.6 and 77.5 ml/min/1.73 m^2), magnesium (0.79 and 0.78 mmol/l) and blood pressure levels (135/85 and 134/84 mmHg) remained stable. Calciuria significantly decreased (9.5 to 6.2 mmol/24 h, $P=0.018$) and calcium and calcitriol dosages were non-significantly reduced.
Conclusion
Out data show that thiazide diuretics significantly lower calciuria in patients with hypoparathyroidism, but they do not impact serum calcium, magnesium, eGFR or blood pressure levels.

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OC13.6

Growth hormone-releasing hormone (GHRH) promotes transdifferentiation of myoblasts and white adipocytes into brown/beige adipocytes

Alessia Bertoldo, Giuseppina Granato, Iacopo Gesmundo, Ezio Ghigo & Riccarda Granata
Division of Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy

Brown adipocytes dissipate energy through the production of heat, acting as a defense against cold and obesity, and secrete batokines, that positively regulate metabolic functions. Thus, identifying brown-promoting molecules is crucial for developing novel therapeutic strategies against obesity and metabolic disorders. Of note, differentiation into myoblasts and later myocytes of myogenic factor 5 (Myf5) positive progenitors, the same from which brown adipocytes originate, is controlled by several transcription factors, such as Myf5, myogenic differentiation 1 (MyoD1), myogenin (MyoG) and myogenic regulatory factor 4 (MRF4). Moreover, different compounds can induce myoblasts to transdifferentiate into non-muscle cells, including brown adipocytes. Similarly, in response to different stimuli, white preadipocytes transdifferentiate into beige adipocytes, morphologically and functionally similar to brown adipocytes. Growth hormone-releasing hormone (GHRH), a hypothalamic neuropeptide that regulates synthesis and secretion of pituitary growth hormone (GH), exerts peripheral effects through binding to GHRH receptor (GHRH-R), expressed in many extrapituitary tissues, including adipocytes and skeletal muscle cells. Although studies have shown that GHRH counteracts skeletal muscle atrophy and ameliorates dyslipidaemia, its role in browning remains unknown. Thus, we evaluated the role of GHRH in transdifferentiation of murine C2C12 myoblasts and 3T3-L1 preadipocytes into brown/beige adipocytes. C2C12 myoblasts were treated with brown adipogenic differentiation medium for 7 days, in either absence or presence of GHRH (0.1 and 0.5 μM). Instead, 3T3-L1 preadipocytes were first differentiated into white adipocytes for 10 days (in whitening medium), then transdifferentiated for 72 h into beige adipocytes (in browning medium), in either absence or presence of GHRH (0.5 and 1 μM). In C2C12 myoblasts, GHRH (0.5 μM) suppressed the mRNA expression of myogenic markers *MyoD1*, *MyoG*, *Myf5* and *MRF4*, whilst increasing brown/beige genes *UCP1*, *PGC-1α*, *PRMD16*, *DIO2*, *CIDEA*, *Tmem26* and *CD137*. These results were confirmed by a decrease in protein levels of MyoG and increase in UCP1, PGC-1α and PRMD16. Similarly, in 3T3-L1 preadipocytes, GHRH (1 μM) increased mRNA and protein levels of brown/beige markers. Furthermore, in both cell types, Oil Red O staining showed that GHRH enhanced the number of small lipid droplets, characteristics of brown/beige adipocytes. Overall, these preliminary findings suggest that GHRH promotes transdifferentiation of both myoblasts and preadipocytes into beige/brown adipocytes, suggesting a potential therapeutic role in obesity and metabolic diseases.

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Rapid Communications

Rapid Communications 1: Reproductive and Developmental Endocrinology

RC1.1

Comparative study of the legal framework for the medical care of people with differences of sex developmental (DSD) across the world

Nicolas Kalfa[1], Beth Drzewiecki[2], Luis Braga[3], Marco Castagnetti[4], Jacques Birraux[5], Magdalena Fossum[6], Alexander Springer[7], Anka Nieuwhof-Leppink[8], PJ Lopez[9], Abraham Cherian[10], Piet Hoebeke[11], Clementine Vialla[12], Francoise Paris[1] & François Vialla[12]
[1]Hospital Center University De Montpellier, Montpellier, France; [2]Mass-General Hospital for Children, Boston, United States; [3]McMaster University, Hamilton, Canada; [4]Bambino Gesù Children's Hospital, Roma, Italy; [5]Hôpitaux Universitaires de Genève (HUG), Genève, Switzerland; [6]Karolinska Institute, Sweden; [7]Medical University of Vienna, Wien, Austria; [8]UMC Utrecht, Utrecht, Netherlands; [9]Universidad De Chile Facultad De Medicina Division Sur, San Miguel, Chile; [10]Great Ormond Street Hospital for Children, United Kingdom, [11]Ghent University Hospital, Gent, Belgium; [12]Faculty of Law and Political Science, Montpellier, France

Purpose
Some countries have introduced legislation to regulate medical practices regarding DSD. We performed an international comparative law study to better understand how to integrate our medical decisions into these regulations.
Material and Methods
With an international medical law research unit 1- we extracted legislative texts, decrees, ministerial recommendations from different countries 2- we sent a questionnaire to surgeons caring for DSD-children to understand the medical decision-making procedures.
Results
Data from 19 countries and 8 US states were analyzed. Legislation was enacted in only 6 countries and ministerial orders or case-law were issued in 4. Legislation is still in preparation in 11 countries while 6 have none. Laws range from a ban on surgery (Malta, Iceland) to the establishment of a multidisciplinary decision-making circuit in case of medical necessity. The decision is made at the local level (14 cases: Belgium, Italy, UK…), at the national level (8 cases: Nordic countries, France…) or after a court decision (Germany, Australia). Most countries recognize the person's consent as essential and the parents' decision cannot replace it (24/27). Age of consent varies from 5 to 18 years but most texts don't stipulate clear limits or defer to the child's maturity. Risks of sanctions for practitioners are most often unspecified, of a professional medical board nature ($n=8$) or rarely criminal ($n=2$). Posterior hypospadias are included in this process in 74% of cases, either systematically or when associated with micropenis or undescended testis (Switzerland, Australia, France).
Conclusions
Rarely has a medical activity been subject to such legislative framework while medical data and long- term studies remain sparse. This raises the question of how far we should genetically explore minor genital variations and if the patients with minor phenotypes but with genetic variants are included in this legal frame. This situation illustrates the special position pediatric urologists occupy at the interface of society, law and scientific knowledge and profoundly changes the way we practice, think and make therapeutic decisions.
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Public funding from the National Reference Network for Rare Disease, Genital Development DSD DevGen.

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RC1.2

Endometrial transcriptome alterations following short-term liraglutide treatment in infertile women with polycystic ovary syndrome and obesity

Mojca Jensterle[1], Vesna Salamun[2], Eda Vrtacnik Bokal[2], Luca Lovrecic[2], Ales Maver[2], Borut Peterlin[2], Rok Herman[1] & Andrej Janez[1]
[1]University Medical Centre Ljubljana, Slovenia, Department of Endocrinology, Diabetes and Metabolic Diseases, Ljubljana, Slovenia; [2]University Medical Centre Ljubljana, Slovenia, Division of Obstetrics and Gynecology, Department of Human Reproduction, Ljubljana, Slovenia

Objective
Obesity and polycystic ovary syndrome (PCOS) affect endomertial receptivity and may cause implantation failure, defective placentation, and pregnancy loss. Glucagon-like peptide-1 (GLP-1) receptor agonist (RA) improved the endometrial function in animal models, presumably by anti-inflammatory action and reduction of endometrial fibrosis. The impact of GLP-1RA on human endometrioum has not yet been investigated.
Aim
We compared endometrial transcriptome of women with obesity and PCOS pre-treated with liraglutide and endometrial transcriptome of treatment-naive BMI and age-matched controls.
Design
Cross-sectional study.
Methods
Endometrial biopsies were collected during the window of implantation from 20 infertile women with PCOS and BMI ≥ 30 kg/m^2 before in-vitro fertilization (IVF) procedure. The endometrium transcriptome of ten women who had been pretreated with low-dose liraglutide 1.2 mg QD for 12-weeks and achieved at least 5% weight loss from baseline were compared with 10 BMI and age matched PCOS controls who were treatment naïve and had a stable weight over the previous 12 weeks. Next-generation sequencing was conducted using the Illumina HiSeq 2000 platform to analyze RNA samples. The resulting data were processed through Ingenuity® Pathway Analysis to discern key canonical pathways and predict activations or inhibitions. Additionally, gene networks were constructed based on established published associations to further interpret the findings.
Results
Endometrial biopsy analysis demonstrated distinct gene expression profiles between both groups. A total of 1036 genes displayed differential expression with statistical significance (P-value <0.05); 478 genes were upregulated, and 558 genes downregulated in the treatment group, including ones already demonstrated to be associated with liraglutide treatment (*PCSK2*, *ACTN3*, *NOS2*). Functional analysis identified that the most important canonical pathways that differed between the comparison groups included GLP-1 receptor activation, modulation of inflammation and oxidative stress response, alterations in glucose homeostasis and energy consumption, with *YWHAG* being a notable central gene in the associated network. The results indicate a possible involvement of the AKT pathway in the liraglutide's mode of action.
Conclusions
Short-term low-dose liraglutide treatment prior to IVF was associated with changes in the endometrial transcriptome that could potentially be important for improving endometrial receptivity and fertility in infertile women with obesity and PCOS.

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RC1.3

Clinical and genetic characterization of a large cohort of patients with premature ovarian failure

Silvia Federici[1,2], Dario Messetti[1], Raffaella Rossetti[2], Silvia Moleri[2], Luca Persani[1,2] & Marco Bonomi[1,2]
[1]University of Milan, Dept. of Medical Biotechnology and Translational Medicine; [2]IRCCS Istituto Auxologico, Dept. of Endocrine and Metabolic Diseases

Primary ovarian insufficiency (POI) affects 1% of women before age 40 years, and in 70-90% of cases is defined as idiopathic. Although numerous POI-associated genes have been identified in recent years, the prevalence and pathogenicity of individual rare gene variants is still difficult to establish. The aim of our study was to retrospectively analyze the correlation between genotype and phenotype in patients with idiopathic POI, providing a more detailed characterization of POI-associated gene variants. 83 patients were enrolled, clinical data at diagnosis were collected and genetic analysis was performed with NGS technique to search for rare variants (RVs) in 9 candidate genes (*BMP15*, *FIGLA*, *FOXL2*, *GDF9*, *NOBOX*, *NR5A1*, *FSHR*, *SYCE1*, *STAG3*). We also classified the RVs we found according with ACMG criteria. Thus, RVs "of uncertain significance," "probably pathogenic," and "pathogenic" were defined as "potentially pathogenic variants" (PPRVs). Family history of POI was present in 27.5% of patients with secondary amenorrhea (SA) and 6.7% of patients with primary amenorrhea (PA). Patients with PA presented phenotypic abnormalities associated with ovarian failure in 25% percent of cases, while those with of SA in 8.7% of cases. However, none of these differences were found to be statistically significant. Genetic analysis showed the presence of several RVs and PPRVs in the 9 genes analyzed, with STAG3 being the gene with the highest enrichment in rare variants in our sample. In patients with PA we observed a greater enrichment, statistically significant, in RVs (respectively 43.5% in PA vs in 13.7% SA) and PPRVs, as well as in biallelic and oligogenic RVs (respectively 8.7% and 13% in PA vs 0% and 2% in SA). In addition, we found the presence of family history in 40% of PPRV carrier patients (vs 20% in PPRV-negative cases). Finally, no difference in prevalence of associated phenotypes was found in patients carrying RVs or not. Our analysis showed that higher enrichment in RVs, especially those with likely pathogenetic impact, correlates with greater clinical severity. In

particular, the presence of oligogenicity and homozygosity/ compound heterozygosity appears to correlate with PA. In contrast, the more blunted clinical forms, presenting with SA, seem to associate less frequently with RVs in candidate genes, while showing even more prevalent family history: genetic background may consist of a combination of polymorphic variants or rare variants in genes not classically associated with POI, combined with the effect of stochastic and environmental factors.

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RC1.4

The role of rare human PROK2/R2 mutations in the reproductive and metabolic health of the general population: A recall-by-genotype study

Maria Stamou[1], Crystal Chiu[1], Shreya V. Jadhav[1], Kathryn B. Salnikov[1], Lacey Plummer[1], Stephanie B. Seminara[1] & Ravikumar Balasubramanian[1]
[1]Massachusetts General Hospital, Reproductive Endocrinology, Boston, United States

Mutations in the genes of *PROK2/R2* cause isolated hypogonadotropic hypogonadism (IHH) in humans, and defects in the PROK2/R2 pathway metabolic disturbances in mice. The role of naturally occuring mutations in the reproductive and metabolic health of the general population remains unknown. We hypothesized that individuals with naturally occurring rare *PROK/R2* variants will display dysregulation of their reproductive and metabolic fitness. We examined whole exome sequencing data of participants of the large dataset of the Massachusetts General Brigham Biobank (MGBB) (N = 53,408). Using a recall-by-genotype approach, we recruited and examined the reproductive and overall health of 25 individuals with rare *PROK2/R2* deleterious variants (cases) compared to 24 non-carrier controls. Evaluation of medical histories, physical exams, laboratory test results and dedicated questionnaires were used for assessment of the reproductive and overall health of the participants. A frequently sampled intravenous glucose tolerance test was performed in a subset of individuals to assess the β-cell function and insulin sensitivity of the participants. While no differences were observed in the overall health of individuals with *PROK2/R2* variants compared to health controls, *PROK2/R2*-positive male participants were at higher risk for being evaluated for infertility compared to healthy controls [41% of *PROK2/R2* positive participants were evaluated for infertility compared to 6% of non-carrier controls, OR 12.5 (1.19-130), *P* value 0.04]. In addition, they demonstrated a lower adult size testicular volume at exam compared to non-carrier controls [19 (2.7) mls vs 21 (2.9) mls, *P* value 0.02]. No differences in glucose regulation was noted between the two groups. In conclusion, impaired PROK2/R2 signaling may contribute to subtle deficits in reproductive fitness of male carriers in the general population. This study highlights the importance of recall by genotype studies in assessing the phenotypic expressivity, the full phenotypic spectrum, and the penetrance of disease associated human genetic variants.

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RC1.5

Characterization of the role of LEAP-2 in the metabolic control of puberty

Carmen Torres Granados[1,2,3], Miguel Ruiz-Cruz[1,2,3], Yolanda Guerrero Ruiz[1,2,3], Esperanza Uceda Rodríguez[1,2,3], Elvira Rodríguez Vázquez[1,2,3], Álvaro Aranda Torrecillas[1,2,3], Manuel Tena-Sempere[1,2,3,4] & Juan Roa-Rivas[1,2,3,4]
[1]Instituto Maimónides de Investigación Biomédica de Córdoba, Córdoba, Spain; [2]University of Córdoba, Department of Cell Biology, Physiology and Immunology, Córdoba, Spain; [3]Hospital Universitario Reina Sofia (IMIBIC/ HURS), Córdoba, Spain; [4]CIBER Fisiopatología de la Obesidad y Nutrición, Instituto de Salud Carlos III, Madrid, Spain

Puberty is a key maturational process that culminates with the acquisition of reproductive capacity. This event demands significant energy resources to support the profound biological changes that occur during this period, including the activation of the reproductive axis. To this end, a plethora of signals operate for transmitting metabolic information to the reproductive axis in order to precisely regulate pubertal awakening depending on energy availability. Among others, ghrelin is an orexigenic hormone, primarily secreted by the stomach, exerting its effect via activation of the growth hormone secretagogue receptor (GHS-R1a), with crucial implications in the control of metabolism and puberty onset. In recent years, special attention has been also paid to the hepatic peptide LEAP-2, identified as a potential antagonist of ghrelin receptor, particularly in the context of energy homeostasis. However, the influence of LEAP-2 on pubertal maturation has not yet been explored. Therefore, the aim of this project was to unveil the contribution of LEAP-2 to the metabolic control of puberty. To this regard, we investigated the impact of LEAP-2 treatment during the pubertal transition in intact female Wistar rats under different metabolic conditions. In addition, we analyzed the effect of chronic administration of LEAP-2 to ovariectomized peripubertal rats replaced with physiological levels of estradiol (OVX + E2) to avoid the potential confounding effects of fluctuating sex steroid levels. Our results revealed that acute central administration of LEAP-2 increases luteinizing hormone (LH) release in a dose-dependent manner in peripubertal rats subjected to 24 h fasting, an experimental condition known to elevate circulating ghrelin levels. In the same line, chronic central administration of LEAP-2 to prepubertal female rats, either fed ad libitum (normonutrition) or subjected to 20% food restriction, induced a significant advance in puberty onset. This effect was defined by earlier vaginal opening, increased LH levels and accelerated ovarian maturation, regardless the nutritional status of the animals, being this effect more pronounced in undernourished animals. Similar effect on LH levels was detected in OVX + E2 animals treated with LEAP-2. Notably, central treatment with LEAP-2 in OVX + E2 rats led to an increase in Kiss1 mRNA levels, smggesting a potential implication of this neuropeptide in the actions of LEAP-2 on puberty onset under different metabolic conditions. Altogether, our data provide the first evidence about the important role of LEAP-2 in the metabolic control of pubertal maturation, potentially via Kiss1 neurons.

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RC1.6

The prevalence of serious autoimmune diseases is increased in women with premature ovarian insufficiency in Finland – A population-based study

Susanna Savukoski[1,2,3], Heidi Silvén[1,2,3], Paula Pesonen[4], Eero Pukkala[5,6], Mika Gissler[7,8], Eila Suvanto[1,2,3], Meri-Maija Ollila[1,2,9] & Maarit Niinimäki[1,2,3]
[1]University of Oulu, Research Unit of Clinical Medicine, Oulu, Finland; [2]University Hospital and University of Oulu, Medical Research Center, Oulu, Finland; [3]University Hospital of Oulu, Department of Obstetrics and Gynecology, Oulu, Finland; [4]University of Oulu, Infrastructure for Population Studies, Faculty of Medicine, Oulu, Finland; [5]Tampere University, Health Sciences Unit, Faculty of Social Sciences, Tampere, Finland; [6]Institute for Statistical and Epidemiological Cancer Research, Finnish Cancer Registry, Helsinki, Finland; [7]THL Finnish Institute for Health and Welfare, Department of Knowledge Brokers, Helsinki, Finland; [8]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [9]University Hospital of Oulu, Department of Internal Medicine, Oulu, Finland

Introduction
Autoimmunity is an important etiological factor of premature ovarian insufficiency (POI, menopause <40 years). It has been estimated that 4-50 % of POI cases are of autoimmune origin. Only a few studies, with sample sizes of dozens to hundreds POI cases, have investigated the prevalence of autoimmune diseases in women with POI. We aimed to assess in an essentially larger data set the prevalence of severe autoimmune diseases treated in tertiary care prior to POI diagnosis compared to matched controls.
Materials and Methods
Women diagnosed with POI between the years 1988-2017 (n = 5,714) in Finland were identified from the reimbursement registry of the Social Insurance Institution by their right for hormone replacement therapy. Women with a history of cancer or bilateral oophorectomy (n = 1,742), were excluded leaving 3,972 women spontaneous POI cases into the study population. Four population controls matched by age and municipality of residence (n = 15,708) were searched for each POI case. Severe autoimmune disease diagnoses for years 1970-2017 were identified from the Hospital Discharge Registry. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using binary logistic regression for having autoimmune diseases preceding the index date (the date when reimbursement for HRT was granted for the POI case in the case-control set) among POI cases compared to controls.
Results
In women with POI, 5.6% had a severe autoimmune disease before the index date. The prevalence of having any severe autoimmune disease prior to the index date was higher among women with POI (OR 2.6, 95% CI 2.2–3.0). Women with POI had an increased prevalence of several specific autoimmune diseases: polyglandular autoimmune diseases (OR 25.8, 95% CI 9.0-74.1), Addisońs

disease (OR 22.9, 95% CI 7.9-66.1), vasculitis (OR 10.2, 95% 4.3-24.5), systemic lupus erythematosus (OR 6.2 95% CI 4.2-20.3), rheumatoid arthritis (OR 2.3, 95% CI 1.7-3.2), sarcoidosis (OR 2.3, 95% CI 1.2-4.5), inflammatory bowel diseases (OR 2.2, 95% CI 1.5-3.3), and hyperthyroidism (OR 1.9, 95% CI 1.2-3.1). The prevalence of diabetes type 1 and ankylosing spondylitis did not differ between cases and controls.
Conclusion
Women with severe autoimmune diseases have a more than two-fold increased risk of developing POI, smggesting that immunological mechanisms play a pivotal role in POI. Future studies should focus on specific autoimmune mechanisms behind POI from a preventive perspective.

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RC1.7

Characterisation of the daily rhythm of salivary androgens in healthy women and in women with polycystic ovary syndrome by liquid chromatography-tandem mass spectrometry

Laura Rotolo[1,2], Alessandra Gambineri[1,2], Valentina Bissi[1], Francesca Zauli[1,2], Greta Galante[1], Carolina Cecchetti[1,2], Paola Dionese[1,2], Elisabetta Belardinelli[1,2], Beatrice Solmi[1,2], Uberto Pagotto[1,2] & Flaminia Fanelli[1]
[1]Center for Applied Biomedical Research, Dept. Of Medical and Surgical Sciences, Alma Mater Studiorum - Bologna University, Bologna, Italy; [2]Endocrinology and Diabetes Prevention and Care Unit, IRCCS Azienda Ospedaliero-Universitaria, Bologna, Italy

Background
PCOS is characterised by increased production of ovarian and adrenal androgens. Obesity is closely connected to excess androgens and to the disruption of hormone circadian rhythmicity. To date, it is not clear whether hyperandrogenism in PCOS, complicated or not by obesity, is associated with androgen rhythm dysregulation.
Aim
To investigate androgen diurnal rhythmicity and overall daily androgen exposure by measuring testosterone(T), androstenedione(A4) and dehydroepiandrosterone(DHEA) in saliva of healthy women(HW) and women with PCOS fulfilling the three Rotterdam diagnostic criteria, according to their BMI status.
Methods
HW ($n=24$), aged 23-37 y, showed no PCO morphology (PCOm), menstrual irregularity or hyperandrogenism. PCOS ($n=18$) were 15-38 y old and showed oligo-amenorrhea, PCOm and either clinical or biochemical hyperandrogenism. Both groups were subdivided into normal weight (NW:BMI <25kg/m^2; HW:$n=20$, PCOS:$n=5$) and overweight/obese (OW/OB:BMI ≥ 25kg/m^2; HW:$n=4$, PCOS:$n=13$). All were in early follicular phase, had standardised meals at 8, 13 and 20am, and self-collected saliva hourly from 7 until 23am. Salivary T, A4 and DHEA were measured by a validated LC-MS/MS method.
Results
All women presented elevated androgen levels upon awakening, decreasing until bedtime (all $P<0.001$). Compared to HW, PCOS displayed higher T and A4 levels at each time point, and higher DHEA at 9, 11 and 16 am (all $P<0.050$). Throughout the day, minor androgen peaks were detected at 14 (A4,DHEA), 18 (DHEA) and 23 (T,A4,DHEA) am in HW, and at 11 (T,A4,DHEA), 17 (T,A4,DHEA) and 23 (T) am in PCOS. The AUC for daily T and A4 profiles was significantly greater in PCOS vs HW, irrespectively of BMI, whereas DHEA AUC was higher in OW/OB PCOS compared to NW PCOS and to both NW and OW/OB HW (all $P<0.050$). Multiple regression, including androgen AUC as the dependent variable and age, BMI and PCOS status as covariates, showed an independent impact of PCOS on T and A4 (both $P<0.001$) and of BMI on DHEA ($P=0.031$).
Conclusions
Our study provides novel insights into circadian androgen regulation in healthy and PCOS women, enabled by a highly sensitive and specific LC-MS/MS technology. While overall diurnal androgen rhythmicity was preserved, PCOS exhibited a time-specific dysregulation of small androgen surges. Excess T and A4 were detectable in saliva throughout the day in PCOS, whereas DHEA excess was only noticeable in the mid-morning and afternoon. While increased T and A4 secretion characterised PCOS condition regardless of BMI, excess DHEA specifically typified the obese PCOS phenotype, smggesting a specific adrenal contribution to PCOS-related dysmetabolic sequelae.

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Rapid Communications 2: Calcium and Bone | Part I

RC2.1

Genetics of congenital hypoparathyroidism and pseudohypoparathyroidism: results of a multigenic screening in an Italian cohort of affected patients

Francesca Marini[1], Francesca Giusti[2], Filomena Cetani[3], Giovanna Mantovani[4,5], Paolo Garagnani[6] & Maria Luisa Brandi[1,2]
[1]Fondazione FIRMO Onlus, Firenze, Italy; [2]Donatello Bone Clinic, Villa Donatello Hospital, Sesto Fiorentino, Italy; [3]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [4]University of Milan, Department of Clinical Sciences and Community Health, Milano, Italy; [5]Fondazione IRCCS Cà Granada Ospedale Maggiore Policlinico, Endocrinology Unit, Milano, Italy; [6]University of Bologna, Department of Medical and Surgical Sciences (DIMEC), Bologna, Italy

Introduction
Hypoparathyroidism (HPT), pseudohypoparathyroidism (PHP), and end-organ parathyroid hormone (PTH)-resistance are rare metabolic disorders characterized by low serum calcium and increased serum phosphorus due to a PTH-deficient or resistant state. Various genes/loci have been identified as responsible for the development of congenital/familial forms of HPT, PHP and related diseases.
Patients and Methods
A total of 39 patients with a clinical diagnostic suspicion of congenital forms of HPT ($n=30$) or PHP ($n=9$), previously resulted negative to monogenic genetic screening with PCR-based Sanger sequencing ($n=13$) or not yet being genetically analyzed ($n=26$), were collected by 4 major endocrinology centers in Italy. They were all analyzed by Next Generation Sequencing (NGS) using a customized multigenic panel containing 24 human genes whose mutations have been associated with the development of congenital forms of HPT and PHP. Obtained sequences were mapped on the HG38 human reference genome; genetic variants were annotated and analyzed using human gene variant databases and variant allele frequency projects. Variants were classified as "common" or "rare" with a frequency over or less than 1% in the general population, respectively, and then as benign (B), likely benign (LB), variants of uncertain clinical significance (VUS), likely pathogenic (LP), or pathogenic (P), according to the Standards and Guidelines for the Interpretation of Human Sequence Variants of the American College of Medical Genetics and Genomics (ACMG).
Results
Twenty-two patients (56.4%) were found not bearing any rare genetic variant, while in 4 patients (10.3%) we identified 4 different rare variants classified as benign. Thirteen patients (33.3%) were found to be carriers of at least one rare variant classified as VUS, LP, or P, out of them 8 (20.5%) had a single VUS, 3 (7.7%) had one VUS and one LP variant, one (2.6%) had a single LP variant, and one (2.6%) had a P variant. A total of 14 different VUS, LP and P variants were identified, all being heterozygous, 3 in *AIRE* gene (2 VUS, 1 P), 2 in *GCM2* gene (1 VUS, 1 LP), and one in *ACADM* (VUS), *CaSR* (LP), *CDH7* (VUS), *FAM111A* (VUS), *GATA3* (LP), *GNAS* (VUS), *PTH1R* (VUS), *TBCE* (VUS) and *TBX1* (VUS) genes.
Conclusions
Multigenic panel screening by NGS allowed the identification of rare VUS, LP, or P variants in patients previously resulted negative to monogenic Sanger's sequencing (6/13; 46.2%). Segregation analysis is needed to assess the real clinical significance of identified variants.

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RC2.2

Irisin levels are correlated with age and behavioural performance in Post-surgical HypoPT condition

Federica Saponaro[1], Grazia Chiellini[1], Beatrice Polini[1], Caterina Ricardi[1], Patrizia Pignataro[2], Roberta Zerlotin[3], Angela Oranger[3], Silvia Colucci[2], Manuela Di Carlo[3], Graziana Colaianni[3], Alessandro Saba[1] & Maria Grano[3]
[1]Biochemistry Unit, Department of Surgical, Medical and Molecular Pathology and Critical Care, University of Pisa, Pisa, Italy; [2]Department of Translational Biomedicine and Neuroscience, University of Bari, Bari, Italy; [3]Department of Precision and Regenerative Medicine and Ionian Area, University of Bari, Bari, Italy

Introduction
Hypoparathyroidism (HypoPT) is a rare endocrine disease and Post-surgical HypoPT (PS-HypoPT) is the most common cause, caused by accidental parathyroid injury. From a neuropsychological standpoint, patients with PS-HypoPT present cognitive and neuropsychological symptoms. Irisin is a myokine secreted by contracting muscle, which mediates beneficial effects on several targets, including brain. The aim of this study was to evaluate irisin in the context of PS-HypoPT condition.

Methods
a surgical rat model of PS-HypoPT was obtained, treated with gluconate-calcium to maintain normocalcemia. A cohort of 40 animals was included, divided in 4 subgroups: $n=10$ PS-HypoPT rats (PTx) 11 weeks of age, $n=10$ PTx rats 28 weeks of age, $n=10$ controls shamed-operated (Crl) 11 weeks of age and $n=10$ Crl 28 weeks of age. All animals underwent serum calcium and irisin measurement and behavioural testing Morris Water Maze (MWM).
Results
Both PTx ($n=20$) and Crl rats ($n=20$) showed a normal growth and comparable serum calcium levels. In the whole animal cohort, serum irisin levels were statistically significantly lower in younger animals compared to elderly (16.5 ± 3.3 vs 13.0 ± 3.5, $P=0.014$), regardless the belonging group (PTx or Crl). In the ANOVA analysis including the 4 groups, we observed that PTx old animals (28 weeks of age) showed the lowest levels of irisin ($P=0.04$) and the rate of irisin decrease between 11 and 28 weeks of age was significantly higher in PTx animals, compared with Crl ($P=0.03$). We also observed that in MWM test, animals with lower levels of irisin (<14 mg/dl as median cut-off), showed a worse performance at the test, measured as parameters in the probe day (last day): number of entries in the zone of the platform ($P=0.04$), time spent in the zone of platform ($P=0.03$), total distance ($P=0.02$), resting time in the zone of platform ($P=0.02$). Moreover, PTx animals with lower levels of irisin, showed a higher Escape Latency Time compared to the other groups ($P=0.01$).
Conclusions
Irisin is a myokine, with potential protective effects on CNS. We observed that irisin is decreased with age and it is reduced in the animal model of PS-HypoPT. Moreover, irisin levels are correlated with the worse performance at behavioural testing evaluating locomotory capacity and memory in the PS-HypoPT group of animals. This mechanism could explain the known neuropsychological and cognitive symptoms of patients with PS-HypoPT. Further studies are ongoing to understand the role of irisin and its downstream effectors on CNS in PS-HypoPT.

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RC2.3

Metformin prevents glucocorticoid-induced bone resorption in healthy subjects

Stéphanie Pfammatter[1], Zanetti Lisa[1], Susanne Thierry[1], Christian Meier[1] & Eleonora Seelig[1,2]
[1]Universitätsspital Basel, Endocrinology, Diabetology and Metabolism, Basel, Switzerland; [2]Cantonal Hospital Baselland, University Clinic of Medicine, Liestal, Switzerland

Background
Glucocorticoids are crucial for treating various medical conditions due to their beneficial immunosuppressive effects. However, glucocorticoids also carry a high risk for osteoporosis. Notably, within just a few months of glucocorticoid therapy, bone density can be significantly reduced, and up to 5% of patients undergoing such treatment may experience fractures. There is promising evidence from preclinical studies and observations in patients with type 2 diabetes that metformin may prevent glucocorticoid-induced osteoporosis. We aim to investigate whether metformin prevents glucocorticoid-induced osteoporosis as assessed by biochemical markers of bone turnover in healthy subjects.
Methods
In a randomized, placebo-controlled, cross-over trial, we compared metformin to placebo during high-dose glucocorticoid treatment in 18 lean, healthy males. All participants received prednisone 30 mg/d for two 7-day periods separated by a 28-day washout period. During one period, participants additionally had metformin; during the other, they received a placebo. In an exploratory analysis, we assessed changes in bone turnover markers before and after glucocorticoid treatment in both study phases.
Results
18 male subjects (mean age 27, standard deviation [SD] ±5.2 years, BMI 22.9 ± 1.8 kg/m^2) were enrolled in the study. During glucocorticoid treatment, serum C-terminal telopeptide (CTX) increased with placebo but remained stable with metformin (placebo: 0.2 ± 0.2 ng/ml; metformin 0.06 ± 0.2 ng/ml, $P=0.03$). Serum procollagen I Intact N-terminal (PINP) decreased with both treatments (placebo: -20.6 ± 11.8 ng/ml; metformin -22.3 ± 16.7 ng/ml, $P=0.7$). Serum osteocalcin decreased with both treatments (placebo -10.8 ± 6.9 mg/l; metformin -12.1 ± 9.4 mg/l, $P=0.3$).
Conclusion
Our study demonstrated that metformin has a protective effect during GC-therapy with diminished bone resorption, while no effect on bone formation can be observed. These findings indicate that metformin may have a promising role in mitigating some of the detrimental effects of glucocorticoids on bone health.

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RC2.4

Primary hyperparathyroidism in children and adolescents: Clinical features and treatment outcomes from an Italian multicenter study

Filomena Cetani[1], Simone Della Valentina[2], Alfredo Scillitani[3], Anna Dal Lago[2], Laura Pierotti[2], Chiara Sardella[1], Bruno Madeo[4], Elisa Cairoli[5], Cristina Eller Vainicher[6], Massimo Procopio[7], Marco Barale[8], Serena Palmieri[9,10], Laura Gianotti[11], Elena Castellano[12], Andrea Lania[13], Marco Pitea[14], Roberto Lanzi[15], Riccardo Maggiore[16], Cristiana Cipriani[17], Jessica Pepe[18] & Sabrina Corbetta[19,20]
[1]Unit of Endocrinology, University Hospital of Pisa, Pisa, Italy; [2]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [3]Unit of Endocrinology, Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy; [4]Unit of Endocrinology, Department of Medical Specialist, Azienda Ospedaliera-Universitario of Modena, Ospedale Civile of Baggiovara, Modena, Italy; [5]Bone Metabolism Disorders and Diabetes Unit, IRCCS Istituto Auxologico Italiano, Milan, Italy; [6]SC Endocrinologia, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy; [7]Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [8]Oncological Endocrinology, Department of Oncology, University of Turin, Turin, Italy; [9]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy, [10]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Policlinico Maggiore, Milan, Italy, [11]Struttura Complessa di Endocrinologia e Diabetologia Territoriale, ASL Cuneo 1, Cuneo, Italy, [12]Endocrinology, Diabetology and Metabolism, Santi Croce & Carle Hospital, Cuneo, Italy, [13]Humanitas University and Endocrinology Unit, IRCCS Humanitas Research Hospital, Rozzano, Italy, [14]Department of Pediatrics, San Raffaele Hospital, University of Milan, Milan, Italy, [15]Internal Medicine Day Case, San Raffaele Hospital, Milan, Italy, [16]Endocrine Surgery Unit, IRCCS San Raffaele Scientific Istitute, Milan, Italy, [17]Department of Clinical, Internal, Anaesthesiological and Cardiovascular Sciences, Sapienza University of Rome, Rome, Italy, [18]Department of Clinical, Internal, Anaesthesiological and Cardiovascular Sciences, Sapienza University of Rome, Rome, Italy, [19]Bone Metabolism Disorders and Diabetes Unit, IRCCS Istituto Auxologico Italiano, Milan, Italy, [20]Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy

Primary hyperparathyroidism (PHPT) is rare in the pediatric population, with an estimated incidence of 0.5–5 cases per 100,000 person-years in children. Data regarding the clinical phenotype, the surgical outcomes are scarce. The objective of our study was to retrospectively analyze the phenotype of apparently sporadic PHPT in patients ≤21 years in major endocrinology reference centers in Italy. None of the patients had known familial syndromes. A total of 41 patients were included, 14 males and 27 females with a median age at diagnosis of 18 years (IR 16-20). Twenty-nine percent of diagnoses ($n=12$) were made incidentally through laboratory evaluation performed for other reasons while 71% ($n=29$) had PHPT-related symptoms. The most common symptom was nephrolithiasis in 58.6% of the symptomatic cohort ($n=17$), followed by bone pain (11.1%) and acute pancreatitis (6.9%). Median total serum calcium concentration was 11.7 mg/dl (IR 11.1-12.5), ionized calcium was 1.58 mmol/l (IR 1.43-1.71) and PTH levels, evaluated as fold increase of the upper limit of reference range, were 2.96. Fifty-nine percent (19/32 with available 24-hour urinary calcium) had hypercalciuria with a median value of 342 mg (IR 258-498). Fifty-three percent (15/28 with available dual-energy x-ray absorptiometry) had low bone mineral density (mean lumbar Z-score -2.8; femoral neck -2.6; total femur -2.9; 1/3 distal radius -3.7 DS). Genetic analysis of genes that have been associated with the development of genetic PHPT was performed in 34 patients. Eleven patients (33.3%) carried a heterozygous germline variant: 7 in *CDC73* gene, 1 in *MEN1* gene, 1 in *AP2S1* gene, 1 in *GCM2* gene, 1 in CASR of uncertain significance. The latter two variants were classified of uncertain significance. Thirty-one (75%) patients underwent surgery, 15 of them had bilateral cervical exploration. Histology was consistent with the diagnosis of chief cell adenoma in 27 (87%) patients, atypical adenoma in 2 (6.5%) and carcinoma in 2 (6.5%). The post-surgical follow-up (median 5 years) was available in 23 patients. The cure rate following primary surgery was 95.7%. Persistence of PHPT was evident in one patient. No recurrence was evident. Our findings smggest that PHPT in children and adolescence is frequently sporadic, although a substantial proportion of patients (approximately one-third) have a genetic predisposition. Therefore, an appropriate familial screen should be performed clinically and if relevant, tested genetically. Most cases are seemingly due to isolated adenomas.

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RC2.5

Genetic testing for syndromic conditions in patients referred with primary hyperparathyroidism: a retrospective observational analysis

Kyi Pyar Than Yu[1], Andrew Gregory[1], Mustafa Abdulkareem[1], Biju Jose[1] & Lakshminarayanan Varadhan[1]
[1]University Hospital of North Midlands, Diabetes and Endocrinology, Stoke-on-Trent, United Kingdom

Background and Aim
Primary hyperparathyroidism (PHPT) is a common endocrine disorder. A small proportion of these patients may have syndromic conditions such as multiple endocrine neoplasia (MEN) or familial hypocalciuric hypercalcemia (FHH). The UK national guidelines recommend genetic testing for familial hyperparathyroidism in individuals under 50 or any age with specific criteria such as family history, multi glandular disease, hyperplasia, or parathyroid carcinoma. Genetic testing for familial hypocalciuric hypercalcemia (FHH) is recommended in patients with hypercalcemia with hypocalciuria (urinary calcium creatinine clearance ratio $<$ 0.02). The aim of our study was to assess the uptake and utility of genetic testing and its diagnostic yield in patients referred to endocrine clinic with possible primary hyperparathyroidism.
Methods
A retrospective analysis of the genetic tests performed in patients with primary hyperparathyroidism over 7 years was done. Along with routine testing with PTH, bone profile and vitamin D, all patients underwent screening for FHH with urinary calcium/creatinine ratio and/or 24 h urine calcium excretion. Data on additional hormonal tests (fasting gut hormone profiles, pituitary profile, catecholamine level), and imaging to evaluate pathological glands (Ultrasound (US) and MIBI scan) was collected.
Results
A total of 33 patients underwent genetic testing for PHPT, and results were available for 26. 70% ($n=23$) were females. The mean age at diagnosis was 44 years (range 16-66). Additional hormonal testing was conducted for 25 patients. Ultrasound of parathyroid glands was performed in 30 patients, with 21 positive results. Additionally, 28 patients underwent Nuclear Medicine Parathyroid MIBI scans with 12 positive results. Various indications and numbers tested were: a) 14 patients due to age $<$50 years old. b) 8 for failed localization on imaging modalities. c) 4 for low urine calcium creatinine ratio. d) 2 for recurrence of primary hyperparathyroidism. e) 2 for parathyroid hyperplasia on post-operative histology. f) 2 for associated hormone problems (one each with elevated gastrin and chromogranin A). 1 for coexistent pituitary adenoma. Genetic tests confirmed CASR gene mutation in 2 patients confirming FHH. None of the patients had MEN-1 or MEN-2 gene mutations.
Conclusion
Our data indicates that, despite a high index of suspicion for MEN and FHH based on risk factors and clinical presentation, the actual prevalence is low in this highly selected cohort, with sporadic occurrence being the most common presentation.

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RC2.6

Role of FGF23 in patients with transfusion-dependent β-thalassemia and hypercalciuria

Alberto Gobbo[1], Fatima Chamekh[2], Camilla Alice Cattaneo[1], Martina Verrienti[1], Stefano Pizzicotti[3], Filomena Longo[4], Maria Chiara Zatelli[1] & Maria Rosaria Ambrosio[1]
[1]University of Ferrara, Section of Endocrinology and Internal Medicine, Department of Medical Sciences, Ferrara, Italy; [2]University of Ferrara, Ferrara, Italy; [3]University Hospital of Ferrara, Laboratorio Unico Provinciale, Ferrara, Italy; [4]University Hospital of Ferrara, Regional HUB Centre for Thalassaemia and Haemoglobinopathies, Department of Medicine, Ferrara, Italy

Introduction
Patients with transfusion-dependent β-thalassemia (TDT) frequently exhibit elevated urinary calcium excretion, contributing to kidney stone formation and osteoporosis. The underlying mechanism of hypercalciuria in β-thalassemia remains elusive, with FGF23 playing a potential role. FGF23, a bone-derived hormone, primarily acts on the kidneys by inhibiting phosphate reabsorption in the proximal tubules while enhancing calcium uptake in the distal tubules. Few studies have evaluated FGF23 levels in β-thalassemic patients as compared to the general population with contradictory results.
Objective
This study aims to investigate FGF23 levels in patients with TDT and hypercalciuria vs those without.
Methods
Our study included 126 patients referring to the Regional HUB Centre for Thalassaemia and Haemoglobinopathies in Ferrara in 2023. The parameters we assessed are shown in the Table. Hypercalciuria was defined as a 24-hour urinary calcium level $\geq$4 mg/kg/day. The intact FGF23 polypeptide was quantified using the chemiluminescence immunoassay "LIAISON® FGF 23 test".
Results

	Normocalciuric	Hypercalciuric
$N=126$	39 (31%)	87 (69%)
Sex (F/M)	27/12	44/43
	Median [IQR]	**Median [IQR]**
Age (years)	51 [45; 56]	49 [44; 53]
BMI (kg/m^2) *	23.8 [21.4; 26.7]	21.9 [20.2; 24.8]
FGF23 (pg/ml) **	42.6 [30.1; 58.7]	32.5 [23.8; 42.7]
Urinay creatinine (g/day) *	0.9 [0.8; 1.1]	1.1 [0.8; 1.4]
Urinary phosphate (g/day) ***	0.55 [0.3; 0.7]	0.8 [0.6; 1]
Urinary proteins (mg/day)	131 [101; 207]	176 [114; 242]
Calcium (mg/dl)	9.3 [9; 9.7]	9.5 [9.3; 9.8]
Phosphate (mg/dl)	3.6 [3.2; 3.9]	3.5 [3.3; 3.9]
Vitamin D (ng/ml) *	34.9 [27.2; 37.5]	28.8 [19.4; 34.6]
PTH (pg/ml)	28 [21.5; 41.5]	25 [19; 33.8]
Magnesium (mg/dl)	2.2 [2; 2.4]	2.1 [2; 2.3]
Ferritin (ng/ml)	548 [334; 889]	447 [298; 676]
Iron (ug/dl)	223.5 [195.8; 272.3]	241 [215.5; 270]
eGFR (ml/min)	91.6 [75; 109]	90.8 [77.1; 116.7]
Creatinine (mg/dl)	0.74 [0.59; 0.89]	0.73 [0.61; 0.9]

Mann-Whitney test was applied. $P<0.05$*; $P<0.01$**; $P<0.001$***

Conclusions
Hypercalciuric patients exhibited lower FGF23 levels combined with higher urinary creatinine and phosphate levels as compared to normocalciuric patients. This smggests a potential role of FGF23 in the development of hypercalciuria, but additional mechanisms (i.e., renal impairment due to iron overload or chelation therapy) may contribute to the increased phosphate and calcium renal losses in these patients. Further studies are warranted to better explore this issue.

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Rapid Communications 3: Adrenal and Cardiovascular Endocrinology | Part I

RC3.1

Biochemical control with dose reduction in chronic glucocorticoid therapy over 4 years: A phase III extension study of Chronocort (Efmody) in the treatment of Congenital Adrenal Hyperplasia (CAH)

Richard John M. Ross[1], Deborah P. Merke[2], Wiebke Arlt[3], Aude Brac De La Perriere[4], Angelica Hirschberg[5], John D.C. Newell-Price [1], Alessandro Prete[6], Aled Rees[7], Nicole Reisch[8], Marcus Quinkler[9], Philippe A. Touraine[10], Kerry Maltby[11], Jo Quirke[11], Naila Aslam[11], Helen Coope[11] & John Porter[11]
[1]The University of Sheffield, United Kingdom; [2]National Institutes of Health, Bethesda, United States; [3]MRC Laboratory of Medical Sciences, United Kingdom; [4]Louis Pradel Hospital, Bron, France; [5]Karolinska Institute, Sweden; [6]University of Birmingham, United Kingdom; [7]Cardiff University, United Kingdom; [8]Klinikum der Universität München, München, Germany; [9]Charlottenburg, Berlin, Germany, [10]University Hospitals Pitié Salpêtrière - Charles Foix, Paris, France, [11]Diurnal, United Kingdom

Background
Management of CAH involves replacing cortisol deficiency and reducing raised adrenal androgens, however the supraphysiological glucocorticoid doses often required to treat hyperandrogenism are associated with poor long-term health outcomes. Modified-release hydrocortisone (MRHC) capsules, Efmody, replicate cortisol diurnal rhythm and improve control of CAH compared to standard glucocorticoid therapy. Here we report changes in glucocorticoid daily dose and 9am 17-hydroxyprogesterone (17-OHP) and androstenedione (A4) in MRHC-treated patients after 48 months in the MRHC single-arm extension study.
Methods
Participants completing MRHC Ph2 and Ph3 studies were eligible to enter a single-arm, open-label extension study. Visits occurred at baseline, weeks 4, 12, 24 and 6-monthly thereafter. MRHC doses were adjusted on the basis of an adrenal insufficiency checklist, and measurement of A4 and 17-OHP at 9am and 1pm, targeting 17-OHP to $<$36 nmol/l and A4 into the reference range. Participants that completed 48 months in the extension study were reviewed. Participants were considered responders when 9am 17OHP $\leq$36 nmol/l or A4 $\leq$7nmol/l and hydrocortisone (HC) dose $\leq$25 mg/day.
Results
Data were available for 91 participants at baseline and 71 participants (61 with hormone blood results) at 48 months. The median daily HC dose (Inter-Quartile Range [IQR]) at baseline and 48 months were 30 mg (IQR 20–35) and 20 mg (IQR 15–25), respectively (nominal $P<0.0001$). Geomean (95% CI) 17-OHP

was 15.84 (10.32–24.31) and 11.34 (7.048–18.23) nmol/l at baseline and 48 months, respectively. Geomean A4 (95% CI) was 2.242 (1.669–3.012) and 2.092 (1.604–2.727) nmol/l at baseline and 48 months, respectively. Quadrant analysis showed the following:

		Dose	
		≤25 mg/day	>25 mg/day
Baseline	>36 nmol/l 17-OHP	14/91 (15%)	21/91 (23%)
	≤36nmol/l 17-OHP	29/91 (32%)	27/91 (30%)
48 months	>36 nmol/l 17-OHP	15/61 (24%)	3/61 (5%)
	≤36 nmol/l 17-OHP	31/61 (51%)	12/61 (20%)

Responder status 51% vs 32% at baseline, $P=0.0274$ by Fisher's exact test.

		Dose	
		≤25 mg/day	>25 mg/day
Baseline	>7 nmol/l A4	6/91 (7%)	14/91 (15%)
	≤7nmol/l A4	37/91 (41%)	34/91 (37%)
48 months	>7n mol/l A4	5/61 (8%)	1/61 (1%)
	≤7nmol/l A4	41/61 (67%)	14/61 (23%)

Responder status 67% vs 41% at baseline, $P=0.0016$ by Fisher's exact test.

Conclusions

After 48 months of MRHC treatment the median daily HC dose was reduced from a median of 30mg to 20mg and the number of patients achieving responder status based on 9am 17-OHP or A4 while receiving HC ≤25 mg/day increased.

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RC3.2

Combined [18F]Fluorodeoxyglucose PET and [123I]Iodometomidate-SPECT for diagnostic evaluation of indeterminate adrenal neoplasias – The prospective cross-sectional diagnostic test performance study FAMIAN

Stefanie Hahner[1], Philipp Hartrampf[2], Felix Beuschlein[3], Matthias Miederer[4], Konstanze Miehle[5], Schlötelburg Wiebke[2], Carmina Teresa Fuss[1], Thomas Pflmger[6], Christian Fottner[7], Anke Tönjes[5], Ken Herrmann[8], Holger Amthauer[9], Mathias Schreckenberger[4], Osama Sabri[10], Johanna Werner[1], Miriam Reuter[1], Stefan Kircher[11], Wiebke Arlt[12], Martin Fassnacht[1], Andreas Buck[2], Hans Helge Müller[13] & Schirbel Andreas[2]

[1]University Hospital Würzburg, Division of Endocrinology and Diabetology, Würzburg; [2]University Hospital Würzburg, Department of Nuclear Medicine, Würzburg; [3]Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, UniversitätsSpital Zürich (USZ) und Universität Zürich (UZH), Switzerland, Switzerland; [4]Department of Nuclear Medicine, University Medical Center of the Johannes Gutenberg University Mainz, Germany, Germany; [5]University Hospital Leipzig, Medizinische Klinik und Poliklinik III – Endokrinologie, Nephrologie, Rheumatologie, Leipzig, Germany; [6]Klinikum der Universität München, Department of Nuclear Medicine, Munich, Germany; [7]Department of Endocrinology and Metabolism, I Medical Clinic, University Medical Center of the Johannes Gutenberg University Mainz; [8]Department of Nuclear Medicine, West German Cancer Center (WTZ), University Hospital Essen, University of Duisburg-Essen; German Cancer Consortium (DKTK), Partner Site University Hospital Essen; [9]Charité - Universitätsmedizin Berlin, Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Nuclear Medicine, [10]Klinik und Poliklinik für Nuklearmedizin, Universitätsklinikum Leipzig, [11]Institute of Pathology, University of Würzburg, [12]Medical Research Council Laboratory of Medical Sciences, London, UK, [13]Institute of Medical Bioinformatics and Biostatistics, Philipps University of Marburg

Adrenal tumours are frequently detected by conventional cross-sectional imaging, which, however, has limited specificity in identifying the most prevalent tumour type, benign, non-functional adrenocortical adenomas (ACA) not requiring surgery. We assessed the diagnostic accuracy of adrenal molecular imaging with [^{18}F]Fluorodeoxyglucose-positron emission tomography (FDG-PET) and [^{123I}]Iodometomidate-single photon emission tomography (IMTO-SPECT). We performed a prospective, multicentre study in adult patients (≥30 years) with indeterminate adrenal masses (diameter >3 cm and unenhanced computed tomography [CT] tumour attenuation ≥10 Hounsfield units [HU]). We assessed the diagnostic performance of combined FDG/IMTO imaging in detecting ACA, using a reference standard of histopathology. Low FDG uptake (=FDG-negative) with high IMTO uptake (=IMTO-positive) was considered indicative of ACA. We also assessed the utility of FDG and unenhanced CT tumour attenuation in detecting malignancy. Between July 2015 and December 2020, 85 patients were enrolled and 77 included in the final analysis; 53 harboured benign and 24 malignant adrenal masses. Combined FDG/IMTO-imaging identified ACA with high specificity (95·7% [95%CI 85·2-99·5%]; positive predictive value 87·5% [95%CI 61·7-98·5%]; positive likelihood ratio 11·1 [95%CI 3·2-122·2%]). However, sensitivity was low (48·3% [95%CI 29·4-67·5%]) due to moderate or high FDG uptake in 14 of 30 ACAs. Malignant masses were identified with high sensitivity but low specificity both by unenhanced CT (cut-off HU ≥20 sensitivity 100% [95%CI 85·8-100%], specificity 26·4% [95%CI 15·3-40·3%]) and FDG (sensitivity 95·8% [95%CI 78·9-99·9%], specificity 62·3% [95%CI 47·9-75·2%]). Combined FDG/IMTO-imaging identifies ACA with high specificity in this cohort with indeterminate masses. However, the presence of a sub-cohort of FDG-positive ACA decreases sensitivity.

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RC3.3

Quantifying variability in ambulatory 24-hour tissue hormones for personalised management of hormonal replacement in patients with adrenal insufficiency

Ileana R. Botusan[1,2], Katarina Berinder[1,2], Paal Methlie[3,4], Thomas Upton[5], Eder Zavala[6], Georgina Russell[5], Katerina Simunkova[3], Dimitra Vassiliadi[7], Isabella Marinelli[6], Marianne Aardal Grytaas[3,4], Stylianos Tsagarakis[7], Stafford Lightman[5], Eystein Sverre Husebye[3,4], Olle Kämpe[1,2], Marianne Øksnes[3,4] & Sophie Bensing[1,2]

[1]Karolinska Institutet, Stockholm, Sweden; [2]Karolinska University Hospital, Stockholm, Sweden; [3]University of Bergen, Bergen, Norway; [4]Haukeland University Hospital, Bergen, Norway; [5]University of Bristol, Bristol, United Kingdom; [6]University of Birmingham, Birmingham, United Kingdom; [7]Evangelismos Hospital, Athens, Greece

Background

Recently, we have shown that ambulatory 24-hour dynamic steroid profiling using the newly developed U-RHYTHM system is possible and presented the circadian and ultradian rhythmicity of adrenal hormones in a healthy cohort. With U-RHYTHM, multiple hormones can be sampled simultaneously, and the free active hormones can be measured in local tissue where the effect is exerted. Thus the hormone fingerprint resulting from replacement therapy in individual patients can be visualized and compared to the normative references throughout the day.

Aim

To assess 24-hour profiles of free cortisol and metabolites in patients with Addisońs disease (AD) on different glucocorticoid replacement therapies (GRT) and compare the results with healthy volunteers (HV).

Material and Methods

The study was performed within the frame of a multi-center EU-funded H2020 ULTRADIAN study. HV group, enrolled 214 subjects, aged 18 to 68 years and with BMI 16 to 29.9 kg/m^2. Patients group enrolled 41 subjects with established AD within the same age span. All were 21 hydroxylase autoantibody positive. Median duration of AD was 6.5 years (IQR: 3.25-19.75). Median BMI was 25.2 kg/m^2. (IQR: 22.75-27). The enrollment was independent of their GRT regimes: 27 hydrocortisone, 9 cortisone-acetate, 4 modified release hydrocortisone and 1 pump. Their regular medication was not changed. Twenty-minute microdialysis fractions were collected ambulatory from subcutaneous tissue over 24 h using the portable fraction collector, U-RHYTHM. Steroid hormones were analyzed by ultrasensitive liquid chromatography tandem mass spectroscopy (LC-MS/MS). Dynamic biomarkers: area under the curve, concentration peak post -dose and time to peak were used to define hormone pattern differences, and to assess the "time in range" for patients compared with the profiles of HV.

Results

The U-RHYTHM ambulatory system was well tolerated, not disturbing the normal daily activities or sleep and 24-hour dynamic steroid profiling revealed marked interindividual variations partially depending on GRT and dosing-regime. Continuous overnight steroid profiling in patients was possible in ambulatory, without disturbing sleep. Tissue cortisol exposure expressed as a percentage of total (cortisol + cortisone) showed higher levels in patients AD compared with HV, throughout the day (8 am to 2 am) with levels even higher than in HV with high BMI (>25 kg/m^2). The exception was during night when, cortisol was very low in patients with AD.

Conclusion

Ambulatory 24-hour microdialysis sampling may provide a tool for precision medicine in AD, creating the opportunity for individual dose adjustment particularly in patients who are not well on current GRT.

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RC3.4

CHAMPAIN study: Initial results from a phase II study of efficacy, safety and tolerability of modified-release hydrocortisones: Chronocort® (Efmody®) versus Plenadren®, in primary adrenal insufficiency

Alessandro Prete[1,1], Verena Theiler-Schwetz[1], Wiebke Arlt[2], Irina-Oana Chifu[3], Birgit Harbeck[4,5], Catherine Napier[6], John D.C. Newell-Price[7], Aled Rees[8], Nicole Reisch[9], Günter K. Stalla[10], Naila Aslam[11], Helen Coope[11], Kerry Maltby[11], John Porter[11], Jo Quirke[11] & Richard John M. Ross[7]

[1]University of Birmingham, United Kingdom; [2]MRC Laboratory of Medical Sciences, United Kingdom; [3]University Hospital Würzburg, Würzburg, Germany; [4]amedes experts, Hamburg, Germany; [5]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [6]Newcastle University, United Kingdom; [7]The University of Sheffield, United Kingdom; [8]Cardiff University, United Kingdom; [9]Endokrinologie, Nephrologie und weitere Sektionen, München, Germany, [10]Ludwig Maximilian University of Munich, München, Germany, [11]Diurnal, United Kingdom

Background

Current glucocorticoid replacement regimens for patients with primary adrenal insufficiency (PAI) mean patients wake with either low or undetectable cortisol levels[1], associated with fatigue and a reduced quality of life (QoL)[2]. Plenadren® (Takeda, UK) is a once-daily modified-release formulation of hydrocortisone that replaces daytime cortisol levels whereas Chronocort® (modified-release hydrocortisone hard capsules, Diurnal, UK) when taken twice-daily, has been shown to replicate the normal overnight rise in serum cortisol concentration and provide physiological levels throughout the day. We have undertaken a double-blind, double-dummy, two-way cross-over, randomised, phase II study of efficacy, safety and tolerability of modified-release hydrocortisones: Chronocort® Versus Plenadren®.

Aim

To test the hypothesis that Chronocort® provides more physiological waking cortisol levels than Plenadren®.

Methodology

The study was conducted across 8 sites in the UK and Germany. Male and female patients, aged $\geq$18 with confirmed PAI (defined as morning pre-dose cortisol $<$ 50 nmol/l) on stable therapy over the preceding three months and not currently treated with Chronocort®/Plenadren®. Participants with congenital adrenal hyperplasia (CAH), secondary or tertiary AI were excluded. Each participant was randomised on a 1:1 basis to either; treatment sequence I (Chronocort® first) or treatment sequence II (Plenadren® first) taking a 25 mg total daily dose for 4 weeks; either Plenadren® 25 mg in the morning or Chronocort® 10 mg in the morning and 15 mg at night with the associated dummy preparation followed immediately by the other treatment. The pre-dose morning serum cortisol level was assayed at baseline and after each treatment period. A physiological morning cortisol level was defined as a pre-dose level of $>$140 nmol/l. Secondary measures included: morning fatigue measured using the Multidimensional Assessment of Fatigue (MAF) questionnaire and the PROMIS® 7b questionnaire; QoL was assessed using the EuroQol 5-level Standardised Health Questionnaire (EQ-5D-5L™); Health-related Quality of Life in Addison's disease (AddiQoL) questionnaire and the 36-Item Short Form Health Survey (SF-36®) questionnaire.

Results

Of 49 evaluable participants with PAI, 45 achieved a physiological morning cortisol after four weeks of Chronocort® compared with 2 after four weeks of Plenadren® ($P<0.0001$). The mean (standard deviation) waking cortisol was 422.85 (203.50) vs 36.98 (113.87), respectively.Conclusion: Chronocort® provides more physiological waking cortisol levels than Plenadren®. Further analysis will test the hypothesis that waking with physiological cortisol levels improves fatigue and QoL in patients with PAI.

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RC3.5

The saline infusion test with mass spectrometric measurements of aldosterone in patients tested for primary aldosteronism

Christina Pamporaki[1], Hanna Remde[2], Georgiana Constantinescu[1], Lydia Kuerzinger[2], Carmina Teresa Fuss[2], Mirko Peitzsch[3], Manuel Schulze[4], Myron Lee[5], Jun Yang[6], Lisa Mueller[7], Tracy Ann Williams[7], Martin Reincke[7], Sven Gruber[8], Felix Beuschlein[8], Jacques Lenders[9] & Graeme Eisenhofer[1]

[1]Medical Faculty, University Hospital Carl Gustav Carus, Technische Universität Dresden, Department of Medicine III, Dresden, Germany; [2]University Hospital, University of Würzburg, Division of Endocrinology and Diabetes, Würzburg, Germany; [3]University Hospital Carl Gustav Carus, Technische Universität Dresden, Germany, Institute of Clinical Chemistry and Laboratory Medicine; [4]Center for Interdisciplinary Digital Sciences, TU Dresden, Department Information Services and High Performance Computing, Dresden, Germany; [5]Prince of Wales Hospital, Sydney, New South Wales, Australia; [6]Hudson Institute of Medical Research, Clayton, Australia, Centre for Endocrinology and Metabolism, Melbourne, Australia; [7]University Hospital, Ludwig Maximilian University Munich, Department of Medicine IV, Munich, Germany; [8]University Hospital Zurich and the LOOP Zurich Medical Research Center, Zurich, Department of Endocrinology, Diabetology and Clinical Nutrition, Zurich, Switzerland; [9]Radboud University Medical Center, Nijmegen, Department of Internal Medicine, Nijmegen, Netherlands

Background

Confirmation of primary aldosteronism (PA) with the saline infusion test (SIT) requires accurate measurements of plasma aldosterone, best achieved by mass spectrometry. Performance of the test and appropriate cut-offs remain inadequately defined.Design and methods: This prospective multicenter cohort study involved 451 patients with suspected PA who underwent a seated SIT. Among these, there were 90 and 76 in whom PA was respectively confirmed and excluded based on outcome assessment. Thirty-one patients who were not adrenalectomized underwent a repeat SIT at outcome assessment. Diagnostic performance and optimal cut-offs were determined from receiver operating characteristic (ROC) curves.

Results

Analysis of ROC curves indicated higher ($P=0.020$) areas under curves for the SIT than the aldosterone:renin ratio (0.968 vs 0.905). A cut-off of 141 pmol/l for the post-SIT aldosterone provided 100% sensitivity at a sub-optimal specificity of 87% for disease confirmation. A cut-off of 219 pmol/l provided improved specificity of 95%, though at a sensitivity of 87%. Among the 31 patients in whom the SIT was repeated, there were five (16%) in whom post-SIT aldosterone concentrations fell discordantly on both sides of the 141-219 pmol/l concentration range.

Conclusions

The SIT with mass spectrometric measurements of aldosterone provides superior performance over the ARR for diagnosis of PA, but is suboptimal as confirmatory test. Inaccuracy and discordance of the SIT indicate need for care in application and interpretation of the test. A cut-off for aldosterone above 219 pmol/l limits the false-positive rate to 5%, which may be suitable to select patients for adrenal venous sampling.

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RC3.6

Mismatch repair deficiency and microsatellite instability in adrenocortical carcinoma: Diagnosis, prevalence, and clinical impact

Barbara Altieri[1], Sabine Herterich[2], Stefan Kircher[3], Arne Jahn[4], Maria-Veronica Teleanu[5], Juliane Lippert[1], Laura-Sophie Landwehr[1], Otilia Kimpel[1], Miriam Reuter[1], Hanna Remde[1], Albrecht Stenzinger[6], Hanno Glimm[7], Ralf Bargou[8], Stefan Froehling[5], Cristina L Ronchi[1,9], Silke Appenzeller[8], Martin Fassnacht[1,2,8] & Kroiss Matthias[1,10]

[1]Department of Internal Medicine I, Division of Endocrinology and Diabetes, University Hospital, University of Würzburg, Würzburg, Germany; [2]Clinical Chemistry and Laboratory Medicine, University Hospital, University of Würzburg, Würzburg, Germany; [3]Institute of Pathology, University of Würzburg, Würzburg, Germany; [4]Institut für Klinische Genetik, Dresden, Germany; [5]National Center for Tumor Diseases (NCT) Heidelberg and German Cancer Research Center (DKFZ), Heidelberg, Germany; [6]Institute of Pathology, University Hospital of Heidelberg, Heidelberg, Germany; [7]National Center for Tumor Diseases (NCT) Dresden, Dresden, Germany; [8]Comprehensive Cancer Center Mainfranken, University Hospital of Würzburg, Würzburg, Germany; [9]College of Medical and Dental Sciences, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom, [10]Department of Internal Medicine IV, University Hospital Munich, Ludwig-Maximilians-Universität München, Munich, Germany

Background

DNA mismatch repair (MMR) maintains genomic integrity and stability. Inactivation of the MMR genes *MLH1*, *PMS2*, *MSH2*, and *MSH6* by somatic or germline variants or gene methylation causes MMR deficiency (dMMR) leading to microsatellite instability (MSI) and high tumour mutational burden. In many tumour entities, patients with dMMR/MSI respond well to immune checkpoint inhibitor (ICI) therapy. The clinical relevance of dMMR and MSI in adrenocortical carcinoma (ACC) remains uncertain.

Objective
To systematically investigate MMR gene variants and methylation, MMR protein expression, and MSI in patients with ACC and to test for their association with clinical variables including response to ICI.
Methods
Immunohistochemistry of MLH1, PMS2, MSH2, and MSH6 was performed in 109 ACC tissues with available germline and somatic MMR gene variants by whole-genome ($n=14$), exome ($n=7$) or targeted-panel sequencing ($n=88$). Pathogenic/likely pathogenic *MMR* variants were confirmed by Sanger-sequencing. Methylation status was evaluated by multiplex ligation-dependent probe amplification in patients with dMMR tumours. Microsatellite analysis of dinucleotide and mononucleotide microsatellite loci *NR21*, *NR27*, *BAT40*, and *KCNJ5* were analysed by plex PCR in 99 patients. Clinicopathological data were analysed retrospectively.
Results
Immunohistochemistry showed dMMR in 15/109 cases (13.8%) with prevalence of MSH6-loss either alone ($n=3$) or associated with MSH2-loss ($n=4$), MLH1/PMS2-loss ($n=1$), or as tetra-loss ($n=1$). Hormone secretion ($P=0.31$), ENSAT stage ($P=0.53$), Ki67% ($P=0.12$), S-GRAS score ($P=0.23$), history of other malignancy ($P=0.19$), progression-free (HR=1.21, 95%CI=0.63-2.31, $P=0.57$) and disease-specific survival (HR=1.26, 95%CI=0.58-2.71, $P=0.56$) did not differ between patients with and without dMMR. Weiss score was significantly higher in dMMR tumours ($P=0.008$). Ten patients with dMMR tumours had pathogenic/likely pathogenic germline ($n=4$) or somatic ($n=5$) *MMR* variants or *MLH1* hypermethylation ($n=1$), but plex PCR showed MSI only in 3 cases. Among patients without dMMR, few cases had germline ($n=1$) or somatic ($n=1$) *MMR* variants or MSI ($n=1$). 4/5 patients with dMMR and/or *MMR* variants who received ICI did not respond. A single patient with germline *MSH6* variant, tumoural dMMR, but lack of MSI, was stable on immunotherapy for 12 months.
Conclusion
This is the first large systematic multiparameter study of dMMR/MSI in ACC. Loss of MMR protein expression is rare in ACC. MSI is infrequent even in patients with dMMR at immunohistochemistry. Germline variants in MMR genes (Lynch syndrome) are found in 4.5% of ACC and not always associated with dMMR/MSI. Different from other cancers, dMMR in ACC is not associated with histopathological and clinical characteristics or prognosis, including response to immunotherapy.

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RC3.7

Factors that influence pheochromocytoma penetrance in MEN2A Syndrome

Sofia-Maria Lider-Burciulescu [1,2], Monica Livia Gheorghiu[1,3], Andrei Muresan[3], Stanescu Laura-Semonia[1,3], Anda Dumitrașcu[3] & Corin Badiu[1,3]
[1]Carol Davila University of Medicine and Pharmacy, București, Romania; [2]"Ana Aslan" National Institute of Geriatrics and Gerontology, Endocrinology, Bucharest, Romania; [3]C.I. Parhon National Institute of Endocrinology, București, Romania

Introduction
It is known that phaeochromocytoma penetrance in MEN2A syndrome steadily increases with age. In general, MEN2A related pheochromocytomas (PHEOs) have a benign evolution; however, some of them have an aggressive behaviour despite the same genetic background as the benign forms.
Aim
To evaluate potential factors that may influence PHEO penetrance and tumor dimensions (age at diagnosis, MTC aggressiveness or genetic status).
Material and Methods
Patients with PHEOs in MEN2A syndrome were retrospectively retrieved from the database of a Tertiary Reference Centre from Romania. Genetic status, age at diagnosis, tumor dimensions, localisation, and the presence of other syndromic components were collected.
Results
Twenty-two patients from fifteen families were included in this study. Fourteen patients (63.6%) were women and 8 (36.4%) were men. Mean age for diagnosis was 36.6±2.8 years. Mean tumour diameter was 46.4±3.5 mm. Eighteen patients (12 families) had a pathogenic variant of exon 11 [p.Cys634Trp (55.5%), p.Cys634Arg/Tyr (22.2%/16.6%); p.Asp631Tyr (5.5%)] while 4 (3 families) of them had a pathogenic variant (PV) of exon 10 [p.Cys618Arg (75%), and p.Cys618Tyr (25%)]. Mean age in families with exon 11 was lower (35.6±2.9 years) than in exon 10 (41±9.2 years). Mean tumor diameter was non-significantly higher in exon 11 PV than in exon 10 (48±4 vs 38±5.8). In 3 patients PHEO was the first manifestation of the syndrome all with PV of exon 11, while in 4 CMT was the first manifestation of the disease. In other 15 patients CMT and PHEO were simultaneously diagnosed. Patients with exon 10 had a more aggressive form of CMT than those with exon 11. Regarding PHEO localisation, 31.8% ($n=7$) were right sided, 27.3% ($n=6$) were left sided, and 40.9% ($n=9$) presented bilateral PHEOs, four synchronous and five metachronous. Patients with bilateral disease tended to have a familial lateralisation pattern. Regarding tumor natural evolution, maximal tumor diameter did not correlate to age of diagnosis in any of the families.
Conclusion
Exon 11 mutation is the most frequently reported in MEN2A related PHEOs. p.Cys634Trp is the most pathogenic variant of exon 11, while in exon 10 was p.Cys618Arg. Patients with mutation in exon 11 tended to develop PHEOs in younger age than those with mutation in exon 10, and to have more rapidly evolving tumors. MTC was more aggressive in patients with exon 10 mutations. PHEOs in MEN2A tended to have a familial lateralisation pattern.

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Rapid Communications 4: Diabetes, Obesity, Metabolism and Nutrition | Part I

RC4.1

Baseline hormonal profiling and post-surgical outcomes in patients with obesity undergoing bariatric surgery: Results from the novara experience

Edoardo Luigi Maria Mollero[1], Chiara Mele[1], Maria Teresa Samà[1], Flavia Prodam[1,2], Marina Caputo[1,2], Martina Romanisio[1], Edda Cava[2], Sergio Riso[3], Gianluca Aimaretti[1] & Paolo Marzullo[1]
[1]SCDU Endocrinologia, University of Eastern Piedmont, Department of Translational Medicine, Novara, Italy; [2]University of Eastern Piedmont, Department of Health Sciences, Novara, Italy; [3]Dietetica e Nutrizione Clinica, AOU Maggiore della Carità, Novara, Italy

Purpose
Obesity is a chronic disease with a high risk of cardiovascular and metabolic comorbidities, hence a decrease > 5-10% of the initial body weight (BW) is essential to achieve improvement of cardiometabolic dysfunction. Bariatric surgery currently represents a valid therapeutic option in this clinical setting, especially in patients unresponsive to a dietary-nutritional approach. Obesity instigates adaptive hormone changes, yet the role of baseline hormone setting on postsurgical outcomes in terms of excess weight loss (%EWL) and post-nadir weight regain (%PNWR) remains unclear and warrants investigation.
Methods
Out of 202 patients with morbid obesity candidate to bariatric surgery enrolled between January 2017- December 2022, 79 patients (M/F: 16/63; age: 47.3±1.2 years; BMI: 44.2±0.5 kg/m^2) eventually admitted to sleeve gastrectomy ($n=72$) or gastric bypass ($n=7$) after multidisciplinary assessment were retrospectively analyzed for clinical, and biochemical data at baseline and after 6, 12 and 24 months since surgery. Baseline hormone assessment included TSH, 24 h urinary free cortisol (UFC) IGF-I and prolactin levels.
Results
As expected, bariatric surgery caused a progressive reduction in BW, with nadir BW being reached after 12 months (ΔBMI -29±0.9%; %EWL, 70.3±2.9%) and 77% of patients achieving a %EWL ≥50%, regardless of the surgical technique. Surgical treatment resulted in remission of hypertension and type 2 diabetes mellitus in 62.5% and 64% of patients, respectively. Patients who did not go into complete remission achieved an improvement in disease that required a reduction in therapy. The glycolipid profile of the patients showed statistically significant differences at 12 months following surgery. At baseline, no abnormalities in hormone levels were observed. The influence of hormone setting on patients' response in terms of %EWL ≥ 50% and %PNWR was null. Likewise, we failed to record associations between UFC, IGF-I or prolactin levels and post-surgical changes in BW or waist, although TSH was associated with 6-mo changes in BW ($r=$−0.74, $P<0.05$) after controlling for age and gender. Alternatively, there were correlations between %EWL and baseline BMI (r−0.39, $P<0.001$), %PNWR (r0.22, $P=0.05$), and age (r−0.20, $P=0.03$). The inverse correlation between baseline BMI and %EWL was confirmed by stepwise multivariate regression analysis (β=−0.45, $P=0.002$).
Conclusion
Bariatric surgery is an effective tool in inducing weight loss in adults with obesity and its effectiveness relates inversely to initial BMI. Baseline hormones play no role on postsurgical outcomes except for TSH, which potentially hints at the influence of the thyrostat on individual responsiveness to this weight-reducing approach.

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RC4.2

Dysregulation of RNA-Exosome machinery in MASLD-HCC progression

Víctor J. Fernández-Ramírez[1,2,3,4], Samanta Lozano de la Haba[1,2,3,4], María Isabel Pozo-Relaño[1,2,3,4], Rafael J. Nieto-Santiago [1,2,3,4], Natalia Hermán-Sánchez[1,2,3,4], Prudencio Sáez-Martínez[1,2,3,4], Manuel Rodriguez-Peralvarez[1,4,5], Raúl M. Luque[1,2,3,4], Juan Luis López-Cánovas[1,2,3,4] & Manuel D. Gahete[1,2,3,4]
[1]Maimonides Institute for Biomedical Research of Cordoba (IMIBIC), Cordoba, Spain; [2]University of Cordoba, Department of Cell Biology, Physiology and Immunology, Cordoba, Spain; [3]Reina Sofía University Hospital, Cordoba, Spain; [4]Reina Sofía University Hospital, Department of Hepatology and Liver Transplantation, Cordoba, Spain; [5]CIBER Hepatic and Digestive Diseases (CIBERehd), Cordoba, Spain

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common cause of chronic liver disease and is the leading cause of liver-related morbidity and mortality. MASLD is rapidly becoming a major aetiology for the development of hepatocellular carcinoma (HCC), the most common liver cancer. As the incidence of MASLD continues to rise, it is crucial to understand the molecular alterations that lead to HCC. Previous studies have revealed a significant alteration of the mechanisms controlling RNA processing and metabolism in MASLD-related HCC. However, the implication of the RNA-Exosome machinery, which is crucial for RNA processing, degradation, and quality control, is still to be fully defined. This work aims to elucidate the alteration of the RNA–Exosome components in MASLD and MASLD-related HCC, and its correlation with clinical parameters, in order to identify early biomarkers and new therapeutic opportunities. Therefore, we analyzed in silico the mRNA and/or protein expression levels of RNA-Exosome components in MASLD, MASLD-related HCC, Metabolic Dysfunction Associated Steatohepatitis (MASH), HCC and control (healthy and/or non-tumor) samples from fourteen cohorts: two retrospectives ($n=94$ and $n=62$ respectively) and twelve in silico (Zhou, GSE63067, Roessler 2, Mas, GSE135251, Wurmbach, TGCA, GSE147304, GSE167523 GSE185051, Arendt and Pinyol). Different bioinformatics approaches were performed, using software such as R, MetaboAnalyst, Gene Set Enrichment Analysis (GSEA) and Single-sample GSEA (ssGSEA). The results revealed a heterogeneous pattern of dysregulation in gene/protein expression of most of the RNA-Exosome components, with percentages of altered elements ranging from 7,7% (retrospective cohort) to 76,7% (Zhou cohort). The most consistently altered elements in MASLD cohorts were EXOSC10, ZFC3H1, PABPN1, EXOSC8, EXOSC4 and EXOSC9; standing out PABPN1, EXOSC4 and ZFC3H1, as they were also the most dysregulated genes in HCC patients. Expression of these components was associated with the enrichment in oncogenic traits (e.g., DNA repair pathway and expression of MYC targets), smggesting important clinical implications. In conclusion, analysis of gene expression dysregulation patterns in RNA-Exosome elements reveal a strong dysregulation in MASLD and MASLD-related HCC samples, which were associated with clinical parameters and with the dysregulation of oncogenic pathways.

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RC4.3

Irrespective of diet composition, cycles of low-calorie intake imprint a unique hepatic signature throughout the secretome to influence organismal energy balance

Juan Luis López-Cánovas[1], Beatriz Naranjo-Martinez[1] & Alberto DIaz-Ruiz[1,2]
[1]IMDEA Food Institute/Instituto IMDEA Alimentación, Madrid, Spain; [2]CIBER Pathophysiology of Obesity and Nutrition (CIBERobn)

Identifying effective strategies and underneath molecular signatures is crucial to combat certain metabolic diseases with increasing incidence such as obesity and MASLD (metabolic dysfunction-associated steatotic liver disease). The hepatic secretome plays a crucial role at controlling global energy metabolism and inflammation in MASLD. However, the interplay between diet composition and the eating architecture on the dynamic response of secretome as a tool to improve disease outcomes remains unknown. Under these conditions, we aim to elucidate the influence of the hepatic secretome on the energetic homeostasis as a potential therapeutic mechanism in metabolic diseases. To this end, male C57BL/6 mice (1 year old) were subjected to 5 months of 4:10 feeding cycles [4 days of very low-calorie intake (VLCI) followed by 10 days of ad libitum feeding] under Standard (SD) and high-fat diet (HFD) feeding regime. Liver RNAseq was performed, and the modulation of secretome genes was studied by associating their expression with physiological data, mouse parameters, and biological energy homeostasis. VLCI effectively reduces body weight and fat mass, improving physical performance and glucose regulation. Hepatic RNAseq identified a total of 1607 secretome genes. A Heatmap and PCA analysis significantly distinguished the secretome profile between VLCI and ad libitum (AL) mice, under SD and HFD feeding regime. Subsequently, a Volcano Plot analysis between VLCI and AL mice, identified a molecular signature of 269 and 135 differentially expressed secretome genes [$FC>1.2$, $P<0.05$] induced by VLCI under Standard and high-fat diets, respectively, of which, a VLCI-specific signature of 46 genes were over-expressed and down-expressed identically in both SD and HFD. Moreover, a Gene Ontology analysis revealed specific metabolic pathways (cholesterol metabolism, regulation of kinase activity, etc.) related with VLCI intervention, independently of diet composition (SD or HFD). Finally, the VLCI-imprinted signature correlated with energy balance signals in the liver and plasma, including insulin, mTOR pathway, or beta-hydroxybutyrate. In summary, this study not only upholds the effectiveness of fasting-based strategies to enhance physiological health but also identifies a strong and dynamic modulation of the secretome, identifying VLCI-specific signature independent of diet composition. Therefore, our data smggest that secretome modulation could have a therapeutic impact on metabolic diseases involving energy balance dysregulation.

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RC4.4

The beta-2-adrenoreceptor agonist fenoterol increases resting enery expenditure without activation of brown adipose tissue in humans

Laila Füchtbauer[1], Jaël Senn[1], Carole Baumann[1], Anninja Isenrich[1], Laura Ehlen[2], Marceline Fuh[2], Jörg Heeren[2] & Matthias Betz[1]
[1]University Hospital Basel and University of Basel, Department of Endocrinology, Diabetes and Metabolism, Basel; [2]University Medical Center Hamburg-Eppendorf, Center for Experimental Medicine, Department of Biochemistry and Molecular Cell Biology, Hamburg, Germany

Brown adipose tissue (BAT) may directly dissipate energy into heat and is associated with a metabolically favorable phenotype. Cold exposure activates BAT via the sympathetic nervous system and its transmitter norepinephrine. In rodents, the activation is facilitated by the β3-adrenoreceptor (β3-AR). In humans treatment with the β3-AR agonist mirabegon leads to a rather weak activation of BAT as compared to a cold stimulus. In vitro studies in cell lines from human BAT and have pointed towards the β2-AR as a possible activator. We studied the effect of an infusion with the potent and selective β2-AR agonist fenoterol on human resting energy expenditure (REE) and BAT activity compared to a mild cold stimulus in normal weight volunteers. REE was measured continously with indirect calorimetry, skin and core temperature were recorded, and BAT activity was quantified in the supraclavicular BAT depot by 18F-FDG-PET/CT after each intervention. Blood was sampled for metabolic analysis. Resting EE at baseline was similar before the two interventions. Cold exposure resulted in a mean increase in EE of 195 kcal/24 h ($P=0.044$ vs baseline) and fenoterol infusion increased EE by 358 kcal/24 h ($P<0.0001$). The mean standardized uptake value (SUVmean) of supraclavicular BAT was 3,06 (IQR 2,19;3,64) g/ml after cold exposure but only 1,66 g/ml [1,63;1,70] after fenoterol infusion. Correspondingly, the active BAT volume was 90 (26;190) ml vs 3 (1;16) ml, respectively. Analysis of the lipidome revealed higher levels of mono- and poly-unsaturated fatty acids after both interventions, which was stronger after fenoterol than after cold exposure ($P<0.0001$). In contrast, in all other lipid categories, fenoterol failed to replicate the pattern, which a cold stimulus induces in the lipidome. The main side effect of fenoterol was a feeling of warmth and a mild tachycardia. In conclusion fenoterol increased REE more than cold exposure but did not activate human BAT. This indicates that the human β2-AR does not play an important role in BAT activation which is underscored by differential lipid profiles after both interventions. However, β2-AR mediated increases in REE might be an attractive therapeutic target to treat obesity.

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RC4.5

Precision medicine in type 2 diabetes mellitus: Unraveling the role of TCF7L2, CTRB1/2, and GLP-1R genetic variants in response to treatment with glucagon-like peptide-1 receptor agonists

Artemis Kyriakidou[1], Angeliki Kyriazou[1], Theocharis Koufakis[2], Yiannis Vasilopoulos[3], Iakovos Avramidis[4], Stefanos Baltagiannis[5], Dimitrios Goulis[6], Pantelis Zebekakis[1] & Kalliopi Kotsa[1]
[1]AHEPA University Hospital, Division of Endocrinology and Metabolism - Diabetes Center, 1st Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Hippokration General Hospital, 2nd Propedeutic Department of Internal Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; [3]University of Patras, Department of Biology, Section of Genetics, Cell Biology and Development, Patras, Greece; [4]G. Papanikolaou General Hospital, Diabetes Center, Department of Internal Medicine, Thessaloniki, Greece; [5]General Hospital of Kastoria, Diabetes Outpatient Clinic, Kastoria, Greece; [6]Medical School, Aristotle University of Thessaloniki, Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Thessaloniki, Greece

Background and Aims
Our objective was to assess the association between genetic polymorphisms in *TCF7L2*, *CTRB1/2* and *GLP-1R* genes and inter-individual variability in response to treatment with glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in terms of glycemic control and weight loss among Greek individuals with type 2 diabetes mellitus (T2DM) and to identify potential predictors of response to GLP-1 RA therapy.
Materials and Methods
Patients ($n=191$) treated with either liraglutide, exenatide, or lixisenatide for at least 6 months were enrolled in the study. Genotyping of *TCF7L2* rs7903146 (C>T), *CTRB1/2* rs7202877 (T>G) and *GLP-1R* rs367543060 (C>T) variants was conducted, using real-time PCR, while clinical and laboratory assessments were performed at baseline, 3- and 6-months post-treatment. Glycemic responders were defined as patients meeting one of the following criteria: i) HbA_{1c} <7% at 3 or 6 months after GLP-1 RA initiation, ii) reduction of baseline HbA_{1c} by ≥1% after 3 or 6 months of therapy, and iii) maintenance of HbA_{1c}<7% that a patient had before switching to GLP-1 RA, after 3 or 6 months of treatment. Weight loss responders were defined as individuals who achieved weight reduction ≥3% from their baseline weight after 3 or 6 months of GLP-1 RA administration.
Results
The minor allele frequencies for *TCF7L2* rs7903146, *CTRB1/2* rs7202877 and *GLP-1R* rs367543060 genetic polymorphisms were 79.1, 15.7 and 0%, respectively. 136 (71%) individuals were classified as glycemic responders and 125 (65%) as weight loss responders. Carriers of at least one rs7903146 "T" allele and rs7202877 "G" allele demonstrated a comparable glycemic control and weight loss response to GLP-1 RAs with the respective homozygous wild-type genotypes [odds ratio (OR): 1.08, 95% confidence interval (CI): 0.5, 2.31, $P=0.85$ and OR: 1.35, 95% CI: 0.66, 2.76, $P=0.42$; OR: 1.4, 95% CI: 0.56, 3.47, $P=0.47$ and OR: 1.28, 95% CI: 0.55, 2.98, $P=0.57$, respectively). Weight and BMI decreased in both glycemic responders ($P<0.0001$) and non-responders ($P<0.0001$) after 6 months of treatment. Weight loss responders and non-responders exhibited a significant reduction in fasting glucose ($P=0.003$ and $P=0.0004$, respectively) and HbA_{1c} at 6 months ($P<0.0001$). Female sex (OR: 0.5, 95%, CI: 0.26, 0.94, $P=0.03$) and lower baseline weight (OR: 0.97, 95%, CI: 0.95, 0.99, $P=0.024$) were associated with improved glycemic and weight loss response to GLP-1 RA administration, respectively.
Conclusion
Our findings do not indicate a role of the studied variants in predicting response to treatment with GLP-1 RAs in Greek patients with T2DM.

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Rapid Communications 5: Pituitary and Neuroendocrinology | Part I

RC5.1

Clinical use of 18F-fluoro-ethyl-tyrosine PET co-registered with MRI for diagnostic dilemmas in prolactinoma

Victoria van Trigt[1], Leontine Bakker[1], Ling Lu[2], Iris Pelsma[1], Marco Verstegen[3], Wouter van Furth[3], Lenka Pereira Arias-Bouda[2] & Nienke Biermasz[1]
[1]Leiden University Medical Center, Department of Medicine, Division of Endocrinology, Leiden, Netherlands; [2]Leiden University Medical Center, Department of Radiology, Section of Nuclear Medicine, Leiden, Netherlands; [3]Leiden University Medical Center, Department of Neurosurgery, Leiden, Netherlands

Purpose
To assess the utility of (^{18}F)fluoroethyl-L-tyrosine PET co-registered with magnetic resonance imaging (FET-PET/MRI^{CR}) in patients with difficult-to-localize prolactinoma to inform clinical decision making and treatment planning.
Methods
Retrospective cohort study of 17 consecutive patients with difficult-to-localize prolactinoma undergoing FET-PET/MRICR between October 2020 and Amgust 2022 for either (1) additional information in case of difficult remnants after transsphenoidal surgery (TSS) or pharmacological treatment, or (2) diagnosis in absence of a (clear) adenoma on conventional MRI at diagnosis or after treatment.
Results
FET-PET/MRI^{CR} identified a lesion in 14/17 patients, yet failed to identify active lesions in 2 patients with negative conventional MRI but prolactin >7.5 times upper limit of normal. FET-PET/MRI^{CR} results were inconclusive in 1 patient due to diffuse tracer uptake 10 weeks post-surgery. Foci on FET-PET/MRI^{CR} corresponded completely with the lesion on conventional MRI in 10 patients, partially in 3 patients, and new foci were identified in 4 patients. Functional imaging influenced clinical decision making in 15/17 patients: 7 patients underwent TSS after functional imaging, and 8 patients did not. One patient underwent surgery despite negative FET-PET/MRI^{CR} due to a high need for alternative treatment, and 1 patient underwent additional diagnostics due to inconclusive FET-PET/MRI^{CR} results. FET-PET/MRI^{CR} results were confirmed in all patients undergoing surgery: intraoperatively by identification of adenoma tissue in 5/8 patients, by positive histopathology in 6/8 patients, and by significant decrease in prolactin postoperatively in 7/8 patients. The surgical goal was achieved in 7/8 patients.
Conclusion
FET-PET/MRI^{CR} can be of added value in the preoperative decision-making process for selected patients with difficult to localize prolactinoma (remnants), or patients lacking a substrate on conventional MRI.

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RC5.2

Lanreotide in patients with a 68Ga-DOTATATE PET-positive, clinically non-functioning pituitary macroadenoma (GALANT study): A randomised, double-blind, placebo-controlled trial

Tessel M. Boertien[1], M.L. Drent[2], Jan Booij[3], Charles B.L.M. Majoie[3], Marcel P.M. Stokkel[4], Jantien Hoogmoed[5], Alberto M. Pereira[1,6], Nienke Biermasz[6], Suat Simsek[7], Ronald Groote Veldman[8], Annick J. Weterings[1], Juan M. Vink[1], Michael W.T. . Tanck[9], Eric Fliers[1] & Peter H. Bisschop[1]
[1]Amsterdam UMC location AMC, Endocrinology and Metabolism, Amsterdam, Netherlands; [2]Amsterdam UMC location VUMC, Endocrinology and Metabolism, Amsterdam, Netherlands; [3]Amsterdam UMC location AMC, Radiology and Nuclear Medicine, Amsterdam, Netherlands; [4]Netherlands Cancer Institute, Nuclear Medicine, Amsterdam, Netherlands; [5]Amsterdam UMC location AMC, Neurosurgery, Amsterdam, Netherlands; [6]Leiden University Medical Centre (LUMC), Endocrinology, Leiden, Netherlands; [7]Northwest Clinics location Alkmaar, Internal Medicine, Alkmaar, Netherlands; [8]Medical Spectrum Twente, Internal Medicine, Enschede, Netherlands; [9]Amsterdam UMC location AMC, Epidemiology and Data Science, Amsterdam, Netherlands

Background
Patients with non-functioning pituitary macroadenoma (NFMA) currently have no established medical treatment options. Somatostatin analogues may decrease tumour size, but randomised controlled trials are lacking. In vivo somatostatin receptor assessment with ^{68}Ga-DOTATATE PET could help in selecting patients for treatment. We aimed to determine the effect of the somatostatin analogue lanreotide on tumour size in patients with a ^{68}Ga-DOTATATE PET-positive NFMA.
Methods
The GALANT study was an investigator-initiated, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial performed in the Netherlands and funded by Ipsen Farmaceutica BV (EudraCT 2015-001234-22; NTR NL5136). We included adult patients with a suprasellar extending NFMA (≥10 mm), either surgery-naïve or postoperative remnant. Important exclusion criteria were previous sellar radiotherapy and use of dopamine receptor agonists. Somatostatin receptor expression in the NFMA was determined by ^{68}Ga-DOTATATE PET/CT, co-registered with pituitary MRI. A predefined sample of 44 patients with PET-positive NFMA were randomly assigned (1:1) to lanreotide 120 mg or placebo subcutaneous injections every 28 days for 72 weeks. The primary outcome was change from baseline in cranio-caudal tumour diameter in the intention-to-treat population. Participants, investigators and outcome assessors were masked to treatment allocation.

Results
49 patients were included in order to randomise 44 PET-positive patients between lanreotide ($n=22$) and placebo ($n=22$). Study treatment was completed in 13 (59%) lanreotide and 19 (86%) placebo participants; outcome data were available for all participants. The mean (SD) change in cranio-caudal tumour diameter was +1.2 (2.5) mm with lanreotide and +1.3 (1.5) mm with placebo; ANCOVA adjusted mean difference vs placebo –0.1 mm (95% CI –1.3 to 1.2, $P=0.93$). Sensitivity analyses corroborated the main results. Treatment discontinuation due to tumour progression occurred in three lanreotide and three placebo participants. Four participants in the lanreotide group withdrew due to adverse events and two due to other reasons. Adverse events occurred in 22 (100%) lanreotide and 21 (95%) placebo participants. Gastrointestinal complaints were most common, reported by 18 (82%) lanreotide and 8 (36%) placebo participants. There were no treatment-related serious adverse events.
Conclusion
Compared with placebo, lanreotide treatment did not reduce tumour size or growth of ^{68}Ga-DOTATATE PET-positive NFMA. The results of this first successfully completed double-blind and placebo-controlled intervention trial in NFMA patients do not support the use of somatostatin analogues in these patients.

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RC5.3

Hypogonadotropic hypogonadism in patients with non-functioning pituitary adenomas before and after transsphenoidal surgery – A prospective study

Victor Hantelius[1,2], Gudmundur Johannsson[1,2], Tobias Hallen[3,4], Thomas Skoglund[3,4] & Oskar Ragnarsson[1,2]
[1]Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Department of Internal Medicine and Clinical Nutrition, Gothenburg, Sweden; [2]Sahlgrenska University Hospital, Department of Medicine, Gothenburg, Sweden; [3]Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Department of Clinical Neuroscience, Gothenburg, Sweden; [4]Sahlgrenska University Hospital, Department of Neurosurgery, Gothenburg, Sweden

Background
Hypopituitarism is common in patients with pituitary tumors. Still, the influence of pituitary tumor surgery on gonadal function and reproductive health remains underexplored.
Objective
a) To assess gonadal function and its impact on quality of life (QoL) in patients with non-functioning pituitary adenomas (NFPA) before and after transsphenoidal surgery (TSS), b) to identify factors that predict recovery of gonadal function following TSS, and c) to investigate sex-specific disparities related to hypogonadotropic hypogonadism (HH).
Methods
From September 2015 to December 2021, 122 patients with NFPA planned for TSS were evaluated. Health related QoL was assessed with two questionnaires, EQ-5D and The Psychological General Well-Being (PGWB) Index.
Results
Before surgery, 74 (61%) of 122 patients had HH. Of 49 women, 24 (49%) had preoperative HH, of whom 9 (38%) had recovered 12 months after TSS. Similarly, 50 (68%) of 73 men had preoperative HH of whom four (8%) recovered. Of 48 patients without preoperative HH, 16 (33%) developed it postoperatively. Of 49 women, 13 (27%) were of reproductive age (<50 years). Eight of these 13 (62%) had preoperative HH, of whom 5 (63%) recovered postoperatively and regained regular menstrual cycles. In contrast, 10 out of 13 (77%) men <50 years of age had preoperative HH, of whom only one (8%) recovered. After 12 months following TSS, the mean EQ-5D-index for the whole cohort ($n=122$) increased from 0.86 (interquartile range (IQR): 0.77–0.96) to 0.90 (IQR: 0.85–0.98) ($P<0.001$) and their PGWB-index from 94 (IQR: 80–112) to 104 (IQR: 93–119) ($P<0.001$). There was no difference in QoL between patients with and without HH, neither before nor after surgery. In the group of 76 with postoperative HH the mean EQ-5D-index increased from 0.86 (IQR: 0.76–0.96) to 0.89 (IQR: 0.82–0.96) ($P=0.011$) and the PGWB-index increased from 96 (IQR: 84–113) to 103 (IQR: 90–119) ($P=0.003$). In a multivariable logistic regression analysis, male sex ($P=0.022$) and high BMI ($P=0.036$) were associated with postoperative HH, but central hypothyroidism, adrenal insufficiency and growth hormone deficiencies were not.
Conclusions
HH is common in both men and women with NFPA requiring surgical intervention. The recovery rate following TSS is higher in women than in men. The QoL improves for the whole group after surgery. Male sex and high BMI are predictors for persistent postoperative HH.

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RC5.4

A phase 1 clinical study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of AZP-3813, a novel, small peptide growth hormone receptor antagonist, in healthy subjects

Soraya Allas[1], Guillaume Ravel[1], Colm Farrell[2], Sophie Fillon[1], Taha Ould Rouis[1], Michael Culler[3], Michel Ovize[1], Mark Sumeray[3] & Aart Jan van der Lelij[4]
[1]Amolyt Pharma, Ecully, France; [2]ICON PLC, Reading, United Kingdom; [3]Amolyt Pharma, Cambridge, MA, United States; [4]Erasmus University Medical Center, Rotterdam, Netherlands

Background
Acromegaly is a rare disease typically caused by a benign growth hormone (GH)-secreting pituitary adenoma that stimulates over-production of insulin-like growth factor-1 (IGF1) from the liver. Treatment with somatostatin analog (SSA) monotherapy does not provide optimal control of circulating IGF-1 levels in the majority of patients. AZP-3813, a 16-amino acid, bicyclic GH receptor antagonist (GHRA) binds to the GH receptor and prevents endogenous GH from stimulating the production of IGF-1. In normal animals, AZP-3813 potently decreases circulating levels of IGF-1 and further suppressive effects are observed when combined with the SSA, octreotide. AZP-3813 is being developed as an add-on therapy for the treatment of acromegaly in patients insufficiently controlled with SSAs.
Aim
To evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of AZP-3813 in healthy subjects.
Methods
Randomized double-blind placebo-controlled single and multiple ascending dose studies (SAD and MAD, respectively) are being conducted. In the SAD study, 5 subjects received a single subcutaneous administration of 3 mg AZP-3813 or placebo (3:2) and 8 subjects received 10, 20, 40, 60, 90, 120 mg AZP-3813 or placebo (6:2). In the MAD study, 8 subjects received 10, 20, 40 mg AZP-3813 or placebo (6:2) QD for 14 consecutive days.
Results
Treatment was well tolerated in all subjects with no safety concerns. Cmax and AUC increased in a dose-proportional manner. The half-life of AZP-3813 was estimated to be 18-22 hours. In the SAD study, AZP-3813 induced a dose-related decrease in circulating IGF-1 levels at doses of 10 mg and above with a more prolonged reduction up to 72 hours at higher doses. In the MAD study, AZP-3813 induced a gradual and sustained dose-related decrease in circulating IGF-1 levels at 20 and 40 mg/day, with a larger effect after 2 weeks of dosing as compared to single administration at the same dose, consistent with a cumulative effect of repeated administration. Mean placebo-adjusted % change from baseline for the 20 and 40 mg cohorts were 19% and 44%, respectively. This study is ongoing, and updates on additional MAD cohorts will be reported at the meeting.
Conclusion
These data clearly demonstrate that the novel GHRA, AZP-3813, substantially decreases circulating IGF-1 levels in healthy individuals, thereby supporting further testing in patients with acromegaly.

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RC5.5

CRH-stimulated oxytocin in patients with hypopituitarism and hypothalamic damage: A randomized, single-blind, crossover, placebo-controlled trial

Queralt Asla Roca[1,2,3], Maite Garrido Sánchez[4], Eulàlia Urgell Rull[2,5], Silvia Terzan Molina[5], Alicia Santos Vives[2,6], Mercè Fernández Miró[7], Nimmy Varghese[8,9], Cihan Atila[10,11], Anna Calabrese[12], Betina Biagetti[13], Mirjam Christ-Crain[10,11], Anne Eckert[8,9], Susan M Webb[2,6,14], Elizabeth A Lawson[15,16] & Ana Aulinas Maso[1,2,3,6]
[1]Hospital de la Santa Creu i Sant Pau, Endocrinology and Nutrition, Barcelona, Spain; [2]Institut de Recerca - Hospital Santa Creu i Sant Pau, Barcelona, Spain; [3]University of Vic, Department of Medicine, Vic, Spain; [4]Institut de Recerca Sant Pau (IR-SANTPAU), CIM, Barcelona, Spain; [5]Hospital de la Santa Creu i Sant Pau, Biochemistry, Barcelona, Spain; [6]ISCIII, Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBER-ER, Unit 747), Majadahonda, Spain; [7]Hospital Dos de Maig, Endocrinology and Nutrition, Barcelona, Spain; [8]Universität Basel,

Research Cluster Molecular and Cognitive Neurosciences, Basel, Switzerland; [9]University Psychiatric Clinics Basel, Neurobiology Lab for Brain Aging and Mental Health, Basel, Switzerland, [10]Universitätsspital Basel, Endocrinology, Diabetology and Metabolism, Basel, Switzerland, [11]Universität Basel, Department of Clinical Research, Basel, Switzerland, [12]University of Turin, Internal Medicine, Department of Clinical and Biological Sciences, S. Luigi Hospital, Torino, Italy, [13]Vall d'Hebron University Hospital, Endocrinology and Nutrition, Barcelona, Spain, [14]Universitat Autònoma de Barcelona, Department of Medicine, Bellaterra, Spain, [15]Massachusetts General Hospital, Neuroendocrine Unit, Boston, United States, [16]Harvard Medical School, Department of Medicine, Boston, United States

Introduction
Disruption of the hypothalamic/pituitary axes may lead to hypopituitarism. Anterior pituitary deficiencies (APD) and arginine-vasopressin deficiency (AVP-D) are well established and are treated with hormone replacement. Over the last decade, preliminary studies support the presence of an oxytocin (OXT)-deficient state that might be clinically relevant in patients with hypopituitarism and hypothalamic damage (HHD). Therefore, identifying a provocative test to diagnose an OXT deficiency will be important. The corticotropin-releasing hormone (CRH) – commonly used for the differential diagnosis of ACTH-dependent Cushing's syndrome – is a promising candidate for such a test as it increases peripheral OXT secretion in animal models. This study aimed at examining the effects of CRH on endogenous OXT release in patients with HHD compared to healthy controls (HC). We hypothesized that OXT release after CRH would be lower in patients with HHD compared to HC.
Methods
This single-blind, randomized, placebo-controlled proof-of-concept study (NCT 04902235) with crossover assignment (CRH:placebo) was conducted at an academic medical center. Nineteen patients with HHD (10 females) and 20 HC (11 females) completed two main visits. We randomly assigned participants to receive either CRH (1.0 µg/kg) or placebo (0.9% normal saline) in the first visit. After a washout of $\geq$48 h participants received the alternative treatment. Fasting AM samples were collected over 120 minutes (T0, T15, T30, T45, T60, T90, T120) to assess OXT levels. The primary outcome was the change in OXT levels over time in response to CRH vs placebo in patients with HHD and HC. We used three-way ANOVA (factors treatment*participant*time) to evaluate the effects of CRH on OXT levels.
Results
Participants were balanced by age (median (IQR) 50.3 (22.8) years) and body mass index (27.5(5.6) kg/m^2). HHD had more depression symptoms, alexithymia and impulsivity (all $P<0.05$), as well as worse quality of life ($P<0.001$) and sexual function ($P<0.025$) compared to HC; 80% of patients with HHD presented with $\geq$3 APD and 75% had AVP-D. Baseline OXT concentrations were similar across groups ($P=0.822$). CRH administration did not impact OXT levels across groups over time, three-way interaction was not significant ($P=0.524$). No significant differences in OXT levels overtime were observed in the subgroup of patients with HHD and AVP-D compared to those without AVP-D.
Conclusion
The response of OXT after CRH administration does not seem sufficient for CRH to be pursued as a provocative test to diagnose an OXT-deficient state in HHD. The identification of a safe and feasible provocative test is required.

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RC5.6

Etiology, treatment, and outcomes of sellar metastases: A single-center institutional experience

Julia Breu, Yining Zhao, Michael Buchfelder & Natalia Kremenevski
Friedrich-Alexander-Universität Erlangen-Nürnberg, Neurosurgery, Erlangen, Germany

Background
Metastases to the sellar region are extremely rare tumours in surgical series. The reported incidence has recently increased with advances in neuroimaging. Survival of patients with metastatic cancer has improved due to progress in oncologic therapies and diagnostics. Patients with sellar metastases (SM) follow a variable disease course that is not well defined.
Objective
The objective was to evaluate the clinical characteristics, surgical approaches, and survival outcomes of SM diagnosed and treated at our institution.
Methods
56 patients (29/51·8% women and 27/48·2% men) with histologically confirmed SM were identified between the years 1982 and 2022. Their data were retrospectively collected and analyzed.
Results
Breast cancer in women (23·2%) and renal cell cancer in men (14·3%) were the most common primary malignancies. The median age at diagnosis of SM was 64·8 years (range 19·8-83·7). Patients presented with visual deficits (92·3% [36/39]), cranial nerve palsies (50·0% [28/56]), and headaches (23·2% [13/56]). Diabetes insipidus was noted in four patients (7%). The mean tumor volume was 9·4$\pm$10·8 cm^3 (median 6·0 cm^3 [range 0·04-52·9]). In 13 patients (23·2%), SM were found before the diagnosis of the primary cancer. These were all cases of lung cancer. The mean time in months from primary cancer diagnosis to SM was 96·7$\pm$61·5 for breast, 99·5$\pm$50·4 for renal cell, 37·0$\pm$31·1 for gastrointestinal, and 46·0$\pm$14·1 for prostate cancer. SM occurred intra- and parasellar (8, 14%), supra- (17, 30%), and intra- and suprasellar (21, 38%). In most cases, surgery was performed through a transsphenoidal approach (58·8%) and the transcranial approach was used in 17 cases (30·4%). Seven patients (12·5%) underwent other procedures. Gross total resection was achieved in only 5 patients (9%). 35 patients (62·5%) received adjuvant radiotherapy. One year after surgery, 26 of 53 patients (49·1%) were alive, 19 (35·8%) were alive after two years, and only one (1·9%) was alive after five years. The mean duration of follow-up in months was 23·4$\pm$39·5 (median 9·6 [range 0·3-265·5]).
Conclusions
The diagnosis of SM has always been delayed. Lung cancer patients are most at risk for sellar metastasis at primary tumor diagnosis. The overall survival of patients diagnosed with SM is poor. The extent of the resection of the SM does not affect survival. Surgery is effective for mass reduction and rapid symptomatic improvement of vision and headache. In some cases, it provides a definitive diagnosis of the primary tumor.

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RC5.7

Changes of hepatic metabolism and lipidomic profile with biochemical improvement of acromegaly

Paul Fellinger[1], Lorenz Pfleger[2], Hannes Beiglboeck[1], Clemens Baumgartner[1], Nara Marella[3], Alexander Micko[4], Stefan Wolfsberger[4], Greisa Vila[1], Anton Lmger[1], Alexandra Kautzky-Willer[1], Martin Krssak[1,2], Thomas Scherer[1], Peter Wolf[1], Michael Krebs[1] & Yvonne Winhofer[1]
[1]Medical University of Vienna, Endocrinology and Metabolism, Wien, Austria; [2]Medical University of Vienna, Biomedical Imaging and Image-Guided Therapy, Hochfeld MR Zentrum (High Field MR Center), Wien, Austria; [3]CeMM Forschungszentrum für Molekulare Medizin GmbH, Wien, Austria; [4]Medical University of Graz, Neurosurgery, Graz, Austria

Overview
Despite marked insulin resistance, patients with active acromegaly have low hepatocellular lipid content (IHL) and an unfavourable hepatic lipid composition (UI). As previously shown, inadequate mitochondrial activity in the liver might counteract lipid accumulation in the liver. The purpose of this study was to understand changes in hepatic metabolism, and lipidomic profile with therapy of acromegaly.
Methods
We prospectively included thirteen subjects (5 female; age: 48.3$\pm$12.7 years) with active acromegaly, which was diagnosed by elevated serum IGF-1 concentrations and lack of GH level suppression ($>$1 ng/ml) after ingestion of 75 mg glucose during a standardized two-hour oral glucose tolerance test (OGTT). For further metabolic characterization, participants underwent 31P/1H-7T-MR-spectroscopy of the liver, an OGTT, as well as plasma metabolomic and lipidomic profiling at baseline and twelve months after inclusion.
Results
As expected IGF-I decreased in all patients after therapy with 7 out of 11 patients reaching biochemical control, defined as IGF-1 below age and sex specific upper limit of normal (IGF-I-ULN) of 120% (IGF-I ULN: before 296.1$\pm$119.7%; after 115.3$\pm$52.4%; $P=<0.001$). Two patients were lost to follow up after twelve months. Insulin resistance, measured with HOMA-IR decreased significantly (median difference -20; $P<0.01$). IHL increased (median difference: 0.92%; $P=0.016$), whereas UI decreased significantly after twelve months (median difference -3.6%; $P=0.016$). The hepatic mitochondrial ATP synthase activity parameter relative to the IHL content also decreased significantly after twelve months. The lipid classes of ceramides, sphingomyelins, as well as lysophosphatidylcholines decreased significantly, whereas alkyl-phosphatidyl-ethanolamines increased significantly with improvement of acromegaly.

Conclusion

This study shows that with biochemical improvement of acromegaly, lipid composition as well hepatic mitochondrial activity changes significantly and might therefore indicate a causal relation between growth hormone (GH) excess and hepatic lipid accumulation. Furthermore, a reduction in lipid classes, like ceramides and sphingomyelins, which are associated with insulin resistance gives a more detailed insight into mechanisms of insulin resistance associated with acromegaly. In conclusion, this study offers valuable insight into direct antisteatotic pathways of GH as well as the direct effects of GH on the metabolomic profile.

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RC5.8

Outcomes of transsphenoidal surgery for producing pituitary adenomas in spain

Miguel Paja Fano[1], Felicia Hanzu[2], Mª Angeles Gálvez[3], Rocío Villar[4], Dolores Moure[5], Edelmiro Menéndez[6], Laura González-Fernández[7], Nerea Egaña[8], Rosa Cámara[9], David Peñalver[10], Andreu Simó[11], Diego Asensio-Wandosell[12], Carmen Tenorio[13], Cristina Novo[13], María Calatayud[14], Antonio Pico[15], Johana Sottile[15], Gonzalo Díaz-Soto[16], David Peñalver[17], Marta Araujo-Castro[18], Alfonso Soto[19], Pedro De Pablos[20], Anna Aulinas[21], Fernando Muñoz[22] & Betina Biagetti[23]
[1]Basurto University Hospital, Endocrinology, Spain; [2]Hospital Clinic Barcelona, Endocrinology; [3]Hospital Reina Sofía, Endocrinology; [4]Complejo Hospitalario Universitario de Santiago, Endocrinology; [5]Hospital Universitario de Cruces, Endocrinology; [6]Hospital Universitario Central de Asturias, Endocrinology; [7]Hospital Gregorio Marañón, Endocrinology; [8]Hospital Universitario Donostia, Endocrinology; [9]Hospital Universitari i Politècnic la Fe, Endocrinology, [10]Hospital Universitario Río Hortega, Endocrinology, [11]Hospital Universitario Mutua de Terrassa, Endocrinology, [12]Hospital German Trías i Pujol Badalona, Endocrinology, [13]Hospital Universitario Virgen de las Nieves, Endocrinology, [14]Hospital 12 de Octubre, Endocrinology, [15]Hospital General Universitario de Alicante, Endocrinology, [16]Hospital Clínico Universitario de Valladolid, Endocrinology, [17]Hospital Universitario Río Hortega Valladolid, Endocrinology, [18]Hospital Universitario Ramon y Cajal, Endocrinology, [19]Hospital Virgen del Rocío, Endocrinology, [20]Hospital Universitario Doctor Negrín, Endocrinology, [21]Hospital Sant Pau, Endocrinology, [22]Hospital Sant Pau - Hospital del Mar, Neurosurgery, [23]Hospital Universitario Vall de Hebron, Endocrinology

In our country, as in others, there is a lack of data on the success rate of transsphenoidal surgery for producing pituitary adenomas. We evaluated the results reported in TESSPAIN, a retrospective multicenter nationwide project that includes all the TSS performed in the participating centers in the period between 2018 and 2022, both included. Surgical treatment success is defined according to the published criteria for each disease: normal IGF-1 and GH after 75 g of oral glucose less than 0.4 ng/ml for GH-producing adenomas; adrenal insufficiency for Cushinǵs disease (CD); serum prolactin less than 10 ng/ml for prolactinomas; and resolution of hyperthyroidism for TSH-producing adenomas. We evaluated the global success rate in each center, its correlation with the volume of surgeries and with the number of neurosurgeons performing the surgeries, and the relative success rate including only adenomas retrospectively deemed as curable by an expert endocrinologist in each center, I.e. excluding those with unresectable invasion (Knosp 3b or 4). A total of 911 patients were enrolled in the study: 436 patients with acromegaly, 323 patients with CD, 127 patients with prolactinomas, and 25 TSH-producing adenomas. Overall, the rate of successful surgery was 58.5% for GH-producing adenomas (255/425), which increased to 85.0% when only those considered potentially curable were included (255/370). The surgical success rate for CD was 71.5% (231/323), increasing to 74.8% when only surgically resectable adenomas were included (231/309). The cure rates for PRL-secreting adenomas were 39.4% (50/127) and 76.9% (50 of 65 surgically resectable adenomas), and for TSH-secreting adenomas were 88% (22/25) and 92% (22 of 23 surgically resectable adenomas). The success rate did not correlate with surgical volume, although it showed a positive trend for GH-secreting adenomas (p: 0.43). Although the overall surgical success rate showed no statistically significant differences between centers with a dedicated neurosurgeon and centers with more than one neurosurgeon, the mean surgical success rates were not significantly higher in acromegaly (60.4 ± 11.0 vs 52.1 ± 26.1; *P*: 0.24) and Cushing's disease (74.8 ± 18.6 vs 55.5 ± 34.3; *P*: 0.06). We show the results of TSS for producing pituitary adenomas in our country, with success rates similar to those reported in other countries. We note the high success rate in TSH-secreting adenomas, which probably reflects the earlier actual diagnosis, before the tumor develops invasiveness, and the trend towards better results in centers with a dedicated neurosurgeon, probably not significant because of the low volume of surgeries.

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Rapid Communications 6: Thyroid | Part I

RC6.1

Age-specific reference intervals for TSH and FT4 to optimize diagnosis of thyroid disease

Heleen Jansen[1,2,3], Niek Dirks[2,4,5], Jacquelien Hillebrand[2,3], Edwin Ten Boekel[5], Jacoline Brinkman[6], Madelon Buijs[4], Ayse Demir[7], Ineke Dijkstra[8], Silvia Endenburg[9], Paula Engbers[10], Jeannette Gootjes[4], Marcel Janssen[11], Stephan Kamphuis[12], Wilhelmina Kniest-de Jong[13], Adrian Kruit[14], Etienne Michielsen[15], Albert Wolthuis[16], A.S. Paul van Trotsenburg[3,17], Martin den Heijer[3,18], Eveline Bruinstroop[3,19], Anita Boelen[2,3,20], Annemieke C Heijboer[1,2,3,20] & Wendy den Elzen[21,22]
[1]Amsterdam UMC location Vrije Universiteit Amsterdam, Department of Laboratory Medicine, Endocrine Laboratory, Amsterdam, Netherlands; [2]Amsterdam UMC location University of Amsterdam, Department of Laboratory Medicine, Endocrine Laboratory, Amsterdam, Netherlands; [3]Amsterdam Gastroenterology, Endocrinology and Metabolism, Amsterdam, Netherlands; [4]Atalmedial Diagnostic Centers, Amsterdam, Amsterdam, Netherlands; [5]Northwest Clinics, Alkmaar, Department of Clinical Chemistry, Hematology & Immunology, Alkmaar, Netherlands; [6]St. Jansdal Hospital, Harderwijk, Department of Clinical Chemistry, Harderwijk, Netherlands; [7]Meander Medical Center, Amersfoort, Laboratory for Clinical Chemistry and Hematology, Amersfoort, Netherlands; [8]St Antonius Hospital, Nieuwegein, Department of Clinical Chemistry, Nieuwegein, Netherlands; [9]Dicoon, Gelderse Vallei Hospital, Ede, Department of Clinical Chemistry and Hematology, Ede, Netherlands, [10]Treant Zorggroep, Hoogeveen, Department of Clinical Chemistry, Hoogeveen, Netherlands, [11]VieCuri Medical Center, Venlo, Laboratory of Clinical Chemistry and Hematology, Venlo, Netherlands, [12]Eurofins Clinical Diagnostics, Eurofins Gelre, Apeldoorn, Netherlands, [13]Saltro Diagnostic Center, Unilabs Netherlands, Utrecht, Netherlands, [14]Nij Smellinghe Hospital, Drachten, Medical Laboratory, Drachten, Netherlands, [15]Diagnostiek voor U, Eindhoven, Eindhoven, Netherlands, [16]Stichting Certe Medische Diagnostiek en Advies, Groningen, Groningen, Netherlands, [17]Emma Children's Hospital, Amsterdam UMC location University of Amsterdam, Department of Paediatric Endocrinology, Amsterdam, Netherlands, [18]Amsterdam UMC location Vrije Universiteit Amsterdam, Department of Endocrinology and Metabolism, Amsterdam, Netherlands, [19]Amsterdam UMC location University of Amsterdam, Department of Endocrinology and Metabolism, Amsterdam, Netherlands, [20]Amsterdam Reproduction & Development Research Institute, Amsterdam, Netherlands, [21]Amsterdam UMC location University of Amsterdam, Department of Laboratory Medicine, Laboratory Specialized Diagnostics & Research, Amsterdam, Netherlands, [22]Amsterdam Public Health, Amsterdam, Netherlands

Introduction

Thyroid disorders are generally diagnosed based on thyroid stimulating hormone (TSH) outside the reference interval (RI), and subsequent free thyroxine (FT4) concentrations. Most laboratories do not provide age-specific RIs for TSH and FT4 beyond childhood, although it is known that TSH concentrations vary with age which may be important to take into account. Therefore, we aimed to establish age-specific RIs for TSH and FT4 throughout life using an indirect method for four commonly used immunoassay platforms. Also, we determined whether using age-specific RIs would result in reclassification of thyroid disease diagnoses in adults.

Methods

Indirect RIs for TSH (TMC) and FT4 (RefineR) using four different immunoassay platforms (Roche, Abbott, Siemens, Beckman) were established using retrospective data from 13 Dutch laboratories (>7 million TSH and >2 million FT4 unique requests). RIs were evaluated per manufacturer. Age groups were established from 2 to 20 years by 2-year categories, followed by decade categories between 20 and 100 years.

Results

TSH upper reference limits (URLs) and FT4 lower reference limits (LRLs) were higher until the age of 10 to 12 years and decreased towards adulthood. The URLs of FT4 were stable with a dip during puberty. In adulthood, TSH URLs increased

from the age of 60 years onwards, and even from 50 years in women, while FT4 URLs increased from 70 years onwards. The LRLs of TSH and FT4 remained stable during ageing. The use of our adult age-specific RIs resulted in a decrease in diagnoses of subclinical and overt hypothyroidism in women above 50 (15.7 to 7.3% and 2.7 to 2.3%, respectively), and in men above 60 years of age (13.7 to 8% and 2.0 to 1.6%, respectively) in our Roche dataset.
Conclusion
This study stressed the known importance of using age-specific RIs in children. In adulthood, age-specific reference intervals are currently not used in clinical practice. However, this study showed an important clinical relevance by reducing the diagnoses of subclinical hypothyroidism, and to a lesser extent, overt hypothyroidism. Therefore, implementation of adult TSH age-specific RIs in clinical practice should be strongly considered. Data is less uniform regarding FT4 age-specific RIs and more research should be performed before implementing these in clinical practice.

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RC6.2

Interpretation of TPOAb measurement in pregnancy: An individual participant data meta-analysis

Yindi Liu[1,2], Joris Osinga[1,2], group Consortium on Thyroid and Pregnancy working on TPOAb[3], Ulla Feldt-Rasmussen[4], Sofie Bliddal[4], Robin Peeters[1,2], Arash Derakhshan[1,2] & Tim Korevaar[1,2]
[1]Erasmus University Medical Center, Department of Internal Medicine, Rotterdam, Netherlands; [2]Erasmus University Medical Center, Academic Center for Thyroid Diseases, Rotterdam, Netherlands; [3]Multiple (see https://www.consortiumthyroidpregnancy.org); [4]Copenhagen University Hospital, Rigshospitalet, Department of Medical Endocrinology and Metabolism, Copenhagen, Denmark

Objective
Thyroid peroxidase antibody (TPOAb) positivity is the most important risk factor for overt/subclinical hypothyroidism and partly guides levothyroxine treatment indications during pregnancy. TPOAb positivity is usually defined by manufacturer cutoffs which are typically derived in non-pregnant populations with concentrations ≥95th percentile. Besides the general lack of assay uniformity, current TPOAb positivity cutoffs are likely to underestimate gestational thyroid autoimmunity due to immune tolerance of pregnancy. To improve the clinical interpretation of TPOAb measurement and cutoffs during pregnancy, we investigated the association of TPOAb concentrations and commonly used thresholds with maternal thyroid function during pregnancy.
Methods
This study was embedded in the Consortium on Thyroid and Pregnancy. Participants with multiple gestation, pre-existing thyroid diseases, thyroid (interfering) medication usage, or pregnancy by IVF/ICSI were excluded. We assessed the nonlinear association of TPOAb percentiles with SD-scores of thyroid stimulating hormone (TSH) and free thyroxine (FT4), which indicated an effect threshold between the 80th-85th percentile. With ≤80th percentile as the reference group, we assessed the association of each consequent TPOAb percentile with maternal thyroid function, the risk of TSH 2.5-4.0 mU/l, and the risk of TSH >4.0 mU/l.
Results
The final study population comprised individual-participant data of 69,713 pregnant women from 24 cohorts. For TPOAb concentrations from the 89th percentile and upwards there was a higher TSH (effect estimates, range +0.13 SD to +1.05 SD), and from the 91st percentile and upwards there was a lower FT4 (effect estimates, range -0.08 SD to -0.49 SD). Pregnant women with TPOAb concentrations ≥89th percentile had a statistically significant higher risk of TSH 2.5-4.0 mU/l (range ORs: 1.40 for the 89th percentile to 5.96 for the 100th percentile) and a higher risk of TSH >4.0 mU/l (range ORs: 1.92 for the 89th percentile to 38.46 for the 100th percentile). The associations of TPOAb percentiles with TSH and FT4 SD-scores were stronger during early pregnancy than during late pregnancy, fitting with patterns of hCG stimulation and immune tolerance (P for interaction <0.001 for TSH and <0.001 for FT4).
Conclusion
We show that TPOAb concentrations below the manufacturer cutoffs may already reflect clinically relevant thyroid autoimmunity during pregnancy. High normal TPOAb concentrations could be interpreted differently in pregnant women, especially for those in whom the TPOAb status could (partly) define a treatment indication.

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RC6.3

Maternal thyroglobulin and thyroid function during pregnancy and offspring neurodevelopment

Tessa Mulder[1], Mònica Guxens[2], Sarah Bath[3], Mariana Dineva[3], Amaia Irizar Loibide[4], Nerea Lertxundi[4], Maria Luisa Rebagliato Ruso[5], Henning Tiemeier[1,6], Robin Peeters[1] & Tim Korevaar[1]
[1]Erasmus University Medical Center, Rotterdam, Netherlands; [2]ISGlobal, Barcelona, Spain; [3]University Of Surrey, United Kingdom; [4]Biodonostia Health Research Institute, San Sebastian, Spain; [5]Jaume I University, Castelló de la Plana, Spain; [6]Harvard T.H. Chan School of Public Health, Boston, United States

Background
Low maternal urinary iodine concentration (UIC) during pregnancy has been associated with lower child IQ and differences in brain morphology. However, UIC is highly variable as it is a reflection of 24-h urinary intake rather than long-term iodine status. Thyroglobulin (Tg) might be a more sensitive biomarker of the long-term maternal iodine status.
Aim
To study whether maternal Tg is associated with maternal and newborn thyroid hormone concentrations, offspring IQ and brain morphology and if these associations differ by UIC.
Methods
We selected participants from two population-based prospective cohorts: Generation R (the Netherlands) and INfancia y Medio Ambiente (INMA; Spain) with available measurements of maternal Tg and thyroid function at 13 weeks of gestation (n=4,438 women) or at birth (n=2,082 mother-child pairs), early childhood IQ (n=2,984; age 4.5 and 6 years) or late childhood IQ (n=2,569; age 9 and 13 years), and offspring brain morphology at 10 years (n=1,197). The associations of Tg with TSH and FT4 concentrations, IQ and brain MRI outcomes were studied with multivariable linear regression.
Results
Higher maternal Tg was associated with lower TSH (P<0.001), higher FT4 (P<0.001) and lower IQ in early childhood (-0.06 point per 1 ng/ml Tg, P=0.02). Tg was not associated with cord blood TSH or FT4, late childhood IQ or brain morphology. We found no clear evidence of effect modification by UIC.
Conclusions
Tg is associated with thyroid function during pregnancy and some markers of offspring neurodevelopment. However, further research should determine the added value of Tg in addition to UIC for defining iodine status.

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RC6.4

Local treatment improves outcome of RAI - Refractory differentiated thyroid carcinoma (DTC) patients irrespectively of tyrosine kinase inhibitors (TKI) treatment: a single center experience

Olga Karapanou[1], Kanella Kantreva[2], Stavroula A. Paschou[2], Marina Michalaki[3], Maria Alevizaki[2] & Katerina Saltiki[2]
[1]Endocrine Department, 401 General Military Hospital of Athens, Athens, Greece; [2]Endocrine Unit, Department of Clinical Therapeutics, National and Kapodistrian University, Athens, Greece; [3]Division of Endocrinology-Department of Internal Medicine, School of Health Sciences, University of Patras, Patras, Greece

Purpose
Although the majority of differentiated thyroid cancer (DTC) patients have favorable outcome, approximately up to 20% of them may develop metastatic and/or locoregional disease persistence. One-third of those patients may not respond to the treatment with radioiodine (RAI refractory DTC, RAI-R DTC). There are few reports of real-life experience concerning the clinical course and the treatment modalities that have been used in patients with RAI-R DTC.
Methods
We conducted a retrospective study focusing on the clinical characteristics at diagnosis, the location and time interval of the appearance of metastatic lesions and the characterization of RAI-refractory tumors, the treatment modalities performed (local therapies and/or systemic treatment), the response to therapy and the disease progression rate.
Results
Patients with radioiodine refractory thyroid cancer (RAI-R DTC, n=122, 44.3% men, age-at-diagnosis 51.98±15.8 years, were followed-up for 9.5 years (1.4-50). Patients ≥55 yrs at-diagnosis had more frequently follicular/oncocytic DTC, increased tumor size, metastatic disease and worse outcome (P=0.015) compared to younger. Patients were divided in two groups: those with only cervical persistence (Group 1), n=27 (22.1%), and those with distant

metastases (Group 2), $n=95$(87.9%). In Group1 29.6% underwent >2 surgeries, 14.8% cervical external beam radiation therapy (EBRT), one radiofrequency-ablation (RFA), one sorafenib. The final outcome was: partial response (PR) 4(14.8%), stable disease (SD) 23/27(85.2%). In Group2 40% underwent >2 locoregional surgeries, 28.4% EBRT, 6.3% RFA. For distant metastases 42.1% received local therapies, 47.4% TKIs. Metastases stabilization with local procedures was achieved in 33.7% (18/45 while receiving TKI). Group1 patients were younger, with smaller tumors, had more frequently classical PTC ($P=0.005$) and more favorable outcome ($P<0.001$). In Group2 *sorafenib* was administered in 30 patients (median PFS 1.5 yrs, OS 2.7 yrs), lenvatinib in 31 (median PFS 2 yrs, OS 3.581 yrs), cabozantinib in 7. Overall, for *patients with metastatic disease* the final outcome was: PR 7/95 (7.4%) SD 38 (40%) PD 50(52.6%), 34/95 (35.8%) died of disease progression, 7/95 (7.4%) died of unrelated causes; in Cox-proportional-hazard analysis, for the total follow-up period, when age-at-diagnosis, TKI administration, local therapies, local surgeries, soft-tissue invasion, tumor size and histology were included in the analysis, the age-at-diagnosis and the administration of local therapies were predictors of more favorable OS and CSS ($P<0.02$).

Conclusions

In RAI-R thyroid cancer patients with metastatic disease younger age at diagnosis and the implementation of local therapies are associated with a more favorable outcome

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RC6.5

Unusual manifestation of thyroid hormone receptor ß resistance

Dovile Denaite[1], Edward Visser[2] & Ruta Navardauskaite[1,3]
[1]Department of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Academic Center For Thyroid Disease, Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands; [3]Lithuanian University of Health Sciences, Medical Academy, Institute of Endocrinology, Coordinating center for rare and undiagnosed diseases Lithuanian University of Health Sciences hospital Kauno Klinikos, Kaunas, Lithuania

Introduction

Resistance to thyroid hormone beta (RTHβ) is a rare genetic disorder characterized by impaired responsiveness to thyroid hormone in tissues expressing TRβ. This case report explores the clinical manifestation of RTHβ in a 15-year-old male presenting with acute and intensive chest pain and subsequent diagnostic challenges.

Case Report

At midnight, a 15-year-old male reported acute, sharp chest pain, prompting medical attention. Elevated troponin I levels initially raised concerns about myocardial infarction, but electrocardiogram and echocardiography excluded it. The patient is the third child in the family, denied chronic illnesses, and reported regular physical activity in the swimming pool. Family history revealed an older brother's sudden cardiac death at 29 during cycling. Physical examination revealed an asthenic constitution (BMI: 16.2 kg/m^2, -2.18 SD), palpable goiter I grade, and a heart rate of 113 bpm. Holter monitoring detected 365 ventricular extrasystoles and normal arteries were determined in coronography on 1st day of investigation. A cardiac MRI excluded myocarditis on 4th investigation day. Troponin I peaked at 102.95 µg/l, decreasing to 0.09 µg/l (N <0.04). Creatine kinase MB and Lactate dehydrogenase were elevated but eventually stabilized. Coagulation parameters, including D-dimer levels, remained within normal limits. Hormonal investigation revealed elevated concentrations of circulating free thyroxine (fT4 33.99 pmol/l (N 10–19)) and free triiodothyronine (fT3 8.65 pmol/l (N 4.7–7.2)) in the presence of no suppressed thyroid stimulating hormone (TSH 2.05 mU/l (N 0.48–4.7)). Autoantibodies (TgAb, TRAb, TPOAb) were negative; catecholamines were normal. The coronary spasm and myocardial infarction with non-obstructive coronary arteries (MINOCA) related to thyrotoxicosis were considered. Methimazole 10 mg daily was initiated, which led to an increase in TSH with persistently elevated FT4 and FT3 levels A diagnosis of TSHoma was considered but brain MRI showed a normal pituitary gland. Next, RTHβ was suspected, and genetic testing (Rotterdam Thyroid Centre), revealed a known R320C mutation in the thyroid hormone receptor ß gene. The treatment with thyrostatics was stopped after confirmed RTHβ. The beta-blocker is used due to tachycardia up to now.

Conclusion

This case underscores the challenges in diagnosing thyroid hormone receptor resistance, emphasizing the importance of accessibility of genetic testing and a multidisciplinary approach for comprehensive patient care.

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Rapid Communications 7: Endocrine-related Cancer

RC7.1

PRAP study - Partial versus radical adrenalectomy for hereditary pheochromocytomas

Kai Xu[1], Johannes Langenhuijsen[2], Charlotte Vietor[3], Richard Feelders[4], Tessa van Ginhoven[3], Yasir Elhassan[5], Fabio Bioletto[6], Mirko Parasiliticaprino[6], Wouter Zandee[7], Schelto Kruijff[8], Tobias Åkerström[9], Christina Pamporaki[10], Nicole Bechmann[10], Charlotte Lussey-Lepoutre[11], Letizia Canu[12], Rebecca Steenaard[13], Natacha Driessens[14], Marieke Velema[15], Koen Dreijerink[16], Anton Engelsman[17], Henri Timmers[1] & Marieke de Laat[1]
[1]Radboud University Medical Center, Department of Internal Medicine, Division of Endocrinology, Nijmegen, Netherlands; [2]Radboud University Medical Center, Department of Urology, Nijmegen, Netherlands; [3]Erasmus MC, Department of Surgical Oncology and Gastrointestinal Surgery, Rotterdam, Netherlands; [4]Erasmus MC, Department of Internal Medicine, Division of Endocrinology, Rotterdam, Netherlands; [5]University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, United Kingdom; [6]University of Turin - Campus Luigi Einaudi, Department of Medical Sciences, Division of Endocrinology, Diabetes and Metabolism, Torino, Italy; [7]University Medical Center Groningen, Department of Internal Medicine, Division of Endocrinology, Groningen, Netherlands; [8]University Medical Center Groningen, Department of Surgery, Groningen, Netherlands; [9]Uppsala universitet Inst f kirurgiska vetenskaper, Department of Surgical Sciences, Uppsala, Sweden, [10]University Hospital Carl Gustav Carus Dresden, Department of Internal Medicine III, Dresden, Germany, [11]Faculty of Medicine Pierre et Marie Curie, nuclear medicine department, Paris, France, [12]University of Florence, Department of Experimental and Clinical Biomedical Sciences, Endocrinology Unit, Firenze, Italy, [13]Máxima Medisch Centrum, Department of Internal Medicine, Division of Endocrinology, Veldhoven, Netherlands, [14]Hospital Erasme, Department of Endocrinology, Bruxelles, Belgium, [15]Slingeland Hospital, Department of Internal Medicine, Division of Endocrinology, Doetinchem, Netherlands, [16]VU University Medical Center, Department of Internal Medicine, Section of Endocrinology, Amsterdam, Netherlands, [17]VU University Medical Center, Department of Surgery, Amsterdam, Netherlands

Introduction

Pheochromocytoma, a rare catecholamine-secreting adrenal tumor, can cause hypertension and life-threatening complications. Hereditary cases have an increased risk of developing bilateral disease. Standard treatment involves radical adrenalectomy, leading to adrenal insufficiency in bilateral cases. Partial adrenalectomy aims to preserve adrenal function but has higher recurrence rates. This study compares outcomes of partial vs radical adrenalectomy in hereditary pheochromocytoma, focusing on cases with initial unilateral disease.

Methods

Standard treatment involves radical adrenalectomy, leading to adrenal insufficiency in bilateral cases. Patients were categorized by initial disease presentation and type of surgery. Patients were categorized by initial presentation and surgery type. Outcomes included contra- and ipsilateral recurrence, adrenocortical insufficiency, metastasis, and disease-specific survival.

Results

256 patients with hereditary pheochromocytoma were included of which 108 (42%) with *RET*, 67 (26%) NF1, 62 (24%) VHL, 11 (5%) *TMEM127* and 8 (3%) *MAX* mutations. There were 191 (75%) patients that initially presented with unilateral tumors. Radical adrenalectomy was performed in 223 patients (87%), in 75 of whom bilaterally. A partial adrenalectomy was performed in 33 (13%). Median follow-up was 100 months. In 191 patients who presented with unilateral pheochromocytomas, 50 (26%) developed contralateral tumors, at a median follow-up time of 56 months. Incidence of metachronous contralateral disease was highest in *VHL*, *RET* and *MAX* mutations. Ipsilateral recurrence was low, 6% in the partial group and 3% in the radical group ($P=0.47$). In patients who developped contralateral pheochromocytoma, partial adrenalectomy as first intervention resulted in 3/4 (75%) adrenal insufficiency compared to 1/7 (14%) when the second adrenalectomy was partial ($P = 0.09$). Overall, 153 (60%) patients underwent unilateral surgery and 103 (40%) bilateral (synchronously or metachronous). Among 103 patients with bilateral adrenalectomies, adrenal insufficiency risk was 13/28 (46%) in partial cases and 75/75 (100%) in radical cases ($P < 0.001$). Recurrence rate was 5/28 (18%) for cases with partial adrenalectomy vs 7/75 (9%) those with radical operation ($P = 0.30$). In survival analysis time till ipsilateral recurrence was significantly shorter in the partial group ($P=0.035$). Metastasis and disease-specific survival did not differ between groups.

Conclusion

In hereditary pheochromocytoma, partial adrenalectomy offers lower rates of adrenal insufficiency compared to radical surgery, with slightly higher recurrence rate for the partial adrenalectomy. Risk of metastasis and disease-specific survival was similar between groups. In patients with metachronous bilateral disease,

preserving adrenal function possibly more succesful when partial adrenalectomy was performed as the second intervention.

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RC7.2

The presence of abortive changes in thyroid tumors serves as a strong indicator of underlying DICER1 mutations

Vincenzo Condello[1], James Roberts[2], Adam Stenman[3], Catharina Larsson[1], Kartik Viswanathan[4] & Christofer Juhlin[1]

[1]Karolinska Institutet, Department of Oncology-Pathology, Stockholm, Sweden; [2]Children's Healthcare of Atlanta, Department of Pathology and Laboratory Medicine, Atlanta, United States; [3]Karolinska University Hospital, Department of Breast, Endocrine Tumors and Sarcoma, Stockholm, Sweden; [4]Emory University School of Medicine, Pathology and Laboratory Medicine, Atlanta, United States

Background

Somatic and bi-allelic DICER1 mutations have been reported in subsets of sporadic thyroid tumors, affirming a clear involvement of this gene in the development of thyroid tumors. As a recent study has highlighted associations between *DICER1* mutations and macrofollicular patterns, abortive changes, and papillary structures, we aimed to investigate these observations in a bi-institutional cohort.

Methods

A total of 61 thyroid lesions (54 tumors and 7 cases of thyroid follicular nodular disease; TFND), including 26 *DICER1* mutated cases and 35 *DICER1* wildtype controls underwent histological re-investigation and clinical follow-up.

Results

DICER1 mutated cases showed a statistically significant association with younger age at surgery (29.2 ± 12.5 vs 51.3 ± 18.8, $P = 0.0001$), a predominant macrofollicular growth pattern (20/26 mutated cases vs 18/35 wildtype; $P = 0.01$) and abortive changes (20/26 mutated cases vs 2/35 wildtype; $P = 0.0001$). Similar results were obtained when excluding TFND cases. We also present clinical and histological triaging criteria for *DICER1* sequencing of somatic tissues, which led to the identification of *DICER1* variants in 16 out of 26 cases (62%) when followed. In cases with available germline data ($n = 12$), 3 cases (25%) were found to carry germline *DICER1* mutations. This observation smggests that the majority of *DICER1* variants are somatic – however, it implies that sequencing of constitutional tissues could be clinically motivated.

Conclusion

We conclude that *DICER1* mutations are amassed in younger patients with macrofollicular-patterned tumors and, most strikingly, abortive changes. Considering the rate of germline involvement, our findings hold potential clinical value, allowing the pathologist to triage cases for genetic testing based on histological findings.

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RC7.3

Activating the intratumoral IFNγR-pathway in adrenocortical carcinoma potently enhances antitumor functionality of CAR-T cells by modulating immune cell adhesion and responsiveness

Marc Philipp Schauer[1,2], Laura-Sophie Landwehr[1], Justus Weber[2], Barbara Altieri[1], Silviu Sbiera[1], Matthias Kroiss[1,3,4], Martin Fassnacht[1,4] & Michael Hudecek[2]

[1]University Hospital Würzburg, Department of Internal Medicine I, Division of Endocrinology & Diabetes, Germany; [2]University Hospital Würzburg, Department of Internal Medicine II, Chair for Cellular Immunotherapy, Germany; [3]LMU Hospital Munich, Department of Internal Medicine IV, Division of Endocrinology & Diabetes, Germany; [4]Comprehensive Cancer Center Mainfranken, University of Würzburg, Germany

Background

Adrenocortical carcinoma (ACC) is a rare and aggressive endocrine disease in which 60% of patients show endogenous glucocorticoid (GC) secretion that potentially contributes to a lack of immune cell infiltration and limited efficacy of immunotherapeutic approaches. In another study, we already demonstrated potent antitumor efficacy or ROR1 CAR-T cells in preclinical models of ACC. Nevertheless, solid tumors often show cell intrinsic resistance mechanisms to CAR-T cell cytotoxicity which recently could be attributed to a lack of IFNγR-signalling and immunogenic pathway activation. Here, we report of a new potent small molecule inhibitor* (SMI) that is able to modulate innate antitumor immune-response pathways and potently enhances CAR-T cell functionality by activating the IFNγR-pathway in ACC.

Methods

We evaluated target gene expression in 62 ACC patients at mRNA and protein level. We evaluated efficacy of our SMI in five ACC cell lines and activation of immunogenic proinflammatory tumor signalling pathways using RNA Nanostring nCounter analysis, qRT-PCR and Western Blot. Cytokine secretion was measured by Enzyme-linked Immunosorbent Assay (ELISA). We evaluated antitumour functionality alone and in combination with several CAR-T cell modifications using different preclinical models of ACC.

Results

We show significantly higher expression of our required target gene in five ACC cell lines and ACC tissues when compared to normal adrenal glands (0.073 vs 0.713; $P = 0.004$). Moreover, target expression strongly correlates with glucocorticoid secretion and other clinicopathological parameters including Ki67, Weiss-score and survival supporting its potential utility as biomarker in ACC. The SMI shows potent antitumor functionality alone (NCI-H295R: IC50 195 nM, respectively) by reshaping cell autonomous and immune-stimulating activity in ACC cell lines. We demonstrate strong intratumoral upregulation of PD-L1 (11.5-fold change; $P = 0.003$) and IDO1 (17-fold change; $P = 0.033$) as well as strong secretion of immunogenic upstream signals and a significant increase of IFNγR expression (2.9-fold change, $P = 0.019$) in all five ACC cell lines after co-culture for 48 hours (NCI-H295R cells shown respectively). Consistent with these findings, after selectively activating the IFNγR-pathway when combined with the SMI, we show enhanced immune cell adhesion and responsiveness of different CAR-T cell modifications in ACC upon antigen contact in preclinical models using subtherapeutic effector-to-target-ratios.

Conclusion

Our results illustrate an enhanced immunotherapeutic approach using the combination of a new potent SMI and CAR-T cells by activating immunogenic intratumoral signalling and the IFNγR pathway in adrenocortical carcinoma.

*The small molecule inhibitor will be kept confidential for patent law reasons

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RC7.4

Decrease in anticortisolic drmg osilodrostat plasma exposure in patients treated with mitotane for adrenocortical carcinoma

Louis Thomeret[1], Alicja Puszkiel[2], David Balakirouchenane[2], Lucas Bouys[1,3], Jonathan Poirier[3], Annabel Berthon[1], Bruno Ragazzon[1], Anne Jouinot[1], Laurence Guignat[3], Laura Bessiene[3], Rossella Libe[3], Léopoldine Bricaire[3], Marie-Clémence Leguy[4], Jean Guibourdenche[4], Lionel Groussin-Rouiller[1,3], Guillaume Assie[1,3], Benoît Blanchet[2], Jérôme Bertherat[1,3] & Fidéline Bonnet-Serrano[1,4]

[1]Institut Cochin, INSERM U1016 - CNRS UMR8104, Université Paris-Cité, Team "Genomics and signaling of Endocrine Tumors", PARIS, France; [2]Hôpital Cochin, Assistance Publique - Hôpitaux de Paris, Department of Pharmacokinetics and Pharmacochemistry, PARIS, France; [3]Hôpital Cochin, Assistance Publique - Hôpitaux de Paris, Endocrinology department, PARIS, France; [4]Hôpital Cochin, Assistance Publique - Hôpitaux de Paris, Hormonology department, PARIS, France

Introduction

The steroidogenesis inhibitor osilodrostat (OSI), indicated for the medical treatment of endogenous Cushing's syndrome, exhibits significant interindividual variability regarding the response to treatment (*Pivonello et al*., 2020), *a fortiori* in the context of adrenocortical carcinoma (Tabarin et al., 2022). Plasma exposure may contribute to this variability. Our objective was to investigate the effect of concomitant use of mitotane (MITO), a potent inducer of CYP450 (3A4), on

circulating OSI concentrations in patients treated for an adrenocortical carcinoma (ACC).
Materials and Methods
Plasma OSI concentrations were determined every 4 hours over 24 hours (sampling at 8 h, 12 h, 16 h, 20 h, 24 h and 4 h) by LC-MS/MS (*Balakirouchenane et al*., 2023) in 29 patients treated for different etiologies of endogenous Cushing's syndrome: Cushing's disease ($n=19$), ectopic Cushing's syndrome ($n=4$), primary bilateral macronodular adrenal disease ($n=3$) and adrenocortical carcinoma ($n=3$). Twenty-seven patients were treated with OSI as a monotherapy ("OSI" group, 33 cycles) and 3 patients were treated ith OSI in association with MITO ("OSI-MITO" group, 8 cycles) for an ACC. OSI was administered twice daily in all patients. Daily doses of OSI and plasma MITO concentrations were expressed as median [min-max].
Results
Even after a long period of treatment (> 6 months), high fluctuations of OSI concentrations were observed along the day (median CV = 55%). The area under the OSI concentration curve (AUC-OSI) was thus used as pharmacokinetic endpoint. The AUC-OSI was well correlated with the daily dose of osilodrostat in both the "OSI" group (Spearman *r*0.84; OSI 10 [2-40] mg/day) and the "OSI-MITO" group (Spearman *r*0.85; OSI 60 [20-60] mg/day; plasma MITO concentration 14.1 [0.5-26.6] mg/l). However, the slope of the linear regression line was lower in "OSI-MITO" group. The AUC-OSI based on the daily dose was also statistically decreased in the "OSI-MITO" group compared to the "OSI" group (medians: 11.92 vs 26.81 ng/ml.h; $P<0.001$).
Discussion
Mitotane significantly decreases plasma exposure to Osilodrostat in patients treated for a cortisol-secreting ACC. This is likely explained by the induction of CYP450 by Mitotane and should be taken in account to adjust the Osilodrostat dose in patients treated with Mitotane.
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RC7.5

Fibroblast-mediated modulation of GI-NETs: Implications for drmg response and tumor invasion
Eleonora Malavasi, Lara Toffoli, Marilyn Dainotto, Angeliki Ditsiou & Teresa Gagliano
University of Udine, Department of Medicine (DMED), Udine, Italy

Introduction
The intricate interplay between fibroblasts and cancer cells significantly contributes to cancer invasion, extracellular matrix (ECM) modulation, and the development of drmg resistance. This study delves into understanding the specific influence of fibroblasts on Gastro-Intestinal neuroendocrine tumor (GI-NET) cell lines.
Materials and Methods
Utilizing GOT1 and COLO320 cell lines, we incorporated Normal Human Dermal Fibroblasts (NF) in our investigation. Lipophilic tracers were employed in 3D co-culture to distinguish between cell types. FAK (BI-0319) and SYK (BI1002494) kinase inhibitors, previously identified as antiproliferative on GI-NET cells, were administered. Elisa assays were conducted to quantify protein secretion levels.
Materials and Methods
The study employed the GI-NET cell lines GOT1 and COLO320, alongside Normal Human Dermal Fibroblasts (NF). A 2D invasion assay was conducted using cell inserts, followed by crystal violet staining for visualization. Cell viability assessment in 3D cultures utilized the cell-titer glow method, with fluorescent lipophilic tracers distinguishing between cell types in 3D co-culture. FAK (BI-0319) and SYK (BI1002494) kinase inhibitors, recognized for their antiproliferative effects on GI-NETs cells, were administered as drmg treatment. Protein secretion levels were quantified using Elisa.
Results
In 3D culture, fibroblasts demonstrated a partial impact on the response to FAK and SYK inhibition. In 2D invasion assay, fibroblasts strongly stimulated cancer cell invasion, yet this effect was effectively counteracted by treatment with FAK (BI-0319) and SYK (BI1002494) inhibitors. Notably, fibroblasts were observed to diminish the secretion of TIMP2, a protein recognized for its anti-invasive propertie, preventing excessive extracellular matrix (ECM) degradation and hindering tumor cell migration.
Conclusion
Although fibroblast influence on cancer cells invasion and ECM remodeling is substantial, inhibiting the focal adhesion pathway was shown to partially counteract these effects. This dual role of fibroblasts, both influencing and being influenced by FAK and SYK inhibition, underscores the complexity of their interactions in the context of cancer invasion and highlights the potential therapeutic significance of targeting these pathways.
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RC7.6

The expression and prognostic value of somatostatin and glucagon-like peptide 1 receptors in insulinoma
Elina Peltola[1,2,3], Tiina Vesterinen[4,5], Helena Leijon[4], Päivi Hannula[1,6], Heini Huhtala[7], Markus Mäkinen[8], Lasse Nieminen[9], Elina Pirinen[10], Mikko Rönty[4], Mirva Söderström[11], Johanna Arola[4] & Pia Jaatinen[1,3,12], and the Finnish Insulinoma Study Group .[13]
[1]Tampere University, Faculty of Medicine and Health Technology, Tampere, Finland; [2]Fimlab laboratories, Department of Clinical Chemistry, Tampere, Finland; [3]Department of Internal Medicine, Tampere University Hospital, Tampere, Finland; [4]HUS Diagnostic Center, HUSLAB, Department of Pathology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; [5]Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; [6]Endocrinology, Department of Internal Medicine, Tampere University Hospital, Tampere, Finland; [7]Tampere University, Faculty of Social Sciences, Tampere, Finland; [8]Department of Pathology, Research Unit of Translational Medicine, Oulu University Hospital, University of Oulu, Oulu, Finland; [9]Fimlab Laboratories, Pathology Department, Tampere University Hospital, Tampere, Finland, [10]Department of Clinical Pathology, Kuopio University Hospital, Kuopio, Finland, [11]Department of Pathology, Turku University Hospital, Turku, Finland, [12]Division of Internal Medicine, Seinäjoki Central Hospital, Seinäjoki, Finland, [13], Finland

Insulinomas are rare insulin-producing pancreatic neuroendocrine tumours. Most insulinomas are non-metastatic and can be cured by surgery, but in 10% of the patients insulinomas metastasize, which is associated with a significantly impaired overall survival. As the metastatic potential of an insulinoma cannot be reliably predicted with the current biomarkers, we aimed to evaluate the expression of somatostatin receptors (SSTRs) and glucagon-like peptide-1 receptors (GLP-1Rs) in insulinomas and to analyse their association with clinicopathological features and long-term patient outcome[1,2]. The study material included formalin-fixed paraffin-embedded primary tumour tissue samples of 52 insulinoma patients diagnosed in Finland 1980–2010. Of these patients, 47 had a sporadic, non-metastatic insulinoma, 3 had a sporadic, metastatic insulinoma and 2 patients had a MEN1-syndrome-related, non-metastatic insulinoma. The median duration of the register-based follow-up was 10 (0–32) years after surgery. After histological re-evaluation, the samples were processed into tissue microarrays (TMA) and stained immunohistochemically with monoclonal SSTR1-5 and GLP-1R antibodies. The scoring was made manually and the immunoreactivity of the strongest stained TMA spot was scored based on membranous staining for GLP-1Rs and on both membranous and cytoplasmic staining for SSTRs. Of the somatostatin receptors, SSTR2 was expressed most frequently (71%), followed by SSTR3 (33%), SSTR1 (27%) and SSTR5 (6%). SSTR3 expression was associated with a larger tumour size, and SSTR3 and SSTR5 expression were associated with impaired overall survival. The expression of GLP-1Rs differed significantly between metastatic and non-metastatic insulinomas, as all sporadic, non-metastatic insulinomas expressed GLP-1R, while all metastatic insulinomas lacked the expression of GLP-1R. Of the two non-metastatic, MEN1-related insulinomas, one expressed GLP-1R and the other did not. In conclusion, the lack of GLP-1R expression is associated with a metastatic disease and impaired survival. Our results indicate that the lack of GLP-1R expression could be used as a negative prognostic marker in insulinomas but additional studies investigating a higher number of metastatic insulinomas are needed. Regarding SSTRs, most insulinomas were found to express SSTR subtype 2, which may be utilized in SSTR-targeted imaging and treatment, but further studies are needed to clarify the association between SSTR expression profile and overall survival.
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Rapid Communications 8: Thyroid | Part II

RC8.1

The role of preexisting diabetes mellitus on the risk for aggressive thyroid cancers

Rodis Paparodis[1,2,3], Dimitra Bantouna[2], Sarantis Livadas[4,5], Nicholas Angelopoulos[2,6], Ioannis Androulakis[2,7], George Simeakis[2,8], Dimitra Zianni[2,5], Ilias Perogamvros[9], Anastasios Boniakos[2,5], Andreas Rizoulis[2,10], Juan Carlos Jaume[1], Evaggelos Karvounis[2,11], Aikaterini Kapezanou[11] & Dimitrios Askitis[2,12]
[1]Loyola Medical Center:, Endcrinology, Diabetes and Metabolism, Maywood, United States; [2]Hellenic Endocrine Network, Athens, Greece; [3]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Patra; [4], Athens, Greece; [5]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Athens, Greece; [6]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Kavala, Greece; [7]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Chania, Greece; [8]401 General Military Hospital of Athens, Endocrine Dept - Thyroid Cancer Outpatient's Clinic, Athens, Greece; [9]University of Manchester, Manchester, United Kingdom, [10]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Larisa, Greece, [11]Euroclinic Hospital, Center of Excellence in Endocrine Surgery, Athens, Greece, [12]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Alexandroupolis, Greece

Introduction
Multiple cancers have been described more commonly in patients with diabetes, and some exhibit increased aggressiveness of the tumor as well. This association has been debated with regard to thyroid cancer. With this work, we aim to clarify whether type 2 diabetes (DM2) or autoimmunity-related diabetes (type 1 diabetes + LADA = DM1) could coexist with thyroid cancers more aggressive as compared to those found in unaffected (non-DM) individuals.
Methods
We collected data from patients who underwent thyroid surgery in 10 referral clinics in Greece over 2 years. Our retrospective collection included the type of diabetes, pre-existing to the thyroid surgery, its treatments and duration, the preoperative thyroid function tests and the surgical pathology report. We compared the presence of different forms of thyroid cancer histology and the features of tumor aggressiveness between patients with and without diabetes.
Results
Overall, $n = 808$ subjects with thyroid cancer were included: $n = 571$ were females (70.7%), age 47.3 ± 14.3 years, BMI 27.0 ± 5.0 Kg/m^2, mean TSH 1.99 ± 2.21 mIU/l; $n = 692$ were non-DM, $n = 10$ had DM1 and $n = 107$ had DM2. Histology revealed $n = 5$ poorly differentiated / anaplastic, $n = 13$ medullary, $n = 12$ Hürthle cell, $n = 17$ follicular and $n = 773$ papillary thyroid cancers (PTC); $n = 20$ (2.5%) with aggressive histological subtypes of PTC, $n = 5$ (0.6%) with distant metastases (MET), $n = 199$ (24.6%) with extrathyroidal extension (ETE), $n = 419$ (51.9%) with capsular invasion (CI), $n = 225$ (27.8%) with lymph nodes involvement (LNi) and $n = 23$ with cancer recurrence (CR) (2.8%). The incidence of aggressive histological types, CR, MET or number of I-131 treatments were not different between groups ($p > 0.05$). ETE, CI and LNi were significantly more common in non-DM compared to both diabetes groups, while gross ETE was more common in DM2 over DM1 and non-DM ($P < 0.001$).
Conclusions
Some protective effects are observed in patients with DM1 more than DM2 on certain features of cancer aggressiveness in patients with diabetes. In addition, ETE seems more common in patients with DM2 compared to those with DM1. Aggressive histological types of thyroid cancer and aggressive variants of PTC incidence do not seem affected by the presence of diabetes. Obviously, the relatively small sample size of the present study limits the ability to detect effects of smaller magnitude, but an interplay between tumor biology, glucose homeostasis, insulin secretion and resistance and autoimmunity could have a significant effect on thyroid cancer development and aggressiveness.

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RC8.2

Somatic RAS mutations in thyroid nodules: possible protective effect?

Martina Verrienti[1], Sabrina Lupo[2], Giacomo De Cao[1], Paola Franceschetti[2], Anna Crociara[2], Andrea Daniele[2], Stefania Bruni[2], Maria Rosaria Ambrosio[1] & Maria Chiara Zatelli[1]
[1]Ferrara, Dept of medical Sciences, Ferrara, Italy; [2]Ferrara, UOC of Endocrinology, AOU Ferrara, Ferrara, Italy

Introduction
Thyroid nodules (TN) may display somatic RAS mutations, that, however, lack of diagnostic value. In our experience, somatic RAS mutation evaluation could be useful since it has a very high negative predictive value. In the past, somatic RAS mutation had been associated with a good prognosis in thyroid cancer.
Objective
This study aims to evaluate whether somatic RAS mutation may associate with TN differential growth pattern.
Methods
Our study included 2174 patients referring our center for TN assessment by ultrasound (US), fine needle aspiration biopsy and subsequent cytological and molecular evaluation, represented by somatic BRAFV600E mutation by a CE-IVD Real-time PCR kit (DIATECH, Italy). In BRAF V600E negative TN displaying a non-malignant cytology, somatic RAS mutations were investigated by by a CE-IVD Real-time PCR kit (DIATECH, Italy). We selected 1092 TN undergoing somatic RAS mutations evaluation with a basal and at least one follow-up US evaluation (median follow-up 2 years) and calculated TN volume with the ellipsoid formula.
Results
Among the 1092 TN with US follow-up somatic RAS mutations were identified in 49 TN (RAS+), while 1043 TN where wild type for somatic RAS mutations (RAS-). Each group was divided in 3 categories: 1) TN displaying a volume increase, 2) TN displaying a volume reduction, 3) TN displaying stable volume during follow-up. We found that somatic RAS mutations were equally distributed among the 3 categories. On the contrary, initial volume was significantly higher in RAS- vs RAS+ TN in both category 1 (3.65 vs 1.08 ml) and 2 (4.71 vs 2.18 ml) ($P < 0.01$). In addition, volume variations RAS+ TN were not significant, while category 1 RAS- TN showed a ~twofold increase in volume ($P < 0.01$) and category 2 RAS- TN showed a ~1.5-fold reduction in volume ($P < 0.01$).
Conclusions
Our data smggest that somatic RAS mutations do not associate with TN volume variations. On the contrary, in our study they associate with a smaller and stable volume, supporting the hypothesis of a protective effect of these mutations.

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RC8.3

Thyroid sequencing: What the cell am i using here?

Nuria Sánchez de la Blanca Carrero, Pablo Sacristán Gómez, Ana Serrano Somavilla, José Luis Muñoz de Nova, Miguel Antonio Sampedro Núñez, Mónica Marazuela Azpiroz & Rebeca Martínez Hernández
Hospital Universitario de La Princesa, Endocrinology, Madrid, Spain

Context
Pathological transcriptomic landscape has been the driver of the Molecular Biology in the recent years. Massive RNA sequencing techniques have been extended from bulk RNAseq, to single cell sequencing (scRNAseq) and spot-based spatial transcriptomics (ST), and sometimes laboratory cannot afford all of them. We tried to answer the question about which would be the best option in thyroid gland using Hashimoto's thyroiditis (HT) context.
Methodology
We performed RNAseq (5 HT, 5 controls) and Visium ST using the 10XGenomics platform (3 HT, 2 controls). We used scRNAseq from four HT patients from a public repository database. For ST, we followed a histological annotation classification and we analyzed each tissue compartment: thyrocytes, connective tissue, vessels, germinal center (GC) and immune infiltrated cells (TILs), separately. All the analysis were executed in R and Seurat package. DESeq was used for differential expression analysis (DEA) in RNAseq. In scRNAseq and ST, DEA was performed under the default option of Seurat.
Results
We first focused our analysis on the **ST** data separating the different tissue compartments. We found two thyrocytes subpopulations ("healthy" and "damaged"), three main fibroblasts subpopulations and a specific marker of vessels permeabilization, PLVAP, with their respective locations. Furthermore, we observed the spatial concentration of dendritic cell markers (such as FDCSP) in GCs, a main characteristic of HT histology. Nevertheless, TILs surrounding the GC were not properly estimated nor classified. In **scRNAseq**, we characterized different immune subpopulations which were not able to be observed in ST. However, it is critical to consider the low number of thyrocytes compared to other cells which smggests a non-uniform coverage of all representative cells in the thyroid tissue. This fact could interfere with the results of the analysis presenting limitations in the description of "damaged" and "healthy" thyrocytes subpopulations. We also found a lack of expression of FDCSP marker in GC cells represents the low capture efficiency or the damaged cells that results in the scRNAseq. In **RNAseq**, the upregulation of some genes is overshadowed by immune cell markers. In the top, we found genes such as CXCL13 and FDCSP. The analysis of pathogenic-fibroblasts markers and PLVAP did not reach statistical significance. It may be caused by the lack of depth/samples in the RNAseq analysis and the overrepresentation of immune cells transcriptomes.

Conclusions
ST provides a robust method to identify different cell type subpopulations similar that in scRNAseq in non-immune cells and offers higher depth than RNAseq.

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RC8.4

The increased FCRL mRNA expression in patients with Graves' disease is associated with hyperthyroidism (but not with positive thyroid antibodies)

Katarzyna Wojciechowska-Durczyńska[1,2], Jan Stępniak[1], Andrzej Lewiński[2,3] & Małgorzata Karbownik-Lewińska[1,2]
[1]Medical University of Lodz, Department of Endocrinology and Metabolic Diseases, Lodz, Poland; [2]Polish Mother's Memorial Hospital, Research Institute, Lodz, Poland; [3]Medical University of Lodz, Department of Pediatric Endocrinology, Lodz, Poland

Fc Receptor-like (FCRL) genes play a role in the immune system by encoding proteins that function as receptors on the surface of immune cells. Peripheral blood B cells, which are positive for FCRL3 and FCRL4, are rarely found in healthy individuals. In previous studies overexpression of FCRL4 was observed in patients with Graves' disease (GD) but without association with thyroid peroxidase (TPOAb) or thyroglobulin (TgAb) antibodies. Nonetheless, the clinical significance of FCRLs expression in GD and Graves orbitopathy (GO) remains unclear. We decided to evaluate the expression of FCRL 2, 3, 4 mRNA in patients with GD and GO and its role in the development and severity of these diseases.
Methods
Peripheral blood samples from patients with GD (diagnosed on the basis of positive TSH receptor autoantibodies, TRAb; $n=26$) or GO (diagnosed on the basis of ophthalmic assessment and positive TRAb currently or in medical history; $n=49$) hospitalized in the Department of Endocrinology and Metabolic Diseases, Medical University of Lodz, were collected. Healthy individuals without thyroid diseases served as Control ($n=16$). Expressions of *FCRL2*, *FCRL3* and *FCRL4* were measured by real-time PCR and analyzed using the $2^{-\Delta\Delta CT}$ method.
Results
FCRL3 mRNA expression was higher in peripheral blood from patients with GD comparing to GO (1.375 vs 0.673, $P=0.004$), as well as comparing specifically to active GO (1.375 vs 0.639, $P=0.005$). Regarding FCRL4 mRNA expression, even more pronounced increase was found in GD patients. Namely, FCRL4 mRNA expression was higher in GD comparing to Control (3.078 vs 0.916, $P=0.003$), comparing to GO (3.078 vs 1.178, $P<0.001$), comparing to active GO (3.078 vs 1.186, $P=0.002$) and comparing to inactive GO (3.078 vs 1.171, $P=0.008$). In turn, FCRL4 mRNA expression was higher in patients with hyperthyroidism (subclinical+overt) than in euthyroid patients (2.509 vs 0.995, $P=0.001$ when the whole group of individuals was considered; 2.509 vs 1.073, $P=0.004$ when GO+GD was considered). This positive association of FCRL4 mRNA expression with hyperthyroidism was confirmed in univariate regression analysis (OR=1.561, 95%CI=2.213, $P=0.012$). No clear relationship was observed between FCRL mRNA expression and thyroid antibodies (TRAb included). FCRL mRNA expression was not related to active/inactive GO.
Conclusion
The increased FCRL mRNA expression in patients with GD is associated with hyperthyroidism (but not with positive TRAb) and our study is the first one to confirm this relationship.

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RC8.5

Color Doppler ultrasound and real-time elastography in patients with hypothyroidism for the prediction of levothyroxine replacement: A cross-sectional study of 338 patients

Nikolaos Angelopoulos[1,2], Rodis Paparodis[2], Sarantis Livadas[2], Anastasios Boniakos[2], Ioannis Androulakis[2] & Ioannis Iakovou[1]
[1]AHEPA University Hospital, Faculty of Medicine, School of Health Sciences, 2nd Academic Department of Nuclear Medicine, Thessaloniki, Greece; [2]Hellenic Endocrine Network, Athens, Greece

Aims
While hormonal assays are commonly used for thyroid function assessment, Doppler sonography provides valuable information on vascularization and blood flow. This study aimed to examine the potential associations between Doppler parameters and clinical characteristics of hypothyroid patients, such as the autoimmune nature of the disease and adequacy of LT4 replacement.
Methods
A total of 338 patients with hypothyroidism, primarily caused by autoimmune thyroiditis (AT), were enrolled in this study. Exclusion criteria comprised specific medical conditions, medication history, and nodular abnormalities of the thyroid gland. Patient demographics (age, sex, BMI), treatment parameters (LT4 daily dose), and thyroid hormone levels (TSH, fT4) were recorded.
Results
Among the enrolled patients, 85.2% had autoimmune thyroiditis. Suboptimal levothyroxine (LT4) replacement was observed in 20.1% of patients at the time of enrollment. Patients with autoimmune thyroiditis had increased elastography ratios compared to those without autoimmune disease and present a positive association of elastography ratios with vascularity. In patients without autoimmune thyroiditis, those with suboptimal LT4 replacement had lower total thyroid volume. Patients with suboptimal LT4 replacement had higher peak systolic velocity (PSV) and end-diastolic velocity (EDV) in the inferior thyroid artery and lower resistive index (RI). The severity of hypothyroidism, as indicated by LT4 dose/body mass index (BMI), was negatively correlated with thyroid volume and EDV values of superior and inferior thyroid arteries. PSV of the inferior thyroid artery can predict suboptimal LT4 replacement (sensitivity 81.8%, specificity 42%).
Conclusions
In situations where obtaining blood tests may be challenging, utilizing color Doppler ultrasound can serve as an alternative method to assess treatment responses and identify patients who require further hormonal examinations.

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Rapid Communications 9: Pituitary and Neuroendocrinology | Part II

RC9.1

Assessment of cardiovascular risk and coronary calcium deposits in women with hypopituitarism

Salma Salhi[1], Ibtissem Oueslati[1], Seif Boukriba[2], Emna Talbi[3], Meriem Yazidi[1], Moncef Feki[1], Habiba Mizouni[2] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia; [2]La Rabta University Hospital, Department of Radiology, Tunis, Tunisia; [3]La Rabta University Hospital, Laboratory of Biochemistry, Tunis, Tunisia

Introduction
Cardiovascular diseases are frequent in patients with hypopituitarism receiving conventional hormone replacement therapy. They represent the main cause of premature death in this population. Emerging evidence smggests that beyond traditional risk factors, evaluating coronary calcium score (CCS) and inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP) provides valuable insights into cardiovascular health in this population. The aims of the present study were to assess the cardiovascular risk (CVR) and to determine CCS in women with hypopituitarism.
Methods
We conducted a cross-sectional study including 50 patients with complete anterior hypopituitarism secondary to Sheehan syndrome (SS), receiving conventional hormone replacement therapy (PG) and an equal number of age- and body-mass index (BMI)-matched women controls (CG). Participants underwent a clinical examination, laboratory tests, and a coronary computed tomography scan to calculate the CCS.
Results
The average age was 62.2 ± 9.4 years in the PG and 60.6 ± 8.4 years in the CG ($P=0.385$). The average delay between postpartum hemorrhage and the diagnosis of SS was 11.1 ± 9.4 years and its average duration was 31.6 ± 9.9 years. The prevalence of hypertension (PG: 78%, CG: 64%, $P=0.123$), insulin resistance (PG: 38%, CG: 56%, $P=0.070$), and diabetes (PG: 24%, CG: 14%, $P=0.202$) were comparable between the two groups. Dyslipidemia (PG: 66%, CG: 38%, $P=0.005$) and metabolic syndrome (PG: 64%, CG: 40%, $P=0.016$) were more prevalent in the PG. PG had higher hs-CRP levels (7.6 mg/l vs 2.5 mg/l, respectively; $P<0.001$) and higher CCS (47.3 vs 6.9, respectively; $P=0.009$) than controls. Two patients had coronary artery disease. No women from the CG had a cardiovascular accident. Based on a CCS > 10, 28% of PG had high CVR compared to 18% of controls ($P<0.001$). Factors associated with high CVR included age >55 years (OR= 1.5; IC95%: 1.25-1.95; $P=0.039$) and hypertension (OR=1.6; IC95%: 1.3-2.1; $P=0.016$). On the other hand, no relationship was observed between high CVR, disease-related parameters, and hormone replacement therapy.

Conclusion
Women with hypopituitarism secondary to SS had a higher CVR than controls. They necessitate a more exhaustive risk assessment strategy by incorporating CCS and inflammatory markers into the evaluation process. Preventive and therapeutic strategies should be early developed to mitigate the cardiovascular consequences associated with SS.

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RC9.2

Elevated prolactin: Do not over investigate, cannulate!

Anna Hawkins, Nancy Enriquez, Raj Tanday, Usman Shah, Carmela Chan, Edel Casey & Khash Nikookam
Barking, Havering and Redbridge University NHS Trust, United Kingdom

Aim
Role of Endocrine Specialist Nurse (ESN) in performing cannulated prolactin and subsequent impact on outpatient clinic activities.
Introduction
Hyperprolactinemia is a common condition in endocrine clinical practice. It may occur in any sex, at any age and its prevalence and incidence depend on study population. The most common physiological causes of elevated prolactin are stress, lactation, pregnancy and exercise. Non-physiological causes include medications, pituitary and systemic disorders and medications[1]. Regardless of underlying aetiology hyperprolactinemia may cause galactorrhoea, amenorrhoea, infertility and erectile dysfunction in addition to several adverse health outcomes such as cardiac disease, cancer, osteoporosis, autoimmune conditions. 40 patients (11 men and 29 women) with a mean age of 32 yrs were referred by the consultant endocrinologists for cannulated prolactin over a 12-month period in 2023. All patients were originally referred by their GP with elevated prolactin following various presentations, pituitary adenomas (4), erectile dysfunction (3), irregular periods (3), fatigue (3), short stature (2), infertility (1), galactorrhoea (1), sweating (1), asymptomatic (22). Their elevated prolactin levels ranged 355 to 1281 miu/l in men and 499 to 2149 miu/l in women, with a mean prolactin of 891 miu/l in both sexes.
Method
All patients underwent a cannulated prolactin following our joint Endocrine guidelines. This involved placing a cannula in the arm and taking a sample of blood at insertion for prolactin. The patient was then left to sit and relax for 60 mins before a second sample of blood was withdrawn from the cannula for prolactin.
Results
21 patients (10 men and 11 women) had a normal cannulated prolactin at 60 mins with a range of 323 to 131 miu/l, mean = 244 miu/l in men and 435 to 260 miu/l, mean 360 miu/l in women. 21 (52%) of patient with normal cannulated prolactin were reassured and discharged back to their general practitioner (GP). 19 patients with non-suppressed prolactin (range of 409 to 1608 miu/l) were subsequently seen in consultant endocrine clinic for further investigation and treatment including two patients who were on Duloxetine and Olanzapine.
Conclusion
The above highlights the importance of a dedicated endocrine team with the role of the ESN being paramount to:
1) facilitate and ensure timely and accurate diagnostic testing.
2) ensure outcome follow up, improved patient care and satisfaction.
3) reduce referrals to Endocrine Clinics hence more capacity for urgent referrals.
4) cost effectiveness.
Prolactin normal reference range: men 86-324 miu/l, women 102-496 miu/l
Reference
1. Soto-Pedre et al. (2017) https://pubmed.ncbi.nlm.nih.gov/27434534/

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RC9.3

Identifying potential small molecule "metabolites" as biomarkers for growth hormone deficiency (GHD): Insights from a novel mouse model

Sarmed Al-Samerria[1,2], Huiting Xu[3], Joseph Phelan[3], Maria Elena Diaz Rubio[3], Sayaka Yamada[1], Ariel Negron[1], Fredric Wondisford[4] & Sally Radovick[1]
[1]The University of Arizona Medical School, Department of Pediatrics, Phoenix, United States; [2]The University of Arizona College of Medicine - Phoenix, Phoenix, United States; [3]Rutgers University, Department of Medicine, New Brunswick, United States; [4]The University of Arizona Medical School, Department of Medicine, Phoenix, United States

Growth hormone deficiency (GHD) diagnosis poses a significant challenge since no test definitively diagnoses GHD. The current diagnostic approach for GHD relies on a determination of auxologic parameters followed by determining Growth Hormone (GH) levels and Insulin-like Growth Factor-I (IGF-I) in serum. However, clinical assessment and interpretation of GH and IGF-1 levels lack sensitivity. Further provocative studies of GH secretion do not have a precise cutoff level that discriminates a normal response from a deficient response; second, they have poor specificity. With the goal of determining biomarkers for GHD, our laboratory developed a unique mouse model, inspired by a severe GHD patient due to a mutation in the *PIT-1* gene, which provides a controlled setting for probing GHD intricacies, overcoming some challenges encountered in human studies. In this study, we utilized a metabolomic approach to analyze serum samples from both wild-type and mutant mice, both with and without GH treatment, aiming to identify potential biomarkers. Metabolomic analysis unveiled several impacted metabolic pathways associated with GHD in the developed mouse model. Among these pathways, the Purine metabolism pathway and Arginine and proline metabolism exhibited the most pronounced alterations, indicating their crucial involvement in GHD-related metabolic changes. Upon closer analysis, 3-hydroxy butyric acid, Glucose, and Hydroxyproline displayed distinctive patterns in male and female mutant mice, smggesting their potential as GHD biomarkers. Furthermore, we established a correlation between metabolomic changes and treatment response, enabling the monitoring of GH therapy effects. This research highlights the pivotal role of metabolomic analysis in identifying a unique biomarker for GHD and evaluating treatment response. Incorporating a novel mouse model with a *PIT-1* gene mutation enriches GHD research, contributing to enhanced diagnostic accuracy and improved monitoring of treatment outcomes in individuals with GHD.

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RC9.4

The novel SST3 agonist ITF2984 exerts antimitotic and proapoptotic effects in human non-functioning pituitary neuroendocrine tumor (NF-PitNET) cells

Genesio Di Muro[1,2], Rosa Catalano[2], Donatella Treppiedi[3], Anna Maria Barbieri[2], Federica Mangili[3], Giusy Marra[2], Sonia Di Bari[2], Emanuela Esposito[2,4], Emma Nozza[2,4], Andrea Lania[5,6], Marco Locatelli[7,8], Daniela Modena[9], Christian Steinkuhler[9], Erika Peverelli[2,3] & Giovanna Mantovani[2,3]
[1]University Sapienza of Rome, Dipartimento di Medicina Sperimentale, Rome, Italy; [2]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [3]Endocrinology unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [4]PhD Program in Experimental Medicine, University of Milan, Milan, Italy; [5]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Italy; [6]Endocrinology and Diabetology Unit, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Hu-manitas Research Hospital, Rozzano, Italy; [7]Neurosurgery Unit, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [8]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; [9]Preclinical R&D, Italfarmaco Group, Cinisello Balsamo, Italy

Non-functioning pituitary neuroendocrine tumors (NF-PitNETs) are still orphan of medical therapy. The drmgs approved for the other types of PitNETs, e.g. somatostatin analogues (SSA) with high affinity for somatostatin receptors (SSTs) type 2 (SST2) and 5 (SST5) are poorly efficacious in NF-PitNETs. Among SSTs, NF-PitNETs express high levels of SST3, a receptor that can mediate antiproliferative and apoptotic signaling. ITF2984 is a pan-SST ligand with high affinity for SST3, able to induce SST3 internalization and phosphorylation, to trigger G-protein signaling in vitro and to exert antitumoral activity in MENX rat model. Aim of the present study was to test the antiproliferative and proapoptotic effects of ITF2984 in NF-PitNET primary cultured cells derived from surgically removed human tumors and to characterize their SSTs expression profile. We treated primary cells derived from 23 NF-PitNETs with ITF2984, octreotide (SSA with high affinity for SST2), pasireotide (SSA with high affinity for SST5) or cabergoline (DRD2 agonist) and we measured cell proliferation (by BrdU incorporation assay) and apoptosis (by caspase 3/7 activity assay). The expression of SST3, SST2 and SST5 in tumor tissues was analysed by qRT-PCR and western blot. Our results demonstrated that ITF2984 reduced cell proliferation (-40.8 (17.08) %, $P<0.001$ vs basal, $n=19$ NF-PitNETs) and increased cell apoptosis (+41.4 (22.1)%, $P<0.001$ vs basal, $n=17$ NF-PitNETs). On the contrary, in the same tumors no

effect was observed after octreotide, pasireotide, or cabergoline treatment. Receptor expression analysis revealed that SST3, SST2 and SST5 transcripts were expressed at similar levels in tumor tissues, and a positive correlation was found between SST3 and SST5 protein levels. In conclusion, our data support a possible use of ITF2984 in the pharmacological treatment of NF-PitNET.

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RC9.5

Pregnancy and acromegaly: Clinical outcomes of retrospectively analysed data from the German Acromegaly Registry

Anke Tönjes[1], Marleen Würfel[1], Marcus Quinkler[2], Ulrich Knappe[3], Jürgen Honegger[4], Nina Krause.Joppig[5], Konrad Bacher[6], Jochen Schopohl[7], Sylvère Störmann[7] & Sebastian Meyhöfer[8]
[1]University of Leipzig Medical Center, Leipzig, Germany; [2]Endocrinology in Charlottenburg, Berlin, Germany; [3]Department of Neurosurgery, Johannes Wesling Hospital, Minden, Germany; [4]University of Tübingen, Department of Neurosurgery, Tübingen, Germany; [5]ENDOKRINOLOGIKUM Hannover, Hannover, Germany; [6]Practice for Endocrinology and Diabetes, Stuttgart, Germany; [7]Medizinische Klinik und Poliklinik IV, LMU Klinikum, München, Germany; [8]Institute of Endocrinology and Diabetes, University of Lübeck, Lübeck, Germany

Context
Acromegaly is a rare disease caused by excessive growth hormone (GH) secretion, mostly induced by pituitary adenomas. The care of pregnant women with acromegaly is challenging, in part due to existing clinical data being limited and not entirely consistent with regard to potential risks for mother and child.
Objective
To retrospectively examine data on pregnancy and maternal as well as neonatal outcomes in patients with acromegaly.
Design and Methods
Retrospective data analysis from 47 pregnancies of 31 women treated in centers of the German Acromegaly Registry.
Results
87.1% of the studied women underwent transsphenoidal surgery before pregnancy. In 51.1% a combination of dopamine agonists and somatostatin analogs were used before pregnancy. Three women did not receive any therapy for acromegaly. During pregnancy only 6.4% received either somatostatin analogs or dopamine agonists. In total, 70.2% of all documented pregnancies emerged spontaneously. Gestational diabetes was diagnosed in 10.6% and gravid hypertension in 6.4%. Overall, no preterm birth was detected. Indeed, 87% of acromegalic women experienced a delivery without complications.
Conclusion
Pregnancies in women with acromegaly are possible and the course of pregnancy is in general safe for mother and child both with and without specific treatment for acromegaly. The prevalence of concomitant metabolic diseases such as gestational diabetes is comparable to the prevalence in healthy pregnant women. Nevertheless, larger studies with more data in pregnant patients with acromegaly are needed to provide safe and effective care for pregnant women with this condition.

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RC9.6

Prevalence and determinants of microvascular and macrovascular complications of diabetes in acromegaly patients: A prospective case-control cross-sectional study

Rosa Pirchio[1], Renata Simona Auriemma[1], Roberta Scairati[1], Antonella Tropiano[1], Ivan De Simone[1], Alice Vergura[1], Guendalina Del Vecchio[1], Claudia Pivonello[2], Rosario Pivonello[1] & Annamaria Colao[1]
[1]Università Federico II di Napoli, Naples, Italy, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]Università Federico II di Napoli, Dipartimento di Sanità Pubblica, Naples, Italy

Context
Although diabetes mellitus is a major complication in patients with acromegaly, prevalence and determinants of microvascular and macrovascular complications of diabetes remains unexplored in this population.
Aim
To investigate prevalence and determinants of microvascular and macrovascular complications in acromegaly patients with diabetes and to compare them with a group of diabetic patients without acromegaly.
Methods
Prospective case-control cross-sectional study evaluating 53 acromegaly patients with diabetes (ACRODIAB) and 53 diabetic patients (DIAB) similar for gender and age.
Results
No significant difference in age at diabetes diagnosis, diabetes duration, fasting glucose, and HbA1c levels were found between ACRODIAB and DIAB groups. Prevalence of retinopathy was similar between the two groups (18.4% vs 14.3%,$P=0.602$), whereas ACRODIAB patients had a significantly higher eGRF ($P=0.01$) and a significantly lower prevalence of chronic kidney failure ($P<0.001$) compared to DIAB group. Albuminuria was slightly but not significantly lower in ACRODIAB than in DIAB group (12.7 ± 18.4 vs 22.3 ± 38.3,$P=0.185$). Prevalence of ischemic heart disease (27.3% vs 41.5%, $P=0.03$) and cerebrovascular disease (1.9% vs 14.3%,$P=0.03$) were significantly lower in ACRODIAB than DIAB group. Similarly, atherosclerotic plaques (78.4% vs 95.2%,$P=0.09$) and lower limb peripheral arterial disease (14.7% vs 28.6%, $P=0.211$) were slightly less frequent in ACRODIAB than DIAB group. In ACRODIAB group, patients with retinopathy were significantly younger both at the evaluation ($P=0.02$) and at diabetes diagnosis ($P=0.009$) and had slightly higher IGF-I levels ($P=0.06$) as compared to those without retinopathy. In ACRODIAB group, patients diagnosed with diabetes before the age of 52 years (median) had a significantly higher prevalence of retinopathy (37.5% vs 4.3%,$P=0.008$), mainly proliferative (18.7% vs 4.3%, $P=0.07$), and a slightly higher prevalence of lower limb peripheral arterial disease (23.1% vs 9.5%, $P=0.278$) as compared to those diagnosed at older age. ACRODIAB patients in whom diabetes onset occurred before acromegaly exhibited a significantly higher prevalence of atherosclerotic plaques (55.5% vs 16.7%, $P=0.04$) and of lower limb peripheral arterial disease (32.3% vs 0%, $P=0.01$) as compared to those diagnosed with diabetes after acromegaly. Retinopathy was slightly more frequent in ACRODIAB patients diagnosed with diabetes before acromegaly than those in whom the diagnosis was simultaneous (42.8% vs 9.1%, $P=0.09$).
Conclusions
ACRODIAB patients are affected by a lower number of diabetes complications, particularly macrovascular, as compared to DIAB. So far, a protective role of GH and IGF-I on diabetes complications cannot be excluded. In ACRODIAB patients, age at diagnosis of diabetes and diabetes occurrence before acromegaly are the main determinants of diabetes complications.

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RC9.7

Pituitary apoplexy: A retrospective canadian single center cohort study

Ellen Parker[1], S. Ali Imran[2], Andrea Hebb[1], Nelofar Kureshi[1] & David Clarke[1]
[1]Dalhousie University, Division of Neurosurgery, Halifax, Canada; [2]Dalhousie University, Division of Endocrinology and Metabolism, Halifax, Canada

Introduction
Pituitary apoplexy is a rare clinical syndrome that often involves headache, visual deficits, and endocrine dysfunction resulting from infarction or hemorrhage of a pituitary tumor. Due in part to the rare nature of this condition, there are few large studies on pituitary apoplexy described in the literature. Here, we present a large single center retrospective cohort study of patients with pituitary apoplexy managed surgically or conservatively.
Methods
This is a retrospective cohort study; data was collected from prospectively entered information in our Halifax Neuropituitary Clinic's database. Medical records of patients with symptomatic pituitary apoplexy treated at from January 2000 to October 2022 were reviewed. Patients treated surgically typically presented with deterioration of vision or loss of consciousness, whereas conservative management was typically selected for patients with no visual field deficits or who were otherwise unable to undergo surgery due to patient-specific medical factors. Patient demographics, endocrinologic values, clinical outcomes, and cases of tumor recurrence were analyzed. Descriptive statistics were reported as means, percentages, and standard error of the mean. Independent two-samples *t*-tests (and $\alpha=0.05$) were used for statistical analyses between patients treated surgically versus conservatively.
Results
Eighty-three ($n=83$) patients with symptomatic pituitary apoplexy met our inclusion criteria. The average age at diagnosis was 50.4 ± 1.6 years. Seventy-two percent of tumours ($n=60$) were non-functioning adenomas. Functioning (but hormonally uncontrolled) adenomas made up 8.4% of cases ($n=7$), and other parasellar lesions comprised 13.2% ($n=11$). Sixty (72.3%) patients were treated surgically, while the remaining twenty-three patients (27.7%) were treated conservatively. At time of initial presentation, mean endocrinological values were

as follows: GH 1.1 ± 0.6 µg/l (n = 28), IGF-1 155.1 ± 29.6 µg/l (n = 38), Prolactin 318.0 ± 286.1 µg/l (n = 49), FSH 7.6 ± 1.3 IU/L (n = 50), LH 3.8 ± 0.8 IU/L (n = 7), TSH 1.39 ± 0.17 mIU/l (n = 52), Cortisol 330.4 ± 35.8 nmol/l (n = 54). There were no significant differences in endocrinological values at time of presentation between patients treated surgically compared to those treated conservatively. At time of presentation, patients treated surgically had a tumor size in maximum dimension of 2.7 ± 1.4 cm vs 1.6 ± 0.5 cm for those treated conservatively (P = 0.0003). Fifteen percent (n = 9) of patients treated surgically underwent an additional surgery (mean 2.8 ± 2.0 years from index), of which 67% (n = 6) were secondary to tumor recurrence.

Conclusions

This is one of the largest reported series of pituitary apoplexy with long-term follow-up. A subset of surgically treated patients will require additional intervention, highlighting the importance of ongoing follow up in this population.

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Rapid Communications 10: Calcium and Bone | Part II

RC10.1

First-line F18-choline PET/CT Versus Tc99m-sestaMIBI SPECT/CT in the surgical management of primary hyperparathyroidism: a diagnostic randomized phase III trial

Elske Quak[1], Audrey Lasne-Cardon[2], Marie-Béatrice Cavarec[3], Barbara Lireux[1], Vianney Bastit[2], Nathalie Roudaut[4], Pierre-Yves Salaun[3], Nathalie Keromnes[3], Gael Potard[5], Patricia Vaduva[6], Annabelle Esvant[6], Franck Jegoux[7], Olivier De Crouy-Chanel[7], Anne Devillers[8], Clémence Guery[8], François Christy[9], Jean-Michel Grellard[9], Stéphane Bardet[1] & Bénédicte Clarisse[9]

[1]François Baclesse Cancer Centre, Nuclear Medicine and Thyroid Unit, Caen, France; [2]François Baclesse Cancer Centre, Head and Neck Surgery, Caen, France; [3]University Hospital of Brest, Nuclear Medicine, Brest, France; [4]University Hospital of Brest, Endocrinology, Brest, France; [5]University Hospital of Brest, Head and Neck Surgery, Brest, France; [6]Rennes University Medical Center, Endocrinology, Rennes, France; [7]Rennes University Medical Center, ENT, Rennes, France; [8]Emgene Marquis Cancer Institute, Nuclear Medicine, Rennes, France; [9]François Baclesse Cancer Centre, Clinical Research, Caen, France

Introduction

Whether F18-choline PET/CT (FCH PET/CT) should replace Tc99m-sestaMIBI SPECT/CT (MIBI SPECT/CT) as a first-line imaging technique for preoperative localisation of parathyroid adenomas in primary hyperparathyroidism (pHPT) is unclear.

Methods

We conducted a multicentre randomized open diagnostic intervention phase III trial in adults with primary hyperparathyroidism and indication for surgical treatment. Patients were assigned in a 1:1 ratio to receive first-line FCH PET/CT (FCH1) or MIBI SPECT/CT (MIBI1). In case of negative or inconclusive first-line imaging, patients received second-line FCH PET/CT (FCH2) after MIBI1 or MIBI SPECT/CT (MIBI2) after FCH1. The main aim of the trial was to compare the proportions of patients in whom the first-line imaging method resulted in successful mini-invasive parathyroidectomy (MIP) and normalisation of serum calcium levels at 1 month. We hypothesized a 30% superiority of FCH1 over MIBI1 for sample size determination (Quak et al, BMC Endocr Disord. 2021, PMID: 33413316).

Results

Overall, 57 patients received FCH1 (n = 29) or MIBI1 (n = 28). Baseline patient characteristics were similar between groups. Normocalcemia at 1 month after positive first-line imaging guided MIP was observed for 23 (85%) patients in the FCH1 group and 14 (56%) patients in the MIBI1 group (P = 0.022). Diagnostic performances were superior for FCH1 than for MIBI1: sensitivity was 82% and 63%, and diagnostic accuracy was 79% and 64%, for FCH1 and MIBI1, respectively. Follow-up at 6 months with biochemical measures was available for 43 patients, confirming normocalcemia for all patients with normocalcemia at 1 month post-surgery. Ten patients received FCH2 and 6 patients received MIBI2. FCH2 was positive in 8/10 patients, leading to 7/9 MIP and 2/9 bilateral cervical explorations (surgery recused in 1 patient), and normocalcemia in 9/9 patients. MIBI2 was positive in 2/6 patients, leading to 1 MIP and 1 VATS; normocalcemia was obtained in all 6 patients. No adverse events related to imaging and 4 adverse events related to surgery were reported.

Conclusions

First-line FCH PET/CT is a suitable and safe replacement for MIBI SPECT/CT. FCH PET/CT leads more PHPT patients to correct imaging-guided MIP and normocalcemia than MIBI SPECT/CT due to its superior diagnostic accuracy.

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RC10.2

Clinical features of a multicenter Italian cohort of adult patients with X-linked hypophosphatemia

Silvia Carrara[1], Silvia Vai[2], Simone Della Valentina[3], Gaetano Arcidiacono[4], Marco Torres[4], Federica Giambo[5], Alessia Pusterla[6], Federica Fraire[6], Andrea Palermo[7], Francesca Pigliaru[8], Valentina Camozzi[9], Cristina Eller Vainicher[10], Elena Castellano[11], Laura Gianotti[12], Filomena Cetani[13], Massimo Procopio[14], Marco Barale[15], Sandro Giannini[4], Giuseppe Vezzoli[5] & Sabrina Corbetta[16]

[1]Bone Metabolism Disorders and Diabetes Unit, IRCCS Istituto Auxologico Italiano, Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [2]Bone Metabolism Disorders and Diabetes Unit, IRCCS Istituto Auxologico Italiano, Milan, Italy; [3]Department of Translational Researche and Innovative Technology in Medicine and Surgery, University of Pisa, Pisa, Italy; [4]UOC Clinica Medica 1, Dipartimento di Medicina, Università degli Studi di Padova, Padua, Italy; [5]Nephrology Unit, IRCCS Ospedale San Raffaele, Università Vita Salute San Raffaele, Milan, Italy; [6]Endocrinology, Diabetes and Metabolism; Department of Medical Sciences, University of Turin, Turin, Italy; [7]Unit of Endocrinology and Diabetes, Department of Medicine, Campus Bio-Medico University of Rome, Rome, Italy; [8]Endocrinology Unit, AOU Cagliari, Cagliari, Italy; [9]UOC Endocrinologia Endo-Ern, Azienda Ospedale, Università degli Studi di Padova, Padua, Italy, [10]SC Endocrinologia, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy, [11]Division of Endocrinology, Diabetology and Metabolism, Department of Internal Medicine, Santi Croce & Carle Hospital, Cuneo, Italy, [12]Struttura Complessa di Endocrinologia e Diabetologia Territoriale, ASL Cuneo 1, Cuneo, Italy, [13]Endocrine Unit, University Hospital of Pisa, Pisa, Italy, [14]Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy, [15]Oncological Endocrinology, Department of Oncology, University of Turin, Turin, Italy, [16]Bone Metabolism Disorders and Diabetes Unit, IRCCS Istituto Auxologico Italiano, Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy

X-linked hypophosphatemia (XLH) is a rare genetic disease due to inactivation of the PHEX gene, which results in enhanced secretion of the phosphaturic hormone fibroblast growth factor 23 (FGF23); the latter induces renal phosphate wasting and hypophosphatemia. Skeletal and dental anomalies and recently described increase in cardiovascular risk are typical clinical findings. We retrospectively evaluated 58 adult patients with XLH from 9 Italian tertiary centres [34 females, 24 males, aged 42.6 ± 14.5 (19-72, min-max) years]. Median age at diagnosis was 4.0 (IQR, 2.0-14.0; min-max, 1-66) years; 12 patients (20.7%) were diagnosed in their adulthood. Twenty-six patients (44.8%) reported a family history of XLH and two females passed the condition on to their child. PHEX gene mutations or deletions were identified in 95% of patients. Circulating FGF23 levels were assayed in 23 patients (111.5 ± 71.5 pg/ml); FGF23 was increased in only 11 (47.8%) patients. Fractures or pseudofractures were reported in 30 patients (51.7%); 45 patients (77.6%) had marked signs of skeletal deformities, mainly varus of the lower limbs, or underwent multiple orthopedic surgeries; 18 (31.0%) patients had marked osteophytosis particularly affecting the spine. Enthesopathies were described in 16 (27.6%) patients, mostly affecting the knees. About two third of patients had severe dental disease, especially abscesses. Kidney stones/nephrocalcinosis developed in 6 patients. Regarding their cardiometabolic profile, 10 patients (aged 59.4 ± 10.6 years) had hypertension, and 7 patients were dyslipidemic. None of the patients had diabetes mellitus or a history of major adverse cardiovascular events. In the present series, 5 patients were diagnosed with hypoacusia. Autoimmune diseases, namely rheumatoid arthritis, Sjogren syndrome, thyroid diseases, and inflammatory bowel diseases, occurred in 17% of patients. About two third of patients were on conventional therapy with phosphate supplements and/or calcitriol, whereas 22 patients were on burosumab, a recombinant human IgG1 anti-FGF23 monoclonal antibody. Most patients proposed for treatment with burosumab, had experienced previous fractures/pseudofractures compared with patients on conventional therapy (82.6 vs 34.4% P = 0.0008), while they did not differ for age, age at diagnosis, and FGF23 levels. In conclusion, Italian adult XLH patients include lower limb deformities and severe dental disease as major clinical features; the presence of enthesopathies and ossifications that limit patients' quality of life is significant. Conversely, major cardiovascular events did not appear to be prevalent. Finally, Italian bone specialists propose burosumab to adult XLH patients with prevalent fractures/pseudofractures.

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RC10.3

Autosomal dominant hypocalcemia type 1 (ADH1): Experience from an Italian center

Simone Della Valentina[1], Laura Pierotti[1], Chiara Sardella[2], Anna Dal Lago[1], Elena Pardi[1], Simona Borsari[1] & Filomena Cetani[2]
[1]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]Unit of Endocrinology, University Hospital of Pisa, Pisa, Italy

Autosomal dominant hypocalcemia type 1 (ADH1) is a genetic disorder characterized by low serum calcium and low or inappropriately normal levels of PTH. It is caused by a heterozygous activating mutation of the calcium-sensing receptor (*CASR*) gene, resulting in decreased sensitivity of the receptor to low serum calcium. The aim of our study was to describe a series of patients with ADH1 followed at our outpatient clinic from 2011 to 2023. A total of 7 patients (4 females and 3 males) carrying a missense variant of the *CASR* gene, were collected. Median age at diagnosis was 46 years (IQR 35-50), with only one patient diagnosed at birth. Two probands (71.4%) belonged to two kindreds with ADH1 and two (28.6%) were sporadic cases. Four patients (57%) were symptomatic at the time of the diagnosis (2 had recurrent kidney stones, 2 had cramp-like muscle pain with paresthesias and one recurrent hypocalcemic seizures since childhood). The remaining three patients were asymptomatic. At the time of our first evaluation, all patients had median albumin-corrected serum calcium of 7.72 mg/dl (IQR 6.9-8.1), PTH 17 ng/ml (IQR 15.5-20.7), phosphate 3.4 mg/dl (IQR 3.25-4.75), magnesium 1.9 mg/dl (IQR 1.68-2.0), creatinine 0.85 mg/dl (IQR 0.70-1.12), eGFR 90.8 mg/ml (89-105) and 24-h urinary calcium 202 mg IQR 179-225). Only one patient was on therapy with calcium carbonate, alfacalcidol and magnesium. Four of seven patients (57 %) had at least one target organ involvement (bilateral nephrolithiasis in three, nephrocalcinosis in four and reduced eGFR in two). One of six patients (17%) with available brain CT scan had basal ganglia calcifications. Bone mineral density at lumbar spine, femur and 1/3 distal radius was normal in five and low in two (median BMD 0.69; Z-score -2.2) at 1/3 distal radius. One patient started treatment with calcium carbonate and calcitriol and one also teriparatide. The median follow-up after our first evaluation was 5 years (IQR 4-8) and available only in five patients. Of the two patients on therapy, the median albumin-corrected serum calcium concentration was 8.9 mg/dl (IQR 8.9-8.9), phosphates 3.55 mg/dl (IQR 3.23-3.78), magnesium 1.85 mg/dl (IQR 1.77-1.92) and 24-h urinary calcium 345 mg/24 h (IQR 322-367). The three patients who were not on therapy had median values of serum calcium of 8.1 mg/dl (8.05-8.1), phosphate 3.85 mg/dl (3.78-3.92) and magnesium 1.9 mg/dl (1.85-1.95). Our data confirm a variable phenotype of ADH1 ranging from asymptomatic to mild-severe symptomatic profile.

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RC10.4

Increased bone fragility over time in women with chronic hypoparathyroidism: Real-world data from the HypoparaNet Italian Cohort

Francesca Giusti[1], Francesca Marini[2], Blandine Weiss[3], Michel Ovize[3], Salvatore Benvenga[4], Filomena Cetani[5], Annamaria Colao[6], Sabrina Corbetta[7,8], Ettore Degli Uberti[9], Maurizio Iacobone[10], Andrea Lenzi[11], Giovanna Mantovani[12], Rosaria Maddalena Rmggeri[13] & Maria Luisa Brandi[1,2]
[1]Bone Clinic, Villa Donatello Hospital, Sesto Fiorentino, Italy; [2]Fondazione FIRMO Onlus, Firenze, Italy; [3]Amolyt Pharma, Ecully, France; [4]University of Messina, Department of Clinical and Experimental Medicine, Messina, Italy; [5]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [6]University of Naples Federico II, Department of Clinical Medicine and Surgery, Napoli, Italy; [7]IRCCS Istituto Auxologico Italiano, Center for Metabolic Bone Diseases and Diabetology, Milano, Italy; [8]University of Milan, Department of Biomedical, Surgical and Dental Sciences, Milano, Italy; [9]University of Ferrara, Section of Endocrinology & Internal Medicine, Department of Medical Sciences, Ferrara, Italy, [10]University of Padua, Endocrine Surgery Unit, Department of Surgery, Oncology and Gastroenterology, Padova, Italy, [11]University of Rome "La Sapienza", Department Experimental Medicine, Section Medical Pathophysiology, Endocrinology and Nutrition, Roma, Italy, [12]University of Milan, Department of Clinical Sciences and Community Health, Milano, Italy, [13]University of Messina, Department of Human Pathology Patologia DETEV, Messina, Italy

Introduction
The HypoparaNet database includes 509 patients (110 men and 399 women) with chronic hypoparathyroidism (cHP), recruited and followed in 20 clinical centers in Italy from 2014 onwards. cHP etiology included 363 post-surgical cases (71.3%), 78 idiopathic cases (15.3%), and 64 patients with a genetic background (12.6%). Bone health is an important clinical aspect to be considered in patients with cHP, whose skeleton is exposed both to the cHP-induced alteration of bone mass and microarchitecture and to the occurrence/progression of osteopenia/osteoporosis related to ageing, specifically in post-menopausal (or over 50 years) women.
Patients and Methods
In the HypoparaNet cohort, dual x-ray osteodensitometry (DXA) was available in $n=173$ cHP patients. Among them, we specifically assessed the prevalence of osteopenia and osteoporosis in relation to menopause (or age below or above 50 years) in cHP women. Osteoporosis was defined as the presence of at least one of the measured bone sites presenting a *T*-score (or a *Z*-score for individuals <50 years) <-2.5. Osteopenia was defined as the presence of at least one of the measured bone sites presenting a *T*-score (or a *Z*-score for individuals <50 years) $<$-1.0, and all the measured bone site >-2.5.
Results
Female patients ($n=45$) at or below 50 years ($F\leq 50$) and female patients ($n=97$) above 50 years ($F>50$) showed comparable mean values of albumin-adjusted serum calcium, PTH, phosphate, 25(OH) vitamin D, $1,25(OH)_2$ vitamin D and magnesium. The overall prevalence of osteopenia was high, and it resulted to be comparable in the $F\leq 50$ and $F>50$ subgroups, averaging 38% and 34%, respectively. The prevalence of osteoporosis was clearly higher in the $F>50$ group with respect to the $F\leq 50$ group, averaging 4% and 24%, respectively.
Conclusions
These real-world data indicate that nearly half of cHP women, who represent the majority of the hypoparathyroid population, exhibit a high prevalence of osteopenia or osteoporosis that increases in relation to age. In this context, new treatment modalities (including PTH replacement therapy) for this patient population should aim at restoring a balanced bone turnover, preventing further bone loss and granting a better bone health at any age.

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RC10.5

Determinants of vertebral fractures and effectiveness of anti-resorptive drmgs in pre-menopausal women with early breast cancer under hormone deprivation therapies: A multicenter real-world study

Giacomo Cristofolini[1,2], Rebecca Pedersini[3], Andrea Palermo[4], Walter Vena[1,3], Barbara Presciuttini[6], Maria Francesca Birtolo[1,2], Gaia Tabacco[4], Anda Mihaela Naciu[4], Stella Pigni[1,2], Marta Lagana[3], Federica Mazzoleni[5], Deborah Cosentini[3], Antea Ciafardini[1,2], Mauro Pagani[6], Davide Farina[7], Luca Balzarini[8], Alberto Zambelli[1,9], Rosalba Torrisi[9], Luisella Cianferotti[10], Nicola Napoli[4,11,12], Antonio Carlo Bossi[5], Alfredo Berruti[3], Andrea Lania[1,2] & Gherardo Mazziotti[1,2]
[1]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy; [2]IRCCS Humanitas Research Hospital, Endocrinology, Diabetology and Medical Andrology Unit, Rozzano, Italy; [3]University of Brescia, ASST Spedali Civili, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, Medical Oncology, Brescia, Italy; [4]Unit of Metabolic Bone and Thyroid Diseases, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy; [5]Humanitas Gavazzeni, Diabetology and Endocrinology, Bergamo, Italy; [6]ASST Carlo Poma, Endocrinology Unit, Department of Medicine, Mantua, Italy; [7]University of Brescia, ASST Spedali Civili, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, Radiology, Brescia, Italy; [8]IRCCS Humanitas Research Hospital, Department of Radiology, Rozzano, Italy; [9]IRCCS Humanitas Research Hospital, Cancer Center, Rozzano, Italy, [10]University of Florence, Department of Experimental and Clinical Biomedical Sciences "Mario Serio", Florence, Italy, [11]University Campus Bio-Medico di Roma, Unit of Endocrinology and Diabetes, Department of Medicine, Rome, Italy, [12]Washington University in St Louis, Division of Bone and Mineral Diseases, St Louis, MO, United States

Management of skeletal fragility in women with early breast cancer (BC) under hormone-deprivation therapies (HDTs) may be a challenge and it is still unknown whether anti-osteoporotic therapies could be active in preventing fractures in pre-menopausal women exposed to HDTs. In this real-world, multicenter study, we evaluated the effectiveness of bone-active drmgs and determinants of vertebral fractures (VFs) in 306 pre-menopausal women (mean age 47.15 ± 5.09, range: 30-54) with early BC treated undergoing HDTs [gonadotropin-releasing hormone agonist (GnRHa) plus aromatase inhibitors (AIs) in 223 cases, GnRHa plus tamoxifene in 26 cases, AIs alone in 53 cases, tamoxifene alone in 4 cases]. In all 306 women, menopause was induced by treatment of BC (chemotherapy in 57 cases; GnRHa in the remaining 249 cases). All enrolled women were retrospectively evaluated for bone mineral density (BMD) and morphometric VFs by 12 months from starting of HDTs and after at least 24 months of

treatment. Treatment was guided by national guidelines, current Italian regulation for drmg reimbursement, patient's preference, comorbidities and overall clinical judgement. After the first bone evaluation, bone-active drmgs were prescribed in 237 women out of 306 (64 oral bisphosphonates, 28 zoledronate 5 mg iv yearly, 145 denosumab 60 mg every 6 months). At baseline, familiar history of osteoporotic fractures, personal history of clinical fractures, osteopenia, osteoporosis and morphometric VFs were found in 41 (13.40%), 21 (6.90%), 172 (56.20%), 39 (12.70%) and 19 (6.20%), respectively. After 47.01 ± 20.10 months of follow-up, 16 women (5.20%) experienced either new VFs or progression of pre-existing VFs. Incident VFs occurred more frequently in women who were untreated as compared to those treated with bone-active drmgs (14/69, 20.80% vs 2/237, 0.80%; $P<0.001$). Risk of VFs was associated with baseline diagnosis of osteoporosis [odds ratio (OR) 4.14, 95% confidence interval (C.I.) 1.10-15.58; $P=0.036$), familiar history of osteoporotic fractures (OR 3.19, 95% C.I. 1.05-9.73; $P=0.041$), baseline morphometric VFs (OR 25.36, 95% C.I. 8.03-80.13; $P<0.001$) and body mass index (BMI; OR 1.07; 95% C.I. 1.01-1.14; $P=0.034$). Duration of HDTs was significantly shorter in women experiencing incident VFs with vs those who did not fracture (38.00 ± 16.80 months vs 47.50 ± 20.10 months; $P=0.047$). In conclusion, risk of VFs in pre-menopausal women exposed to HDTs for early-BC could be effectively prevented by bisphosphonates or denosumab. This study smggests that bone-active drmgs might be indicated in women with pre-existing osteoporosis, familiar history of osteoporotic fractures and in those with higher BMI.

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Rapid Communications 11: Adrenal and Cardiovascular Endocrinology | Part II

RC11.1

Changing clinical presentation of pheochromocytomas in a tertiary centre

Matej Rakusa[1], Gaj Vidmar[2], Ludemila Silva[3], Ursa Gerl[3] & Tomaž Kocjan[1]
[1]UMC Ljubljana, Endocrinology, Diabetes and Metabolic Diseases, Ljubljana, Slovenia; [2]University Rehabilitation Institute, Ljubljana, Slovenia; [3]Faculty of Medicine, Ljubljana, Slovenia

Context
Pheochromocytomas and paragangliomas (PPGLs) are rare tumours with potentially harmful cardiovascular complications. Traditionally, they were detected in patients with symptoms and signs of catecholamine excess or during genetic surveillance. However, according to recent reports, PPGLs are increasingly being diagnosed in the setting of incidentally discovered adrenal masses.
Aim
To assess the initial clinical presentation of our PPGL patients with emphasis on the characteristics of the incidental subgroup.
Methods
We retrospectively reviewed our cohort of patients diagnosed with and operated on PPGLs between January 2005 and December 2020 at the national tertiary care centre. The diagnosis was pathohistologically verified.
Results
We included 126 patients (68 women) with PPGL, mean age 55 years (range 16-80), mean BMI 26.1 (range 17.3-45.5). Most tumours were located in the adrenal (92%; right 52%, bilateral 2%), the remaining minority being paragangliomas (8%). Tumour size ranged from 10 to 121 mm (mean 47 mm). Overall, 80 PPGLs (63%) presented incidentally, 39 (31%) with adrenergic symptoms and signs, and 7 (6%) were diagnosed via genetic screening. Incidentally detected patients were older (mean age 58 years) on average than symptomatic individuals (52 years) and patients with hereditary syndromes (35 years; $P<0.001$). Annual number of PPGLs has been increasing over the studied period from about five to about 10. The presenting age has significantly increased since 2010 (mean 57 vs 48 years; $P=0.01$) in parallel with the proportion of patients with incidentalomas (69% vs 47%; $P=0.03$). However, targeted clinical assessment revealed that 48% of the incidentaloma group had at least one of the typical clinical manifestations (e.g. headache, palpitations, perspiration, pallor), and 37% had stage 2 or 3 hypertension. Genetically detected patients exhibited statistically significantly lower levels of urinary and plasma metanephrines, while values in symptomatic and incidentaloma patients were similar and varied widely. Five tumours appeared nonfunctional (2 hereditary and 3 incidental PPGLs). Imaging was mostly done by CT (120 patients or 94%). The density of the adrenal lesions ranged from 11 to 50 Hounsfield units. Nuclear medicine procedures were performed in 113 patients (89%). MIBG scintigraphy was used in 93% of these cases, the others had PET with positive findings in 91% overall.
Conclusion
Our observations are in line with recent reports that the majority of PPGLs are diagnosed incidentally. As a significant proportion of these patients were not truly asymptomatic, awareness of the clinical presentation of PPGLs still seems lifesaving.

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RC11.2

Contralateral suppression in adrenal venous sampling predicts clinical and biochemical outcome in primary aldosteronism

Jessica Okubo[1], Paula Frudit[1], Aline Cavalcante[2], Ana Alice Maciel[1], Thais Castanheira[1], Bruna Pilan[2], Gustavo Fagundes[1], Nara Queiroz[1], Matheo Stumpf[1], Victor Souza[1], Eduardo Kawahara[1], Tatiana Goldbaum[1], Maria Adelaide Pereira[1], Vinicius Calsavara[3], Luciano Drager[4], Maria Candida Fragoso[5], Ana Claudia Latronico[5], Berenice Mendonca[5], Francisco Carnevale[2] & Madson Almeida[1]
[1]Unidade de Adrenal, Laboratório de Endocrinologia Molecular e Celular LIM25, Divisão de Endocrinologia e Metabologia, Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo, Sao Paulo, Brazil; [2]Divisão de Radiologia Intervencionista, Instituto de Radiologia InRAD, Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo, Sao Paulo, Brazil; [3]Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, United States; [4]Unidade de Hipertensão, Divisão de Nefrologia, Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo, Sao Paulo, Brazil; [5]Unidade de Adrenal, Laboratório de Hormônios e Genética Molecular LIM42, Divisão de Endocrinologia e Metabologia, Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo, Sao Paulo, Brazil

Context
The role for hormone parameters at adrenal venous sampling (AVS) in predicting clinical and biochemical outcome remains controversial.
Objective
To investigate the impact of hormone parameters at AVS under cosyntropin stimulation on lateralization and on complete biochemical and clinical outcome.
Methods
We retrospectively evaluated 168 sequential AVS under cosyntropin infusion. Bilateral successful cannulation rate was 83.3% ($n=$ 140), 47.9% bilateral and 52.1% unilateral. The lateralization index (LI), aldosterone/cortisol ratio (A/C) in the dominant adrenal vein (AV), relative aldosterone secretion index (RASI = A/C in AV divided by A/C in inferior vena cava) were assessed. The contralateral suppression (CS) percentage was defined by (1 – nondominant RASI) ×100.
Results
A nondominant RASI <0.5 (CS >50%) had 86.84% sensitivity and 92.96% specificity to predict contralateral lateralization. An A/C ratio in dominant AV > 5.9 (74.67% sensitivity and 80% specificity) and dominant RASI >4.7 (35.21% sensitivity and 88.06% specificity) had a worst performance to predict ipsilateral lateralization. Complete biochemical and clinical cure were significantly more frequent in the patients with CS >50% [98.41% vs 42.86% (p <0.001) and 41.94% vs 0% ($P<0.001$)]. CS correlated with high aldosterone at diagnosis (p <0.001) and low postoperative aldosterone levels at 1 month ($P=0.019$). Postoperative biochemical hypoaldosteronism was more frequent in patients with CS >50% (70% vs 16.67%, $P=0.014$). In multivariable analysis, a CS >50% was associated with complete biochemical cure (OR 125, 95%CI 11.904–5,000; $P=0.001$) and hypertension remission (OR 12.19, 95%CI 2.074–250; $P=0.023$).
Conclusion
A CS >50% was an independent predictor of complete clinical and biochemical cure. Moreover, it can predict unilateral PA and postoperative biochemical hypoaldosteronism. Our findings underscore the usefulness of CS for clinical decision-making.

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RC11.3

Light chromatography and mass spectrometry proteomic analysis of formalin fixed tissue of Bilateral Macronodular Adrenocortical Disease (BMAD) reveals various class correlating with molecular groups

Florian Violon, Anne Jouinot, Bruno Ragazzon, Patricia Vaduva, Lucas Bouys, Annabel Berthon, Mathilde Sibony & Jerome Bertherat
Cochin Institute, Endocrine tumor genomic and signaling pathway, Paris, France

Introduction
Bilateral macronodular adrenocortical disease (BMAD) is an adrenal cause of Cushing's syndrome explained in a subset of patients by inactivation of the tumor suppressor genes *ARMC5* or *KDM1A*. Genetic and transcriptomic studies cluster BMAD in 3 distinct molecular groups: one with *ARMC5* inactivation, one with *KDM1A* inactivation and a third group with no known genetic cause. Although *ARMC5* and *KDM1A* are involved in the post-translational regulation of proteins, the protein studies in BMAD tissues are mainly limited to immunohistochemistry targeted on steroidogenesis enzymes. The aim of this work was to study the proteomic heterogeneity in a BMAD cohort and its correlation with the molecular causes.
Patients and Methods
The cohort includes 24 BMAD (7 *ARMC5*-altered, 4 *KDM1A*-altered and 13 of unknown genetic cause) and 12 samples used as controls (10 adenomas and 2 normal adrenal glands). All patients underwent surgery in our center between 2006 and 2021. Samples were obtained from formalin-fixed and paraffin-embedded material by macrodissection. After protein extraction, identification and protein quantifications were performed by Light chromatography and mass spectrometry (LC-MS/MS) on the Cochin Institute Proteomic platform.
Results
PCA showed a rather homogeneity of *ARMC5* and *KDM1A*-altered BMAD, whereas BMAD with no known genetic cause were more heterogeneous. In accordance with *ARMC5* role in the regulation of the RNA polymerase II, several of its subunits including POLR2A are the most overexpressed proteins in ARMC5-mutated BMAD compared to the others BMAD groups. However, they have a low expression of several cholesterol biosynthesis enzymes (such as FDFT1 or NSDHL) compared to other BMAD. *KDM1A*-altered BMAD were also a homogeneous group characterized by the systematic loss of KDM1A protein and the overexpression of proteins involved in lipid metabolism (such as LDLR or SULT2A1).
Discussion
Our study is the first to explore the BMAD proteome using LC-MS/MS. We confirmed the high expression of ARN polymerase II subunits in *ARMC5*-altered BMAD and showed a high expression of ARN polymerase II partners smggesting its important role in the pathogenesis of BMAD mediated by *ARMC5* alterations. Compared to other BMAD, ARMC5-altered BMAD expressed lower levels of cholesterol biosynthesis enzymes that could partially explain the low cortisol production of cells with bi-allelic inactivation of *ARMC5*. *KDM1A* altered BMAD showed an overexpression of proteins involved in lipid metabolism that probably play a role in the production of cortisol dysregulation. BMAD with no known genetic cause showed various proteomic pattern smggesting different pathogenic mechanisms to be identified.

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RC11.4

Urine steroid metabolomics to diagnose endocrine hypertension: results from the ENS@T-HT project

Alessandro Prete[1,2], Lida Abdi[3], Onnicha Suntornlohanakul[1,4], Katharina Lang[1], Roland Veen[3,5], Marco Canducci[6], Julien Riancho[7,8], Aida Lazkani[9], Casper K. Larsen[7], Anne-Paule Gimenez-Roqueplo[7,10], Alessio Pecori[11], Martina Tetti[11], Silvia Monticone[11], Lisa M. Müller[12], Christian Adolf[12], Henri JLM Timmers[13], Stephanie Hampson[14], Graeme Eisenhofer[15], Filippo Ceccato[16], Felix Beuschlein[12,17], Marek Kabat[18], Jerome Bertherat[19], M. Conall Dennedy[20], Eleanor Davies[14], Jaap Deinum[13], Martin Reincke[12], Gian Paolo Rossi[21], Paolo Mulatero[11], Laurence Amar[7,8], Maria-Christina Zennaro[22], Alice J. Sitch[2,23], Peter Tino[6], Michael Biehl[5,24], Angela E. Taylor[1] & Wiebke Arlt[1,3,25]
[1]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK; [2]NIHR Birmingham Biomedical Research Centre, University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; [3]Medical Research Council Laboratory of Medical Sciences, London, UK; [4]Endocrinology and Metabolism Unit, Division of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Thailand; [5]Bernoulli Institute for Mathematics, Computer Science and Artificial Intelligence, University of Groningen, Groningen, the Netherlands; [6]School of Computer Science, University of Birmingham, Birmingham B15 2TT, United Kingdom; [7]Université Paris Cité, PARCC, INSERM, F-75006 Paris, France; [8]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Unité Hypertension artérielle, Paris, France; [9]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Centre d'Investigations Cliniques 9201, Paris, France; [10]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Service de Génétique, F-75015 Paris, France; [11]Division of Internal Medicine and Hypertension Unit, Department of Medical Sciences, University of Torino, Italy; [12]Medizinische Klinik und Poliklinik IV, Klinikum der Universität München, LMU München, Munich, Germany; [13]Department of Internal Medicine, Radboud University Medical Center, Nijmegen, The Netherlands; [14]School of Cardiovascular and Metabolic Health, BHF Glasgow Cardiovascular Research Centre, University of Glasgow, Glasgow G12 8TA, UK; [15]Department of Medicine III, University Hospital Carl Gustav Carus, TU Dresden, Dresden, Germany; [16]UOC Endocrinologia, Dipartimento di Medicina DIMED, Azienda Ospedaliera-Università di Padova, Padua, Italy; [17]Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, UniversitätsSpital Zürich (USZ) und Universität Zürich (UZH), Zurich, Switzerland; [18]Department of Hypertension, National Institute of Cardiology, Warsaw, Poland; [19]Department of Endocrinology, French Reference Center for Rare Adrenal Disorders, Hôpital Cochin, Université Paris Cité, Institut Cochin, Inserm U1016, CNRS UMR8104, F-75014, Paris, France; [20]The Discipline of Pharmacology and Therapeutics, School of Medicine, National University of Ireland 33 Galway, Ireland; [21]Internal & Emergency Medicine- ESH Specialized Hypertension Center, Department of Medicine-DIMED, University of Padova, Padua, Italy; [22]Université Paris Cité, PARCC, INSERM, F-75006 Paris, France; Service de Génétique, Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, F-75015 Paris, France; [23]Institute of Applied Health Research, University of Birmingham, Birmingham B15 2TT, United Kingdom; [24]Centre for Systems Modelling and Quantitative Biomedicine, University of Birmingham, Birmingham, UK; [25]Institute of Clinical Sciences, Imperial College London, London, UK

Background
Hypertension affects more than 30% of the adult population worldwide and is a major cardiovascular risk factor. Identifying secondary causes of hypertension is key to offering targeted treatments and mitigating adverse health outcomes. We tested the performance of urine steroid metabolomics (USM), the computational analysis of 24-hour urine steroid metabolome data by machine learning, for diagnosing endocrine forms of hypertension.
Methods
1400 hypertensive adults with and without endocrine causes were recruited through the ENS@T-HT EU-funded Horizon 2020 research and innovation project; of these, 351 and 1049 were collected retrospectively and prospectively, respectively. Liquid chromatography-tandem mass spectrometry (LC-MS/MS)-based multi-steroid profiling was used to quantify the excretion of 27 steroid metabolites in 24-hour urine samples. The prospective cohort underwent standardised measurement of the aldosterone-renin-ratio (ARR) to screen for primary aldosteronism (PA). Data were analysed by generalised matrix learning vector quantisation, a prototype-based algorithm of supervised machine learning, using the retrospective cohort (RC) for training and the prospective cohort (PC) for validation.
Results
We included 610 patients with PA (110 RC, 500 PC), 126 with phaeochromocytoma-paraganglioma (PPGL; 82 RC, 44 PC), 83 with Cushing's syndrome (CS; 48 RC, 35 PC), and 581 with primary hypertension (PHT; 111 RC, 470 PC). USM demonstrated high accuracy (area under the receiver-operating characteristics curve [AUC-ROC] 0.93) in identifying CS cases, which showed higher urinary excretion of glucocorticoid and glucocorticoid precursor metabolites. USM yielded moderate accuracy (AUC-ROC 0.73) in differentiating PHT from PA. However, the performance improved considerably (AUC-ROC 0.87) when comparing PA cases to low-renin PHT ($n=235$), with the major aldosterone metabolite – 3α,5β-tetrahydroaldosterone – being the most discriminatory. Within the prospective cohort, USM had similar accuracy to the ARR in differentiating PHT from PA (AUC-ROC 0.87 and 0.88, respectively). The performance improved when combining USM results with renin alone (AUC-ROC 0.90) or the ARR (AUC-ROC 0.93). Expectedly, USM could not reliably differentiate PHT from PPGL (AUC-ROC 0.57).
Conclusions
Urine steroid metabolomics is a non-invasive candidate test for accurately diagnosing hypertension secondary to cortisol and aldosterone excess and can improve diagnosis and delivery of appropriate treatment in affected individuals.

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RC11.5

Assessment of adrenal function after prednisolone treatment in patients with polymyalgia rheumatica and/or giant cell arteritis – Data from the double edge-replace study

Simon Bøggild Hansen[1,2], Anja Fenger Dreyer[3,4], Nanna Thurmann Jørgensen[3,6], Hajir Al-Jorani[3,4], Lise Sofie Bislev[1,2], Victor Brun Boesen[6], Stina Willemoes Borresen[6], Louise Lehmann Christensen[3,4], Dorte Glintborg[3], Ellen Hamge[7], Merete Lund Hetland[8], Richard Christian Jensen[3], Søren Andreas Just[9], Kresten Keller[10], Marianne Klose[6], Kristina Lamgesen[2,11], Marie Louise Lund[5,6], Jelena Stankovic[1,2], Paul M Stewart[12], Henrik Toft Sørensen[2,11], Randi Tei[1], Anne Voss[13], Ulla Feldt-Rasmussen[5,6], Jens Otto Jørgensen[1,2] & Marianne Andersen[3,4]

[1]Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus N; [2]Aarhus University, Department of Clinical Medicine, Aarhus N; [3]Odense University Hospital, Department of Endocrinology, Odense C, Denmark; [4]University of Southern Denmark, Research Unit OPEN, Department of Clinical Research, Odense, Denmark; [5]University of Copenhagen, Department of Clinical Medicine, Faculty of Health and Clinical Sciences, Københavns, Denmark; [6]Copenhagen University Hospital, Rigshospitalet, Department of Endocrinology and Metabolism, Københavns, Denmark; [7]Aarhus University Hospital, Department of Rheumatology, 8200 Aarhus N, Denmark; [8]Copenhagen University Hospital, Rigshospitalet, Center of Rheumatology and Joint Diseases, Denmark; [9]Odense University Hospital, Svendborg Hospital, Department of Rheumatology, Denmark, [10]Aarhus University Hospital, Department of Rheumatology, Denmark, [11]Aarhus University Hospital, Department of Clinical Epidemiology, Denmark, [12]University of Leeds, Faculty of Medicine and Health, United Kingdom, [13]Odense University Hospital, Department of Rheumatology, Denmark

Introduction

Pharmacological glucocorticoid (GC) treatment may cause iatrogenic adrenal insufficiency (GIA), although the prevalence and clinical implications are debated. With 3% of the Danish population redeeming prescriptions of systemic GC annually, the number of patients at risk is potentially extensive. Taken together, there is an unmet need for a prospective and unbiased assessment of the GIA prevalence.

Materials and Methods

The data for this report stem from an ongoing randomized clinical trial – REPLACE. The study systematically investigates adrenocortical function in patients with polymyalgia rheumatica (PMR)/giant cell arteritis (GCA), 2-12 weeks after patients have stopped long-term (>12 weeks) prednisolone treatment. We used the standard 250 µg ACTH test (SST) and analyzed plasma cortisol at 0 and 30 minutes with Liquid Chromatography Mass Spectrometry and/or Electrochemiluminescence immunoassay (Roche Elecsys Cortisol II) with GIA defined as 30-minute cortisol <420 nmol/l. The participants also completed a 30-item disease-specific (AddiQoL-30) quality of life questionnaire with scores from 30 (worst) to 120 (best).

Results

Among 238 patients who were tested, four (1.6%) patients exhibited an insufficient response to the SST. 64/192 (33%) of patients with completed AddiQoL-30 displayed marked symptoms, with an AddiQoL-30 score ≤85 (average for AI patients in literature). AddiQoL-30 score ≤85 was related to lower basal plasma cortisol levels taken at median time 11:30 (IQR 10:09-12:50) of 261 (95%CI: 239-283) nmol/l vs 307 (95%CI: 292-322) nmol/l, $P<0.001$. Linear regression adjusted for age, sex, BMI and sample time revealed a positive correlation between AddiQoL-30 score and basal cortisol of 1.5 (95%CI: 0.3-2.9) points/50 nmol/l ($P=0.015$). Risk factors associated with low Addiqol-30 score included upper quartile body fat percentage (OR: 7.3, 95%CI: 1.8-30.7) compared to lower quartile, lower quartile hand grip strength (OR: 6.2, 95%CI: 1.9-20.6) compared to upper quartile and female sex (OR: 1.9, 95%CI: 1.0-3.7) compared to male (all $P<0.05$). There was no association with age, type of or duration of PMR/GCA, cumulative 6-month prednisolone exposure or levels of C-reactive protein.

Conclusions

- The risk of GIA defined by the SST after finished prednisolone treatment in patients with PMR/GCA is much lower than previously reported, but the prevalence of GIA symptoms is high and accompanied by lower cortisol levels.
- It remains to be experimentally tested, if patients with symptoms attributable to adrenal insufficiency after planned cessation of prednisolone treatment benefit from hydrocortisone replacement therapy.
- Our data add important information about the so-called steroid withdrawal syndrome, which merits future research.

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RC11.6

Modulation of calcium signaling on demand to decipher the molecular mechanisms of primary aldosteronism

Bakhta Fedlaoui[1], Cosentino Teresa[1], Al Sayed Zeina[1], Giscos-Douriez Isabelle[1], Fernandes-Rosa Fabio[1], Hulot Jean-Sebastien[1,2], Faedda Nicolo[1], Fayad May[1], Magnus Chris[3], Sternson Scott[3], Travers-Allard Simon[1,4], Baron Stephanie[4], Zennaro Maria-Christina[1,5] & Sheerazed Boulkroun[1]

[1]PARCC, INSERM, Université Paris Cité, Paris, France; [2]CIC1418 and DMU CARTE, Assistance Publique Hôpitaux de Paris (AP-HP), Hôpital Européen Georges Pompidou, Paris, France; [3]Howard Hmghes Medical Institute & Department of Neurosciences, University of California, San Diego, United States; [4]Service de Physiologie, Assistance Publique Hôpitaux de Paris (AP-HP), Hôpital Européen Georges Pompidou, Paris, France; [5]Service de Génétique, Assistance Publique Hôpitaux de Paris (AP-HP), Hôpital Européen Georges Pompidou, Paris, France

Primary aldosteronism (PA) is the most frequent form of secondary hypertension and is due to autonomous aldosterone production by the adrenal gland. During the last decades, major advances have been made in our understanding of the disease with the identification of germline or somatic mutations in ion channels and pumps. These mutations enhance calcium signaling, the main trigger of aldosterone biosynthesis. The objective of our work was to elucidate, using chemogenetic tools, the molecular mechanisms underlying the development of PA by modulating sodium entry into the cells "on demand" leading to calcium signaling activation. We have developed an adrenocortical H295R-S2 cell line stably expressing a chimeric ion channel receptor formed by the extracellular ligand-binding domain of the a7 nicotinic acetylcholine receptor fused to the ion pore domain of the serotonin receptor 5HT3a named α7-5HT3. Its activation by a selective agonist, the PSEM-817, leads to sodium entry into the cells and activation of calcium signaling. In parallel, we have developed a mouse model expressing the α7-5HT3 receptor specifically in the adrenal cortex. The cells expressing the α7-5HT3 receptor recapitulated the major features of *KCNJ5* mutations, the most frequent genetic alteration identified in Aldosterone-Producing-Adenoma. Stimulation of the α7-5HT3 receptor by PSEM-817 resulted in a significant increase in intracellular calcium concentrations, *CYP11B2* mRNA expression, and aldosterone biosynthesis and was associated with a decrease in cell proliferation. RNA sequencing and steroidome analyses revealed unique profiles associated with sodium entry. Exploration of adult mice expressing the α7-5HT3 receptor specifically in the adrenal cortex, generated in our laboratory, is ongoing. Preliminary results revealed a significant increase in plasma aldosterone and 18-hydroxycorticosterone levels in male and female mice expressing the a7-5HT3 receptor after four weeks of treatment with PSEM-817 but no major adrenal abnormalities. Our results smggest that increased sodium influx leading to increased calcium signaling is not sufficient to promote both increased aldosterone production and cell proliferation, thus strongly supporting the requirement of additional mechanisms for the development of APA. Altogether, this work offers valuable insights into the role of sodium-induced calcium signalling in PA development and paves the way for developing new therapeutic strategies.

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RC11.7

An artificial intelligence-based decision support system for classifying patients with adrenal tumors

Dimitrios Binas[1], Theodore Economopoulos[1], Grigoria Betsi[2], Paraskevi Xekouki[2], Anna Angelousi[3] & George Matsopoulos[1]

[1]National Technological University of Athens, Biomedical Engineering Laboratory, School of Electrical and Computer Engineering, Athens, Greece; [2]University of Crete School of Medicine, Endocrinology and Diabetes Clinic, Heraklion Crete, Greece; [3]National and Kapodistrian University of Athens, First Department of Internal Medicine, Athens, Greece

Background

Adrenal Incidentaloma's (AI) incidence has been increased 10-fold in the past two decades and more specifically, up to 7% in the general population and up to 9% in elderly patients. Determining whether an adrenal mass is malignant or hormonally active is of great clinical and socioeconomical importance, in order to select the best medical approach and follow up. Artificial Intelligence techniques could provide useful clinical tools for predicting the nature of AI with acceptable accuracy.

Methods

A total of 96 patients diagnosed with AI were selected from two tertiary centres. Their clinical data were collected and randomly grouped into training and validation sets in a ratio of 4:1. Two different experimental approaches were adopted. The first approach, concerned the analysis of twelve routine clinical features [functionality, age at diagnosis, hypokalemia, lateralisation, size max, baseline cortisol morning levels, adrenocorticotropic hormone (ACTH), 17-OH progesterone levels, 24 h urinary free cortisol, 1 mg overnight dexamethasone suppression cortisol levels, Hb1Ac, Computed Tomography imaging (baseline non-contrast Hounsfield)] for developing a predictive model for benign and non-benign adrenal tumors. The second approach included eight more features [age, gender, hypertension, hyperlipidaemia, anti-lipidemic therapy, Diabetes Mellitus (DM), anti-DM therapy, dehydroepiandrosterone (DHEAS)] for classifying

patients into the same groups (benign and non-benign tumors). Eleven Machine Learning (ML) models were applied and tested in each of the above-mentioned experimental approaches to construct the best performing predictive model. In order to evaluate the performance of the proposed classification systems, precision, sensitivity, F1-score and accuracy were examined.
Results
The first tested Machine Learning model, based on the combination of 12 features, resulted in predictions with an average accuracy of over 97% using a K-Neighbors classifier. Equally, the second tested model based on the combination of 20 features resulted in a prediction with an average accuracy of over 96%, using a Ridge classifier. The statistical comparison between the results of the two different experimental approaches did not show statistically significant difference, as verified through a Mann Whitney test.
Conclusion
This study proposes the use of Machine Learning methods to establish a prediction model for benign and non-benign adrenal tumors. A high predictive performance was achieved even based on relatively few clinical cases. This study provides a decision support model which could constitute a helpful and practical clinical tool, accelerating the decision process in the healthcare system resulting to early screening, which ultimately results in time and cost savings.

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RC12.1

Effects of semaglutide, Peptide YY3-36 and empagliflozin on metabolic dysfunction associated fatty steatotic liver disease in diet-induced obese rats with chronic nitric oxide synthase-inhibition

Niklas Geiger[1], Simon Kloock[1], Jana Gerner[2], Aisha-Nike Landthaler[2], Alexander Nickel[2], Michael Kohlhaas[2], Andreas Geier[3], Martin Fassnacht[1] & Ulrich Dischinger[1]
[1]University Hospital Wuerzburg, Department of Internal Medicine, Division of Endocrinology and Diabetes, Wuerzburg, Germany; [2]University Hospital Wuerzburg, Comprehensive Heart Failure Center, Wuerzburg, Germany; [3]University Hospital Wuerzburg, Department of Hepatology, Wuerzburg, Germany

Background and Aims
Metabolic dysfunction-associated steatotic liver disease (MASLD) is a common comorbidity of obesity. In this study, we sought to determine hepatic metabolic and mitochondrial effects of the Glucagon-like Peptide-1-agonist semaglutide, the sodium-glucose linked transporter 2-inhibitor empagliflozin and Peptide YY_{3-36} in diet-induced obese rats with additional chronic inhibition of nitric oxide synthase via N^{ω}-nitro-L-arginine methyl ester (L-NAME), to induce accelerated liver injury.
Method
Following an eight-week feeding period with a high-fat/fructose-diet (HFD) and L-NAME, male wistar rats were randomized into the following treatment groups: semaglutide, empagliflozin, PYY_{3-36}, semaglutide in combination with empagliflozin or PYY_{3-36}, a food restricted body weight matched group (BWM) and saline control. After an additional 8 weeks, qRT-PCR was performed to quantify hepatic mRNA expression of metabolic and inflammatory marker genes. Serum was analysed for insulin, glucose, adiponectin and leptin levels. Moreover, in isolated mitochondria, mitochondrial respiration in different states using Oroboros O2K-FluoRespirometer was examined.
Results
In the liver, the de-novo lipogenesis regulating genes MLXIPL and SREBF-1 were downregulated in the BWM, semaglutide and PYY_{3-36} -mono groups and significantly lower in the semaglutide + PYY_{3-36} group ($P<0.05$) compared to saline treated controls. HOMA-index was significantly lower in PYY-mono treated animals ($P<0.05$) and in the semaglutide + empagliflozin- group ($P<0.05$), adiponectin-leptin-ratio was significantly higher in semaglutide + PYY_{3-36} ($P<0.01$) and BWM treated animals in comparison to saline ($P<0.01$). Moreover, there was a significant downregulation of IL-1b mRNA in the semaglutide-mono treated group ($P<0.05$). In the semaglutide + empagliflozin treated group, TNF-alpha-levels were lower compared to saline. Regarding mitochondrial respiration, fatty acid-dependent state 3 respiration, empagliflozin ($P<0.001$) as well as semaglutide + empagliflozin ($P<0.05$) decreased O_2-consumption significantly in comparison to controls. In the uncoupled state, empagliflozin and PYY_{3-36} mono-treatment decreased the O_2-rate significantly ($P<0.05$) compared to saline control. Moreover, semaglutide in combination with PYY_{3-36} or empagliflozin lowered O_2-consumption.
Conclusion
In summary, the presented data indicate a strong improvement of insulin sensitivity shown by presented metabolic parameters and associated genes. O_2-consumption of the respiratory chain in mitochondria is decreased in semaglutide, PYY_{3-36}, and empagliflozin treated rats, supposing reduced metabolic stress in these groups. The strongest effect was detected in semaglutide + PYY_{3-36} treated animals, which points towards PYY_{3-36} as a promising additive substance in the treatment of MASLD.

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RC12.2

Predictors of poor response to semaglutide for weight management

Ploutarchos Tzoulis[1,2] & Michael Batavanis[3]
[1]UCL Medical School, London, United Kingdom; [2]IASO Hospital, Department of Endocrinology, Athens, Greece; [3]University of Cambridge School of Clinical Medicine, Cambridge, United Kingdom

Introduction
The prevalence of obesity, a chronic disease with significant morbidity, has rapidly increased in recent decades. Semaglutide, an injectable glucagon-like peptide-1 agonist, has gained global popularity after its approval for weight management in 2021. All studies have reported marked variability in semaglutide response, with a small proportion of patients (10-16%) showing inadequate response. Data about the predictors of poor response to semaglutide for weight loss is lacking.
Methods
This is a retrospective case review of patients treated with semaglutide for weight loss in an endocrine clinic in Athens, Greece. This included 40 adults without diabetes mellitus who either had a body mass index (BMI) > 30 kg/m^2, or a BMI of 27-29.9 kg/m^2 and at least one weight-related co-morbidity. The aim was to assess the association of baseline characteristics with the magnitude of weight loss and determine predictors of poor response.
Results
This real-world chart review included 28 females and12 males with a median age of 47 years old, weight of 111.7 kg and BMI of 39.7 kg/m^2. The median weight reduction was 6.6% and 13.3%, following 3 and 6 months of semaglutide treatment, respectively. This study showed significant heterogeneity in response to semaglutide, with nine individuals (22.5%) being non-responders, defined as achieving a weight loss $<3\%$ at 3 months or $<5\%$ at 6 months. Baseline BMI was not associated with 3-month percentage weight loss ($P=0.086$). Regarding the effect of gender on semaglutide-induced weight loss, the median 3-month percentage weight loss was similar: 6.9% in females and 6.4% in males ($P=0.46$). However, the percentage of non-responders was higher amongst males (41.6% compared to 14.2% among females, but not statistically significant; $P=0.057$). Patients with a history of psychiatric illness were overrepresented in the non-responders group, with 4 out of 9 patients (44.4%) not showing a favourable response. The only three individuals who experienced weight gain at 3 months were all females with active major depressive disorder.
Discussion
This retrospective study confirmed the great variability in semaglutide-related weight loss outcomes, with males having a higher likelihood of suboptimal response compared to females. The novel finding was the link of psychiatric disease, especially active depression, with poor response to semaglutide, highlighting the need to evaluate the efficacy of semaglutide in patients with active psychiatric disease. Determining the predictors of response to semaglutide is essential to facilitate personalised treatment of obesity.

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RC12.3

Adipose tissue analysis toolkit (ATAT) for automated analysis of adipocyte size and extracellular matrix in white adipose tissue

Jacob Robino[1], Alexander Plekhanov[2], Qingzhang Zhu[3], Michael Jensen[4], Philipp Scherer[3], Charles Roberts[1] & Oleg Varlamov[1,5]
[1]Oregon National Primate Research Center, Beaverton, United States; [2]California Institute of Technology, Pasadena, United States; [3]UT Southwestern Medical Center, Dallas, United States; [4]Mayo Clinic, Rochester, United States; [5]Oregon Health and Science University, Oregon Primate Research Center, Beaverton, United States

The pathological expansion of white adipose tissue (WAT) in obesity involves adipocyte hypertrophy accompanied by expansion of collagen-rich pericellular extracellular matrix (ECM) and the development of crown-like structures (CLS). Traditionally, WAT morphology is assessed through immunohistochemical analysis of WAT sections. However, manual analysis of large histological

sections is time-consuming, and available digital tools for analyzing adipocyte size and pericellular ECM are limited. To address this gap, we developed the Adipose Tissue Analysis Toolkit (ATAT), an ImageJ plmgin facilitating analysis of adipocyte size, WAT ECM and CLS. ATAT utilizes local and image-level differentials in pixel intensity to independently threshold background, distinguishing adipocyte-free tissue without user input. It accurately captures adipocytes in histological sections stained with common dyes and automates the analysis of adipocyte cross-sectional area, total-field, and localized region-of-interest ECM. ATAT allows fully automated batch analysis of histological images using default or user-defined adipocyte detection parameters. ATAT provides several advantages over existing WAT image analysis tools, enabling high-throughput analyses of adipocyte-specific parameters and facilitating the assessment of ECM changes associated with WAT remodeling due to weight changes and other pathophysiological alterations that affect WAT function.

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RC12.4

Hypoglycaemia following the 2-hour 75g OGTT in pregnancy – investigating maternal and foetal outcomes

Edward Jude, Callum Blunt & Roopa Krishnamurthy
Tameside and Glossop Integrated Care NHS Foundation Trust, United Kingdom

Aims
To investigate differences in maternal and foetal outcomes in pregnancy, where patients developed hypoglycaemia following the 2-hour 75 g oral glucose tolerance test (OGTT).
Method
A retrospective cohort study of 200 pregnancies attending the Antenatal Clinic at Tameside General Hospital between 2018 and 2022. Outcomes were compared between 4 groups: normal OGTT [G1; ($n=39$, 20%], hyperglycaemia following OGTT [G2; BG $\geq$5.6 mmol/litre or 2-hour OGTT $\geq$7.8 ($n=41$, 21%)], hypoglycaemia [G3; 2 hr OGTT 3.0-3.9 mmol/l ($n=93$, 47%)], or clinically significant hypoglycaemia [G4; 2 hr OGTT $<$3.0 mmol/l ($n=27$, 14%)]. Maternal BMI, foetal body-weight (FBW), neonatal complications, neo-natal intensive care unit (NICU) stay and conversion to GDM were assessed.
Results
Maternal BMI was lower in G3 and G4 (27.3 kg/m^2 and 28.1 kg/m^2 respectively) compared to G1 (30.4 kg/m^2) ($P=0.02$). NICU stay was more frequent in G3 (12%, $n=11$) and G4 (8%, $n=2$) compared to G1 (5%, $n=2$). Foetal complications occurred in 39% of G3 ($n=36$) and 44% of G4 ($n=12$) compared to 23% in G1 ($n=9$) and 22% in G2 ($n=9$). FBW was similar in G1 when compared to G3 and G4 ($P=0.34$). Of the 120 patients in G3 and G4, 25 patients self-monitored blood glucose for two weeks. 28% ($n=7$) subsequently developed GDM.
Conclusion
Higher rates of NICU stay and foetal complications were seen in both hypoglycaemic groups. In patients with hypoglycaemia following OGTT there is evidence to support monitoring BG as a proportion were later diagnosed with GDM.

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RC12.5

Effects of antagonists of the NPY-2 receptor, semaglutide, PYY3-36, and empagliflozin on metabolic dysfunction-associated steatotic liver disease in diet-induced obese rats

Simon Kloock[1], Niklas Haerting[1], Gloria Herzog[2], Marie Oertel[1], Niklas Geiger[1], Andreas Geier[3], Alexander Nickel[4], Kohlhaas Michael[4], Martin Fassnacht[1] & Ulrich Dischinger[1,4]
[1]Center for Internal Medicine at the University of Würzburg ZIM, Endocrinology and Diabetes, Würzburg, Germany; [2]Institute of Pathology at the University of Würzburg, Würzburg, Germany; [3]Center for Internal Medicine at the University of Würzburg ZIM, Hepatology, Würzburg, Germany; [4]Comprehensive Heart Failure Center, Cardiology, Würzburg, Germany

Metabolic dysfunction-associated steatotic liver disease (MASLD) frequently accompanies obesity, posing a significant health concern. The Neuropeptide Y (NPY) system, a key player in energy metabolism regulation, has implications for liver health, yet the impact of NPY receptor antagonists remains largely unexplored. This study investigates the effects of antagonists targeting the NPY-2 receptor (Y2R) in comparison to known MASLD-beneficial substances.
Methods
Diet-induced obese (DIO) male Wistar rats were divided into the following treatment groups: empagliflozin, semaglutide, semaglutide $\pm$PYY3-36, Y2R antagonist JNJ-31020028, a food-restricted group, and a control group. After 8 weeks of treatment, livers were assessed for weight and histology. QrtPCR was utilized to examine liver inflammation and de novo lipogenesis in both liver and adipose tissue. Serum samples were analyzed for metabolic parameters.
Results
The combination of semaglutide and PYY3-36 resulted in weight loss, significantly reducing liver steatosis compared to controls ($p = 0.05$). Markers of inflammation, insulin resistance, and leptin levels were also reduced. Empagliflozin exhibited limited impact on the measured parameters. JNJ-31020028 did not induce significant weight loss but prevented steatosis ($P=0.03$), with no effect on inflammation. The de novo lipogenesis regulating genes SREBP1 and MLXIPL were downregulated in livers of JNJ-31020028 treated DIO rats compared to controls ($p \leq 0.0001$), with no observed effect in visceral adipose tissue. Food restriction led to significant reductions in weight, steatosis, and de novo lipogenesis.
Discussion
Body weight reduction, achieved through methods like food restriction or drmgs such as semaglutide $\pm$PYY3-36, proved effective in ameliorating liver steatosis in DIO rats. Notably, the weight-neutral Y2R antagonists showed promise in preventing liver steatosis through a reduction in de novo lipogenesis. Further investigations are needed to elucidate the molecular impact of the NPY system on liver pathophysiology.

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Rapid Communications 13: Late Breaking

RC13.1

MTHFR 677 TT and CT genotype related epigenetic changes and hyperhomocysteinemia in Hypothyroidism and its management, a family case report

Tamar Kvaratskhelia[1], Elene Abzianidze[2], Sandro Surmava[2] & Eka Kvaratskhelia[2]
[1]New Vision University Hospital, Internal department, Tb, Georgia; [2]Tbilisi State Medical University, T'bilisi, Georgia

Introduction
Hypothyroidism is a clinical syndrome resulting from a deficiency of thyroid hormones, which in turn results in a generalized slowing down of metabolic processes. There are consistent reports demonstrating that many diseases, including the thyroid gland dysfunction are associated with changes of serum homocysteine (tHcy) level, with its genetic and epigenetic causes.
Case report
In 2018 we reported 51 and 52-year-old sisters diagnosed with subclinical and manifested hypothyroidism accordingly. One of them was enrolled to a research study related to the link between MTHFR gene polymorphisms, DNA methylation status and hypothyroidism (T. Kvaratskhelia et al.). Both siblings revealed MTHFR gene 677 TT genotype. We also investigated two other siblings from the same family without history of hypothiroidism: 54-year-old female and 47-year-old male who showed CC genotype and their 82-year-old mother with CT genotype and an episode of thyroid failure in the past. After 6 years we report 88-year-old mother who developed subclinical hypothyroidism soon after initial study and the results of hyperhomocysteinemia management with vitamin supplements in all effected family members.
Methods
MTHFR gene was investigated by the PCR-RELF method using HinfI (NEB Inc) enzyme. Levels of DNMT1-3a and DNMT1 were measured in nuclear extracts of PBMC (Abcam). Total serum homocysteine concentrations were also measured. DNA samples underwent bisulfite modification (Qiagen) and methylation levels of Alu and LINE-1 were examined by the combined bisulfite restriction analysis-interspersed repetitive sequences (COBRA-IRS). We have added vitamin B group supplements for hyperhomocysteinemia management.
Results
Family members with TT and CT genotype had elevated levels ofDNMT3a compared with CC genotype. There was no significant difference in DNMT1 levels. tHcy levels were significantly elevated in study subjects with TT genotypes and slightly elevated in the individual with CT genotype in initial measurement, which increased at the presentation of hypothyroidism. Hypermethylated loci (mCmC) at Alu elements were significantly lower and LINE-1 hypermethylated loci (mCmC) were also lower in TT and CT genotypes compared with CC family members. Hyperhomocysteinemia management with

supplemets lead to the reduction of levothyroxine replacement doses in sisters, it improved thyroid function test results in mother who was not initiated levothyroxine replacement treatment and significantly improved dyslipidemia in all study subjects.
Conclusions
We smggest that molecular studies of MTHFR gene and its related epigenetic changes could be valuable for refining the clinical diagnosis of hypothyroidism, leading to its more precise management.

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RC13.2

Comprehensive genetic analyses of sporadic and seemingly idiopathic hypoparathyroidism by whole-exome sequencing: Identification of novel GCM2 and AIRE mutations

Saroj Sahoo[1], Takasi Anush Babu[1] & Kausik Mandal[2]
[1]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Endocrinology, Lucknow, India; [2]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Medical Genetics, Lucknow, India

Objective
We aimed to identify the genetic defect in patients labelled as sporadic and idiopathic hypoparathyroidism (HP) by using whole-exome sequencing (WES).
Methods
Patients with sporadic nonsurgical HP, aged <30 years were recruited. Those with a known genetic or autoimmune aetiology were excluded from the study. Thirty such patients were screened for antibodies against interferon-α, a highly sensitive and specific marker of autoimmune polyendocrine syndrome type 1 (APS1). Eight patients had an elevated titer and all of them carried double mutations in the *AIRE*, responsible for APS1. The remaining 22 were screened for DiGeorge syndrome via multiplex-ligand dependent probe amplification (MLPA) and five had deletions diagnostic of DiGeorge syndrome. The remaining 17 were subjected to WES. Mutations were confirmed by Sanger sequencing, and the pathogenicity of novel variants were confirmed by *in-silico* functional analyses.
Results
Of the 17 patients who underwent WES, pathogenic variants causing HP were detected in five (29%) patients. Patient #1 (current age 32 years, age of onset of disease 24 years) had a known pathogenic variant c. 1504A>C, Asn502His in the *GCM2* gene. Patient #2 (current age 19 years, age of onset of disease at 1 month) and patient #3 (age of onset of the HP 20 years, current age 32 years) had novel mutations in the *GCM2* gene; homozygous mutation c.391C>T, Arg131* and heterozygous variant c.319G>A, Asp107Asn, respectively. Patient #4 (current age 21 years, age of onset of disease 14 year) carried a heterozygous variant in exon 6 of the *AIRE* gene (c.739C>T, Arg247Cys). Patient #5 with HP and additional features such as sensory neural hearing loss and dysmorphic facies carried a heterozygous variant c.1608G>T (Met536Ile) in the *AIRE*. All the novel variants were pathogenic as assessed in the *in-silico* functional analysis. The patients carrying the *AIRE* mutations did not have other endocrine and ectodermal components on further investigations.
Conclusion
Muations in the *GCM2* and *AIRE* were common in patients with seemingly sporadic and idiopathic hypoparathyroidism. In contrast to the classic homozygous/compound heterozygous mutations in the *AIRE* which is responsible for childhood-onset APS1 and widespread endocrine and ectodermal manifestation, heterozygous mutations in the *AIRE* can manifest as isolated HP and negative for antibodies againt interferon-α. All young patients with sporadic and idiopathic hypoparathyroidism should be evaluated for genetic basis especially *GCM2* and *AIRE*.

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RC13.3

Comparison of metyrapone, osilodrostat and ketoconazole in the therapy of endogenous Cushing's syndrome: The MOSKETEER study

Mario Detomas[1], Filippo Ceccato[2], Chiara Simeoli[3], Pasquale Dolce[4], Ana Aulinas Maso[5], Aleksandra Gilis-Januszewska[6], Mirko Parasiliti Caprino[7], Mohamed Bassiony[8], Maria Stelmachowska-Banaś[9], Emanuele Ferrante[10], James Pittaway[11], German Rubinstein[12], Felicia A Hanzu[13], Soraya Pmglisi[14], Andrea Corsello[15], Simone Antonini[16], Lana Sambula[17], Marianna Minnetti[18], Linus Haberbosch[19], Timo Deutschbein[20], Ulrich Dischinger[1], Giacomo Voltan[2], Nicola Di Paola[3], Alicia Santos Vives[5], Mari Minasyan[6], Roberta Giordano[21], Vanessa Fell[8], Karolina Cylke-Falkowska[9], Alessandra Mangone[10], Christina Plowman[11], Arturo Vega[13], Leah Braun[12], Alessandro Mazzarella[3], Pietro Locantore[15], Antongiulio Faggiano[22], Massimo Terzolo[14], Andrea Lania[16], Darko Kastelan[17], Andrea Isidori[18], Martin Reincke[12], Irina Bancos[8], Emanuela Arvat[23], Susan M Webb[5], Scaroni Carla[2], Rosario Pivonello[3], Martin Fassnacht[1] & Barbara Altieri[1]
[1]University Hospital of Würzburg, Endocrinology, Würzburg; [2]Endocrine Disease Unit, University-Hospital of Padova; [3]Department of Clinical Medicine and Surgery, Division of Endocrinology, University of Naples "Federico II", Naples Italy; [4]Department of Public Health, University of Naples Federico II, 80131 Naples, Italy; [5]Department of Endocrinology, Hospital S Pau, Barcelona; IIB-Sant Pau, Research Center for Pituitary Diseases, Barcelona; CIBERER Unit 747, ISCIII and Department of Medicine, Univ Autonoma Barcelona, Spain; [6]Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland; [7]Division of Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [8]Division of Endocrinology, Diabetes, Metabolism, and Nutrition, Department of Medicine, Mayo Clinic, Rochester, MN; [9]Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland, [10]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [11]Centre for Endocrinology, Charterhouse Square, Queen Mary University of London, London EC1M 6BQ, United Kingdom; [12]Medizinische Klinik und Poliklinik IV, Klinikum der Universität, Ludwig-Maximilians-Universität München, Munich 80336, Germany, [13]Endocrinology and Nutrition Department, Hospital Clinic, University of Barcelona, IDIPAS, Barcelona, Spain; [14]Internal Medicine, San Luigi Hospital, Department of Clinical and Biological Sciences, University of Turin, 10043 Orbassano, Italy; [15]Department of Translational Medicine and Surgery, Unit of Endocrinology, Università Cattolica del Sacro Cuore-Fondazione Policlinico Universitario A. Gemelli IRCCS, Largo Gemelli 8, I-00168 Rome, Italy; [16]Endocrinology, Diabetology and Andrology Unit, IRCCS Humanitas Research Hospital, 20089 Rozzano, Italy; [17]Department of Endocrinology, University Hospital Centre Zagreb, Zagreb, Croatia; [18]Department of Experimental Medicine, Sapienza University of Rome, Viale Regina Elena, 324, 00161, Rome, Italy; [19]Department of Endocrinology and Metabolism, Charité - Universitätsmedizin Berlin, 10117, Berlin, Germany; [20]Medicover Oldenburg, MVZ, [21]Division of Endocrinology, Diabetes and Metabolism, Department of Biological and Clinical Sciences, University of Turin, Turin, Italy, [22]Endocrinology Unit, Department of Clinical and Molecular Medicine, Sant'Andrea Hospital, ENETS Center of Excellence, Sapienza University of Rome, Rome, Italy; [23]Oncologic Endocrinology, Department of Medical Sciences, University of Turin, Turin, Italy

Background
Metyrapone, osilodrostat, and ketoconazole are steroidogenesis inhibitors used as second-line treatment in endogenous Cushing's syndrome (CS). However, a direct comparison of these three drmgs is missing.
Objective
To compare the efficacy of the three drmgs after short-term therapy (≤ 12 weeks) for CS.
Methods
Multicenter, real-life retrospective study involving 20 centers worldwide. Patients with CS treated with metyrapone, osilodrostat or ketoconazole as monotherapy were included. Main outcomes were changes in 24 h urinary free cortisol (24 h-UFC) and morning serum cortisol, both normalized to upper limit of normal (ULN) for each measurement, after 2(T1), 4(T2), and 12(T3) weeks of treatment. Mixed-effects models were used to evaluate how drmgs influenced main outcomes over time, considering baseline values and controlling for dosage variations. The interaction between drmgs and time was tested.
Results
531 patients (76% women; 77% ACTH-dependent CS) were identified; 35 patients with adrenocortical carcinoma were excluded for this analysis. Among the remaining 496 cases, 199 (40%) were treated with metyrapone, 122 (25%) with osilodrostat, 175 (35%) with ketoconazole. Median daily dose of metyrapone and osilodrostat significantly increased from 750 (interquartile range 500-1000) mg and 3 (2-4) mg at baseline to 1000 (500-1250; $P<0.01$)mg and 6 (2-10; $P<0.0001$) mg at T3, respectively. No significant changes were observed for ketoconazole (median 400mg over time). Median baseline 24 h-UFC was slightly higher in patients under metyrapone (2.6×ULN, 1.5-7.9) than ketoconazole (2.1×ULN, 1.2-3.6, $P=0.04$), but not than osilodrostat (2.3×ULN, 1.3-4). The three drmgs showed same impact in decreasing 24 h-UFC over time (interaction $P=0.51$). Morning serum cortisol at baseline was not different among the groups. Osilodrostat reduced morning serum cortisol more than the other drmgs (interaction $P=0.002$), mostly at T3 (average mean difference: metyrapone/osilodrostat=0.23, 95%CI=0.07-0.38, $P<0.001$; ketoconazole/osilodrostat=0.28, 95%CI=0.45-0.12, $P<0.001$). No differences between ACTH-dependent and -independent CS were found regarding the efficacy of the three drmgs. At T1, the number of antihypertensives was reduced in 7% of patients under metyrapone, 17% under osilodrostat, and 7% under ketoconazole ($P<0.005$), whereas at T2-T3 no differences were found. At T3, 19% of patients under osilodrostat required potassium supplementation compared to 10% under metyrapone and 10% under

ketoconazole ($P=0.15$). Treatment was discontinued because of adverse events in 5% of cases under metyrapone, 10% under osilodrostat, 8% under ketoconazole.
Conclusion
Our results showed comparable efficacy of these three drmgs in decreasing 24 h-UFC. However, considering dose variations, osilodrostat might be more efficient in decreasing morning serum cortisol and faster in reducing blood pressure than metyrapone and ketoconazole.

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RC13.4

Development and validation of an LC-MS/MS method to measure 7-alpha-hydroxy-4-cholesten-3-one (C4) for the assessment of bile acid dysregulation in PCOS

Jonathan S Atkins[1], Brian Keevil[1], Christian Ludwig[2] & James M. Hawley[1]
[1]Wythenshawe Hospital, Department of Clinical Biochemistry, Manchester, United Kingdom; [2]University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, United Kingdom

Introduction
7α-Hydroxy-4-cholesten-3-one (C4) is the common intermediary of the primary bile acids (BAs). Its concentration in serum correlates with the rate of activity of hepatic CYP7A1 and therefore with the rate of hepatic BA production. Previous work has smggested a role for BA pool dysregulation in the metabolic syndrome and gut dysbiosis seen in polycystic ovary syndrome (PCOS). However, the mechanism of this is still to be elucidated. Here we report a novel LC-MS/MS method for the analysis of C4 for this purpose and an assessment of preanalytical stability to ensure reliable results.
Methods
The method was developed using a Waters TQS mass spectrometer. Accuracy was underpinned by calibrating to quantitative nuclear magnetic resonance analysis. C4 was analysed in a high-throughput 96-well plate format using deuterated C4 as an internal standard and liquid-liquid extraction for sample clean-up. The assay was validated according to 2018 FDA guidelines. To assess C4 stability, healthy volunteers ($n=12$) donated 8 samples each. Samples were incubated at 20°C for up to 72 hours and retrieved, centrifmged, aliquoted and frozen for storage at different time points prior to C4 analysis.
Results
The C4 method demonstrated excellent analytical performance and passed all validation criteria. The method was found to be accurate, precise, free from matrix effects and not susceptible to assay interference. Concentrations up to 1000 nmol/l could be reliably quantitated with an LOQ of 5 nmol/l. Over 72, hours concentrations of C4 gradually declined by up to 14% from their baseline concentrations. However, the change was not significant for up to 12 hours.
Conclusions
We present a robust method of analysing serum C4 that is metrologically traceable to SI units. C4 was found to be stable enough in unseparated serum for laboratory processing prior to analysis. This method is suitable for the assessment of BA production rate in patients with PCOS and may help to investigate the role this plays.

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RC13.5

Dose response relationship between Denosumab treatment and germ cell proliferation of humanized RANKL mice in vivo and in testicular tissue cultures

Nadia Krarup Knudsen[1], Christine Hjorth Andreassen[1], Charles O'Brien[2], Anne Jørgensen[1] & Martin Blomberg Jensen[1]
[1]Herlev and Gentofte Hospital, Department of Endocrinology and Internal Medicine, Herlev, Denmark; [2]University of Arkansas

Today there exist no treatment that can improve semen quality in more than 85% of infertile men. Interaction between germ and Sertoli cells is critical for sperm production, and Denosumab, an inhibitor of RANKL, has previously been shown to stimulate sperm production in a fraction of infertile men. Here, we show in a humanized RANKL mouse that Denosumab dose dependently increase germ cell proliferation and testicular weight. RANKL was modified so it can be blocked by Denosumab. Fragments of mouse testis were cultured with the RANKL inhibitor Denosumab and compared with vehicle treatment. Testis tissue were cultured for 48 hours. Germ cell proliferation was assessed by BrdU incorporation and Denosumab treatment 1-100 ng/ml increased germ cell proliferation compared with vehicle although no effect on germ cell apoptosis was observed. This effect is physiologically relevant as the seminal fluid concentration reached 120 ng/ml following Denosumab injection of 60 mg dosing sc. once. Mice with humanized RANKL were treated with Denosumab 0,1-3 mg/kg once and sacrificed after 6 weeks. All mice treated with Denosumab had increased testicular weight and an increased serum AMH and Inhibin B although only statistically significant for 0.1 mg/kg. This shows that transient RANKL inhibition leads to increased germ cell output after 1 full spermatogenesis that takes 35 days in mice. This study smggests that even low doses of Denosumab can stimulate mouse spermatogenesis; however, further investigation is critical for understanding the interplay between Sertoli cell function, spermatogenesis, and RANKL inhibition in humans.

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RC13.6

The clinical profile of silent and subclinical somatotroph PitNETs according to the immunohistochemical staining

Mariana Solovey[1,2], Olena Danevych[1], Mykola Guk[1] & Valeria Musulevska[1]
[1]Romodanov Neurosurgery Institute, Kyiv, Ukraine; [2]Komisarenko Endocrinology and Metabolism Institute, Kyiv, Ukraine

Background
Somatotroph PitNETs represent a polymorph group of GH-secreting pituitary neuroendocrine tumors with great variety of clinical presentation, which may graduate from totally silent without clinical and biochemical signs of hormonal hypersecretion to functioning with subtle or classic acromegaly symptoms. The grade of GH and somatostatin receptors expressoin as well as the other pituitary hormones and receptors co-expression may contribute to the tumor biological behavior.
Objective
To discover the clinical profile of silent and subclinical somatotroph PitNETs according to the immunohistochemical staining.
Materials and Methods
We have conducted a retrospective analysis of 33 cases of GH-immunopositive PitNETs surgically resected in our center without clinical signs of acromegaly. Tumors were classified according to the immunohistochemical staining: pure somatotroph, mammosomatotroph, mixed somatotroph-lactotroph, somatotroph-thyrotroph, plurihormonal Pit-1- lineage tumors. The clinical presentation and the grade of GH, somatostatin and estrogen receptors expressoin were compared in these groups.
Results
Silent somatotroph PitNETs represented 10·4% from all consecutive cases of nonfunctional PitNETs and 21.8% of all cases of GH-positive PitNETs. Pure somatotroph tumors constituted 48·5% of all GH-positive tumors, mammosomatotroph – 12·1%, mixed somatotroph-lactotroph – 21·2%, somatotroph-thyrotroph – 12·1%, plurihormonal Pit-1- lineage tumors – 6% respectively. Pure somatotroph tumors were divided into 2 groups: totally silent (24·25%) and subclinical (24·25%). The prevalent symptoms in cases of totally silent GH-tumors were visual disturbances and oligomenorrhea/amenorrhea. Headache was the most frequent presenting complaint in mixed somatotroph-lactotroph tumors. The presence of hypopituitarism and invasiveness depended on the immunohistochemical type of the tumor. The grade of GH expression didn't correlate with somatostatin receptors expression. The SSTR2 and SSTR5 expression was negative or lower than in acromegaly. All silent somatotroph tumors were negative for estrogen receptors.
Conclusions
Clinical presentation of silent somatotroph PitNETs is variable and depends on the variant of the immunohistochemical staining.

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Poster Presentations

Adrenal and Cardiovascular Endocrinology

P1

Reversal of cardiac damage after treatment for aldosterone-producing adenoma and idiopathic hyperaldosteronism – A Prospective Cardiac Magnetic Resonance Imaging study

Chenxiao Xu[1], Jiayu Sun[2], Tao Wu[2], Tao Chen[1], Lu Tang[2], Wei Wang[1], Fangli Zhou[1], Deying Wen[2] & Yan Ren[1]
[1]Department of Endocrinology and Metabolism, Adrenal Center, West China Hospital, Sichuan University, Chengdu, China; [2]Department of Radiology, West China Hospital, Sichuan University, Chengdu, China

Objective
At present, there are no studies in which authors report the use of cardiac magnetic resonance imaging (CMR) to evaluate the differences in myocardial strain between patients with aldosterone-producing adenomas (APAs) and those with idiopathic hyperaldosteronism (IHA) or the improvement in myocardial strain after treatment.
Methods
In this study, 71 patients with APA and 51 patients with IHA were prospectively enrolled from the Department of Endocrinology and Metabolism, West China Hospital, and all patients underwent CMR examination at the time of diagnosis. Differences in cardiac chamber volume, mass index and myocardial strain, including global radial strain (GRS), global circumferential strain (GCS) and global longitudinal strain (GLS), were compared between the two groups. Among them, 41 patients were re-examined via CMR one year after treatment, and the changes in cardiac parameters were also analyzed.
Results
Sex, duration of hypertension, blood pressure, fasting blood glucose, and lipid levels were comparable between the APA patients and the IHA patients at the time of diagnosis, and the IHA patients were older. There were no significant differences in the LVEF; native T1 time; or global radial, circumferential, or longitudinal peak strain (all $P>0.05$), but the APA patients had higher LV massi, LVEDVi, LVESVi, and RVEDVi (all $P<0.05$). Correlation analysis revealed that the log PAC and log ARR were positively correlated with the LV massi, LVEDVi, and LVESVi ($R=0.19$–0.27, $P=0.003$–0.042) and negatively correlated with the serum potassium concentration ($R=-0.24$–0.28, $P=0.002$–0.008). At the 1-year post-treatment follow-up assessment, patients showed significant decreases in the LVEDVi, LVESVi and LV massi and an increase in the global circumferential peak strain (all $P<0.05$).
Conclusion
Patients with APAs have more significant chamber enlargement and ventricular hypertrophy than patients without APAs, but the extents of myocardial strain and fibrosis may not be significantly different from those in patients with IHA. Improvements in the left ventricular structure and myocardial function 1 year after treatment are also noteworthy.
Key words: aldosterone-producing adenoma, idiopathic hyperaldosteronism, cardiac magnetic resonance, cardiac damage

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P2

Prospective, multi-country, observational study of patients with endogenous Cushing's syndrome exposed to Ketoconazole (using the existing European Registry on Cushing's Syndrome (ERCUSYN)), to assess drug use, safety and effectiveness

Susan Webb[1], Alicia Santos[1], Anna Aulinas Maso[1], Karin Zibar Tomsic[2], Claudia Amaral[3], Richard Feelders[4], Oskar Ragnarsson[5], Emanuele Ferrante[6], Filippo Ceccato[7], Olivier Chabre[8], Justine Cristante[8], Felicia Hanzu[9], Martin Reincke[10], Philippe Chanson[11], Antoine Tabarin[12], João Sequeira Duarte[13], Daniela Guelho[14], Carmen Fajardo[15], Martine Bostnavaron[16], Myriam Bou Nader[16], Jerôme Bertherat[17] & Thierry Brue[18]
[1]Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau, Ciberer Unit 747, UAB, Department of Endocrinology, Barcelona, Spain; [2]University Hospital, Zagreb, Department of Endocrinology, Zagreb, Croatia; [3]Centro Hospitalar Universitário do Santo António, Department of Endocrinology, Porto, Portugal; [4]Erasmus University Medical Center Rotterdam, Department of Endocrinology, Rotterdam, Netherlands; [5]Sahlgrenska University Hospital, Department of Endocrinology, Göteborg, Sweden; [6]Fondazione IRCC Ca' Granda Ospedale Maggiore Policlinico, Department of endocrinology, Milan, Italy; [7]University Hospital of Padova, Department of Endocrinology, Padova, Italy, [8]Centre Hospitalier Universitaire Grenoble Alpes, Department of Endocrinology, Grenoble, France; [9]Hospital Clinic Univesity Barcelona, Idibaps, Department of Endocrinology, Barcelona, Spain; [10]University Hospital of Münich, Medical Department IV, Münich, Germany; [11]APHP-Université Paris Saclay, Hôpital Bicêtre, Department of Endocrinology, Le Kremlin Bicêtre, France; [12]Centre Hospitalier Universitaire, Department of Endocrinology, Bordeaux, France; [13]Egas Moniz Hospital, Centro Hospitalar de Lisboa Ocidental, Department of Endocrinology CLO, Lisboa, Portugal; [14]CHUC-HUC, Serviço de Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal; [15]Hospital Universitario de La Ribera, Department of Endocrinology, Alzira, Spain; [16]HRA Pharma Rare Diseases, Rare Diseases, Châtillon, France; [17]Hôpital Cochin, Department of Endocrinology, Paris, France; [18]Hôpital de la conception, Department of Endocrinology, Marseille, France

Background
Ketoconazole is a steroidogenesis inhibitor approved in Europe for the treatment of endogenous Cushing's syndrome (CS) based on retrospective studies published over 3 decades. We present interim data from the first prospective observational, multicenter, international study on ketoconazole, a non-interventional PASS (Post-Authorization Safety study) requested by EMA at the time of registration to confirm ketoconazole good tolerance and effectiveness. This study is performed in collaboration with ESE owner of ERCUSYN (European Registry on CS).
Methods
Main inclusion criteria are: Patients (>12 years of age) with endogenous CS starting treatment with HRA ketoconazole® in routine clinical practice. The primary endpoint is to document liver (hepatotoxicity) and cardiac (QT prolongation, QTc >450 msec and/or QTc increase >60 msec tolerability profile of ketoconazole. The main secondary endpoints are overall safety of ketoconazole and effectiveness evaluations.
Results
Last interim results (August 2023) included 93 patients (73 Females, 20 Males) from 17 centers in 5 countries. At baseline, median age was 47 years (17–85), main etiology was pituitary-dependent CS and median final dose was 400 mg/day. Median treatment duration was 212 days (3 to 2160 days). No case of QTc prolongation was reported. Liver function tests (LFT) abnormalities were reported in 37.5% (33/88) patients, occurring up to 4 weeks after ketoconazole start. Only 10.2% (9/88) patients had AST ≥ 3 ULN (Upper Limit of Normal) without increase of Total Bilirubin (TB) >2×ULN. Among these patients, 7 had liver injury with ALT ≥5× ULN assessed as hepatocellular (4), cholestatic (2) and mixed injury (1), which resolved after ketoconazole discontinuation. In 5 patients concomitant medication was also suspected. For 5 patients, 9 study-drug related serious adverse events (SAEs) other than severe hepatotoxicity occurred (pneumonia, acute kidney injury (2), hypokalemia, acute adrenal insufficiency (2), hyperkalemia (2), angioedema). Among the 45/91 (49,4%) patients for whom urinary free cortisol (UFC) and/or serum cortisol data were available, 31/45 (47.2%) patients had normalized UFC levels and/or serum cortisol at the last visit. A treatment benefit was evaluated by the physician in 90/91 (98.9%) patients. At the last visit, twelve 12/91 (13.2%) patients had at least one less drug for comorbidities by drug class (antihypertensive, antidiabetics, anti-osteoporosis, lipid lowering, ischemic heart disease medications or other treatments for comorbidities).
Conclusions
This prospective observational study in patients with CS confirms that ketoconazole has a tolerability profile similar to the previously reported safety profile and effectively lowers cortisol levels.

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P3

Fingerprints of increased susceptibility to adrenal crisis in patients with chronic adrenal insufficiency

Janik Freytag[1], Irina Chifu[1], Sabine Herterich[2], Stefanie Hahner[1], Marcus Quinkler[3] & Burger-Stritt Stephanie[4]
[1]University Hospital Würzburg, Division of Endocrinology and Diabetes, Würzburg, Germany; [2]University Hospital Würzburg, Clinical Chemistry and Laboratory Medicine, Würzburg, Germany; [3]Endocrinology in Charlottenburg, Germany; [4]University Hospital, Uppsala, Sweden

Background
Potentially fatal adrenal crises (AC) still occur in educated patients with adrenal insufficiency (AI). Our study investigates clinical and biochemical fingerprints of increased susceptibility to AC.
Material and methods
199 patients with chronic AI (disease duration ≥6 years), classified into tertiles according to the frequency of AC/patient-years (group 1 no AC, group 2 ≤0.07 AC/py, group 3 >0.07 AC/py). Following parameters were assessed: 24 h urinary cortisol, salivary cortisol day profile, predefined glucocorticoid (GC) replacement score based on clinical and biochemical parameters of GC exposure, plasma and urinary catecholamines, polymorphisms (SNPs) of the glucocorticoid receptor

(*NR3C1*), mineralocorticoid receptor (*NR3C2*), *FKBP5*, HSD11B1 and HSD11B2 and crisis management.
Results
One-hundred patients (50%) never experienced AC, whereas sixty-seven patients (34%) had frequent AC (group 3). This group received significantly higher GC replacement doses (13 ± 5 mg hydrocortisone-equivalent /m^2/day) compared to group 1 (11 ± 3 mg hydrocortisone-equivalent /m^2/day, $P < 0.01$) and group 2 (11 ± 3 mg hydrocortisone-equivalent /m^2/day, $P < 0.01$). On the contrary, mean GC under-replacement score was lowest in patients with frequent AC (-2.3 ± 1.7) compared to both group 1 (-1.4 ± 1.4, $P = 0.017$) and group 2 (-1.0 ± 1.1, $P = 0.012$). 24 h-urinary metanephrine levels were lower, whereas 24 h-urinary normetanephrine levels were higher in patients from groups 2 and 3 compared to those without AC. Among patients with frequent AC, crises frequency correlated with HSD11B2 activity assessed by salivary cortisol/cortisone ratios Two *NR3C1* SNPs (rs1005297, rs860457) linked to glucocorticoid resistance and three *NR3C2* SNPs (rs6810951, rs11099680, rs4835493) linked to blood pressure regulation were associated with AC frequency. No significant differences in crisis management were observed between groups 2 and 3. Gastrointestinal and psychiatric comorbidities were more frequent among patients from group 2 (24% and 21%, respectively) and group 3 (22% and 21%, respectively) compared to patients without AC (10%, $P = 0.08$ and 7%, $P = 0.04$, respectively).
Conclusion
Higher glucocorticoid replacement doses in patients with frequent AC fit to previous observations and could simply reflect increased caution but might also be an indicator of increased vulnerability, as also suggested by the lower GC replacement scores and by the correlation with HSD11B2 activity. Gastrointestinal comorbidities might impair cortisol absorption and increase susceptibility to AC. The association between AC frequency and SNPs of *NR3C1* and *NR3C2*also implies a genetic susceptibility to AC. These observations require validation in prospective studies.

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P4

The truth hidden behind a case of resistant hypertension

Xiaoxiao Song[1] & Xin Pan[1,2]
[1]The Second Affiliated Hospital, Zhejiang University School of Medicine (East Gate 1), Department of Endocrinology, Hang Zhou, China; [2]The First People's Hospital of Xiaoshan District, Department of Endocrinology, Hangzhou

Introduction
Resistant hypertension(RHTN) is an increasingly prevalent clinical condition associated with target organ damage and a poor prognosis, encompassing endocrine hypertension(EH). In this report, we describe a rare case of EH complicated by the application of a cytochrome P450(CYP450) enzyme inducer, which manifested as RHTN.
Case summary
A 56-year-old man with an 18-year history of hypertension and one month documented spontaneous hypokalemia(K+, 3.01 mmol/l),was admitted to the Endocrinology Department. The patient had undergone a 2-week washout period with double doses of doxazosin and diltiazem before admission. Physical examination revealed a BP of 170/85 mmHg and overweight. Screening investigations for EH showed abnormal response to the overnight 1 mg dexamethasone suppression test (DST) and low-dose 2-day dexamethasone test (cortisol of 113 nmol/l and 193 nmol/l, respectively), indicating Cushing's syndrome(CS) probably; secondly, a positive aldosterone–renin ratio(ARR) and a positive captopril challenge test(CCT) demonstrating primary aldosteronism(PA). Adrenal CT revealed slight nodular thickening of the bilateral adrenal glands. Pituitary MRI and renal artery ultrasound showed normal findings, leading to suspicion of EH as the underlying cause. Although spironolactone and amlodipine at near-maximum doses were added for the treatment of PA, there was no response. The BP sometimes still could achieve 200/100 mmHg. Subsequent treatment involved bisoprolol, terazosin, clonidine and olmesartan. However, systolic blood pressure had no significant change. MDT discussion and a review of medical history revealed that the patient had been taking rifampicin for brucellosis before being hospitalized. Previous research showed that almost all antihypertensive medications are substrates of CYP450 enzymes, which can be induced by rifampicin. This induction may lead to decreased blood concentration, diminished medicinal efficacy, and elevated BP. And the CYP-induction effect of rifampicin accelerates the metabolism of dexamethasone, rendering a false-positive DST. Consequently, we discontinued rifampicin, causing an improvement in BP control. During the 1-month follow-up, the patient's ARR and CCT were positive, and the overnight 1 mg DST (cortisol of 17.6 nmol/l) was negative. Further AVS supported idiopathic hyperaldosteronism (IHA). Thus, the etiology of the patient's RHTN was confirmed as IHA complicated by drug–drug interactions due to the CYP450 enzyme inducer, with CS excluded. Three months later, his BP was well controlled with serum potassium levels normal. The defined daily doses of antihypertensive medications had decreased by more than 50% compared with the previous treatment.
Conclusion
Drug–drug interactions caused by CYP450 inducers is prone to be neglected, especially when combined with another cause of EH, which complicates the etiology of RNTH further.

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P5

A case of a composite pheochromocytoma with a spindle cell sarcoma exhibiting aggressive behavior

Vasiliki Venetsanaki[1], Maria Sfakiotaki[1], Mickey J. M. Kuo[2,3], Eleni-Konstantina Syntzanaki[1], Amalia Sertedaki[4], Labrini Papanastasiou[5], Athanasios Fountas[5], Georgios Zografos[6], Mayank Patel[3,7], Theodosia Choreftaki[8], Georgios Kyriakopoulos[9], Karel Pacak[3] & Paraskevi Xekouki[1]
[1]University General Hospital of Heraklion, Department of Endocrinology, Metabolism and Diabetes, Heraklion, Greece; [2]National Institutes of Health, National Human Genome Research Institute, Medical Genetics Branch, Bethesda, Maryland, United States; [3]National Institutes of Health, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Section on Medical Neuroendocrinology, Bethesda, Maryland, United States; [4]'Agia Sophia' Children's Hospital, Division of Endocrinology, Diabetes and Metabolism, First Department of Pediatrics, Athens, Greece; [5]'Georgios Gennimatas' General Hospital, Endocrinology, Metabolism and Diabetes Center, Athens, Greece; [6]'Georgios Gennimatas' General Hospital, Third Department of Surgery, Athens, Greece; [7]National Cancer Institute, Center for Cancer Research, Laboratory of Pathology, Bethesda, Maryland, United States; [8]'Georgios Gennimatas' General Hospital, Department of Pathology, Athens, Greece; [9]'Evangelismos' General Hospital, Department of Pathology, Athens, Greece

Introduction
Pheochromocytomas (PHEOs) are rare catecholamine-producing tumors with metastatic potential. Composite PHEOs are rare (3% of adrenal tumors) including components other than adrenal chromaffin cells. We report a case of a rare composite neoplasm with a very rapid disease progression.
Case report
A 57-year-old male was referred to the Endocrinology Department for investigation of a retroperitoneal mass. He presented with nonspecific symptoms and mild hypertension. Computed tomography (CT) of the abdomen revealed a left-sided $14.5 \times 12 \times 14$ cm mass with cystic, necrotic and hemorrhagic features. Investigation revealed elevated levels of 24-hour urinary metanephrine [690 μg/24 h (44–261)], normetanephrine [3471 μg/24 h (128–484)] and dopamine [998 μg/24 h (60–440)] and serum chromogranin A (CgA) [>9000 ng/ml (10–110)] suggestive of a PHEO. The ^{123}I-MIBG scintigraphy showed increased uptake in the left adrenal, multiple skeletal sites and the liver. He underwent left adrenalectomy and nephrectomy. The initial pathology report revealed a poorly differentiated PHEO (PASS score 17) composed of a high-grade spindle cell component and an epithelioid cell component. There was focal staining of CgA and Synaptophysin in the areas of better differentiation, while Ki-67 index was high (75%). Extensive necrosis and marked mitotic activity (>30 mitoses/HPF) were also observed. Postoperative 24 h urinary metanephrines decreased significantly although CgA levels remained high and CT scans showed disease progression with multiple liver and bone metastases. Treatment with cyclophosphamide, vincristine, dacarbazine (CVD) and concurrent radiation of left femoral metastasis was decided but after 3 CVD cycles further disease progression was noted. The patient died 6 months after diagnosis due to hepatic failure. Pathology review at the National Institutes of Health (NIH) concluded that this was a sarcomatoid, malignant spindle cell neoplasm immediately associated and commingled with a differentiated PHEO. Immunohistochemistry (IHC) was positive for CgA, S100, and Synaptophysin in the PHEO component. The partially retained expression of H3K27me3 on IHC did not support the possibility of a malignant peripheral nerve sheath tumor (MPNST). Exome sequencing was negative for germline pathogenic variants in genes associated with PHEO; Next generation sequencing performed on tumor tissue detected pathogenic (likely homozygous) deep deletions in *NF1*, *CDKN2A,* and *CDKN2B*.
Conclusion
Composite PHEOs are very rare and their clinical course depends on their components. MPNST is a rare component of composite PHEO with dismal

prognosis. In our case, histology and genetic variants indicated spindle cell sarcoma with no clear evidence of a neurogenic origin. Alternatively, this could represent a PHEO which partially dedifferentiated to a sarcomatoid neoplasm.

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P6

The differential impact of oral classic and 11-oxygenated androgen precursor administration on downstream androgen metabolism and insulin sensitivity in women with polycystic ovary syndrome

Tara McDonnell[1,2], Leanne Cussen[1,2], Clare Miller[2,3], Benson Jacob[3], Angela Taylor[4], Wiebke Arlt[4,5,6], Marie McIlroy[1], Karl Heinz-Storbech[7], Leanne Hodson[8], Jeremy Tomlinson[8], Mark Sherlock[1,2] & Michael W. O'Reilly[1,2]
[1]Royal College of Surgeons in Ireland, Academic Division of Endocrinology, Department of Medicine, Dublin, Ireland; [2]Beaumont Hospital, Department of Endocrinology, Dublin, Ireland; [3]Royal College of Surgeons in Ireland, Academic Division of Endocrinology, Dublin, Ireland; [4]University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, UK; [5]MRC Laboratory of Medical Sciences, UK; [6]Imperial College London, Institute of Clinical Sciences, UK; [7]Stellenbosch University, Department of Biochemistry, Stellenbosch, South Africa; [8]OCDEM, Oxford Centre for Diabetes, Endocrinology, and Metabolism, Headington, UK

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women. Androgen excess is a cardinal biochemical feature of PCOS and correlates closely with markers of insulin resistance. 11-oxygenated androgens are the predominant androgens in PCOS, however their relationship with metabolic dysfunction is unclear. The aims of this study were (i) to evaluate the downstream impact on androgen metabolism of oral classic and 11-oxygenated precursor administration and (ii) to delineate the differential impact of androgen excess on insulin sensitivity in women with PCOS. An interventional, open-label study was conducted in 20 women with PCOS. Metabolic phenotyping including hyperinsulinaemic–euglycaemic clamp (HEC) testing was carried out at baseline and after 7 days of androgen precursor administration. Participants were randomized 1:1 to receive 150 mg of either 11-ketoandrostenedione (11KA4) or dehydroandrostenedione (DHEA) for 7 days Serum and urinary multi-steroid profiling was performed by liquid chromatography–tandem mass spectrometry. Twenty women with PCOS were enrolled ($n=10$ in each intervention arm); 7 women crossed over to complete both study arms. Median age and BMI were 30.9 years (IQR 26–33) and 34.9 kg/m^2 (IQR 28.4–36.2), respectively. The intervention arms were matched for age and BMI. Following 7 days of 11KA4 150 mg daily, we observed priming of the 11-oxygenated pathway, with statistically significant elevations in serum 11KA4, 11β-hydroxyandrostenedione, 11β-hydroxytestosterone and 11-ketotestosterone ($P<0.05$ for each). Urinary 11-oxygenated androgen metabolites including 11β-hydroxyandrosterone and 11β-hydroxyetiocholanolone also increased significantly ($P<0.01$ for each). Serum classic androgens including testosterone did not change significantly after 11KA4. Oral DHEA 150 mg daily resulted in upregulation of classic androgens in both serum and urine, without any significant associated changes in levels of serum or urinary 11-oxygenated androgens. On HEC testing, glucose infusion rates, unadjusted for insulin, did not change significantly after either DHEA or 11KA4 administration (Table 1). Oral administration of the androgen precursors DHEA and 11KA4 is a powerful *in vivo* tool to study downstream classic and 11-oxygenated androgen metabolism, respectively. Further data and studies are required to delineate whether classic and 11-oxygenated androgens have differential effects on insulin sensitivity and metabolic risk in women with PCOS.

Table 1 The effect of androgen precursor administration on glucose metabolised (M-value) during a Two-Step Hyperinsulinaemic Euglycaemic Clamp.

Metabolic Variable	DHEA			11KA4		
	Before	After	P-value	Before	After	P-Value
M value, (mg/kg · min)						
Low insulin	1.71 [0.63–2.40]	1.51 [1.14–2.0]	0.41	1.88 [1.53–2.08	1.63 [1.11–2.03]	0.44
High insulin	7.21 [4.38–8.99]	6.99 [4.80–7.97]	0.79	7.16 [5.59–9.16]	8.42 [5.76–9.16]	0.53

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P7

Inflammation-based scores in a large monocentric cohort of adrenocortical carcinoma and adrenocortical adenoma: role of the hormonal secretion pattern

Vittoria Favero[1,2], Alessandra Mangone[3,4], Alessandro Prete[5,6,7], YasirS Elhassan[5,6,7], Miriam Asia[7], Rowan Hardy[5,8], Giovanna Mantovani[3,4], Iacopo Chiodini[1,2] & CristinaL Ronchi[5,6,7]
[1]Ospedale Niguarda Ca' Granda, Endocrinology Unit, Milan, Italy; [2]University of Milan, Department of Biotechnology and Translational Medicine, Milan, Italy; [3]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [4]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [5]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK; [6]Birmingham Health Partners, Centre for Endocrinology, Diabetes and Metabolism, Birmingham, UK; [7]Queen Elizabeth Hospital, Department of Endocrinology, Birmingham, UK; [8]Institute of Clinical Sciences, University of Birmingham, Birmingham, UK

Background
Serum inflammation-based scores can predict clinical outcomes in several cancer types, including adrenocortical carcinoma (ACC). They may also be altered in benign adrenocortical tumours and correlate with cortisol excess. It is unclear whether the inflammation-based score alterations in ACC reflects malignancy, steroid excess, or both.
Methods
A total of 490 patients were included (429 [87.6%] with adrenocortical adenoma [ACA] and 61 [12.4%] with ACC) with available baseline full blood count and hormonal evaluation. We examined the relationship between different inflammation-based scores [neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), systemic immune-inflammation index (SII), and prognostic nutrition index (PNI)] and both malignancy and steroid secretion patterns.
Results
All inflammation-based scores differ between ACC and ACA. Patients with ACC had higher levels of NLR, PLR, SII and lower levels of LMR and PNI compared to patients with ACA (all P values <0.001). This difference remained significant after adjusting for age, tumour size, and cortisol after the 1 mg-overnight dexamethasone suppression test (1 mg-DST). All the inflammation-based scores correlated with cortisol levels after 1 mg-DST in ACA and ACC patients. NLR showed a positive correlation with cortisol levels after the 1 mg-DST, both in ACC and in ACA ($P<0.001$). Among the inflammation-based scores, NLR demonstrated the highest accuracy in distinguishing ACC from ACA, with an area under the curve of 0.847 (95% CI 0.795–0.894) and an optimal cut-off value of 2.6. A logistic regression analysis showed that NLR >2.6 was independently associated with the presence of ACC, cortisol levels after 1 mg-DST, and age, but not with tumour size. The multivariate analysis showed that both the presence of malignancy (ACC vs ACA, $P<0.001$) and the presence of cortisol excess (cortisol after 1 mg-DST >50 nmol/l, $P<0.001$) were associated with higher NLR values. Considering ACC, NLR and SII were higher and PNI was lower in patients with cortisol excess compared to those without cortisol excess ($P=0.002$, $P=0.007$, and $P=0.044$ respectively). Finally, we studied the inflammation-based score in patients with hormonally inactive tumours; LMR and NLR were significantly different between inactive ACC (n = 10) and inactive ACA ($n=215$) ($P=0.040$ and $P=0.031$, respectively).
Conclusion
Inflammation-based scores are related to steroid secretion both in ACC and ACA. ACCs present a higher grade of inflammation regardless of their secretion, likely as a feature of malignancy *per se*.

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P8

Enhanced well-being in patients with congenital adrenal hyperplasia on modified-release hydrocortisone compared to conventional glucocorticoid replacement

Hannah Choi[1], Selina Ziegler[1], Hanna Nowotny[1], Lea Tschaidse[1], Matthias Auer[1], Ann-Christin Welp[1], Martha Merrow[2] & Nicole Reisch-Pawlu[1]
[1]LMU University Hospital, LMU Munich, Department of Medicine IV; [2]Faculty of Medicine, LMU Munich, Institute of Medical Psychology

Background
Conventional glucocorticoid (GC) replacement for congenital adrenal hyperplasia (CAH) induces unphysiological cortisol spikes. In contrast, modified-release hydrocortisone (MR-HC, Efmody) offers a more accurate imitation of the circadian cortisol release, particularly emphasizing the morning surge. The study

compares quality of life and sleep-wake cycles in patients with CAH with conventional GC treatment and after a switch to MR-HC.
Methods
In this single-center study we included 41 patients with CAH (28 females, 13 males; 34 classic CAH, 7 non-classic CAH) with a median age of 33 years (IQR 12,75) and a median BMI of 24.67 kg/m^2 (IQR 5.44). Baseline treatment distribution included 15 patients on HC with a median dose of 25 mg (IQR 10), 20 patients on prednisolone with a median hydrocortisone dose equivalence (HDE) of 27.5 mg (IQR 12.5), and 6 patients on mixed regimens with a median HDE of 30 mg (IQR 15). These patients were switched to MR-HC (Efmody) with a median dose of 25 mg (IQR 10). The following questionnaires were used to gather biopsychosocial data before and $\geq$3 months after the switch: a self-developed therapy-satisfaction survey, SF-36, Global Fatigue Index, WHOQOL-BREF, PSQI, and MCTQ. In addition, actigraphy watch data was collected from 12 patients using MotionWatch 8 (CamNtech), both before (8 patients with HC, 4 patients with prednisolone) and after the switch to MR-HC, for a median duration of 20 days.
Results
Patients on MR-HC showed significantly increased satisfaction with their replacement regimen, compared to those on conventional GCs (P=0,0048). Patients considered MR-HC more advantageous in managing CAH (P=0,0225). SF-36 survey results indicated less impairment due to mental issues (P=0,0041) and better mental well-being (P=0,0003). Additionally, patients reported an increased subjective health status after a switch to MR-HC compared to one year prior (P=0,0457). However, actigraphy watch data was not different between the two groups, neither the other surveys.
Conclusion
Patients seem to be more satisfied with MR-HC than conventional GC replacement regimen. This was further reflected in a subjective improvement in both physical and mental health status.

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P9

Therapeutic potential of targeting the FLNA-regulated Wee1 kinase in adrenocortical carcinomas

Emanuela Esposito/[1,2], Rosa Catalano[1], Emma Nozza[1,2], Giusy Marra[1], Sara Maioli[1,3], Genesio DiMuro[1,4], Anna Maria Barbieri[1], Hantel Constanze[5,6], Guido DiDalmazi[7,8], JensAlbrecht Ernst Geginat[1], Elisa Cassinotti[9], Ludovica Baldari[9], Serena Palmieri[10], Alessandra Mangone[10], Emanuele Ferrante[10], Giovanna Mantovani[1,10] & Erika Peverelli[1,10]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]University of Milan, PhD Programme in Experimental Medicine, MIlan, Italy; [3]University of Milan, PhD Programme in Translational Medicine, Milan, Italy; [4]University Sapienza of Rome, PhD Programme in Endocrinological Sciences, Rome, Italy; [5]University Hospital Zurich (USZ) and University of Zurich (UZH), Department of Endocrinology, Diabetology and Clinical Nutrition, Zurich, Switzerland; [6]University Hospital Carl Gustav Carus Dresden, Medizinische Klinik und Poliklinik III, Dresden, Germany; [7]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Endocrinology and Prevention and Care of Diabetes Unit, Bologna, Italy; [8]Alma Mater University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy; [9]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Surgery, Milan, Italy; [10]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy

The cytoskeletal acting-binding protein filamin A (FLNA) is poorly expressed in adrenocortical carcinomas (ACC) compared to adenomas (ACA), and this might contribute to sustain the increased cell proliferation by upregulating IGF1R and its downstream signaling. An increased expression of the CDK1 kinase Wee1, a leading gatekeeper for G2/M transition, was shown in mouse neural progenitor cells after loss of FLNA. Wee1 is highly expressed in several tumor types and its pharmacological inhibitor AZD1775 is currently undergoing clinical trials. This project aims to investigate Wee1 expression in ACC, its regulation by FLNA, the anti-tumor effects of Wee1 inhibitor AZD1775, and the impact of FLNA levels on its efficacy in human H295R and MUC-1 cell lines. The analysis of FLNA and Wee1 protein expression in 6 ACC and 8 normal adrenal tissues revealed that ACC express increased levels of Wee1 (0.3-fold(0.2) vs 0.02-fold(0.05), $P<0.001$), while lower levels of FLNA (0.4-fold(0.1) vs 2.1-fold(1.7), $P<0.05$). FLNA silencing induced an increase of about 1.6-fold of Wee1 protein expression in MUC-1 and in primary ACC cultured cells. Accordingly, p-CDK1 and cyclin B1 levels were shown to be higher in FLNA-silenced MUC-1 cells. On the other hand, decreased Wee1 levels (0.4-fold(0.2), $P<0.001$), as well as those of p-CDK1 and cyclin B1, resulted after FLNA overexpression. Lactacystin treatment reverted Wee1 reduction in FLNA-transfected MUC-1 cells, suggesting that FLNA has a role in promoting Wee1 proteasomal degradation. AZD1775 treatment induced a dose-dependent reduction of cell proliferation in MUC-1 (-91(15%), $P<0.001$ vs bas at 500 nM), H295R (-52(28%), $P<0.05$ at 500 nM), and in primary cultured cells derived from 2 ACC (-86(3%), $P<0.05$ at 1 μM). In MUC-1, Wee1 inhibition increased both the early apoptotic (5.7-fold(2.9), $P<0.01$ at 1 μM) and necrotic (2.7-fold(3.1), $P<0.05$ at 1 μM) cell subpopulations. Furthermore, FLNA knockdown increased AZD1775 efficacy in reducing cell proliferation in MUC-1 (-85(8.0%) for FLNA siRNA vs 72(6.4%) for C-siRNA, $P<0.01$ at 250 nM) and in primary ACC cultured cells (-41.4 for FLNA siRNA vs -20.5 for C-siRNA, $P<0.01$ at 100 nM). Similarly, it also potentiated AZD1775 pro-apoptotic effect by increasing the early apoptotic cell subpopulation (3.1-fold(2.6) for FLNA siRNA vs 1.8-fold(2.1) for C-siRNA, $P<0.05$ at 500 nM). In conclusion, this work demonstrates that FLNA regulates Wee1 expression by promoting its proteasomal degradation, suggesting that the low levels of FLNA frequently found in ACC lead to an increase of Wee1 with consequent cancer cells growth. Moreover, it proposes Wee1 inhibition as a new potential therapeutic approach for ACC, particularly for those lacking FLNA.

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P10

Nausea and vomiting, a clue for the diagnosis of pheochromocytoma?

Ramona Teodora Catana, Adela Nechifor-Boilă & Angela Borda
George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Histology, Targu Mures, Romania

Background and Objective
Pheochromocytomas are rare tumors, originating from chromaffin cells of the adrenal medulla. The typical presentations include the Menard triad (headache, palpitations, sweating) accompanied by sustained or paroxysmal hypertension. Some studies on animals support that high levels of catecholamines have been implicated in the development of the vomiting responses, by activating the alpha-adrenergic receptors in the area postrema, which triggers the emetic cascade. Nevertheless, literature data on human studies is sparse. The aim of our study was to document and investigate nausea and vomiting as relevant and key-symptoms in patients diagnosed with pheochromocytoma.
Methods
We performed a 23-year retrospective study on all pheochromocytoma cases registered at Târgu-Mureş Pathology Departments, Emergency and County Mureş Hospitals, respectively, between 2000 and 2022. Demographic and pathological data were retrieved from institutional database registries and original pathological reports. All patients were subject to a phone questionnaire which provided data related to symptoms and body weight changes (before and after surgery for pheochromocytoma).
Results
Thirty-four patients (n=34) with pheochromocytoma were registered in our departments over the study period (women/men ratio:1.26, mean age: 51.66 years, mean tumor size: 67.83 mm). Subsequently, we were able to obtain clinical data for 25/34 of these patients. Approximatively half of them (n=13/25, 52%) complained of nausea and vomiting, symptoms that ceased following surgery for pheochromocytoma. The mean age of the symptomatic patients was 56.07 years, the majority were women (women/men ratio: 3.33) and the mean tumor size was 65.16 mm. When looking at the mean Body Mass Index for these patients we observed an increased postoperative value, from 27.34 kg/m^2 before to 28.84 kg/m^2 after surgery.
Conclusion
Although hypertension is the hallmark sign of pheochromocytoma, some patients complain of atypical symptoms, mimicking many other diseases. Our data revealed that nausea and vomiting could be considered as key-symptoms in the diagnosis of pheochromocytomas and should be documented in the history of these patients.
Ackowledgemets
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P11

A rare case of testicular adrenal rest tumor associated to X-linked adrenoleukodystrophy

Marianna Torchio[1], Elena Pagin[1], Antonio Marzollo[2], Chiara Mainardi[2] & Chiara Sabbadin[1]

[1]University Hospital of Padua, Endocrine Unit, Italy; [2]University Hospital of Padua, Pediatric Hematology, Oncology and Stem Cell Transplant Division, Italy

Testicular adrenal rest tumors (TARTs) are benign masses causing testicular damage and infertility. Their development is attributed to chronic stimulation of elevated ACTH levels. Several diseases are characterized by an increase of ACTH, however TARTs have been described almost exclusively in patients with congenital adrenal hyperplasia (CAH), excluding only rare cases. X-linked adrenoleukodystrophy (X-ALD) is a rare cause of primary adrenal insufficiency (PAI). It is a genetic metabolic disorder of beta-oxidation with accumulation of very long chain fatty acids primarily in the adrenal cortex and central nervous system. In 2021, TARTs were reported for the first time in two patients with X-ALD associated PAI. In this article, we present two brothers with X-ALD-associated PAI. The youngest developed PAI first at the age of 10 after an adrenal crisis. Treatment with hydrocortisone was started with a median daily dose of 10 mg/m^2 body surface area. Following the patient's diagnosis, the oldest brother was also found to have X-ALD: at that time, he was 14 year old and presented symptoms of attention deficit hyperactivity disorder, but no previous episodes of possible unrecognized adrenal crisis. In fact, biochemical exams revealed only a moderate increase of ACTH levels and low normal values of cortisol; however, glucocorticoid treatment was prudently started. The younger brother was deemed eligible for hematopoietic cell transplant to prevent progression of cerebral disease, which was already detectable in his older brother. During screening programs, a left testicular lesion of 7×7 mm was accidentally discovered and then enucleated, resulting compatible with a TART. Even his older brother underwent testicular ultrasound, which resulted normal. This is the third case of TARTs described in a patient with X-ALD-associated PAI. The genetic factors may play a minor role in the onset of TARTs, as reported in these siblings. The development of TARTs seems to be more related to the early onset of the disease and poor hormonal control. Indeed, only the youngest showed a prepubertal onset of PAI, probably unrecognized for several months before the correct diagnosis. Testicular lesions should be always investigated in patients with PAI, regardless of the cause, to avoid misdiagnosis and unnecessary testicular surgery. Considering these recent findings, the prevalence of TARTs is underestimated and should be considered not only in CAH patients, but at least in those patients with an early onset of chronic ACTH elevation, a poor hormonal control, or fertility problems.

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P12

How to assess adrenal function during low dose prednisolone treatment – impact of a 1- vs 2-day prednisolone pause before the ACTH test: Results from the Double Edge-Rescue Study

Stina Willemoes Borresen[1], SimonBøggild Hansen[2,3], Hajir Al-Jorani[4,5], LiseSofie Bislev[2], VictorBrun Boesen[1], LouiseLehmann Christensen[4,5], Ulla Feldt-Rasmussen[1], AnjaFenger Dreyer[4,5], Dorte Glintborg[4], RichardChristian Jensen[4], NannaThurmann Jørgensen[1,6], MarieLouise Lund[1], Sema Okutan[1,6], Jelena Stankovic[2,3], Randi Tei[2,3], MereteLund Hetland[6,7], Henning Locht[8], Ellen Hauge[9], Kresten Keller[9], SørenAndreas Just[10], Anne Voss[11], Henrik Toft Sørensen[12], PaulM Stewart[13], JensOtto Jørgensen[2,3], Marianne Andersen[4,5] & Marianne Klose[1]

[1]Copenhagen University Hospital, Rigshospitalet, Department of Endocrinology and Metabolism, Copenhagen, Denmark; [2]Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus, Denmark; [3]Aarhus University, Department of Clinical Medicine, Aarhus, Denmark; [4]Odense University Hospital, Department of Endocrinology and Metabolism, Odense, Denmark; [5]University of Southern Denmark, Department of Clinical Research, Odense, Denmark; [6]University of Copenhagen, Department of Clinical Medicine, Faculty of Health and Clinical Sciences, Copenhagen, Denmark; [7]Copenhagen University Hospital, Rigshospitalet Glostrup, Center of Rheumatology and Joint Diseases, Glostrup, Denmark; [8]Copenhagen University Hospital, Frederiksberg Hospital, Center of Rheumatology and Joint Diseases, Frederiksberg, Denmark; [9]Aarhus University Hospital, Department of Rheumatology, Aarhus, Denmark; [10]Odense University Hospital, Svendborg Hospital, Department of Rheumatology, Svendborg, Denmark; [11]Odense University Hospital, Department of Rheumatology, Odense, Denmark; [12]Aarhus University Hospital, Department of Clinical Epidemiology, Aarhus, Denmark; [13]University of Leeds, Faculty of Medicine and Health, Leeds, United Kingdom

Background

Correctly identifying glucocorticoid-induced adrenal insufficiency in patients tapering prednisolone treatment to ≤5 mg daily is crucial. Pausing prednisolone before an ACTH-test is standard, yet the optimal pause duration is uncertain.

Aim

To determine the outcome of an ACTH-test after 1 vs 2 days' prednisolone pause before the test.

Methods

Baseline data from an ongoing randomised clinical trial (EudraCT:2021-002528-18) including 281 patients with polymyalgia rheumatica/giant cell arteritis receiving prednisolone treatment for >12 weeks, current dose ≤5 mg/day. Patients were instructed to pause prednisolone on the ACTH-test day, which was performed at any timepoint. Variation in pause duration resulted from different timing of regular prednisolone administration, ACTH-test timing, and compliance (some patients paused longer). A 1-day prednisolone pause was defined as last prednisolone dose taken the day before the ACTH-test (22–33 hours' pause); a 2-day pause as the last prednisolone taken 2 days before the test (34–54 hours' pause). P-cortisol was measured before (basal) and 30 min after (stimulated) 250 g ACTH injection. Adrenal insufficiency: stimulated P-cortisol <420 nmol/l (Roche Elecsys® Cortisol II assay or mass spectrometry); delta cortisol: stimulated minus basal P-cortisol concentrations. Subgroup analyses examined potential confounding from current prednisolone dose.

Results

Overall, 56/281 patients (20%) had an insufficient response to the ACTH-test. Patients who paused prednisolone for 1 day (n=251) vs 2 days (n=30) had 43 nmol/l lower mean basal cortisol [mean(s.d.) 262(86) vs 305(106), P=0.013]; 103 nmol/l lower mean stimulated P-cortisol [498(119) vs 601(140), P<0.0001]; and 61 nmol/l lower mean delta cortisol [235(91) vs 296(125), P=0.015]. The prevalence of adrenal insufficiency was 53/251 (21%) vs 3/30 (10%) in patients who paused prednisolone for 1 vs 2 days (P=0.22). Stimulated P-cortisol was positively associated with hours of prednisolone pause [5 nmol/l per hour, CI 95%: 2.6–6.8, P<0.0001]. There was no difference in current dose between groups (1-day vs 2-day). In the 172 patients treated with current dose 5 mg/day, mean basal, stimulated, and delta P-cortisol was 51 nmol/l, 111 nmol/l, and 61 nmol/l lower, respectively, after 1 vs 2 days' prednisolone pause (all P<0.05). Both after 1- and 2-days prednisolone pause, basal morning (before 0010 h) P-cortisol and random (any timepoint) basal P-cortisol >300 nmol/l provided 100% specificity for passing the ACTH-test.

Conclusion

During ongoing low-dose prednisolone treatment, a 1-day compared with a 2-day prednisolone pause before an ACTH-test resulted in lower basal, stimulated, and delta cortisol concentrations. The clinical implications remain to be examined, but awareness of the length of prednisolone withdrawal before an ACTH-test is important for proper interpretation.

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P13

Morning cortisol levels in patients with established primary adrenal insufficiency

Alessandro Prete[1,1], Verena Theiler-Schwetz[1], Wiebke Arlt[2], Irina-Oana Chifu[3], Birgit Harbeck[4,5], Catherine Napier[6], JohnD.C. Newell-Price[7], Aled Rees[8], Nicole Reisch[9], GünterK. Stalla[10], Naila Aslam[11], Helen Coope[11], Kerry Maltby[11], John Porter[11], Jo Quirke[11] & RichardJohnM. Ross[7]

[1]University of Birmingham, UK; [2]MRC Laboratory of Medical Sciences, UK; [3]University Hospital Würzburg, Würzburg, Germany; [4]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [5]amedes experts, Hamburg, Germany; [6]Newcastle University, UK; [7]The University of Sheffield, UK; [8]Cardiff University, UK; [9]Klinikum der Universität München, München, Germany; [10]Ludwig Maximilian University of Munich, München, Germany; [11]Diurnal, UK

Background

Primary adrenal insufficiency (PAI) is rare: prevalence ~100–140/million and incidence 4:1 000 000/year in Western societies [1]. The diagnosis of PAI is suggested by an early-morning cortisol <140 nmol/l (5 µg/dl) [1]. The commonest cause in adults is autoimmunity (~90% in Western countries) and it is generally considered progressive once the diagnosis is made, although it has been reported that residual cortisol secretion is present in ~30% of patients [2]. We have developed a modified-release formulation of hydrocortisone to replace the physiological cortisol circadian rhythm and are undertaking a Double-Blind, Double-Dummy, Two-Way Cross-Over, Randomised, Phase II Study of Modified-Release Hydrocortisones: Chronocort® Versus Plenadren®, in PAI. During recruitment, we were surprised by the number of patients who were ineligible as they had detectable morning cortisol levels.

Methods

Main inclusion criteria: Participants with known PAI on stable glucocorticoid replacement therapy and an early morning pre-dose cortisol <50 nmol/l

(1.8 μg/dl). Baseline serum cortisol was taken at ~0700 h and measured in a central laboratory by ADVIA Centaur® immunoassay with the lower limit of detection <14 nmol/l (<0.5 μg/dl).
Results
86 patients with PAI (autoimmune aetiology in 71), median age 52 years (range 20–73), 60 female, were screened in 8 centres in UK and Germany. 18 (21%) patients were excluded from the study based on morning cortisol >50 nmol/l (1.8 μg/dl), and of those 68 patients who qualified on the main inclusion criteria 51 (59% of screened) had a cortisol <14 nmol/l (<0.5 μg/dl). Of the 18 patients (autoimmune aetiology in 10) excluded based on their morning cortisol level, 9 (50%) were female and 11 (13% of screened), had morning cortisol ≥140 nmol/l (5.0 μ/dl). 12 patients with morning cortisol of >50 nmol/l (1.8 μ/dl) were retested and only 2 then qualified; their initial morning cortisol levels were 70 and 51 nmol/l. In patients retested the median difference between retest and the initial sample was 13 nmol/l (range 1–421 nmol/l).
Conclusions
In patients with an established diagnosis of PAI, the majority had undetectable morning cortisol, but cortisol was detectable in 41% of patients and above 140 nmol/l in 13% confirming previous publications [2]. Retesting patients with a cortisol >50 nmol/l showed very similar results suggesting that the detectable cortisol was not an artefact and likely due to background cortisol secretion.
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P14

Improved selectivity of adrenal venous sampling with the use of alternative steroids to cortisol

Francesco Alessi[1], Georgiana Costantinescu[1], Mirko Peitzsch[2], Hanna Remde[3], Lydia Kürzinger[3], Manuel Schulze[4], Myron Lee[5], Jun Yang[6], Martin Reinke[7], Felix Beuschlein[8], Stefan Bornstein[1], Jacques Lenders[1,9], Christina Pamporaki[1] & Graeme Eisenhofer[1]
[1]University Hospital Carl Gustav Carus, Technische Universität Dresden, Department of Internal Medicine III, Dresden, Germany; [2]Medical Faculty and University Hospital Carl Gustav Carus, Technische Universität Dresden, Institute of Clinical Chemistry and Laboratory Medicine, Dresden, Germany; [3]University Hospital, University of Würzburg, Department of Internal Medicine I, Division of Endocrinology and Diabetes, Würzburg, Germany; [4]Technische Universität Dresden, Center for Interdisciplinary Digital Sciences, Department Information Services and High Performance Computing, Dresden, Germany; [5]Prince of Wales Hospital, Department of Chemical Pathology, NSW Health Pathology, Sydney, Australia; [6]Hudson Institute of Medical Research, Centre for Endocrinology and Metabolism, Clayton, Australia; [7]University Hospital, Ludwig Maximilian University Munich, Department of Medicine IV, Munich, Germany; [8]University Hospital Zurich and the LOOP Zurich Medical Research Center, Department of Endocrinology, Diabetology and Clinical Nutrition, Zurich, Switzerland; [9]Radboud University Medical Center, Department of Internal Medicine, Nijmegen, Netherlands

Background
Current guidelines recommend adrenal vein sampling (AVS) for the identification of surgically treatable unilateral disease among patients with primary aldosteronism (PA). The cortisol-derived selectivity index (SI) is currently used to assess the success (or selectivity) of adrenal vein catheterization during AVS. However, AVS studies can be non-selective in many cases.
Aim
To examine whether the use of SI derived either from 11-deoxycortisol, DHEA or androstenedione assessed by liquid chromatography with tandem mass spectrometry (LC–MS/MS) could improve the selectivity rate of AVS compared to the cortisol-derived SI measured by immunoassay (IA) methods.
Design and methods
This prospective multicenter cohort study involved 160 patients from 7 centers located in 3 countries who underwent AVS without cosyntropin stimulation. Cortisol was assessed by IA and LC–MS/MS, whereas 11-deoxycortisol, DHEA and androstenedione were assessed only by LC–MS/MS. A SI of 3 was considered the cut-off for selectivity.
Results
The AVS selectivity rate was 76.9% (123/160) using the cortisol-derived SI assessed by IA. For the majority of patients with unsuccessful AVS, selectivity failed on the right side (21/37) or on both sides (12/37). Selectivity rates using cortisol-derived SI assessed by LC–MS/MS did not differ. Nevertheless, the use of SI derived by either 11-deoxycortisol, DHEA or androstenedione increased the selectivity success rate of AVS to 90.6% ($P<0.001$), 90% ($P<0.001$), and 90.6% respectively ($P<0.001$). DHEA showed the highest median SI values compared to all other steroids, with 4-fold higher median SI values for the left side and 8-fold for the right side compared to IA cortisol ($P<0.001$).
Conclusions
SI derived either from 11-deoxycortisol, DHEA, or androstenedione and assessed by LC–MS/MS yields a significantly higher selectivity rate for AVS than that derived from cortisol measured by both IA and LC–MS/MS. Our findings have immediate application in daily clinical practice.
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P15

Dysregulation of salivary cortisol rhythm in non-secreting and mild cortisol-secreting adrenal incidentalomas

Kimberly Coscia[1,2], Flaminia Fanelli[2], Lorenzo Tucci[1,2], Valentina Bissi[2], Greta Galante[2], Ilaria Improta[2], Francesca Donnarumma[1,2], Giacomo Colombin[1,2], Laura Rotolo[1,2], Claudia Lena[2], Sobia Noreen[2], Valentina Vicennati[1,2], Uberto Pagotto[1,2] & Guido DiDalmazi[1,2]
[1]Endocrinology and Diabetes Care and Prevention Unit, IRCCS Sant'Orsola-Malpighi Polyclinic, Bologna, Italy; [2]Department of Medical and Surgical Sciences, Alma Mater Studiorum of Bologna University, Bologna, Italy

Background
Adrenal incidentalomas (AI) are classified into mild autonomous cortisol-secreting (MACS) and non-secreting (NS) based on the 1mg-dexamethasone suppression test (DST). However, the latter test fails to detect alterations in the cortisol rhythm, which might be present in both MACS and NS.
Aim
To characterize the cortisol secretion in terms of daily rhythm and exposure in healthy controls (HC) and patients with AI.
Methods
Benign unilateral and bilateral adrenal adenomas and/or hyperplasia were included. AI were classified in NS ($n=25$) for post-DST serum cortisol values ≤18 ng/ml, and as MACS ($n=57$) for post-DST serum cortisol values >18 ng/ml. Twenty-eight HC with a regular wake/sleep cycle and no recent or chronic disease nor medications were recruited from the general population. On an ordinary day, each subject collected saliva samples at 0700 (awakening), 07:15, 07:30, 10:00, 12:30, 14:00, 16:00, 19:30, 21:00 and 23:00 h (bedtime). Salivary cortisol was measured by liquid chromatography–tandem mass spectrometry. Cortisol rhythmicity was evaluated by the repeated measurements ANOVA and compared among groups through the calculation of the cortisol dynamic range (CDR = log (peak value/nadir value)) between 07 00 and 23 00 h. Cortisol AUC was calculated to evaluate the daily glucocorticoid exposure.
Results
HC (age 29 ± 10 y) were younger than NS (age 61 ± 14 y) and MACS (age 65 ± 8 y) ($P<0.001$). Sex was evenly distributed in the overall cohort (51.8% females, n = 57) and among groups. Each group exhibited a significant cortisol reduction over the day ($P<0.001$). The CDR was significantly different between the 3 groups ($P<0.001$), with both NS (1.20 ± 0.30) and MACS (1.14 ± 0.35) having a lower CDR compared to HC (1.56 ± 0.26) ($P<0.050$). Cortisol AUC displayed an increasing trend in NS and MACS compared to HC ($P=0.012$). Cortisol levels among groups were similar from 07:00 h until 14:00 h, but different from 16:00 to 23:00 h (P: <0.001–0.044). Indeed, compared to HC, cortisol levels were higher at 21:00 h and 23:00 h in NS, and at 16:00, 19:30, 21:00 and 23:00 h in MACS. Moreover, values at 1930 and 2100 h were higher in MACS than NS (all $P<0.050$).
Conclusion
The salivary rhythm is preserved in both NS and MACS. However, we detected a reduced dynamicity in both AI groups. The overall glucocorticoid exposure increased with the functional status of the AI and is mainly related to the cortisol secretion from middle afternoon to evening. Notably, NS and MACS exhibited different secretion profiles before bedtime.
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P16

False-positive and false-negative results during screening, confirmatory testing and subtyping for suspected primary aldosteronism: lessons from Prosaldo

Andreea Georgiana Constantinescu[1], Christina Pamporaki[1], Francesco Alessi[1], Jens Passauer[1], Hanna Remde[2], Lydia Kuerzinger[2], CarminaTeresa Fuss[2], Manuel Schulze[3], Mirko Peitzsch[4], Andrea Horvath[5],

Jun Yang[6], Denise Bruedgam[7], TracyAnn Williams[7], Martin Reincke[7], Sven Gruber[8], Felix Beuschlein[8], Jacques Lenders[9] & Graeme Eisenhofer[1]
[1]Carl Gustav University Hospital, Endocrinology and Internal Medicine, Dresden, Germany; [2]University Hospital Wurzburg, Endocrinology, Würzburg, Germany; [3]Center for Interdisciplinary Digital Sciences, TU Dresden, Department Information Services and High Performance Computing, Dresden, Germany; [4]Institute for Laboratory Medicine, Dresden, Germany; [5]Prince of Wales Hospital, Pathology; [6]Hudson Institute of Medical Research, Center for Endocrinology and Metabolism, Melbourne, Australia; [7]Ludwig Maximiliam University Hospital Munich, Department of Medicine IV, München, Germany; [8]University Hospital Zurich, Department of Endocrinology, Zurich, Switzerland; [9]Radboud University Medical Center, Internal Medicine, Radboud, Netherlands

Background
Diagnostic stratification of patients with suspected primary aldosteronism (PA) is a multistep process reliant on tests that are not infallible. Only through prospective studies can diagnostic accuracy be appropriately assessed.
Methods
The PROSALDO trial enrolled 819 patients between 2019 and 2023 to assess steroid profiles against routine tests for diagnostic stratification. A combination of these tests and outcome assessments, including measurements of aldosterone by mass spectrometry (MS), was used to exclude and confirm PA.
Results
A diagnosis based on routine tests or outcome assessments could not be achieved in 97 patients, leaving 179 and 543 with and without PA. Screening with the aldosterone:renin ratio using a cut-off of 33 pmol/mU that provided 95% sensitivity revealed a false-positive rate (FPR) of 44% (56% specificity). Among 468 patients who underwent a saline infusion test (SIT), that test at a cut-off of 170 pmol/l for immunoassay measurements of aldosterone revealed a FPR of 48%. Even with MS-based measurements of aldosterone, that cut-off was associated with a 9% FPR (91% specificity). This was at a sensitivity of 98% due to three patients with false-negative results for the SIT, all who underwent adrenalectomy. Adrenal venous sampling (AVS) was carried out in 194 patients, including 69 (36%) without evidence of PA in whom subtyping largely reflected the 48% FPR for the SIT by immunoassay measured aldosterone. Among 167 selective AVS procedures, 52 of 62 patients (84%) without evident PA had non-lateralized aldosterone secretion, though 8 showed lateralization to the right and 2 to the left (16% FPR). Among 105 with PA, 78 (74%) showed lateralization; lack of lateralization in some of the other 27 patients may reflect false-negatives. Among 97 patients who underwent adrenalectomy, 87 were confirmed to have PA either by outcome assessments (n = 76) or when these remained unavailable (n = 11) by positive screening and confirmatory tests by MS. Among the 10 patients in whom PA was not confirmed, there were six in whom confirmatory tests by MS were negative and no outcome confirmation of PA was achieved. There were two others for whom masses in the resected adrenals were not aldosterone-producing adenomas and another two who had an alternative presurgical diagnosis.
Conclusions
The data indicate previously unrecognised inaccuracies in the diagnostic process for identification of patients with PA that in a substantial proportion of patients leads to unnecessary AVS and in some unrequired adrenalectomy. These findings emphasize the need for improved diagnostic strategies.

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P17

Plasma catestatin and relaxin-2 levels may predict impaired glucose metabolism in patients with primary hypertension

Olena Pankova & Oleksii Korzh
Kharkiv National Medical University, Department of General Practice – Family Medicine, Kharkiv, Ukraine

Background
Arterial hypertension (AH) and type 2 diabetes mellitus (T2DM) are common non-infectious diseases with a high tendency to co-exist. Catestatin (CTS) and relaxin-2 have antihypertensive, cardioprotective and metabolic effects and can be considered as biomarkers of these diseases.
Objective
To evaluate plasma CTS and RLN-2 levels in hypertensive patients and to investigate their associations with parameters of glucose metabolism and their predictive potential for impaired glucose metabolism.
Materials and methods
The present study was performed in accordance with all ethical principles of the Declaration of Helsinki. The study protocol was approved by the local ethics committee. Each study participant signed a written informed consent prior to any protocol procedures. 106 patients with AH stage 2 and 30 healthy volunteers were enrolled in the study. 55 hypertensive patients had comorbid T2DM. The clinical examination, medical history data and blood samples were collected from all study subjects. Plasma CST levels were measured by an enzyme-linked immunosorbent assay (ELISA), using a commercial kit (E4996Hu, BT Lab, China), RLN-2 (E-EL-H1582, Elabscience, USA). The data are presented as a mean ± S.D. or a median and interquartile range. Statistical significance was defined as $P < 0.05$. Statistical data were analyzed using SPSS statistical software (SPSS 25.0 for Windows, IBM, Armonk, NY, USA).
Results
Patients with AH and T2DM had significantly decreased plasma CTS (4.47 ± 1.16 vs 5.61 ± 0.61; $P < 0.001$) and RLN-2 levels (5.11 [4.97; 5.38] vs 6.71 [6.00; 7.14]; $P < 0.001$) than hypertensive patients without T2DM. CTS and RLN-2 levels are correlated with parameters of glucose metabolism, particularly glucose ($r = -0.45$; $P < 0.001$ and $r = -0.637$; $P < 0.001$), HbA1c ($r = -0.535$; $P < 0.001$ and $r = -0.704$, $P < 0.001$), HOMA-IR ($r = -0.481$; $P < 0.001$ and $r = -0.394$; $P < 0.001$), and lipid profile parameters, especially triglycerides ($r = -0.400$; $P < 0.001$ and $r = 0.480$; $P < 0.001$) and HDL-C ($r = -0.481$; $P < 0.001$ and r = 0.407; p < 0.001). Univariate binary logistic regression established that CTS (0.175 [0.099 − 0.312; $P < 0.001$) and RLN-2 (0.196 [0.095 − 0.405]; $P < 0.001$) are significant predictors of impaired glucose metabolism, as well as insulin levels (1.118 [1.065 − 1.174]; $P < 0.001$), HOMA-IR (2.020 [1.609 − 2.535]; $P < 0.001$) and BMI (1.108 [1.002 − 1.224]; $P = 0.045$).
Conclusions
In the present study, we determined the lower CTS and RLN-2 levels in patients with T2DM. Furthermore, we established that CTS and RLN-2 are significant predictors of impaired glucose metabolism. These findings suggest their possible diagnostic role as biomarkers of cardiometabolic diseases, especially AH with T2DM.

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P18

Clinical, biochemical, histopathological, and metabolic characteristics of patients with pheochromocytomas

Eleftheria Kakargia[1], Athanasios Fountas[1], Athina Markou[1], IRINI Giagourta[1], Dimitra Zerva[1], Theodosia Choreftaki[2], Giorgos Zografos[3], Chrysanthi Aggeli[3] & Labrini Papanastasiou[1]
[1]'G. Gennimatas' General Hospital of Athens, Department of Endocrinology and Diabetes Center, Athens, Greece; [2]'G. Gennimatas' General Hospital of Athens, Department of Pathology, General Hospital of Athens, Athens; [3]'G. Gennimatas' General Hospital of Athens, Third Department of Surgery, Athens General Hospital, Athens, Greece

Introduction
Pheochromocytomas represent a rare clinical entity with an incidence of approximately 0.8 per 100 000 person-years. Due to their rarity, the characteristics of patients with pheochromocytoma have not been thoroughly investigated yet.
Aim
The assessment of pre- and post-operative clinical and biochemical characteristics as well as the evaluation of imaging and histological data of patients with pheochromocytomas.
Design
Observational retrospective study of patients diagnosed with and treated for a pheochromocytoma in a tertiary general hospital between 2012 and 2022.
Methods
Medical records of patients with pheocromocytoma were reviewed and parameters related to patients' metabolic status (BMI, fasting glucose, HbA1c, total cholesterol, triglycerides, HDL, LDL), as well as pheochromocytoma characteristics [tumor size on imaging, 24 h urinary metanephrine (UMN) and normetanephrine (UNM) levels, phenoxybenzamine total daily dose (TDD) and total cumulative dose (TCD), histology PASS score] were recorded. In addition, comparison of patients' metabolic parameters (lipids and fasting glucose levels) at diagnosis and after surgical removal of the pheochromocytoma was performed.
Results
Overall, 48 consecutive patients (50% females, mean age 48 ± 15 years) with pheochromocytoma, diagnosed and surgically treated in our hospital, were included. Pheochromocytomas were incidentally detected in 46% of the patients, 57.4% were hypertensive (33% paroxysmal), 17% diabetic, 17% obese and 51% were symptomatic. At baseline assessment, no significant differences were found regarding the metabolic and tumor parameters between obese and non-obese patients, overweight and non-overweight ones, as well as between patients with incidentally detected pheochromocytoma and those presented with secondary hypertension or pheochromocytoma-related symptoms. Interestingly though, diabetic patients had larger tumors ($P = 0.048$) compared to those without diabetes. Regarding preoperational treatment symptomatic patients ($P = 0.013$)

required significantly higher TDD of phenoxybenzamine than asymptomatic patients. Univariate correlations demonstrated significant positive associations between UMN and both phenoxybenzamine TDD ($P=0.025$) and TCD ($P=0.05$). Larger tumors were associated with higher PASS scores indicating a more aggressive histology ($P=0.007$). Twenty patients were followed-up after adrenalectomy for a mean period of 36 ± 21 months. Follow-up assessment showed a significant improvement in fasting glucose values after pheochromocytoma resection ($P=0.001$), whereas lipid profile was not affected.

Conclusion

Our study demonstrates that the pheochromocytoma-associated metabolic alterations of glucose homeostasis improve after surgical removal of the tumor. Furthermore, tumor size seems to be a significant predictive factor of tumor aggressiveness.

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P19

Intra-tissular profile of adrenal steroids reveals variable levels associated with adrenocortical tumors (ACT) differentiation and suggests alterations in steroids export

Fidéline Bonnet-Serrano[1,2], Louis Thomeret[1], Nesrine Benanteur[1], Patricia Vaduva[1], Lucas Bouys[1,3], Bruno Ragazzon[1], Annabel Berthon[1], Karine Perlemoine[1], Corinne Zientek[2], Martin Gaillard[1,4], Florian Violon[1,5], Mathilde Sibony[1,5], Christelle Laguillier-Morizot[2], Marie-Claude Menet[6], Lionel Groussin[1,3], Jean Guibourdenche[2], Anne Jouinot[1], Guillaume Assié[1,3] & Jérôme Bertherat[1,3]
[1]Institut Cochin, inserm u 1016, cnrs umr8104, Université Paris Cité, Equipe Génomique et Signalisation des Tumeurs Endocrines, Paris, France; [2]APHP-Cochin Hospital, Hormonology, Paris, France; [3]APHP-Cochin Hospital, Endocrinology, Paris, France; [4]APHP-Cochin Hospital, Visceral Surgery, Paris, France; [5]APHP-Cochin Hospital, Anatomopathology, Paris, France; [6]Institut de Chimie Physique, Université Paris-Saclay-CNRS, UMR8000, Orsay, France

Introduction

Adrenal steroidogenesis is alterated in adrenocortical tumors (ACT), leading frequently to abnormal steroid secretion. The development of steroid assays by mass spectrometry (MS) has greatly advanced the characterization of these alterations. However, steroid profiles are classically performed in blood and urine, providing a limited insight into adrenal steroidogenesis, altered by the mixing with gonadal steroids and by the steroid peripheral catabolism. The objective of our work was to evaluate the steroids tissue level in normal adrenals and ACT to better characterize adrenal steroidogenesis process dysregulation.

Materials and methods

Fifty-five samples of fresh-frozen adrenocortical tissue stored in liquid nitrogen in the COMETE tumor bank were included: 9 samples of normal adrenals, 22 samples from adrenocortical carcinomas (ACC) and 24 samples from adrenocortical adenomas (including 10 cortisol-producing adenomas (CPA) and 14 non/mild autonomous cortisol secreting adenomas (NFAT/MACS)). After tissue grinding in liquid nitrogen and sonication in methanol, tissue extracts were injected into a TSQ-ALTIS instrument to determine a profile of 13 steroids (cortisol, 11-deoxycortisol, 17-hydroxyprogesterone, cortisone, 21-deoxycortisol, androstenedione, testosterone, corticosterone, 11-deoxycorticosterone, progesterone, 11-hydroxyandrostenedione, 11-ketoandrostenedione, 11-ketotestosterone) in UPLC–MS/MS. Steroid intratissular concentrations were expressed in nmol/kg of tissue allowing the comparison with blood concentrations in nmol/l.

Results

In tissue of normal adrenals, cortisol was the most abundant steroid as in peripheral blood. However, the ranges of intratissular values observed (median [IQR] $=18790$ [5252–27987] nmol/kg) were 10 to 100 times higher than the usual value of cortisol blood concentration. The other most abundant steroids in normal adrenocortical tissue were corticosterone (6951 [1454–8840] nmol/kg) and 11OH-androstenedione (2189 [1323–9595] nmol/kg). The ratios of intratissular levels to usual blood concentrations were higher for precursors (progesterone, 17OH-progesterone and 11-deoxycortisol) than for cortisol, suggesting a facilitated export of bioactive products. In ACT, besides the high intratissular concentrations measured, the most striking observation was the lower steroid levels measured in ACC tissues in comparison to benign adenomas' tissues. Thus, intratissular cortisol level (nmol/kg) was lower in ACC (2655 [692–7933]) than in benign adenomas: CPA (27066 [21982–64731], Benjamini, Krieger and Yekutieli $q<0.0001$), MACS/NFAT (34241 [20425–43727], $q<0.0001$), and normal adrenals ($q=0.036$).

Discussion

This first study of tissue steroid assay in ACT reveals quantitative and qualitative differences among the tumor types. These differences are likely to be explained by the various mechanisms of tumor cells differenciation. The striking differences in the ratio of intratissular to blood levels between bioactive steroids and their precursors suggest differences in the regulation of steroids export.

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P20

Study on the pathogenesis of adrenocortical adenoma with bilateral independent secretion of aldosterone and cortisol: a case report and literature review

Yan Ren, Yan Xi Chen, Tao Chen & Lu Tan
West China Medical School, West China Hospital, Sichuan University, Endocrine, Cheng Du Shi, China

Aldosterone and cortisol coproducing adrenal adenoma is a rare type of primary aldosterone. Previous reports mostly describe single adrenocortical adenomas that simultaneously secrete aldosterone and cortisol. To date, only 7 cases of bilateral adrenocortical adenomas with independent functions of secreting different hormones have been reported in the published English literature. Here, we study an extremely rare case of a left adrenocortical adenoma secreting aldosterone and a right sebaceous adenoma secreting cortisol and explore the pathogenesis. The patient, a 29-year-old female, was diagnosed with gestational hypertension and hypokalemia. The examination showed that his PTC was significantly elevated (0 min PTC: 858 nmol/l) and ACTH was significantly suppressed (ACTH <1 ng/l). CT showed bilateral adrenal nodules/mass shadows, with the largest cross-sections on the right and left sides. They were 3.3×2.2 cm and 1.3×0.8 cm respectively. After the right adrenal tumor was removed, the pathology showed 'adrenal sebaceous adenoma'. Postoperatively, the patient developed cortical hypofunction, with a PTC of 109 nmol/l at 0800 h, and was given supplementary treatment with hydrocortisone. However, the patient still had hypertension and hypokalemia after the operation. Four months later, biochemical tests showed that the sitting plasma aldosterone and renin concentrations were 14 ng/dl and 0.51 uIU/ml respectively. The captopril test and saline test both showed aldosterone cannot be suppressed. CXCR4 imaging showed that the maximum SUV of the left adrenal adenoma was 8.75 and the maximum SUV of the left normal adrenal tissue was 2.7. Therefore, the left adrenal adenoma was diagnosed as an aldosteronoma and the left adrenal tumor was resected. After surgery, the patient's blood pressure and serum potassium returned to normal, and orthostatic aldosterone dropped to 10.5 ng/dl. Postoperative immunohistochemistry results showed: CYP11B1(+), CYP11B2(−) in the right tumor, and CYP11B2(+), CYP11B1(−) in the left tumor. Full-exome gene testing of the left and right tumors and peripheral blood revealed that the right cortisol tumor PRKACA c.167(exon7)T>G (p.L206R) and the left aldosteronoma KCNJ5 c.503(exon2)T> G(p.L168R) is considered pathogenic, but no abnormal mutations were found in the blood. At this point, through clinical manifestations and hormone testing, postoperative tumor tissue pathology and immunohistochemistry testing, and genetic testing of tumor tissue, we have identified a case of right-sided adrenal cortisoloma caused by PRKACA gene mutation and left-sided adrenal cortisoloma caused by KCNJ5 gene mutation. Adrenal aldosteronoma A case of an adrenocortical tumor secreting different hormones bilaterally.

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P21

Analysis of salivary dexamethasone does not improve the specificity of the dexamethasone suppression test

Marcus Imamovic[1], Nils Bäcklund[1], Staffan Lundstedt[2], Göran Brattsand[2], Tommy Olsson[1] & Per Dahlqvist[1]
[1]Umeå universitet, Public Health and Clinical Medicine, Umeå, Sweden; [2]Umeå universitet, Medical Biosciences, Umeå, Sweden

Objective

The low dose overnight dexamethasone suppression test (1 mg DST) is a sensitive screening test for Cushing's syndrome. The specificity of the test can be improved by simultaneous analysis of plasma dexamethasone concentrations. A simple and accurate alternative to analysis of plasma cortisol is analysis of salivary cortisone or cortisol following 1 mg DST [1]. We evaluated if analysis of salivary dexamethasone following 1 mg DST could further improve the specificity of the test. We also evaluated the stability of cortisone and cortisol in saliva samples stored 6–8 years in -80°C.

Design and methods

Saliva samples from 131 volunteers were collected with Salivette® Cortisol at 0800 h with simultaneous collection of plasma following 1 mg DST, between March 2015 and April 2016. Saliva samples were frozen at -20°C for at least

24 h and then thawed, centrifuged, aliquoted, and stored at −80°C. One aliquot of saliva was analysed for cortisone and cortisol with liquid chromatography tandem mass spectrometry (LC–MS/MS) in April–May 2016 and a second aliquot was analysed in November 2022 with the same LC–MS/MS method, slightly modified to also include dexamethasone. Plasma dexamethasone was analysed using a different LC–MS/MS assay. A lower reference limit (LRL) for salivary dexamethasone was defined as the non-parametric 2.5th percentile of all adequately suppressed saliva samples (cortisone <3.5 nmol/l [1]) after excluding outliers using Dixon's Q test ($n=3$), as recommended by the Clinical Laboratory Standards Institute. Spearman's rank correlation coefficients (r_s) were used to test associations between hormone concentrations.

Results

The LRL for salivary dexamethasone was calculated to 0.30 nmol/l (90% CI: 0.20–0.42). Among the samples with unsuppressed salivary cortisone following 1 mg DST (>3.5 nmol/l), four out of five had a plasma dexamethasone concentration below the LRL of 3.3 nmol/l. In contrast, none had a salivary dexamethasone concentration below the LRL of 0.30 nmol/l,. Salivary and plasma dexamethasone correlated moderately ($r_s=0.56$). There was a high correlation between saliva samples measured in 2022 and 2016 for both cortisone and cortisol ($r_s=0.98$ and 0.81, respectively).

Conclusions

Analysis of salivary dexamethasone does not reflect adequate circulating dexamethasone concentrations following 1 mg DST, potentially due to enzymatic conversion of dexamethasone in the salivary gland or tablet residuals in the oral cavity. Further studies are needed on alternative dexamethasone metabolites in saliva. Salivary cortisone and cortisol concentrations are essentially unaltered after longterm storage in −80°C.

Reference

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P22

Update on autoimmune polyendocrine syndrome type-1 in Norway: Using longitudinal immune cell composition incorporated with clinical features

Isil Kucuka[1], Dorsa Iraji[1], Lars Breivik[1,2], Eystein Sverre Husebye[1,2], Anette Bøe Wolff[1,2] & Bergithe Oftedal[1,2]
[1]University of Bergen, Department of Clinical Science, Bergen, Norway; [2]Haukeland University Hospital, Department of Medicine, Bergen, Norway

Autoimmune Polyendocrine Syndrome type-1 (APS-1) is a rare monogenic disease (1:100 000 frequency), caused by mutations in the autoimmune regulator (AIRE) gene, which plays a crucial role in the thymus for negative selection of self-reacting T cells. With tissue damage caused by self-reactive immune cells from early stages of life and gradually presenting with symptoms in following years, APS-1 is clinically diagnosed by presence of minimum two components of the classical triad: primary adrenal insufficiency, hypoparathyroidism, and chronic mucocutaneous candidiasis. Although two criteria of the triad are enough to make a clinical diagnosis, APS-1 can also present with multiple additional autoimmunity-associated manifestations such as malabsorption, hypothyroidism, vitiligo, or enamel hypoplasia. In this study, our goal is to provide an update on the Norwegian APS-1 cohort, include longitudinal immune profiles and relate this to course of disease, age, additional manifestations, and demographic features. We explore the longitudinal changes in distribution and quantity of immune cell subtypes in peripheral whole blood samples of APS-1 patients using the well-characterized Norwegian biobank, known as Registry of Organ-specific Autoimmune Diseases (ROAS) to obtain longitudinal patient samples. Established in 1996, ROAS is among the biggest biobanks of endocrine autoimmune diseases, containing samples spanning 25 years. We analyzed 154 samples in total, including a collection of 106 samples from 27 APS-1 patients at multiple timepoints across 25 years with 47 age and sex matched controls. The new epigenetic immune cell quantification technology allowed us to explore the longitudinal immune cell profiles in APS-1 patients, by using a panel which includes 14 cell-type specific assays. Our panel includes cell groups such as neutrophils, B-lymphocyte subgroups, Natural Killer cells, monocyte subgroups and T-lymphocyte subgroups including cytotoxic, follicular helper and regulatory cells. Overall results showed that patients having classical triad's 3 components were diagnosed at the mean age of 7, whereas patients with less components of classical triad were diagnosed at age 11 on average. Among 27 patients, 11 had 3 components, 11 had 2 of 3 components, 5 had only 1 component of classical triad. Despite the large individual variety, the longitudinal changes in immune cell composition can be linked to clinical and genetic mutations and autoantibodies. In addition, candidiasis and hypoparathyroidism were observed more frequently than adrenal insufficiency.

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P23

Using basal cortisol cut-off to define adrenal sufficiency in a Southeast Asian population

Vijay Ramadoss[1], Lyeann Tan[1], AdaEeDer Teo[1], Kavita Narula[2], Kate Lazarus[2], Doddabele Srinivasa Deepak[1], LiZhen Ong[3], Karim Meeran[4], ChinMeng Khoo[1] & PeiChia Eng[1]
[1]National University Health Systems, Endocrinology, Singapore, Singapore; [2]Imperial College London, Hammersmith Campus, London, UK; [3]National University Health Systems, Laboratory Medicine, Singapore, Singapore; [4]Imperial College London, Hammersmith Campus, UK

Introduction

The short synacthen test (SST) is used in clinical practice to assess adrenal insufficiency (AI). However, the suggested threshold varies according to the patient cohort studied, assay variation and prevalence of the condition relative to the size of population tested. This study aimed to identify a threshold cortisol value to determine adrenal sufficiency in a Southeast Asian population and to investigate the utility of a stimulated 60-minute cortisol level in the diagnosis of AI.

Methods

We performed a retrospective analysis of 785 SSTs (250 micrograms) performed in our institution between 28 February 2022 to 28 February 2023. A normal response was defined as a stimulated cortisol value of ≥420 nmol/l at 30 or 60 min or at both time points, as measured by an Abbott Alinity Analyzer. Logistic regression analysis was performed to predict a normal response based on the baseline cortisol value.

Results

Median cortisol values at baseline, 30-min and 60-min after Synacthen stimulation were 254 (IQR 191–320) nmol/l, 499 (IQR 415–585) nmol/l, 574 (IQR 476–662) nmol/l respectively. Of the 785 SSTs, 83.0% of results were normal and 16.9% were abnormal. 55 SSTs (7.0%) would have been classified as AI if only the 30-min cortisol was assessed without the 60-min value, compared with 10 (1.4%) of patients would have failed using the 60-min cortisol without the 30-min value. An early morning basal cortisol (0800 h to 1200 h) cut-off value of <300 nmol/l identified a subnormal cortisol with 95% sensitivity and an afternoon cortisol (1200 h to 1700 h) of <312 nmol/l achieved 95.2% sensitivity. A basal cortisol level of <100 nmol/l will confirm AI with 97.3% specificity. Using a basal cortisol level of ≥300 nmol/l, 94.8% of individuals go on to pass the SST. Use of this basal cortisol value would have avoided 252 (32.1%) SSTs.

Conclusion

A single measurement of basal cortisol of ≥300 nmol/l, measured on the Abbott Alinity platform, has the potential to determine a normal response to an SST with 95% sensitivity on in our cohort of patients. Using a threshold cortisol level of 300 nmol/l, at least 32% of the SSTs could be avoided. Furthermore, a stimulated 60-min cortisol level identifies 55 (7%) of individuals who would otherwise be misclassified as AI. We believe this information may help clinician decide on situations where SST could be safely omitted, thus reducing unnecessary healthcare expenses.

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P24

Adrenocortical cells are prone to regulated cell death during *in vitro* septic conditions

Agnès Wlodarczyk[1,2], Uta Lehnert[1], Stefan Bornstein[1,2] & Waldemar Kanczkowski[1,2]
[1]University Hospital Carl Gustav Carus Dresden, Dresden, Germany; [2]TU Dresden, Dresden, Germany

Background

Sepsis is the primary cause of mortality in intensive care units. It is characterized by compromised function of several vital organs, including the adrenal glands. However, little is known about the mechanisms involved in this process. Recent experimental data demonstrated a potential role of iron overload and related iron-dependent, lipid peroxide driven form of regulated necrosis known as ferroptosis in sepsis-induced multiorgan damage. In a previous study, we demonstrated that human adrenocortical carcinoma cells NCI-H295R are sensitive to ferroptosis resulting from glutathione peroxidase 4 (GPX4) inhibition. However, whether sepsis also triggers ferroptosis in the adrenal gland remains unexplored until now.

Objectives

The main objective of this study was to investigate whether sepsis-associated conditions such as enhanced steroidogenesis and inflammation can induce ferroptosis in adrenocortical cells.

Methods

In order to mimic septic conditions *in vitro*, NCI-H295R cells were either exposed to forskolin, a well-known activator of steroidogenesis, or to inflammatory cytokine interleukin 6 (IL6). Necrosis induction (positive annexin V and PI

staining) as well as lipid peroxidation (C11-Bodipy staining) were analyzed 24–48 h thereafter. Furthermore, an expression of ferroptosis-relevant molecules was subsequently analyzed on gene and protein level by qPCR and western blot respectively. Finally, the expression those regulatory molecules was additionally assessed in the adrenals of mice treated with LPS.
Results
Our study demonstrated robust expression of two major modulators of ferroptosis, GPX4 and long-chain-fatty-acid-CoA ligase 4 (ACSL4), in the human and mouse adrenal cortex. Stimulation of NCI-H295R cells with either forskolin or IL6, as well as administration of bacterial LPS to mice, enhanced ACSL4 expression in adrenocortical cells. Furthermore *in vitro*results demonstrated that stimulation with forskolin and IL6 moderately increased lipid peroxidation and number of necrotic NCI-H295R cells, which indirectly suggested ferroptosis induction. However, while addition of the ferroptosis inhibitor ferrostatin-1 mitigated forskolin-mediated induction of lipid peroxidation, it rescued only a fraction of NCI-H295R adrenal cells from necrosis, suggesting potential involvement of a different form of cell death. Indeed, *in vitro* co-treatment of those cells with an apoptosis inhibitor fmk-zVad demonstrated a similar effect. In addition, we have found that IL-6 can decrease RSL3-mediated ferroptosis.
Conclusions
In summary, our findings suggest that septic conditions may promote ferroptosis and/or apoptosis in adrenocortical cells. However, further experiments, including the evaluation of GPX4 activity and caspase activation, as well as the validation of results using primary adrenal cells, are essential to gain a more thorough understanding of this process.

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P25

Prevalence and outcome of primary aldosteronism in PBMAH: A single center study and systematic review of the literature

Annalisa Panarelli[1,2], Elisabeth Nowak[1], Pia Adam[1], Junia Schweizer[1], Isabel Stuefchen[1], Stephanie Zopp[1] & Martin Reincke[1]
[1]Department of Medicine IV, LMU University Hospital, LMU Munich, Germany; [2]Department of Internal Medicine IV, Molinette University Hospital, Turin, Italy

Context
Patients with primary bilateral macronodular adrenocortical hyperplasia (PBMAH) usually present with bilateral benign adrenocortical macronodules at imaging and variable levels of cortisol excess. There is anecdotal evidence that, besides cortisol, other adrenal steroids, like mineralocorticoids, can be over-secreted.
Objective
To assess the prevalence, clinical, biochemical characteristics and imaging features of aldosterone excess leading to primary aldosteronism (PA) in patients with PBMAH.
Methods
We conducted a systematic review according to the PRISMA guidelines. We reviewed single case reports and case series of patients with PBMAH and coexistence of PA, in Pubmed, Embase and Cochrane from database inception to 17 December 2023. Two independent reviewers performed screening and data extraction. PBMAH was defined based on radiological features with ≥ 1 bilateral adrenal nodule ≥ 10 mm. We compared our findings to patients with PBMAH and PA derived from the LMU hospital Munich.
Results
1018 articles were screened, of which 36 articles were assessed for eligibility. We identified 18 articles (8 single case reports and 10 case series), resulting in 68 cases with PBMAH with PA. Of those, 14 had concomitant secretion of aldosterone and cortisol. The prevalence of a PA phenotype in patients with PBMAH in six studies with 166 patients ranged from 2 to 44%. The median age at diagnosis was 51.5 (47.5–56.2) with more male patients (18/26, 69%). Most patients were hypertensive, and the median duration of hypertension at referral was 108 months (48–135). 69.6% (16/23) of the patients were hypokalemic. The baseline aldosterone serum concentration and plasma renin activity (PRA) were 253 ng/l (159.8–436) and 0.25 ng/ml per hour (0.2–0.4), respectively. Treatment modality was reported in 30 cases: 28 patients underwent adrenalectomy (two bilateral, two subtotal, and 15 unilateral, 9 not reported) and two received mineralocorticoid receptor antagonists (MRA). In comparison, in the LMU cohort, fewer patients underwent adrenalectomy (12/20, $P=0.0088$) whereas 8/20 received MRAs. Outcome following surgery or MRA therapy was only described in eight cases derived from the literature (6 treated with surgery and 2 with MRA). Complete biochemical remission was obtained in 4 cases while complete clinical remission in 1 case. In the LMU cohort, 9 surgically treated patients went into complete biochemical remission and 2 obtained complete clinical remission.
Conclusion
Autonomous secretion of aldosterone in PBMAH appears to be more frequent than previously thought. Larger multicenter studies will help to clarify the association between these conditions as well as the most appropriate treatment modality.

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P26

Towards precision medicine in adrenocortical carcinoma; predicting response to mitotane using proteomics

Charlotte Vietor[1,2], Anand Iyer[1], Peter van Koetsveld[1], Fadime Dogan-Oruc[1], Lona Moradi-Zeyenedpour[3], Gaston Franssen[2], Cornelis Verhoef[2], Tessa van Ginhoven[2], Theo Luider[3], Richard Feelders[1] & Leo Hofland[1]
[1]Erasmus Medical Center and Erasmus MC Cancer Institute, Department of Internal Medicine, section Endocrinology, Rotterdam, Netherlands; [2]Erasmus Medical Center and Erasmus MC Cancer Institute, Department of Surgery, Rotterdam, Netherlands; [3]Erasmus Medical Center and Erasmus MC Cancer Institute, Laboratory of Neuro-Oncology/Clinical & Cancer Proteomics, Rotterdam, Netherlands

Background
Adrenocortical carcinoma (ACC) is a rare but devastating malignancy (5-year survival 18–57%), with limited treatment options. Currently, mitotane is the first-line medical treatment for metastatic ACC and is used in the adjuvant setting after surgery to prevent recurrence. Mitotane is an adrenolytic drug that is thought to act by disruption of mitochondria with subsequent activation of apoptosis. However, mitotane treatment comes with many drawbacks, such as severe side-effects and contralateral adrenal gland destruction, whilst both clinical and *in vitro*studies have shown that it is only effective in 25–30% of ACC tumors. We performed a proteomics-based analysis of ACC tissues previously characterized *in vitro*as responders, partial responders and non-responders to mitotane, with the aim of identifying tissue biomarkers to improve future patient selection for mitotane therapy.
Methods
Protein lysates were obtained from fresh-frozen ACC samples ($n=13$ responders, $n=10$ partial responders, $n=7$ non-responders). Label-free liquid chromatography–mass spectrometry shotgun proteomics was performed on these samples. Differential protein abundance was assessed using two statistical methods (DESeq2 and spectral index), followed by pathway analysis using STRING.
Results
On average, 2628 proteins were identified per tumor sample. We found 25 proteins (84% being mitochondrial(-related)) with lower expression in responders compared to non-responders with both statistical methods. Pathway analysis revealed involvement of these proteins in mitochondrial fusion, mitochondrial membrane organization and mitochondrial fatty-acid beta-oxidation. In contrast, only four proteins were higher expressed in responders compared to non-responders.
Conclusion
Mitochondria-associated proteins are differentially expressed in ACC of patients who respond well to mitotane therapy compared to non-responders, fitting well with mitochondria being the presumed target of mitotane. Immunohistochemical validation is necessary to further explore the potential of specific proteins to serve as a biomarker for mitotane treatment response. Furthermore, the mechanism behind the relative upregulation of mitochondrial proteins in non-responders and whether there is a causal relationship with mitotane sensitivity remains to be elucidated.

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P27

Impact on immunophenotype of switching from conventional gluco-corticoids to modified-release hydrocortisone in congenital adrenal hyperplasia

Selina Ziegler[1], Hanna Nowotny[1], Hannah Choi[1], Lea Tschaidse[1], Matthias Auer[1], Ann-Christin Welp[1], Adrian Gottschlich[2,3], Sebastian Kobold[2,4,5], Simon Rothenfusser[2] & Nicole Reisch[1]
[1]LMU University Hospital, LMU Munich, Department of Medicine IV; [2]LMU University Hospital, LMU Munich, Division of Clinical Pharmacology; [3]LMU University Hospital, LMU Munich, Department of Medicine III; [4]German Cancer Consortium (DKTK), Partner Site Munich; [5]Helmholtz Munich, Research Center for Environmental Health (HMGU), Neuherberg, Einheit für Klinische Pharmakologie (EKLiP)

Background
Previous research has revealed variances in the composition of immune cells among patients with congenital adrenal hyperplasia (CAH) on conventional glucocorticoid (GC) replacement therapy compared to healthy controls. Modified-release hydrocortisone (MR-HC) optimizes cortisol pharmacokinetics, aligning with a more physiological circadian cortisol rhythm. This study therefore aims to assess the impact on the immune cell profile when transitioning patients with CAH from conventional GCs to MR-HC.
Methods
A cohort comprising 25 patients with classic CAH, including 14 females and 11 males, with a median age of 37 years (IQR 14.25) and a median BMI of 25.29 kg/m^2 (IQR 3.72), was switched from conventional hydrocortisone ($n=13$) or prednisolone ($n=12$) treatment to an equivalent hydrocortisone dose (HDE) of MR-HC (median HDE 30 mg (IQR 10)). This cohort was compared to a group of 25 sex, age, and BMI matched healthy controls. Peripheral mononuclear blood cells were extracted before, 3 months and 6–10 months after the transition to MR-HC. Immune cell subsets were analysed through multicolour flow cytometry after a four-hour stimulation with PMI/ionomycin.
Results
Patients on conventional GCs exhibited a higher percentage of CD4+CD25+ lymphocytes ($P=0.0063$) compared to healthy controls and MR-HC-treated patients. The transition from conventional GCs to MR-HC resulted in a decrease in the percentage of CD4+CD25+ lymphocytes ($P=0,0327$). While patients under conventional GC treatment showed a smaller proportion of CD4+CD25+ Foxp3+T cells (Tregs) compared to controls ($P=0,0026$), the MR-HC cohort displayed comparable proportions to controls. Reductions in hydrocortisone doses by 5 mg, referable to efficient therapeutic control between 3 and ≥ 6 months post-transition to MR-HC, correlated with an increase in T helper cells ($P=0.0034$) and a decrease in CD94+ NK cells ($P=0.0312$).
Conclusion
Conventional GC substitution precipitates alterations in the immune phenotype of patients with CAH. In contrast, MR-HC, which more accurately imitates the physiological circadian release of cortisol, causes less changes in the immune cell profile. Additional functional analysis could help to draw further conclusions regarding the functionality of the immune system and its clinical impact.
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P28

Insulin tolerance test for the diagnosis of adrenal insufficiency
Sahar Abidi, Nadia Khessairi, Sabrina Ayari, Kammoun Elyes, Ibtissem Oueslati & Melika Chihaoui
Endocrinology Department, Rabta Hospital, Endocrinology Department, Tunis, Tunisia

Introduction
The insulin tolerance test (ITT) is the gold standard for hypothalamic–pituitary adrenal axis assessment. There are different protocols depending on the number and timing of serum samples. Our study aimed to investigate the kinetics of serum glucose and cortisol levels during ITT and to determine the most appropriate times for blood samples.
Methods
Our study was cross-sectional and descriptive. One hundred patients with suspected adrenal insufficiency (AI) were evaluated. The patients had 12 h fasting prior to the ITT. An intravenous rapid insulin bolus of 0.1 to 0.2 units/kg was administrated. Eight serum samples for glucose and cortisol measurements were taken: before the insulin injection (T0), at the time of hypoglycemia (Thypo) and samples every 10 min for 60 min after hypoglycemia (T10, T20, T30, T40, T50 and T60). We considered an adequate response a serum cortisol level above or equal to 18 µg/dl after a serum glucose level below 40 mg/dl.
Results
The mean age was 41.4±15.2 years and the sex ratio (F/H) was 0.2. The mean serum glucose lower cut point was 0.29±0.07 g/l and the mean time to achieve venous hypoglycemia (below 0.40 g/l) was 27.9±8.7 min. Forty-two patients (42%) had an adequate response and 58 patients (58%) had AI. Basal cortisol level was correlated with serum cortisol peak ($r=0.56$ $P<0.001$). A cutoff point of 9.75 µg/dl had a sensitivity of 59% and a specificity of 73% to predict an adequate response, it for. Twenty-six patients (62%) had an early response and 16 patients (38%) had a late response. A basal cortisol level ≤ 11.2 µg/dl had a sensitivity of 62% and a specificity of 82% to predict a late response. Finally, the most appropriate times for serum cortisol measurements were T30, T40 and T50 or T20, T30 and T50 with a sensitivity of 95%.
Conclusions
It is necessary to multiply the number of cortisol level samples after hypoglycemia, especially beyond 30 min, in order to increase the sensitivity of ITT and avoid misdiagnosis.
Key words
cortisol, insulin, hypoglycemia, adrenal insufficiency, diagnosis
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P29

Pheochromocytoma-induced pseudo-Cushing syndrome
Malgorzata Bobrowicz[1,2], Marek Roslon[1], Anna Karpilowska[3], Adrianna Gladka[3], Sadegh Toutounchi[4], Lukasz Koperski[5] & Urszula Ambroziak[1]
[1]Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland; [2]Departament of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland; [3]Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland; [4]Department of General, Endocrine, and Vascular Surgery, Medical University of Warsaw, Warsaw, Poland; [5]Department of Pathology, Medical University of Warsaw, Warsaw, Poland

Introduction
Chronic catecholamine overproduction in pheochromocytoma may lead to a proinflammatory and hypermetabolic state characterized by increased resting energy expenditure and brown adipose tissue activation. Non-neoplastic hypercortisolaemia aka pseudo-Cushing syndrome (PCS) is a physiological overactivation of the hypothalamic–pituitary–adrenal axis by e.g. depression, eating disorders, extreme exercise, obesity, alcoholism, poorly controlled diabetes and cachexia. Here we describe an unusual case of pheochromocytoma-induced PCS.
Case report
A 66-year-old woman was referred to the hospital due to pronounced weakness, loss of appetite, apathy and weight loss of 5 kg within a month, a newly diagnosed diabetes mellitus and poorly controlled hypertension. Because of a rapid weight loss and suspicion of malignancy a chest and abdominal CT was performed, showing a heterogeneous, well-demarcated litho-cystic lesion (measuring 32× 25 mm) in the right adrenal gland, with inhomogeneous contrast enhancement. Metanephines' levels in serum were markedly elevated, as well as ACTH (535 pg/ml), highly increased 24 h urinary free cortisol excretion, high plasma DHEAS and testosterone. The initial differential diagnosis was as follows: a coexistence of pheochromocytoma or an ACTH-dependent hypercortisolemia or ectopic ACTH production by pheochromocytoma. An MRI ruled out pituitary tumors and a Ga^{68} DOTATE PET-CT scan showed a hypodense right adrenal nodule measuring 36×22 mm, probably litho-fluid with heterogeneous but high somatostatin receptor expression (with SUVmax 35.4). Considering clinical features, laboratory and imaging tests results, a suspicion of hypercortisolaemia due to ectopic ACTH-producing pheochromocytoma was raised. The patient was qualified for right adrenalectomy. Before the surgery the patient was treated with doxazosin and metyrapone, received enteral feeding and protein supplementation as well as intensive insulin administration. Interestingly, on this treatment we not only observed decreased cortisol levels (leading to a transient adrenal insufficiency), but also decreased levels of ACTH (150 pg/ml) and metanephrines. A right-sided laparoscopic adrenalectomy was performed. Post-surgery, the patient did not require further antidiabetic medication, experienced gradual weight gain, improved well-being, and did not need glucocorticoid supplementation. Histopathological examination confirmed a pheochromocytoma (pT1 NX, PASS 3, GAPP 2), and considering the immediate cortisol suppression with metyrapone, spontaneous ACTH decrease pre-surgery, absence of secondary adrenal insufficiency, and negative ACTH staining of the tumor, pheochromocytoma-induced PCS was diagnosed.
Conclusions
The case underscores the unique manifestation of PCS induced by pheochromocytoma, evident through clinical, laboratory, and histopathological findings, and highlights the successful resolution through adrenalectomy and supportive care.
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P30

An unexpected Adrenal Lymphangioma: A case report
Kouloud Boujelben, Samir Mkaouer, Dhoha Ben Salah, Rihab Khochtali, mouna mnif, fatma mnif, Faten Haj Kacem Akid, Mohamed Abid & NabilaRekik Majdoub
Hedi Chaker Hospital, Endocrinology Department, Sfax, Tunisia

Introduction
Lymphangioma is a rare benign malformation of the lymphatic system that typically affects the neck and head during childhood. Adrenal glands are an

uncommon and rare location for lymphangioma. Herein, we report an unusual clinical presentation of an adrenal lymphangioma revealed by Cushing syndrome.
Case report
A 69-year-old female was referred to our department for exploration of an adrenal incidentaloma. Her medical history was positive for dyslipidemia and depressive symptoms. She was admitted in the emergency department for a five-month history of diffuse abdominal pain. Clinical and biochemical findings were normal. Abdominal sonography was performed, revealing a large heterogeneous mass measuring 9×8 cm, located in the right adrenal gland. Then, an endocrine assessment was considered. On admission, physical examination revealed fragile skin, easy bruisability and normal blood pressure. Her laboratory results were within reference ranges. The endocrinlogical workup revealed a plasma adrenocorticotropic hormone (ACTH) at 8.17 pg/ml (normal <45 pg/ml), morning serum cortisol of 220 ng/ml and unsuppressed cortisol after 1 mg overnight dexamethasone suppression test. Low-dose dexamethasone suppression testing showed unsuppressed cortisol at 23.5 ng/ml. These results were compatible with ACTH independent Cushing syndrome. Serum metanephrines, normetanephrines and androgens levels were normal. On abdominal computed tomography (CT), there was evidence of a right giant heterogeneous mass with central and peripheral calcifications measuring 10×8 cm, suggestive of an adrenocortical carcinoma. Abdominal MRI confirmed CT scan' findings, showing large necrotic tissue. Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) scan did not demonstrate any metastasis. The patient underwent right adrenalectomy, under hydrocortisone coverage, through a right subcostal incision. Lumbo-aortic lymph node dissection was also performed. Unexpectedly, the histopathological examination was consistent with the diagnosis of a benign adrenal Lymphangioma. The postoperative period was uneventful, with pituitary–adrenal recovery.
Conclusion
Adrenal lymphangiomas remain extremely rare.However, they must be included in the differential diagnosis of adrenal mass.Clincial and radiological features are variable, leading to a misdiagnosis.Pathological examination is essential for the diagnosis.

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P31

Blood pressure changes during smoking cessation on dulaglutide and placebo treatment – a secondary analysis of the randomized, double-blind, placebo-controlled SKIP trial

Beck Julia, Flavia Hasenböhler, Sophia Lengsfeld, Thilo Burkard, Andrea Meienberg, Nica Jeanloz, Tanja Vukajlovic, Katja Bologna, Cemile Bathelt, Deborah Vogt, Laura Werlen, Mirjam Christ-Crain & Bettina Winzeler
Universitätsspital Basel, Basel, Switzerland

Objective
Smoking is an established major risk for atherosclerosis and cardiovascular mortality. However, the impact of smoking cessation on blood pressure remains controversial. Despite strong evidence linking smoking cessation to reduced cardiovascular risk, conflicting studies suggest potential increases in blood pressure after smoking cessation. Post cessational weight gain may contribute to these conficiting findings. We have recently shown that the glucagon-like peptide-1 (GLP-1) analog dulalgutide counteracts post-cessational weight gain. Therefore, the aim of this secondary analysis was to investigate blood pressure changes during smoking cessation in dulaglutide versus placebo treated individuals.
Design and methods
This is a predefined secondary analysis of the SKIP trial, a randomized, double-blind, placebo-controlled trial, conducted at the University Hospital Basel in Switzerland. Participants ($n=218$) underwent a 12-week smoking cessation program including standard of care and weekly injections of dulaglutide 1.5 mg or placebo. A mediation path analysis was performed to quantify the effect of predefined variables and relationships.
Results
In the short term (12 weeks), smoking cessation led to a weight gain of +0.96 kg [CI 0.23, 1.70, *P*-value =0.01], with each kilogram increase associated with a systolic blood pressure rise of +0.55 mmHg [−0.0, 1.11, *P*-value =0.055]. Dulaglutide treatment resulted in a weight reduction of −3.02 kg [CI −3.69, −2.63, *P*-value =0.001], and each kilogram decrease lowered systolic blood pressure by −1.66 mmHg [−3.40, 0.08, *P*-value =0.06]. No direct effect on systolic blood pressure was observed for smoking cessation or dulaglutide without weight influence. In the long term (52 weeks), smoking cessation led to a significant weight increase of +4.20 kg [2.67, 5.74, *P*-value <0.001]. No direct effect of smoking cessation on systolic blood pressure was observed, either independently or through weight change.
Conclusion
Our findings indicate that blood pressure changes during smoking cessation are primarily mediated by weight change. This underlines the importance of weight control and a potential beneficial role of GLP-1 analogues in the context of smoking cessation.

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P32

Physical activity after planned cessation of prednisolone treatment in patients with polymyalgia rheumatica and/or giant cell arteritis: baseline data from the double edge-replace study

Jelena Stankovic[1,2], MarieLouise Lund [3,4], AnjaFenger Dreyer[5,6], Hajir Al-Jorani[5,6], Victor Brun Boesen[3,4], StinaWillemoes Borresen[3,4], LouiseLehmann Christensen[5,6], Ulla Feldt-Rasmussen[3,4], Dorte Glintborg[5,6], Simon Bøggild Hansen[1,2], Richard Christian Jensen[5], NannaThurmann Jørgensen[3,4], LiseSofie Bisley[1], Randi Tei[1,2], Marianne Andersen[5,6] & JensOtto Jørgensen[1,2]
[1]Aarhus Universitetshospital, Department of Internal Medicine and Endocrinology, Aarhus, Denmark; [2]Aarhus University, Department of Clinical Medicine, Aarhus, Denmark; [3]Rigshospitalet, Department of Endocrinology and Metabolism, København, Denmark; [4]The University of Copenhagen, Faculty of Health and Medical Sciences, Department of Clinical Medicine, Københavns, Denmark; [5]Odense University Hospital, Department of Endocrinology, Odense, Denmark; [6]University of Southern Denmark, Department of Clinical Research, Odense, Denmark

Introduction
Myopathy is a known and dreaded adverse effect of pharmacological glucocorticoid (GC) treatment, but its impact on daily physical activity is not known.
Aim
To measure spontaneous physical activity and musculoskeletal function in patients shortly after planned cessation of long-term (>12 weeks) prednisolone treatment.
Patients and methods
Baseline data from an ongoing nation-wide prospective study (DOUBLE EDGE – REPLACE) involving 49 patients [median (range) age 71 (51, 86) years, 29 females and 20 males] diagnosed with polymyalgia rheumatica (PMR) and/or giant cell arteritis (GCA) in GC free-remission for 2−12 weeks. Physical activity was assessed by ActiGraphy (wGT3X-BT, ActiGraph), a wearable wrist-device, capturing 7 consecutive days of activity data. Muscle function in terms of the short physical performance battery (SPPB) and time-up-and-go test (TUG) was also assessed. Finally, symptoms of GC-induced adrenal insufficiency (GIA) were assessed by a disease-specific questionnaire (AddiQoL-30 score), by which presence of GIA-symptoms were defined as a score of ≤85.
Results
Patients spent 57% (95%-CI: 55.0, 60.6) of the recorded time at sedentary activity (SA) levels and 10% (95%-CI: 8.1, 11.4) in moderate-vigorous physical activity (MVPA). The median (IQR) 6 month accumulated prednisolone-dose was 310 (208, 469) mg. Mean (s.d.) morning cortisol-level (nmol/l) was 246 (82) in patients with GIA-symptoms vs 315 (90) in the asymptomatic group ($P<0.001$). Patients who followed the WHO-recommendations of 60 min of MVPA daily performed better on the short physical performance battery (SPPB) (mean (s.d.) 10.3 (2.0) vs 8.4 (3.5)) and time-up-and-go (TUG) (mean (SD) 10.4 (6.4) vs 6.9 (1.7)), compared to those who did not meet the criteria ($P=0.03$ and $P<0.01$ respectively). The low-MVPA group was more comorbid measured by the Charlson comorbidity index ($P=0.03$). Multiple linear regression controlling for age and gender revealed no difference in SA or MVPA between patients with and without GIA-symptoms.
Conclusions
This is the first study to consecutively map spontaneous physical activity and muscle function in a population of PMR and GCA patients at risk of GC-induced myopathy. Only a small proportion of the patients met the WHO-recommendations of 60 min/day of MVPA. Low MVPA levels were associated with higher comorbidity, which illustrates broader health implications of inactivity. Higher GIA-symptoms did not correlate with objective activity measures. However, we hypothesize, that GC-related factors contribute to the so-called steroid-withdrawal syndrome. The ensuing prospective phase of the study will show if this is reversed by either time or low-dose hydrocortisone replacement.
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P208

Webinars for patient education on congenital adrenal hyperplasia

Ann-Christin Welp[1], Lea Tschaidse[1], Matthias Auer[1], Christian Lottspeich[1], Uta Neumann[2], Hanna F Nowotny[1] & Nicole Reisch[1]
[1]LMU Klinikum München, Medizinische Klinik und Poliklinik IV, Munich, Germany, [2]Institut Für Experimentelle Pädiatrische Endokrinologie, Charité – Universitätsmedizin Berlin, Berlin, Germany

Background
In 2020, DSD-Care, a collaborative project involving endocrine reference centres, support groups, and research institutes in Germany was launched funded by the German Ministry of Health. The aim of the project was to improve the quality of care for people with differences in sex development (DSD), who often report feeling poorly treated by healthcare providers and a lack of access to detailed information about their condition. Congenital adrenal hyperplasia (CAH) is one of the diagnoses that has been investigated in DSD-Care. According to current studies, patients with CAH often lack knowledge and education about their disease, which can have severe consequences. Proper treatment is crucial, as CAH is a life-threatening disease and patients must respond correctly in emergency situations.
Objective
To produce informative and objective webinars of high-quality for patient education that offer a structured and detailed overview of CAH for affected patients, their families, and those interested in the disease.
Design and methods
Endocrine specialists with extensive experience in CAH worked together to produce literature- and expert-based manuscripts. These manuscripts were transformed into video presentations for the webinars. The recorded videos present information in a clear and logical manner, using formal language that is still accessible to the layperson. Technical terms are introduced when first used, and current gender standards are adhered to.
Results
Experienced endocrinologists created and recorded seven evidence-based webinars for patient education on CAH. The webinars cover five main topics, providing a structured and detailed overview of CAH. The first topic is an introduction to CAH, presented in two videos. The second topic covers treatment and treatment monitoring of CAH, presented in two videos. The third topic presents the (side-)effects of CAH and emergency treatment. Topic four provides information on genetics in CAH and family planning, while topic five introduces CAH in childhood and adolescence. The videos will be freely available after registration on the LMU Klinikum learning platform for patients with CAH, their relatives and other interested viewers.
Conclusions
To serve the needs of people with CAH for better patient education we recorded webinars containing general information on CAH as well as on therapeutic concepts, side effects, sick day rules, genetics, family planning and CAH in childhood and adolescence. The videos are freely available for patients with CAH and all other interested parties. Evaluation of the webinars will be performed by surveys pre- and post-usage.

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P214

Impact of systematic screening of pheochromocytoma in patients with neurofibromatosis type 1

Audrey AGIUS[1], Abeillon Juliette[1], Mona Amini-Adle[2], Lasolle Hélène[1], Francoise Borson-Chazot[1], Patrick Combemale[2] & Lori Kepenekian[3]
[1]Hospices Civils de Lyon, Lyon, France; [2]Centre Léon Bérard, Lyon, France; [3]Infirmerie Protestante, Lyon, France

Background
In 2016, a prospective study conducted by our team found a prevalence of 7.7% of pheochromocytomas (Pheo) in patients with neurofibromatosis type 1 (NF1) if systematic screening including free metanephrines measurement (DMX) and abdominal imaging was performed. Half of Pheo were secreting, with 16% being symptomatic. This suggested the benefit of a systematic screening by abdominal imaging and DMX assay. The objective of this study was to evaluate the impact of systematic screening in a large cohort of NF1 patients.
Methods
This was an observational retrospective study of NF1 patients followed in the Lyon reference center Leon Berard since 1990 and explored at the Lyon university hospital until August 2023. The files were screened for a history of Pheo and diagnostic circumstances, biological and morphological characteristics, therapeutic modalities and evolution were collected.
Results
The whole cohort comprised 1594 NF1 patients, from whom 585 had undergone abdominal imaging at least once from the age of 25. Forty-eight patients were diagnosed with a Pheo and 1 with an extra-adrenal paraganglioma (PPGL). Prevalence of Pheo/PPGLs was 8.4% in the imaging population and 3% for the whole cohort. Nineteen Pheo/PPGLs were diagnosed on systematic screening (Screening Group (SG)) and 27 were diagnosed either incidentally ($n=10$) or because of symptoms ($n=17$) (Non Screening Group (NSG)). Median age at diagnosis was 44 years in both groups, with more men in SG (58%) than in NSG (26%; $p=0{,}037$). In SG, 26.3% of patients were symptomatic vs 84.6% in NSG, ($P<0.001$) while the proportion of secreting Pheo (DMX >2N) was 66.7% in SG, vs 86.4% in NSG ($P=0.253$). None patient of SG had a Pheo >4 cm vs 24% in NSG ($P=0.072$). Bilateral Pheo were found in 16.7% of cases in SG vs 42.9% in NSG ($P=0.489$), all were synchronous in SG vs 43% in NSG. None SG patient was metastatic vs 8% ($n=2$) in NSG. The number of surgeries was equivalent in both groups; four patients had not been operated on yet. Sparing surgery has been performed in 26.7% of patients in SG ($n=4$) vs 4.2% ($n=1$) in NSG ($P=0.062$).
Conclusion
Systematic screening for Pheo could allow diagnosis of smaller lesions, fewer metastatic and more often asymptomatic despite secreting. It led to more conservatives surgeries.

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P215

Incidence of adrenal crisis in Congenital Adrenal Hyperplasia (CAH) patients during a prospective monitored long-term study of modified-release hydrocortisone (MRHC) capsules, (Efmody)

Richard John M. Ross[1], DeborahP Merke[2], Ashwini Mallappa[2], Wiebke Arlt[3], AudeBrac DeLaPerriere[4], Angelica Hirschberg[5], JohnDC Newell-Price[1], Alessandro Prete[6], Aled Rees[7], Nicole Reisch[8], Marcus Quinkler[9], PhilippeA Touraine[10], Kerry Maltby[11], Jo Quirke[11], Naila Aslam[11], Helen Coope[11] & John Porter[11]
[1]The University of Sheffield, UK; [2]National Institutes of Health, Bethesda, USA; [3]MRC Laboratory of Medical Sciences, UK; [4]Louis Pradel Hospital, Bron, France; [5]Karolinska Institute, Sweden; [6]University of Birmingham, UK; [7]Cardiff University, UK; [8]Medizinische Klinik und Poliklinik I | LMU Klinikum, München, Germany; [9]Charlottenburg, Berlin, Germany; [10]University Hospitals Pitié Salpêtrière - Charles Foix, Paris, France; [11]Diurnal, UK

Background
Adrenal crisis is the leading cause of excess mortality in patients with CAH[1]. Retrospective studies report an adrenal crisis incidence of 5-10/100 patient years (PY), with mortality 0.5/100 PY[2]. Modified-release hydrocortisone (MRHC) capsules, (Efmody), replicate cortisol diurnal rhythm and improve androgen control in CAH compared to standard glucocorticoid therapy[2]. Here, we report the incidence of adrenal crisis in CAH patients from a prospective study of MRHC in CAH patients.
Methods
Patients completing MRHC Ph2 and Ph3 studies were eligible to enter a single-arm, open-label extension study. Study visits occurred at baseline, weeks 4, 12, 24 and 6-monthly thereafter. The primary endpoint was the safety of MRHC over time. Adrenal crisis was defined according to Allolio 2015[3]. MRHC doses were adjusted on the basis of an adrenal insufficiency checklist, and measurement of androstenedione (A4) and 17-hydroxyprogesterone (17-OHP) at 0900 and 1300 h.
Results
91 patients entered the study, mean age 37 years, 68% female, 32% male. 22 discontinued; 11 at patient request, 5 due to pregnancy, 2 undergoing fertility treatment, 2 at physician/sponsor request, 1 due to an AE (carpal tunnel syndrome), and 1 due to death (myocardial infarction). Median treatment duration was 1500 days, range 0.2 to 5.8 years. Median MRHC dose at study entry was 30 mg/day, reducing to 20 mg/day from 24-weeks until end of study. Signs and symptoms of adrenal insufficiency due to under-treatment were reported for 41 (45.1%) participants, most frequently fatigue which was reported at some point by 41.8% of all participants. Signs and symptoms of overtreatment were reported for 25 (27.5%) participants, most frequently sudden weight gain which was reported at some point by 16.5% of all participants. Signs and symptoms of both over- and undertreatment occurred predominantly during the first 24 weeks. The study encompassed 357 participant years, and 18 adverse events considered indicative of adrenal crisis occurred in 7 participants, giving an incidence rate of 5.043 adrenal crises/100 PY.
Conclusions
Data from this longest prospectively monitored study in CAH suggest that the incidence of adrenal crisis on MRHC is at the low end of that reported in retrospective studies and the safety profile of MRHC is otherwise similar to immediate release hydrocortisone.
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P216

Psychotropic drugs in patients with Addison's disease: A Swedish population-based cohort study

Sara Öster[1], Tim Spelman[2], Olle Kämpe[3,4], Sophie Bensing[1,4] & Jakob Skov[1,5]
[1]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [2]Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden; [3]Karolinska Institutet, Department of Medicine Solna, Stockholm, Sweden; [4]Karolinska University Hospital, Department of Endocrinology, Stockholm, Sweden; [5]Karlstad Central Hospital, Department of Medicine, Karlstad, Sweden

Objective
Several autoimmune disorders are known to be associated with an increased risk of psychiatric morbidity. Yet, the effect of autoimmune Addison's disease (AAD) on mental health is not well known. The aim of this study was to examine the use of psychotropic drugs around diagnosis in Swedish individuals with AAD.
Design and methods
In this population-based cohort study, The Swedish national patient register, and the Swedish Addison register were used to find cases with AAD. The Swedish population register was then used to find matched controls. Information on psychotropic drugs prescribed between July 2006 and December 2019 was retrieved from the Swedish prescribed drug register. The primary outcomes were dispensations of antipsychotics (ATC N05A), anxiolytics (ATC N05B), hypnotics/sedatives (ATC N05C) and/or antidepressants (ATC N06A), from three years before to three years after AAD diagnosis in the national patient register.
Results
963 cases of AAD and 9366 matched controls were identified. The most dispensed type of psychotropic medication was hypnotics and sedatives, with 14.2% of cases receiving it during the year of most use. The least dispensed group of psychotropics was anti-psychotics, with only 2.0% of cases and 1.8% of controls receiving it at most. Anti-depressants were prescribed at a lower frequency to the AAD group at all time points except for during the year before diagnosis, where the incidence was higher than in the control group (aOR 1.24; 95% CI 1.02–1.55; $P=0.040$). Patients also received more anxiolytics the year before diagnosis (aOR 1.28; 95% CI 1.03–1.62; $P=0.039$). Hypnotics and sedatives were significantly more common after diagnosis (aOR 1.29; 95% CI 1.02–1.64; $P=0.036$) and the increase did not subside during the study period.
Conclusion
Individuals with AAD receive more anxiolytics, anti-depressants, sedatives and hypnotics around diagnosis. While the dispensation of anxiolytics and anti-depressants return to pre-diagnostic levels after a while, the increased dispensation of sedatives and hypnotics remains elevated.

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P217

Brown adipose tissue activation on 18FDG-PET/CT scan in phaeochromocytoma: A case series

MuhammadNajmiBin MdNor[1], Kate Healy[1], Suzanne Egan[1], John Feeney[1], James Gibney[1], Agnieska Pazderska[2] & Aoife Garrahy[1]
[1]Tallaght University Hospital, Ireland; [2]St James's Hospital, Ireland

Introduction
Prior studies have demonstrated that individuals with phaeochromocytoma and paranganglioma may manifest activation of Brown Adipose Tissue (BAT) as a result of excess catecholamines secretion[1–2]. In this case series, we describe two cases featuring patients with phaeochromocytoma who exhibited increased uptake of BAT on ^{18}-FDG-PET/CT scans.
Case 1
A 74-year-old woman was referred to the Endocrinology department with a 7 cm right adrenal mass detected on CT imaging performed for the investigation of weight loss. Medical history included hypertension requiring three antihypertensives, type 2 diabetes and migraine. Blood work revealed elevated plasma normetanephrines, >25 000 pmol/l (0-1180), metanephrines, >16 000 pmol/l (0-510), and 3-methoxytyramine, 623 pmol/l (0-180). She subsequently had MRI Adrenal which showed 7 cm right adrenal mass and MIBG SPECT/CT which showed intensely MIBG-avid right adrenal mass. ^{18}-FDG-PET/CT arranged prior to the metanephrine results being available showed mild uptake in the right adrenal mass and intense uptake localising in thoracic paravertebral and perinephric fat indicative of BAT activation. Elective open right-sided adrenalectomy was performed, confirming a pheochromocytoma with Phaeochromocytoma Adrenal Scaled Score (PASS) of 7/20. Postoperatively, plasma metanephrines normalised and ^{18}-FDG-PET/CT showed a normalisation of perinephric FDG distribution and no FDG-avid disease.
Case 2
A 56-year-old woman was referred to Endocrinology department due to a 9 cm right retroperitoneal mass which was suspected to arise from right adrenal gland for investigation of recurrent vomiting. Medical history included hypertension and she reported having recurrent palpitations and anxiety. Blood work revealed elevated plasma normetanephrines >25 000 pmol/l (0-1180), metanephrines 1854 pmol/l (0-510) and 3-methoxytyramine, 731 pmol/l (0-180). Further investigations included MRI Adrenal, which identified well-circumscribed, peripherally enhancing 9 cm mass on right adrenal gland. She subsequently had ^{18}-FDG-PET/CT which showed partially cystic/necrotic right adrenal mass with intense FDG uptake in its solid component, with BAT uptake was observed in cervical, subclavicular and paraspinal stations. Subsequently, she had elective right-sided open adrenalectomy with histology confirmed phaeochromocytoma with PASS score of 11/20. Postoperatively, plasma metanephrines normalized and repeat CT TAP 6 months later showed no evidence of recurrence.
Discussions
Norepinephrine-induced beta-adrenoceptor activation in patients with phaeochromocytoma and paraganglioma may lead to brown fat activation, which is associated with increased energy wasting and cachexia[2]. In case 1, this manifested in weight loss and marked BAT activation on ^{18}-FDG-PET-CT, both of which were reversed following removal of the phaeochromocytoma.
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P218

Severe hyponatraemia and hyperkalaemia in pre-eclampsia due to hypoadrenalism/functional hypoadrenalism

Ffion Davies[1], Timothy Green[2], Rhiannon Berkeley[2], Genevieve Tellier[2] & Anthony Wilton[2]
[1]Bangor Hospital, Acute Intervention Team, Bangor, UK; [2]Bangor Hospital, Endocrinology, Bangor, UK

Pre-eclampsia is a life-threatening disease occurring in 4.6% of pregnancies characterised by multi-organ dysfunction. Placental dysfunction is implicated with release of factors causing systemic inflammation and endothelial dysfunction. Mild hyponatraemia (130–135 mmol/l) is regarded as physiological in normal pregnancy. Severe hyponatraemia (<125 mmol/l) is a rare life-threatening complication of pre-eclampsia. Severe hyponatraemia and hyperkalaemia has been reported on one occasion; we report a second case with endocrine data.
Case history
A 27 year old 34-weeks pre-eclamptic twin-pregnancy patient was referred to endocrinology with severe hyponatraemia, hyperkalaemia and metabolic acidosis: sodium 120 mmol/l, potassium 6.2 mmol/l, bicarbonate 16 mmol/l, creatinine 93 mmol/l, eGFR 63 ml/min. Five days earlier: sodium 131 mmol/L, potassium 4.5 mmol/l, creatinine 77 mmol/l, eGFR 78 ml/min. Two weeks earlier: sodium 135 mmol/l, potassium 5.1 mmol/l, creatinine 66 mmol/l, eGFR >90 ml/min. Insulin/dextrose was ineffective causing hypoglycaemia with little effect on potassium. Coincidental with deterioration in sodium and potassium levels a rise in creatinine, CRP and liver enzymes and decrease in eGFR, pH and albumin had occurred. Examination: ill, oedematous, blood pressure 140/90 mmHg on treatment with labetalol 200mg BD. Investigations at 0730 h: cortisol 483 nmol/l, ACTH 118 ng/l, PRA 1.7 nmol/l per hour, (aldosterone 2010 pmol/l, aldosterone/renin ratio 1182, results not immediately available). The abnormal electrolytes, pH and inappropriately normal cortisol level given clinical status, third trimester and elevated ACTH suggested hypoadrenalism. Hydrocortisone 100 mg IV followed by 200 mg/24 h continuous infusion did not prevent further biochemical deterioration: sodium 120 mmol/l, potassium 6.2–8.7 mmol/l, pH 7.23, creatinine 109 mmol/l and eGFR 52 ml/min. Urgent delivery was advised with a 2 healthy males outcome but a post-operative haemorrhage resulted in a hysterectomy. All laboratory data normalised post-delivery.
Conclusion
1) This case confirms severe hyponatraemia (+/− hyperkalaemia) as a risk factor in pre-eclampsia. Existing guidelines do not address this issue. 2) There is evidence of impaired cortisol synthesis/secretion with low cortisol and high ACTH level. The adrenal ACTH receptor is a 7-membrane-spanning G protein-coupled receptor which could be affected by endothelial dysfunction. 3) Angiotensin II is also a transmembrane G protein-coupled receptor which could also be affected by endothelial dysfunction. Hyperkalaemia is a highly potent aldosterone secretagogue acting by depolarisation of the cells of the zona glomerulosa. 4) Aldosterone upregulates and enhances gene transcription of the transmembrane sodium/potassium ATPase pump which again could be affected

by endothelial dysfunction explaining the lack of aldosterone effect on sodium and potassium levels.

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P219

11β-hydroxysteroid dehydrogenase type 1 inhibition unmasks multiple pathways that may mitigate the adverse effects of prescribed prednisolone

Riccardo Pofi[1], Sergi Coll[2], Nantia Othonos[1], Hamish Miller[1,3], Tom Potter[1,4], Jane Escott[5], Andrew Whittaker[6], Núria Monfort[2,7], Rosa Ventura[2] & Jeremy Tomlinson[1]

[1]Oxford, Oxford Centre for Diabetes, Endocrinology and Metabolism, NIHR Oxford Biomedical Research Centre, University of Oxford, Churchill Hospital,, Oxford, UK; [2]Barcelona, Doping Control Research Group, Catalonian Antidoping Laboratory IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain; [3]London, Barts Liver Centre, Blizard Institute, QMUL, London, UK; [4]Oxford, Department of Biological and Medical Sciences, Oxford Brookes University, Oxford, UK; [5]Cambridge, Business Development & Licensing, BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK; [6]Cambridge, Former employee, Emerging Innovations Unit, Discovery Sciences, BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK; [7]Barcelona, Department of Experimental and Health Sciences, Universitat Pompeu Fabra, Barcelona, Spain

Background

Prednisolone is the most commonly prescribed exogenous glucocorticoid(GC) and its use is frequently associated with the development of iatrogenic Cushing's Syndrome. Once administered, prednisolone is rapidly converted to inactive prednisone by renal 11β-hydroxysteroid dehydrogenase type 2(11β-HSD2) and subsequently reactivated by 11β-HSD1. We have shown previously that 11β-HSD1 inhibition(with the selective 11β-HSD1 inhibitor, AZD4017) mitigates prednisolone-induced adverse effects[1]. Other enzymes, including AKR1C1(20α-hydroxylase), Carbonyl reductase 1(20β-hydroxylase, CBR1) and CYP3A4(6β-hydroxylase) are known to have a role in GC metabolism, but their contributions to prednisolone and prednisone metabolism are entirely unexplored.

Aims

To describe the patterns of unique metabolites(plasma and urine) associated with prednisolone and prednisone clearance, define the impact of 11β-HSD1 inhibition and assess correlations between plasma metabolites and clinically significant outcomes.

Methodology

Retrospective analysis of timed overnight urine collections alongside a detailed 8-h assessment period of 2-hourly plasma samples after administering prednisolone (20 mg) with either placebo or AZD4017. Plasma metabolites were quantified using LC–MS/MS. Specific enzyme activity was inferred using the ratio of target metabolite/substrate levels. We employed repeated measure ANOVA, Area Under the Curve(AUC) analysis as well as logistic regression.

Results

Urine sample analysis identified 20 discrete prednisolone metabolites. Following oral prednisolone administration (20 mg), timed (0–8 h) plasma metabolite analysis demonstrated that prednisolone (AUC = 820 ± 213 ng/ml) and prednisone (AUC = 154 ± 50 ng/ml) were the most abundant metabolites, followed by 20β-OH metabolites ($AUC_{20\beta\text{-OH-prednisolone}} = 69.5 \pm 71.2$; $AUC_{20\beta\text{-OH-prednisone}} = 24.8 \pm 16.8$ ng/ml). Inhibition of 11β-HSD1 activity with AZD4017 decreased prednisolone availability by 59% ($P < 0.001$). Interestingly, AZD4017 did not increase prednisone availability ($\Delta_{AUC} = -38.67$, 95%CI −84.42;7.08, $P = 0.113$). Furthermore, 8h after prednisolone administration, prednisone levels were lower in the AZD4017 treated group (Δ −14.88 ng/ml, 95%CI −18.94; −10.83, $P < 0.001$). This observation was driven, at least in part, through increased (+93%, $P = 0.007$) CBR-1 activity assessed by 20β-OH prednisone relative to prednisone concentrations. Logistic regression identified 20β-OH-prednisone(4h) as the only predictor of higher glucose disposal ($B = 0.382$, $P = 0.017$) and osteocalcin levels ($B = 0.727$, $P = 0.006$) after prednisolone, indicative of less significant adverse effects.

Conclusions

11β-HSD1 has a major role to regenerate active exogenous prednisolone. However, preferential prednisone clearance, principally through the activity of CBR1 (but also AKR1C1), further limits the potential for prednisone reactivation and may represent another important mechanism mitigating the adverse effects of prescribed GCs. Finally, 20β-OH-prednisone may emerge as predictor of prednisolone-related adverse effects that may lead to a more precise and personal approach to prednisolone prescribing.

Reference

[1] 11β-HSD1 inhibition in men mitigates prednisolone-induced adverse effects in a proof-of-concept randomised double-blind placebo-controlled trial. *Othonos et al*., *NatComm* 2023; doi:10.1038/s41467-023-36541-w.

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P220

Adrenalectomy improves blood pressure and insulin secretion in adrenal incidentalomas and MACS

Valentina Morelli[1], Antonio Musolino[2], Serena Palmieri[3], Flavia Pugliese[4], Carmen Aresta[1], Sofia Frigerio[2,3], Maura Arosio[3,5], Sabrina Corbetta[1,6], Alfredo Scillitani[4] & Iacopo Chiodini[2,7]

[1]IRCCS Istituto Auxologico Italiano, Department of Endocrine and Metabolic Diseases, Milan, Italy; [2]University of Milan, Department of medical biotechnology and translational medicine, Milan, Italy; [3]Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Unit of Endocrinology, Milan, Italy; [4]"Casa Sollievo della Sofferenza" Hospital, IRCCS, Unit of Endocrinology and diabetology, San Giovanni Rotondo, Foggia, Italy; [5]University of Milan, Department of clinical sciences and community health, Milan, Italy; [6]University of Milan, Department of biomedical, surgical and dental sciences, Milan, Italy; [7]Ospedale Niguarda Cà Granda, Unit of Endocrinology, Milan, Italy

Introduction

In patients with unilateral adrenal incidentaloma (AI) and mild autonomous cortisol secretion (MACS) the best therapeutic approach is still a matter of debate. The only available randomized study showed a short-term beneficial effect of surgery on diabetes and hypertension. Importantly, recent data demonstrated that MACS is associated to an increased risk of mortality, especially due to cardiovascular causes.

Study aim

to evaluate, in the medium term, the effect of adrenalectomy on blood pressure and glycometabolic control, in patients with AI and MACS.

Patients and methods

We performed a prospective randomized study on 62 patients with AI > 1 cm and cortisol after 1 mg dexamethasone suppression test (1 mgDST) between 1.8 and 5 μg/dl. Patients were randomized to adrenalectomy (operated) or conservative approach (non-operated). A total of 46 subjects (20 operated and 26 not operated) completed a 12 months follow-up. Blood pressure (BP), body weight, glycometabolic control, insulin secretion by homeostasis model assessment (HOMA-β) index and the medical therapy changes were assessed.

Results

At 12 months, the frequency of BP improvement was higher in operated (45%) than in non-operated patients (11.5%, $P = 0.01$), while the BP worsening was more frequent in the latter group (30.8%) than in the former one (10.0%, $P = 0.008$). Glycometabolic control ameliorated in the 25% and worsened in the 15% of surgically treated patients and in 11.5% and 30.8% of non-operated ones, respectively (P-for-trend = 0.300). The operated patients showed a significant increase in insulin secretion levels at 12 months compared to non-operated ones (HOMA-β 167.6 ± 79.4 vs 111.4 ± 47.7%, $P = 0.009$; fasting insulin 12.3 ± 4.6 vs 8.8 ± 3.9 μU/ml, $P = 0.018$; insulin AUC after OGTT 12817.1 ± 8006.1 vs 7912.5 ± 2397.0 μU/ml per 120 minutes, $P = 0.050$). BP and/or glycometabolic control improved more frequently in surgically treated patients (55.0%) than in non-operated ones (19.2%, $P = 0.015$), while BP and/or glycometabolic control worsened more commonly among non-operated patients (52.0%) than among surgically treated ones (20.0%, $P = 0.028$). The improvement of BP and/or glycometabolic control was 10.2-fold more frequent in operated patients (confidence interval, 2.82–37.1, $P < 0.001$), regardless for age, gender, and presence of glycometabolic alterations and hypertension at baseline.

Discussion

In patients with AI and MACS surgery leads to a persistent improvement of blood pressure control and insulin secretion and, in more than half of cases, it is beneficial in terms of BP and/or glycometabolic control. At variance, in more than half of patients a conservative approach seems to be deleterious in terms of BP and/or glycometabolic control.

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P221

Constitutional duplication of PRKACA gene is a cause of isolated primary pigmented nodular adrenocortical disease (PPNAD)

Patricia Vaduva[1], Florian Violon[1], Gerald Raverot[2], Espiard Stephanie[3], Amina Attia[1], Lucas Bouys[1,4], Karine Perlemoine[1], Chansavang Albain[5,5], Nicolas Chevalier[6], Vantyghem Marie Christine[3], Michel Polak[7], Bruno Ragazzon[1], Anne Anne Jouinot[1], Eric Pasmant[5] & Jerome Bertherat[1,4,4]

[1]Cochin Institute, Paris, France; [2]Hospices civils de Lyon, Endocrinology, Brons, France; [3]Lille University Hospital, Endocrinology, Diabetology, Metabolism and Nutrition, Lille, France; [4]Cochin Hospital, Endocrinology, Paris, France; [5]Cochin Hospital, Department of Tumors and Cancers Molecular Medicine, Paris, France; [6]Nice University Hospital, Department of Endocrinology, Diabetology and Reproductive medicine, Nice, France;

[7]Necker University Hospital, APHP, Department of Pediatric Endocrinology, Gynecology and Diabetology, Paris

Objective
We have described constitutional duplications of the *PRKACA* gene locus (encoding the catalytic subunit of the Protein Kinase A) in rare cases of bilateral nodular adrenocortical cause of Cushing's (Beuschlein et al, NEJM 2014). Its frequency in macronodular and micronodular adrenal diseases and the occurrence of others manifestation of Carney complex are not clearly established. This study performs its systematic screening in a large cohort of adrenocortical nodular disease patients and describes its phenotype.
Methods
Between 2020 and 2023, 487 consecutive index cases with bilateral macronodular adrenal hyperplasia ($n=442$) or Primary Pigmented Nodular Adrenocortical Disease (PPNAD)/Carney Complex (CNC) ($n=45$) were genotyped with a targeted NGS panel including the exonic and intronic flanking regions of the *ARMC5*, *MEN1*, *PRKAR1A* (CNC) and *PRKACA* genes. Familial screening was then offered to relatives. Whole genome sequencing was performed when accepted in index cases with *PRKACA* duplications.
Results
Constitutional duplications of *PRKACA* were identified in 5 index cases (representing 11% of patients with PPNAD or CNC) and 7 of the 11 screened relatives, supporting the involvement of the *PRKACA* oncogene through a constitutional copy gain mechanism. Sex ratio was 1 male/2 female. The whole genome sequencing performed for 4 index cases did not find any other gene involved in human disease in the duplicated region, nor any other alteration in genes implicated in adrenal tumors. All index cases had PPNAD responsible for Cushing's syndrome and ACTH-independent hypercortisolism, diagnosed at a median of 20 years (range: 9–32). The adrenals were described as normal on conventional imaging in 3/5 cases, but iodocholesterol scintigraphy showed diffuse bilateral uptake. They presented with high 24 h Urinary Free Cortisol (UFC) (range: 2.3 - 9.8 × upper limit of normal) and no response to Dexamethasone suppression test. A paradoxical rise in 24 h UFC after Dexamethasone (Liddle's test) was observed in 3 patients (1 index and 2 relatives). All patients with Cushing syndrome were treated by bilateral adrenalectomy. Almost no significant manifestations of CNC were observed apart from PPNAD (median follow-up of 10 years [5–16]): mainly lentigines and testicular calcifications in one male patient.
Conclusion
Constitutional duplication of *PRKACA* is a rare cause of PPNAD. It does not appear to be involved in other forms of adrenocortical nodular disease, nor is it frequently associated with other manifestations of CNC. Constitutional duplication of *PRKACA* should be searched in the absence of a pathogenic *PRKAR1A* variant in patients with PPNAD.

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P222

Lysophosphatidylcholines and acylcarnitines: Novel markers of physiological glucocorticoid action in adipose tissue

Kate Bennett[1], Terence Garner[1], Dimitrios Chantzichristos[2], Per-Anders Jansson[3], Adam Stevens[1] & Gudmundur Johannsson[3]
[1]The University of Manchester, Division of Developmental Biology and Medicine, Manchester, UK; [2]Sahlgrenska University Hospital, Department of Endocrinology-Diabetes-Metabolism, Sweden; [3]University of Gothenburg, Institute of Medicine, Sweden

Introduction
Glucocorticoids (GCs) play a crucial role in various physiological processes, with adipose tissue (AT) being an important target organ for their metabolic actions. Besides lipolytic action, the mechanistic regulation of GCs in human AT during physiological exposure is still unclear. We integrated transcriptomic and metabolomic data within the AT to identify mechanistic markers of GC action.
Methods
In a randomised, cross-over trial, ten patients with primary adrenal insufficiency received saline i.v. (GC withdrawal) or circadian infusion of hydrocortisone (GC exposure), with > two weeks in-between. At the end of each 26 hour period (0800 h), an abdominal subcutaneous microdialysis (membrane Asahi Kasei Medical, 3MDa) was performed, with dialysate analysed for metabolomics by LC–MS. Abdominal subcutaneous AT biopsy was collected for transcriptomics by Affymetrix Array. Hypergraph network models were used to identify changes in the metabolome between GC exposure and withdrawal, and integrate metabolomic and transcriptomic data.
Results
In subcutaneous dialysate, 22 metabolites were significantly different between GC exposure and withdrawal. The top five metabolites were lysophosphatidylcholine (lysoPC) (16:0(OH)/0:0), octanoylcarnitine, lysoPC(0:0/16:0(OH)), decanoylcarnitine, and hexanoylcarnitine. In near physiological GC exposure, we observed increased concentrations of five acylcarnitines, three fatty acids (FA), proteolytic metabolites such as gamma-glutamylleucine, and three lysoPCs with longer carbon chains (≥20C). Four lysoPCs with shorter carbon chains (<20C) were found at decreased concentration in GC exposure. We identified a relationship between a group of four acylcarnitines and two lysoPCs during physiological GC exposure. This relationship was disrupted in the withdrawal state, suggesting GC-dependent regulation. DEGs ($n=2048$ $P<0.05$) between the interventions were enriched in regulation of lipid metabolic processes by gene ontology. Hypergraphs highlighted a cluster of nine genes, the expression of which was linked to concentrations of acylcarnitines, FA and cortisol. These included several well-known GC-response genes, such as *KLF9*, *PDK4*, and *ZBTB16,* which share positive relationships with these lipolytic and proteolytic metabolites.
Conclusions
Near physiological GC exposure increased lipolysis pathways, with increased concentrations of acylcarnitines, FA, and lysoPCs. A GC-dependent relationship between acylcarnitines and lysoPCs was identified. Acylcarnitines act as transporters of FA across the mitochondrial membrane for beta-oxidation. We observed a shift from shorter chain (C14-16) to longer chain (C20-22) lysoPCs, suggesting increased lipolysis of shorter chain FA. Integration of metabolomics and transcriptomics showed relationships between expression of GC-response genes, and key metabolites in the dialysate, supporting methodology and suggesting an important role of lipolysis, beta-oxidation, and proteolysis in physiological GC action in AT.

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P223

Medication-associated false positive results for plasma normetanephrine, metanephrine and methoxytyramine

Lara Knigge[1], Kristin Potthoff[1], Georgiana Constantinescu[1], Francesco Alessi[1], Sybille Fuld[1], Karolina Zawadzka[2], Stefan Bornstein[1], Jacques Lenders[3], Graeme Eisenhofer[1] & Christina Pamporaki[1]
[1]University Hospital Carl Gustav Carus Dresden, Dresden, Germany; [2]Uniwersytet Jagielloński Collegium Medicum, Kraków, Poland; [3]Radboud University Medical Center, Nijmegen, Netherlands

Background
Measurements of plasma metanephrines provide a sensitive test for diagnosis of pheochromocytoma/paraganglioma (PPGL). However, false positive results can pose a diagnostic dilemma for clinicians. The aim of the study was to determine whether commonly prescribed drugs with potential action on the sympathetic nervous system can falsely elevate plasma free normetanephrine, metanephrine and methoxytyramine.
Methods
This retrospective study included 461 patients among who PPGL was excluded. Data on sex, age, plasma free normetanephrine, metanephrine and methoxytyramine concentrations, cardiometabolic comorbidities and/or seriouschronic illness (CCI), as well as a listing of all medications taken at the time of testingwere collected. Measurements of metabolites were by liquid chromatography with tandem mass spectrometry. For four patients under treatment with tricyclic antidepressants and/or serotonin-norepinephrine-reuptake blockers (NRBs), metabolites were measured at baseline and after discontinuation of the drug for at least five days.
Results
Among 461 patients, 408 were treated with various medications, including 23 with NRBs, 14 with selective-serotonin-reuptake-blockers, five with atypical antipsychotics, ten with anticonvulsants, 19 with hypnotics, 175 with diuretics, 187 with beta-blockers, 189 with dihydropyridines, 18 with non-dihydropyridines, 121 with angiotensin-converting-enzyme-inhibitors, 172 with angiotensin-receptor-blockers, 64 with alpha-blockers, 64 with central-agonists, 14 with vasodilators, and five with renin-inhibitors. Among 369 patients under antihypertensive treatment, 278 were treated with more than one antihypertensive drug. Rates of false positive results for plasma free normetanephrine, metanephrine and methoxytyramine in the entire cohort were 6% (29/461), 1% (4/461) and 1% (5/461) respectively. NRBs were responsible for 10% and 40% of all false positive elevations of normetanephrine and methoxytyramine respectively, whereas treatment with multiple antihypertensive drugs for 59% and 60% respectively. Nevertheless, for the vast majority of patients with multiple antihypertensive drugs and false positive elevations of normetanephrine(12/17), CCI were reported. Multivariable regression analysis after controlling for age, sex and the presence of CCI, indicated that only NRBs have significant impact on plasma free normetanephrine concentrations ($P=0.0014$). Among four patients under NRBs with paired metabolite measurements before and after discontinuation of treatment, all showed drops of normetanephrine levels below upper-cut offs after discontinuation of the medication, whereas for methoxytyramine all but one.

Conlcusion
Plasma free metanephrines and methoxytyramine is a test with a low rate of false positive results. Apart from NRBs, other medications have negligible impact on false positive results for plasma free normetanephrine.

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P224

Comparison of antihypertensive effects between eplerenone and esaxerenone, mineralocorticoid receptor antagonists, in patients with primary aldosteronism

Satoshi Morimoto, Saya Takebe, Kentaro Oyake, Saori Kitayama, Makiko Ikemoto, Yuko Inoue, Hisashi Sano, Kiyotaka Hirata, Noriyoshi Takano, Kaoru Yamashita, Yasufumi Seki, Kanako Bokuda, Daisuke Watanabe & Atsuhiro Ichihara
Tokyo Women's Medical University, Department of Internal Medicine, Tokyo, Japan

Objective
The efficacy of mineralocorticoid receptor (MR) antagonists has been demonstrated in MR-related hypertension, including primary aldosteronism (PA). Non-inferiority in 24-hour blood pressure reduction has been shown for esaxerenone 2.5 mg/day compared to eplerenone 50 mg/day in patients with essential hypertension. However, no trial has compared the antihypertensive effects of these drugs in patients with PA. This study aimed to investigate the effect of switching from eplerenone to esaxerenone and assess changes in various parameters, including blood pressure.
Methods
Patients with PA receiving eplerenone for at least 8 weeks underwent a switch to esaxerenone at 1/20th of the dose. Blood pressure measurements (office, 24-hour ambulatory blood pressure monitoring [ABPM]) and urine and blood tests were conducted before and 12 weeks after the switch, and the obtained data were compared before and after the switch.
Results
Forty-seven cases (21 males) with a mean age of 58±12 years and body mass index of 23.8 (21.7–25.3) kg/m^2 were included. Office blood pressure before the switch was 137±18/81±11 mmHg, 24-hour blood pressure 130 (123–140)/82±6 mmHg, diurnal blood pressure 133 (126–142)/84±6 mmHg, nocturnal blood pressure 119 (110–126)/73±6 mmHg, serum potassium 4.2±0.3 mEq/l, eGFR 70.1±14.3 ml/min per 1.73 m^2, and plasma renin activity (PRA) 0.9 (0.5–1.7) ng/mL per hour. After the switch, office systolic blood pressure was significantly decreased [130 (118–139) mmHg; p=0.002]. ABPM revealed significant reductions in both systolic and diastolic blood pressure over 24 h [127 (120–137) mmHg; P=0.008/80±6 mmHg; P=0.006], during the diurnal period [133 (126–142) mmHg; P=0.015/82±7 mmHg; P=0.009], and throughout the nocturnal period [115 (110–119) mmHg; p=0.039/71±7 mmHg; P=0.023]. Serum potassium did not show significant changes, but PRA [1.5 (0.7–2.1) ng/ml per hour; P<0.001] increased significantly, and eGFR (64.9±14.8 ml/min per 1.73 m^2; P<0.001) significantly decreased.
Conclusion
In PA patients, esaxerenone demonstrated a stronger MR antagonistic effect and a significant and sustained antihypertensive effect compared to eplerenone.

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P225

Baseline characteristics of children and adolescents with classic congenital adrenal hyperplasia enrolled in CAHtalyst pediatric, a phase 3 Study of Crinecerfont, a corticotropin-releasing factor type 1 receptor antagonist

Kyriakie Sarafoglou[1], Mimi Kim[2,3], Maya Lodish[4], Eric Felner[5,6], Laetitia Martinerie[7], Natalie J. Nokoff[8], Maria Clemente[9], Patricia Y. Fechner[10], Maria Vogiatzi[11], Phyllis Speiser[12,13], Julia Sturgeon[14], Eiry Roberts[14], George Jeha[14], Jean L. Chan[14] & Robert Farber[14]
[1]University of Minnesota Medical School, Minneapolis, USA; [2]Children's Hospital Los Angeles, Los Angeles, USA; [3]Keck School of Medicine of USC, Los Angeles, USA; [4]UCSF Benioff Children's Hospital - San Francisco, San Francisco, USA; [5]Emory University School of Medicine, Atlanta, USA; [6]Children's Healthcare of Atlanta, Atlanta, USA; [7]Hospital Robert Debré Ap-Hp, Paris, France; [8]Children's Hospital Colorado Anschutz Medical Campus, Aurora, Aurora, USA; [9]Vall d'Hebron University Hospital, Barcelona, Spain; [10]Seattle Children's Hospital, Seattle, USA; [11]The Children's Hospital of Philadelphia, Philadelphia, USA; [12]Cohen Children's Medical Center, New Hyde Park, USA; [13]Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, USA; [14]Neurocrine Biosciences Inc., San Diego, USA

Objective
To describe the baseline characteristics of individuals enrolled in CAHtalyst Pediatric (NCT04806451), a randomized, double-blind, placebo-controlled, Phase 3 study evaluating the safety and efficacy of crinecerfont (a corticotropin-releasing factor type 1 receptor [CRF$_1$] antagonist) in children and adolescents with classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency (21-OHD CAH).
Methods
Key eligibility criteria included: male or female, age 2-17 years; glucocorticoid (GC) dose >12 mg/m^2/day in hydrocortisone equivalents (HCe) adjusted for body surface area (BSA), on a stable dose for ≥1 month prior to screening; androstenedione (A4) greater than midpoint of reference range; and 17-hydroxyprogesterone (17-OHP) >2× upper limit of normal prior to morning GC dose. Baseline demographics and characteristics were summarized descriptively in all randomized participants.
Results
Of 103 enrolled participants at 46 study centers, 52% were male and 63% were White. Mean (±S.D.) age was 12±3 years (range: 4–17), with 54% ages 12–17 years. Overall, 58% were overweight/obese (body mass index [BMI] ≥85th percentile), BMI standard deviation score (SDS) was 1.2±0.9, height SDS was 0.3±1.3, and mean BSA was 1.5±0.3 m^2. Tanner stages (breast or testicular volume) were as follows: 1 (29%), 2 (12%), 3 (13%), 4 (18%), and 5 (28%). Mean (±S.D.) total daily GC dose was 16.4±3.9 mg/m^2/day HCe, with 92% on hydrocortisone and 8% on a predniso(lo)ne-containing regimen. 87% were taking fludrocortisone (mean dose: 1.1±0.5 mg/day), with 10% on GnRH agonists and 3% on aromatase inhibitors. Mean (±S.D.) hormone concentrations prior to morning GC dose were: ACTH, 329±344 pg/ml; 17-OHP, 8682±6847 ng/dl; A4, 431±461 ng/dl; testosterone (T) in females, 73±67 ng/dl; and A4/T in males, 3.5±7.6. Comorbidities included advanced bone age by ≥1 year (62%), early puberty (33%), irregular menstrual cycles (12% females), hirsutism (12% females), and testicular adrenal rest tumors (6% males). The mean ratio of bone age to chronological age was highest in males at Tanner stage 1 (1.4±0.4) and in females at Tanner stage 2 (1.2±0.2).
Conclusion
In a Phase 3 trial evaluating crinecerfont in children and adolescents with 21-OHD CAH on GC doses >12 mg/m^2/day HCe, there was clinical evidence of GC and androgen excess (e.g., overweight/obesity, advanced bone age, and early puberty). Androgen levels were elevated despite treatment with GC doses >12 mg/m^2/day HCe, highlighting the need for novel treatments for this condition.

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P226

Sphingosine kinase 1 inhibitor safingol as a new possible therapeutic strategy for adrenocortical carcinoma

Emma Nozza[1,2], Rosa Catalano[1], Emanuela Esposito[1,2], Serena Palmieri[3], Barbara Altieri[4], Laura-Sophie Landwehr[4], Hantel Constanze[5,6], Sandra Sigala[7], Emanuele Ferrante[3], Giovanna Mantovani[1,3] & Erika Peverelli[1,3]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]University of Milan, Phd Program in Experimental Medicine, Milan, Italy; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [4]University of Würzburg, Division of Endocrinology and Diabetes, Department of Internal Medicine I, University Hospital, Würzburg, Germany; [5]University Hospital Zurich (USZ) and University of Zurich (UZH), Department of Endocrinology, Diabetology and Clinical Nutrition, Zurich, Switzerland; [6]University Hospital Carl Gustav Carus Dresden, Medizinische Klinik und Poliklinik III, Dresden, Germany; [7]University of Brescia, Section of Pharmacology, Department of Molecular and Translational Medicine, Brescia, Italy

Sphingosine kinase 1 (SphK1) is the enzyme deputed to the phosphorylation of sphingosine in sphingosine-1-phosphate (S1P). S1P promotes ERK phosphorylation with increasing cellular proliferation, AKT phosphorylation, that induces apoptosis resistance and cell migration. It has been recently demonstrated that SphK1 is overexpressed in adrenocortical carcinoma (ACC) in comparison to adenomas (ACA) and that a high expression is related to worse outcome. Different SphK1 inhibitors have been developed to prevent S1P production and induce sphingosine accumulation resulting in cell apoptosis. Among these inhibitors, safingol was used in two phase I clinical trials on solid cancers, also including a small number of ACC patients, where it was clinically active in combination with other chemotherapies. Despite these interesting premises, safingol has never been tested on ACC *in vitro*models. Aim of this study was 1) to assess the expression of SphK1 in ACC, ACA, and normal adrenal tissues (NA) and in 4 human ACC cell lines; 2) to test the effect of safingol on

cellular viability, proliferation, and apoptosis in different ACC cell models. Western Blot analysis revealed that NA tissues ($n=8$) displayed the lowest SphK1 level ($P<0.001$ vs ACC or ACA), while SphK1 expression in ACC ($n=8$) was 2-fold higher than in ACA ($n=8$) ($P<0.05$). Among ACC cell lines, SK showed similarly greater levels in JIL-2266 and MUC-1 compared to H295R and TVBF-7. After 72 h of safingol treatment, all the cell lines displayed a significant reduction of cell viability [H295R safingol 5 μM -52.30 (32.51)%; JIL-2266 safingol 4 μM -51.96 (58.91)%; MUC-1 safingol 3 μM -30.38 (20.90)%; TVBF-7 safingol 8 μM -51.52 (57.50)%]. Cellular proliferation was assessed at the first dosage showing viability reduction, and it was decreased as well ($P<0.05$) in all cell lines [H295R safingol 5 μM -55.73 (57.52)%; JIL-2266 safingol 4 μM -64.53 (16.55)%; MUC-1 safingol 3 μM -51.53 (24.99)%; TVBF-7 safingol 8 μM -57.36 (35.52)%]. Pro-apoptotic effect of safingol was evaluated via caspases 3 and 7 activity quantification and found significantly increased ($P<0.05$) after 24 h of treatment [H295R safingol 7.5 μM + 146.73 (197.5)%; JIL-2266 safingol 4 μM + 141.6 (68.8)%; MUC-1 safingol 5 μM + 38.20 (61.6)%; TVBF-7 safingol 8 μM + 250.14 (258.6)%].
In conclusion, our data demonstrated an overexpression of SphK1 in ACC vs ACA and NA, suggesting that it may represent a novel diagnostic biomarker for ACC. Moreover, our results support the use of SphK1 inhibitor safingol as a novel possible therapeutic strategy for ACC.

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P227

CXCR4-directed [68Ga]Ga-PentixaFor PET/CT as a diagnostic modality in subtyping primary aldosteronism

AmirHosseinChaman Baz[1], Martin Gotthardt[2], Wilko Spiering[3], Jaap Deinum[4] & Johannes Langenhuijsen[1]
[1]Radboud University Medical Center, Urology, Nijmegen, Netherlands; [2]Radboud University Medical Center, Nuclear medicine, Nijmegen, Netherlands; [3]UMC Utrecht, Vascular medicine, Utrecht, Netherlands; [4]Radboud University Medical Center, Vascular medicine, Nijmegen, Netherlands

Introduction
Primary aldosteronism (PA) is a form of secondary hypertension, affecting 2.4% of the hypertensive population. It is caused by autonomous overproduction of aldosterone by either a unilateral aldosterone-producing adenoma (APA) or by bilateral adrenal hyperplasia (BAH). Subtyping is crucial, because PA is cured by adrenalectomy in APA and is treated by medication in BAH. The reference standard in subtyping PA is adrenal vein sampling (AVS). However, it is invasive, costly, has limited availability and is accompanied by risk of serious complications. We propose employing the positron emission tomography-computed tomography (PET-CT) tracer [68Ga]Ga-PentixaFor, which has high accuracy in detecting APAs in PA. The goal of this study is to determine concordance of [68Ga]Ga-PentixaFor PET-CT and AVS. Secondary outcomes are timepoint for scanning, criteria for lateralization and biochemical and clinical success after adrenalectomy.
Methods
This study is part of a two-step diagnostic trial. We included patients with PA from two academic centers, confirmed by an intravenous salt-loading test. Patients underwent AVS and [68Ga]Ga-PentixaFor PET-CT. Patients were treated based on the AVS results. A dynamic scan was performed to determine the optimal timepoint for scanning in the first 6 patients. The main outcome was the concordance of AVS and [68Ga]Ga-PentixaFor PET-CT. The SUVmax was used to determine lateralization in [68Ga]Ga-PentixaFor PET-CT. The PASO criteria for clinical outcomes were used to assess the surgical outcomes at 3 and 6 months post-surgery.
Results
Twenty-five patients underwent adrenal vein sampling and a [68Ga]Ga-PentixaFor PET-CT. The optimal timepoint of scanning was 1h post-injection. Using a cut-off of SUV-max-ratio of 1.4 we reached a concordance of 68%, sensitivity of 60% and specificity of 80%. Using a Bayesian prediction model, the predicted-concordance was: 67% (CI80% = 54–78). At 3 months post-surgery, complete biochemical success was observed in 100% (10/10) of patients and in 83% (5/6) at the 6-month mark. Clinical success rates were noted to be 70% (7/10) at 3 months and 67% (4/6) at 6 months.
Conclusion
[68Ga]Ga-PentixaFor PET-CT is an imaging modality with high concordance with AVS. With these results we have sufficient evidence to proceed to step-2: A randomized controlled diagnostic trial, where patients will be randomized in [68Ga]Ga-PentixaFor PET-CT or AVS.

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Impact of glucocorticoid-induced adrenal insufficiency on health-related quality of life in patients receiving long-term low dose prednisolone treatment: Results from the double edge-rescue trial

MarieLouise Lund[1], Hajir Al-Jorani[2,3], Jelena Stankovic[4,5], LiseSofie Bislev[4], JakobBue Bjørner[6,7,8], VictorBrun Boesen[1], LouiseLehmann Christensen[2,3], Ulla Feldt-Rasmussen[1], AnjaFenger Dreyer[2,3], Dorte Glintborg[2,3], Annette Hansen[9], SimonBøggild Hansen[4,5], RichardChristian Jensen[2], NannaThurmann Jørgensen[1,10], Marianne Klose[1], Henning Locht[11], Randi Tei[4], Torquil Watt[1], PaulM Stewart[12], HenrikToft Sørensen[13], JensOtto Jørgensen[4,5], Marianne Andersen[2,3] & StinaWillemoes Borresen[1]
[1]Rigshospitalet, (1) Department of Endocrinology and Metabolism, København, Denmark; [2]Odense University Hospital, (2) Department of Endocrinology, Odense, Denmark; [3]University of Southern Denmark, (3) Research Unit OPEN, Department of Clinical Research, Odense, Denmark; [4]Aarhus University Hospital, (4) Department of Endocrinology and Internal Medicine, Aarhus, Denmark; [5]Aarhus University, (5) Department of Clinical Medicine, Aarhus, Denmark; [6]University of Copenhagen, (6) Department of Public Health, København, Denmark; [7]QualityMetric incorporated, LLC, Johnston, USA; [8]National Research Centre for the Working Environment, Copenhagen, Denmark; [9]Copenhagen University Hospital Herlev and Gentofte, Gentofte, (7) Center for Rheumatology and Spine Diseases, Gentofte, Denmark; [10](8) Department of Clinical Medicine, Faculty of Health and Clinical Sciences, Copenhagen, Denmark; [11]Copenhagen University Hospital Bispebjerg and Frederiksberg, Frederiksberg, (9) Center for Rheumatology and Spine Diseases, Copenhagen, Denmark; [12]University of Leeds, University of Leeds, Leeds, UK; [13]Aarhus University Hospital, (11) Department of Clinical Epidemiology, Aarhus, Denmark

Objectives
The clinical impact of glucocorticoid-induced adrenal insufficiency in patients on low-dose prednisolone is unclear. We investigated the influence of adrenal function on health-related quality of life (HRQoL) in patients tapering prednisolone.
Method
Baseline data from an ongoing prospective randomised clinical trial including 278 patients with polymyalgia rheumatica/giant cell arteritis treated with prednisolone for ≥12 weeks, current dose ≤5 mg. Adrenal function, evaluated with a 250 μg ACTH-test, remained blinded until after HRQoL assessments. Fatigue was assessed under unstressed conditions five times daily for three days using a smartphone-based momentary item version of the Multidimensional Fatigue Inventory's General Fatigue scale. Answers were provided on visual analogue 100-point scales and analysed with linear mixed models for repeated measures. Generic and disease-specific HRQoL was evaluated with SF36v2 and AddiQoL-30. Subgroup analyses of patients receiving i) 5mg and ii) <5 mg prednisolone/-day were performed.
Results
Of 278 patients 55 (20%) treated with prednisolone for median 18 months (3-271 months), median current dose 5 mg (0.36–5 mg) had adrenal insufficiency. Fatigue measurements were available for 120 patients [response rate 65% (1171/1800 questions)]. Overall, no difference in fatigue was found between patients with normal vs insufficient adrenal function [adrenal insufficient 4.6 points less fatigue, S.E.:5.1, $P=0.36$]. Patients experienced insignificantly more fatigue the higher stimulated P-cortisol [3.6 points/100 nmol/l, S.E.:1.7, $P=0.05$]. No effect of adrenal function on diurnal variation of fatigue was found [$P=0.81$]. Subgroup analyses of patients treated with 5 mg and <5 mg prednisolone/day showed similar results. Among 205 responses, total AddiQoL-30-scores did not differ in patients with insufficient vs normal adrenal function [mean(S.D.) 88.7(12.5) vs 87.9(10.9), $P=0.66$]. Similar results were found for all AddiQoL-30-subscales. For patients treated with 5 mg/day prednisolone ($n=121$), AddiQoL-30 Symptoms was correlated to stimulated P-cortisol (more symptoms with higher cortisol) [−0.58points/100 nmol/l, 95%CI: −1.1 to −0.05, $P=0.031$]. Among 202 responses, no significant difference in SF36v2 scores appeared between patients with normal vs insufficient adrenal function, except the subscale Role Emotion, which correlated with stimulated P-cortisol (worse the higher stimulated P-cortisol) [Spearman correlation coefficient −0.16, $P=0.020$]. Glucocorticoid-subgroup analyses showed similar results.
Conclusions
In patients tapering prednisolone to ≤5 mg/day, we did not find lower HRQoL in patients with adrenal insufficiency. In contrast, SF36v2 Role Emotion and AddiQoL-30 Symptoms scores were significantly worse with higher stimulated P-cortisol, but with small effect sizes and thus unlikely clinically relevant. Patients might experience symptoms during stress. The prospective part of our study will monitor symptoms of adrenal insufficiency during stress.
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Benefits and harms according to intensity of statin therapy in Korean patients with dyslipidemia

SunOk Song[1] & Sunghwan Suh[2]
[1]National Health Insurance Service Ilsan Hospital, Division of Endocrinology and Metabolism, Goyang, Republic of South Korea; [2]Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, Division of Endocrinology and Metabolism, Changwon, Republic of South Korea

Background
This study aimed to investigate the association between the intensity of statin therapy and the development of cardiovascular disease (CVD) and diabetes in individuals without prior diabetes who were being treated for dyslipidemia with statins for the primary prevention of CVD, using the National Health Insurance Service-Health Screening (NHISHEALS) database.
Methods
The database is a longitudinal cohort study of Korean men and women 40 years of age or older who underwent comprehensive biannual screening health examinations by NHIS from January 1, 2002, to December 31, 2015. We included patients in the health screening checkup cohort who underwent health checkups in 2009 and 2010.The primary outcome was the occurrence of a first major cardiovascular or cerebrovascular event, new-onset diabetes.
Results
A total of 20 322 participants without prior diabetes at baseline from 2009 to 2015 were followed up for a mean duration of 81.2 ± 6.6 months. The mean age of all participants at baseline was 59.2 ± 8.4 years and 43.0% of them were male. Their index LDL-C level was 130.4 ± 36.2 mg/dl, the mean duration of taking statins was 337.4 ± 52.3 days, and 93.9% of them had been taking moderate-intensity statins. During follow-up, a total of 641 diabetes cases occurred, 41 from using low-intensity statins, 588 from moderate-intensity statins, and 11 from high-intensity statins. The results indicated no significant differences in the incidence of death, CVD death, or CVD among those in the strong statin group compared with the reference groups.
Conclusion
There was no difference in the occurrence of CVD or CVD death according to statin intensity for the primary prevention of CVD in Korean patients with dyslipidemia. In addition. there was a subtle difference in the incidence of diabetes.

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Description of recreational male and female athletes illicitly using androgenic anabolic steroids

LaustF Buhl[1], LouiseL Christensen[1], Rikke Hjortebjerg[2], Selma Hasific[3], Clara Hjerrild[1], Stefan Harders[4], JonJ Rasmussen[5], Dorte Glintborg[1], MarianneS Andersen[1], Caroline Kistorp[5], JesS Lindholt[3], Axel Diederichsen[6] & Jan Frystyk[1]
[1]Odense University Hospital, Endocrinology, Odense; [2]University of Southern Denmark, KMEB, Odense, Denmark; [3]Odense University Hospital, Vascular Surgery, Odense; [4]Aarhus University Hospital, Radiology, Aarhus, Denmark; [5]Rigshospitalet, Endocrinology, København, Denmark; [6]Odense University Hospital, Cardiology, Odense

Background
The illicit use of androgenic anabolic steroids (AAS) has increased significantly and is nowadays used by many recreational athletes. This raises concerns about the AAS-associated health risks, particularly cardiovascular complications. Therefore, we studied cardiovascular health in the broad population of Danish AAS-using recreational male and female athletes.
Methods
We conducted a cross-sectional study of 107 AAS users (27 women) and 58 healthy, age-matched controls (16 women) ≥18 years of age. Athletes were categorized as active AAS users or previous AAS users. Primary outcome was ultrasound-detected plaques of the carotid and femoral arteries. Secondary outcomes were computed tomography angiography (CCTA)-determined non-calcified and calcified plaques and cardiac function measured by echocardiography.
Results
The prevalence of ultrasound-determined plaques in the femoral artery in controls vs previous vs active AAS users were 0.0%, 6.3%, 16.0%, $P=0.005$, respectively, and in the carotid artery 1.8%, 18.8%, 12.0%, $P=0.025$, respectively. In subgroup analyses, long-term AAS use (>5 years) was significantly linked to non-calcified plaques ($P=0.002$) and coronary artery calcium scores ($P=0.013$). Additionally, both active and previous AAS users had higher prevalence of cardiac hypertrophy (controls vs previous vs active: 3.5%, 21.3%, 32.0%, $P<0.001$). Furthermore, a consistent pattern of decline in biventricular systolic function was observed across groups (controls vs previous vs active), with active AAS users displaying the lowest left ventricular ejection fraction (LVEF) (58.7%, 56.8%, 53.8%; $P<0.001$), LV global longitudinal strain (LV-GLS) (−19.8, −18.8, −17.6; $P<0.001$) and RV-GLS (−22.8, −20.9, −20.2; $P<0.001$). Women showed quantitatively similar changes as men, although not all findings achieved significance, probably due to a lower number of participants.
Conclusion
Long-term AAS use was linked to the development of peripheral and coronary atherosclerosis, cardiac hypertrophy, and reduced systolic and diastolic function. Parallel trends in results were evident in both men and women, underscoring that women share the same risk of developing cardiovascular disease as men.

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3D printed, personalized cortisol for cortisol deficiencies

Sejad Ayyoubi[1], Richard Feelders[2] & Liesbeth Ruijgrok[1]
[1]Erasmus MC, hospital pharmacy, Rotterdam, Netherlands; [2]Erasmus MC, Endocrinology, Rotterdam, Netherlands

Introduction
The current standard of care (SOC) for adrenal insufficiency (AI) is suboptimal due to fluctuating cortisol plasma concentrations. The sub- and supraphysiological cortisol levels, combined with the multi day tablet intake, are associated with negative health outcomes and a poor quality of life. Furthermore, there is a high interindividual difference in the cortisol need, demanding a personalized approach. 3D printing (3DP) has gained momentum within the pharmaceutical field, moving from conceptual products, to clinical trials. This technology makes it possible to adapt the drug dose, release profile, shape and taste, based on the individual patients' need. The aim was therefore to develop a 3D printed, personalized, sustained release (SR) hydrocortisone for patients with AI. Secondary aims were (1) to compare the quality of 3D medication to magistral capsules, which is the current standard of personalizing cortisol dose, and (2) to evaluate the manufacturing costs of 3DP.
Methods
10 mg hydrocortisone tablets were printed using semi-solid extrusion (SSE) and fused deposition modeling (FDM) 3DP. 5 mg Plenadren®, slow-release tablets, and manually filled 10 mg hydrocortisone capsules were purchased and analyzed, as comparators. Hydrocortisone content ($n=3$–10), weights of final products and drug release profiles ($n=3$–6) were determined for each formulation. A micro-costing study was performed to evaluate the manufacturing costs of FDM 3D hydrocortisone in an academic hospital pharmacy setting.
Results
The 3D tablets had a stable release profile, similar to the Plenadren, where >80% of hydrocortisone was released in 24 h. Drug content of 3D printed tablets were closer to 10 mg compared to the purchased capsules. 3D printed tablets contained 103 ± 5% and 98 ± 1% hydrocortisone respectively for SSE and FDM, while capsules contained 92 ± 1% – 94.5 ± 0.5%. Manufacturing costs of 3D hydrocortisone was €1.90–€3.20 per tablet, compared to a purchasing price of €9.00 per capsule.
Conclusion
A 3D printed SR, personalized hydrocortisone formulation was developed for patients with AI. The quality of 3D tablets is higher than the capsules, while the manufacturing costs seem lower compared to the purchase price of capsules. Therefore, 3DP should replace manually filling of capsules in AI. The 3D therapy is once-daily, compared to three times a day of the SOC, reducing pill-burden. Any desired dose can be printed, unlike the Plenadren®. The 3D printed formulation will be tested in a clinical setting. A personalized delayed release 3D product is under development for the morning cortisol need in AI.

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Prevalence and treatment of osteoporosis and bone fractures in Cushing's syndrome across Europe

Aleksandra Zdrojowy-Welna[1], Claudia Amaral[2], Marta Araujo-Castro[3], Nienke Biermasz[4], Marek Bolanowski[1], Jens Bollerslev[5], Thierry Brue[6], Davide Carvalho[7], Frederic Castinetti[8], Filippo Ceccato[9], Olivier Chabre[10], Daniela Dadej[11], Mario Detomas[12], Timo Deutschbein[13], Emanuele Ferrante[14], Atanaska Elenkova[15], Ezio Ghigo[16], Roberta Giordano[16], Aleksandra Gilis-Januszewska[17], Miklos Goth[18], Cecile Greaud[19], Yona Greenman[20], Daniela Guelho[21], Irina Ilovayskaya[22], Sonia Kaniuka-Jakubowska[23], Darko Kastelan[24], Irina Komerdus[22], Michal Krsek[25], Dominique Maiter[26], Olga Moros[27], KatarinaMlekuš Kozamernik[28], Eleni Papakokkinou[29], Oskar Ragnarsson[29],

Giuseppe Reimondo[16], Martin Reincke[30], Alicia Santos[31], Helga Sigurjonsdottir[32], Christian Strasburger[33], Miklos Toth[34], Antoine Tabarin[35], Greisa Vila[36], Susan Webb[31], Birutę Žilaitienę[37] & Elena Valassi[38,39]
[1]Wroclaw Medical University, Department of Endocrinology, Diabetes and Isotope Therapy, Wroclaw, Poland; [2]Centro Hospitalar Universitário de Santo António, Porto, Portugal; [3]Ramón y Cajal University Hospital, Madrid, Spain; [4]Leiden University Medical Center, Leiden, Netherlands; [5]Rikshospitalet Radium Hospitalet, Oslo, Norway; [6]Association pour le Devéloppement des Recherches Biologiques et Médicales, Marseille, France; [7]University of Porto, Porto, Poland: [8]Aix Marseille Université, Marseille, France; [9]University-Hospital of Padova, Padova, Italy; [10]Centre Hospitalier Universitaire de Grenoble, La Tronche, France; [11]Chair, Department of Endocrinology, Faculty of Medicine, Metabolism and Internal Diseases, Poznan University of Medical Sciences, Poznan, Poland; [12]University Hospital of Würzburg, Würzburg, Germany; [13]PI Medicover Oldenburg MVZ, Oldenburg, Germany; [14]Endocrinology Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [15]Medical University of Sofia, Sofia, Bulgaria; [16]University of Turin, Turin, Italy; [17]Department of Endocrinology, Jagiellonian University, Medical College, Kraków, Poland; [18]Division of Endocrinology, 2nd Department of Medicine, State Health Center, Budapest, Hungary; [19]Bicêtre Hospital, Le Kremlin-Bicêtre, France; [20]Tel Aviv University, Tel Aviv, Israel; [21]Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal; [22]Moscow Regional Research Clinical Institute n.a.Vladimirsky, Moscow, Russia; [23]Medical University of Gdańsk, Gdańsk, Poland; [24]University Hospital Zagreb, Zagreb, Croatia; [25]Charles University, Prague, Czechia; [26]University Hospital Saint Luc, Woluwe-Saint-Lambert, Belgium; [27]Zentrum für Endokrinologie, Diabetologie, Rheumatologie Dr. Demtröder & Kollegen im MVZ Dr. Eberhard &Partner und Klinikum Dortmund, Dortmund, Germany; [28]Klinicni Center Ljubljana, [29]Goteborg University, Gothenburg, Sweden; [30]Medizinische Klinik und Poliklinik IV; Campus Innenstadt; Klinikum der Universität München, Munich, Germany; [31]Institut de Recerca de la Santa Creu i Sant Pau, Barcelona, Spain; [32]Landspitali University Hospital, Reykjavik, Iceland; [33]Charité Universitatsmedizin Berlin, Berlin, Germany; [34]Semmelweis University, Budapest, Hungary; [35]Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France; [36]Medizinische Universitat Wien, Vienna, Austria; [37]Lithuanian University of Health Sciences, Kaunas, Lithuania; [38]School of Medicine, Universitat Internacional de Catalunya (UIC), Barcelona, Spain; [39]Germans Trias i Pujol Hospital and Research Institute, Badalona, Spain

Introduction
Real-world data on management of bone alterations in Cushing's syndrome (CS) are scanty. The aim of our study was to assess the prevalence of osteoporosis (OP) and bone fractures (BF) in CS patients included in the European Registry on Cushing's Syndrome (ERCUSYN), and to describe the diagnostic and therapeutic strategies adopted across Europe to address these comorbidities.
Patients and methods
In this retrospective, observational cohort study, we evaluated the prevalence of OP and BF in 1684 patients (81% females; mean age 44 (±14.1) years) of whom 1234 (73%) had a pituitary-dependent (PIT-CS) and 450 (27%) an adrenal-dependent (ADR-CS) CS from 60 European centers in 26 countries. In addition, we created a survey to collect real-life data on bone disease management in CS.
Results
A dual-energy X-ray absorptiometry (DXA) was performed in 766 (51%) patients at diagnosis. Lumbar and hip OP were found in 21% and 13% of patients, respectively. After treatment, lumbar and hip OP were found in 18% and 11% of patients respectively, after a median follow-up of 24 (36) months, with a similar prevalence between patients in remission (78%) and those with persistent disease (22%). Fractures were present in 17% of patients at diagnosis, most in the spine (30%). Patients with BF at the time of diagnosis were older than patients without [mean (± s.d.) age 48.3±13.1 vs 43.4±14.2 years; $P<0.001$] and were more often males ($P<0.001$). Median delay to diagnosis was longer in patients with BF as compared with those without [3 (3.5) vs 2 (2) years, $P=0.02$] at diagnosis. Most of the survey responders (87%) evaluate bone health using DXA in all newly diagnosed patients, whereas the remaining only assess it in high-risk patients. Forty-six percent of responders perform X-ray only in patients with fracture symptoms. Seventy-six percent of the centers start specific treatment in all patients with OP at diagnosis, 21% only treat patients with fractures. After successful treatment, 59% of the responders re-check bone status within two years,whereas the remaining individualize control based on fracture risk stratification. The most widely used medications to treat OP and/or BF are vitamin D with calcium (74%), zolendronate (72%), alendronate (59%), denosumab (49%), risendronate (25%) and teriparatide (25%).
Conclusions
There is a need to optimize the management of bone impairment across Europe. In the ERCUSYN cohort, older age, male sex and longer delay to diagnosis were associated with increased rate of fractures at the time of diagnosis.

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Decoding adrenal marginal zone lymphoma's silent narrative

ShabbarAbbas Naqvi & SingYang Sim
Royal Sussex County Hospital, Endocrinology and Diabetes, Brighton, UK

An 80-year-old patient was referred due to an incidental finding of a right adrenal mass during investigation of Iron Deficiency Anaemia (Ferritin 11.7 µg/l). CT scan of abdomen and pelvis revealed a 10×5 cm ill-defined heterogeneous mass within the right supra-renal space with areas of enhancement in the arterial phase imaging without calcification. Clinically, the patient lacked signs of endocrinopathy, such as (catecholamine or corticosteroid excess). However, the history was positive for drenching night sweats, fatigue and abdominal discomfort for several months. The initial investigations were unremarkable. Plasma metanephrine 10 ng/l (<100). Normetanephrines 57 ng/l (<170), Overnight dexamethasone suppression 0900 h Cortisol-19 nmol/l (0–50), Urine steroid profile showed normal total cortisol metabolite output, ACTH 19 ng/l (<50), Renin 21 mU/l (5-60), Aldosterone 283 pmol/l (100-800), Renin aldosterone ratio <80, Androstenedione <0.5 nmol/l (2-5.4), Total testosterone 0.1 nmol/L (0.1-1.42), SHBG 91 nmol/l (17.3-125), DHEA <0.1 µmol/l (0.9-2.1), 17b Oestradiol 48 pmol/l (114-332),17 hydroxyprogesterone <1, FSH 55.3 iu/l (3.5-12.5) and LH 31 iu/l (2.4-12.6). A dedicated CT adrenal revealed a large right adrenal mass 10.4 cm×5 cm with pre-contrast density of 40 HU, Portal venous phase density approximately 80–100 HU and delayed post-contrast density approximately 60 HU. The case was discussed in the Adrenal MDT and differentials included lymphoma, Sarcoma or inflammatory condition. Patient underwent a CT guided biopsy which showed diffuse staining of monoclonal lymphoplasmacytic infiltrate. Immunohistochemistry revealed positive CD20 B-Cell markers in addition to other B cell marker (BCL2 and IgM) with low proliferation index and no staining for CD10, CD5 and BCL6. These features indicated extra-nodal marginal zone lymphoma. Staging PET CT displayed moderate to intense uptake (SUVmax 8) in the right adrenal mass with no active lymphoproliferative disease elsewhere. Patient was referred to haematology MDT and subsequently started on Rituximab monotherapy for adrenal marginal zone lymphoma. At the point of writing, patient remained under oncology follow up. Primary adrenal lymphoma (PAL) is rare (<1%) of all extranodal lymphomas. While diffuse large B cell lymphoma is more prevalent and associated with a poor prognosis, marginal zone lymphoma, a low grade B cell neoplasm can rarely occur presenting as a relatively indolent condition. The diagnosis is usually challenging and pathological examination is the only approach to establish the diagnosis. The role of surgery for the management remains controversial. Immunochemotherapy typically employing Rituximab, is the standard treatment for symptomatic patients with extra nodal Marginal Zone Lymphoma of various origins.

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Fine needle aspiration cytology of adrenal lesions: A 22-year single center experience

AnaMariaCristina Carasel[1,2], CChristofer Juhlin[3,4], Jan Calissendorff[1,2] & Henrik Falhammar[1,2]
[1]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [2]Karolinska University Hospital, Department of Endocrinology, Stockholm, Sweden; [3]Karolinska Institutet, Department of Oncology-Pathology, Stockholm, Sweden; [4]Nya Karolinska, Department of Pathology and Cancer Diagnostics, Stockholm, Sweden

Background
The nature of adrenal tumors can occasionally be difficult to determine using only laboratory and radiological findings. In those rare cases, obtaining a cytological sample by fine needle aspiration (FNA) can be valuable. Transabdominal ultrasound, endoscopic ultrasound (EUS), and computerized tomography (CT) guided biopsy are the most used methods for obtaining a cytological sample from an adrenal lesion.
Methods
Adrenal FNAs performed between the years 2000–2022 at the Karolinska University Hospital were identified using a search function incorporated in our institutional pathology database. Clinical and histological data were retrieved from medical records.
Results
Of 241 adrenal FNAs identified, 113 (46.9%) were obtained by transabdominal ultrasound, 72 (29.9%) were obtained by EUS, 53 (22%) using CT-guided technique, one FNA was obtained during surgery (0.4%) and in two cases (0.8%) the modality was not mentioned in the available medical charts. Preceding imaging indicated suspected malignant lesions in 184 cases (76.3%). Malignancy was confirmed by cytology in 139 cases (57.6%). A new FNA was performed to obtain the correct diagnosis in 10 cases (4.1%). Adequate material for diagnosis

was retrieved in 98 cases (86.7%) by transabdominal ultrasound, 69 cases (95.8%) by EUS and in 47 cases (88.7%) by CT-guided biopsies. An endocrinological assessment of adrenal function was performed before cytology in 122 cases (50.6%). Using FNA, adrenal lesions were diagnosed as adrenal metastases in 127 cases (52.7%) and adrenocortical cells (indicative of an adrenal cortical lesion) were found in 92 cases (38.1%). Of the latter ones, 4 (1.7%) received a diagnosis of adrenal cortical carcinoma. The remaining FNAs showed lymphoma in 7 cases (2.9%), tuberculosis and acute myeloid leukemia in one case each (0.4%). The diagnosis was unclear in 13 cases (5.4%). Most metastases were from lung carcinoma (71 cases, 55.9%) followed by malignant melanoma (10 cases, 7.9%), renal cell carcinoma (9 cases, 7.1%), gynecological cancers (7 cases, 5.5%), and other malignancies (30 cases, 23.6%) (e.g., breast, prostate, hepatocellular, and gastrointestinal carcinoma). Complications due to the biopsy procedure, such as bleeding and pneumothorax, were reported in 19 cases (7.5%).
Conclusions
Complication rates for FNA were low and an adequate sample was obtained in most cases regardless of imaging method used. FNA of the adrenal glands is a useful tool for diagnosis of adrenal tumors, especially when a metastasis is suspected.

Keywords: fine needle aspiration, adrenal glands.
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SIAH1, a regulator of the Wnt/β-catenin pathway in human adrenocortical cells

Pierre Puygrenier[1], Karine Perlemoine[1], Bruno Ragazzon[1], Anne Jouinot[1], Constantine Stratakis[2,3], Jérôme Bertherat[1] & Annabel Berthon[1]
[1]Institut Cochin, Paris, France; [2]Research Institute, ELPEN, Pikermi, Athens, Greece; [3]Human Genetics & Precision Medicine, Heraklion, Greece

The most frequent molecular alteration in adrenocortical tumors (ACT) is the activation of the Wnt/β-catenin pathway that is associated with poor prognosis in adrenocortical carcinoma. Activating β-catenin mutation (p.S31, p.S37, p.S45, T.41) inhibiting its proteosomal degradation by the canonical destruction complex is responsible for its abnormal activation in roughly 30% of ACT. However, the E3 ubiquitin protein ligase 1, SIAH1 is able to ubiquitinate β-catenin even while mutated in intestinal cells, we then, investigate if SIAH1 regulates both wild-type and mutant β-catenin in H295R human adrenocortical cells. We demonstrate that SIAH1 interacts with β-catenin and increases both wild-type and mutant β-catenin ubiquitination through its catalytic RING finger domain. Overexpression of SIAH1 results then, in a decrease in β-catenin half-life (−25%) that is sufficient to reduce β-catenin transcriptional activity (−50%) measured with the TOPFlash reporter even in presence of β-catenin mutation (p.S45) in H295R cells. However, the overexpression of SIAH1 deleted from its catalytic domain does not affect neither β-catenin activity nor its ubiquitination suggesting that the effect of SIAH1 on β-catenin activity depends on its E3 ubiquitin activity. Altogether, our results suggest that SIAH1 indirectly regulates β-catenin transcriptional activity and that promoting SIAH1 activity could limit the activation of this pro-oncogenic pathway while Wnt/β-catenin signaling is constitutively activated.

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Impact of environmental pollution on adrenocortical carcinoma in Italy

Soraya Puglisi[1], Anna Calabrese[1], Francesco Ferraù[2], Ylenia Alessi[2], Marta Laganà[3], Salvatore Grisanti[3], Filippo Ceccato[4], Carla Scaroni[4], Guido Di Dalmazi[5,6], Antonio Stigliano[7], Barbara Altieri[8], Letizia Canu[9], Michaela Luconi[9], Paola Loli[10], Maria Cristina DeMartino[11], Emanuela Arvat[12], Serena Palmieri[13], Paola Perotti[1], Vittoria Basile[1], Paola Berchialla[14], Alfredo Berruti[3], Anna Pia[1], Giuseppe Reimondo[1], Salvatore Cannavò[2] & Massimo Terzolo[1]
[1]Internal Medicine, Department of Clinical and Biological Sciences, San Luigi Hospital, University of Turin, Orbassano, Italy; [2]Endocrine Unit of University Hospital of Messina, University of Messina, Messina, Italy; [3]Oncology Unit, University of Brescia, Brescia, Italy; [4]Endocrinology Unit, Department of Medicine DIMED, University-Hospital of Padua, Padua, Italy; [5]Division of Endocrinology and Diabetes Prevention and Care Unit, IRCCS, University Hospital of Bologna, Bologna, Italy; [6]Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum-University of Bologna, Bologna, Italy; [7]Endocrinology, Department of Clinical and Molecular Medicine, Sant'Andrea University Hospital, Sapienza University of Rome, Rome, Italy; [8]Division of Endocrinology and Metabolic Diseases, University-Hospital Gemelli, IRCCS, Catholic University of the Sacred Heart, Rome, Italy; [9]Endocrinology Unit, Department of Experimental and Clinical Biomedical Sciences, University of Florence, Florence, Italy; [10]Endocrinology, Clinica Polispecialistica San Carlo, Milan, Italy; [11]Endocrinology Unit, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy; [12]Oncological Endocrinology Unit, Department of Medical Sciences, University of Turin, Turin, Italy; [13]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [14]Statistical Unit, Department of Clinical and Biological Sciences, University of Turin, Orbassano, Italy

Background
Whether environmental pollution may influence adrenocortical carcinoma (ACC) development remains largely unknown. The aim of this study was to evaluate the impact of exposition to environmental pollutants on ACC presentation and prognosis in Italy.
Patients and methods
A retrospective analysis was done on 500 patients affected by ACC, who were diagnosed in 12 reference centers in Italy from 1990 to 2018 and followed-up for a median of 37.5 months (interquartile range, IQR, 11-83). Patients were stratified according to: i) residence in Sites of National Interest (SIN) which are areas with contaminated soil and water, classified as dangerous by the Italian Ministry of Environment and in need of remediation; ii) residence in areas with different degrees of urbanisation, considered as index of exposure to air pollution.
Results
At diagnosis, 50 (10%) patients were resident in SIN (Res-SIN) and 450 (90%) patients were not (Not-SIN). The two groups had similar characteristics in terms of age, ENSAT stage, tumor size, Weiss score and Ki67%. However, incidental diagnosis of ACC was more frequent in Not-SIN patients than in Res-SIN patients (40.0% vs 19.6%; $P=0.011$). Res-SIN patients showed shorter recurrence-free survival (RFS) than Not-SIN patients (21 months *vs* 41 months; $P=0.027$). In multivariate analysis, residence in SIN was an independent negative prognostic factor for RFS (HR 1.82, 95%CI 1.10–3.03; $P=0.021$). Overall survival (OS) showed a similar pattern although the difference between the 2 groups was not significantly different. At diagnosis, 205 (41%) patients were resident in 'cities' (>50% of population in urban centers, with density >1500 inhabitants/km^2 and population >50 000), 230 (46%) in 'towns' and 'suburbs' (>50% in urban clusters with density >300 inhabitants/km^2 and population >5000), and 65 (13%) in 'rural areas' (>50% of population not meeting the previous criteria). No statistically significant differences were observed among the three groups in terms of clinical presentation, RFS and OS.
Conclusions
The different clinical presentation and worse outcome of ACC in patients living in areas with contaminated soil and water suggest that environmental pollutants in these matrices may have a role in conditioning the behavior of this rare tumor. Conversely, air pollution does not seem to influence the ACC disease course.

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Fertility outcomes in women with classic and non-classic congenital adrenal hyperplasia on modified-release hydrocortisone (MR-HC)

Lea Tschaidse[1], HannaF Nowotny[1], Matthias Auer[1], Christian Lottspeich[1], Ann-Christin Welp[1], Martin Bidlingmaier[1], JamesM Hawley[2], Brian Keevil[2] & Nicole Reisch[1]
[1]Klinikum der Universität München, Medizinische Klinik und Poliklinik IV, München, Germany; [2]Manchester University Foundation NHS Trust, Manchester Academic Health Sciences Centre, Department of Clinical Biochemistry, Manchester, UK

Background
Women with classic and non-classic (NC) congenital adrenal hyperplasia (CAH) often struggle with fertility, due to androgen excess, elevated progesterone and 17-hydroxyprogesterone (17OHP) levels, causing anovulation, impaired endometrial development and menstrual irregularities. The typical approach to addressing infertility so far, often involves an increase in glucocorticoid (GC) doses, yet this strategy carries potential side effects. Limited observational data on modified-release hydrocortisone (MR-HC), which better replicates the natural diurnal cortisol rhythm, suggests improved fertility in both female and male patients with classic CAH. Therefore, the aim of this study was to investigate fertility in women with classic and non-classic CAH before and after switching to MR-HC.
Methods
A total of 28 adult female patients with CAH (18 classic; 10 NC), with a median (range) age of 32.0 (30.0) years, premenopausal, without hormonal contraception, participated in this prospective, observational, single-center study. The data

collection took place before (using conventional GC preparation) and after a switch to MR-HC. Clinical parameters, along with morning serum and daily saliva profiles were collected, measuring progesterone, 17OHP, androstenedione (A4), testosterone and 11-oxygenated androgens.
Results
Prior to study inclusion, 7/28 patients had an irregular cycle, 3/28 were amenorrhoeic, and 14/28 desired pregnancy. After switch to MR-HC, the patients received a significantly lower mean (SD) hydrocortisone equivalent dose (26.3 (12.0) vs 23.1 (8.3), $P = .038$). Median (range) morning serum concentrations between 0800 and 0010 h showed no significant differences for progesterone, 17OHP, A4, testosterone, and 11-oxygenated androgens. However, in early morning saliva, median (range) 17OHP levels were significantly lower (67.3 (693.2) vs 28.1 (572.8), $P = .006$) after switching to MR-HC. Menstrual regularisation occurred in 6/10 patients with menstrual disturbance, and 8/14 patients desiring pregnancy became pregnant under MR-HC.
Conclusion
Our preliminary data indicate a clinical improvement in fecundity and fertility in women with classic and non-classic CAH under MR-HC, with even a slight decrease in GC dose. Lower 17OHP concentrations in early morning saliva suggest improved hormonal control overnight, contributing to regulated ovulatory cycles and enhanced fertility.

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Musculoskeletal health and body composition in patients discontinuing long-term prednisolone treatment – prospective data from the replace Study

LiseSofie Bislev[1], MarieLouise Lund[2], AnjaFenger Dreyer[3], Hajir Al-Jorani[3], VictorBrun Boesen[2], Stina Willemoes Borresen[2], LouiseLehmann Christensen[3], Ulla Feldt-Rasmussen[2], Dorte Glintborg[3], SimonBøggild Hansen[1], RichardChristian Jensen[3], NannaThurmann Jørgensen[2], Jelena Stankovic[1], Randi Tei[1], MarianneSkovsager Andersen[3], Marianne Klose[2] & JensOttoLunde Jørgensen[1]
[1]Palle Juul-Jensens Boulevard, Aarhus, Denmark; [2]Blegdamsvej 9, København, Denmark; [3]J. B. Winsløws Vej 4, Odense, Denmark

Background
Pharmacological glucocorticoid (GC) treatment exerts adverse effects on musculoskeletal health and may induce glucocorticoid-induced adrenal insufficiency (GIA), but these features have so far not been characterized in a prospective and unbiased manner.
Aim
To characterize a population, who recently discontinued long-term (>12 weeks) prednisolone treatment with particular emphasis on the presence or absence of symptoms.
Methods
A prospective nationwide study (REPLACE) including baseline data from 116 patients with polymyalgia rheumatica/giant cell arteritis in GC-free remission for 2–12 weeks. The participants completed a disease-specific questionnaire (AddiQoL-30) where a score <85 was defined as presence of GIA symptoms. Musculoskeletal health and body composition were assessed by DXA scans, functional tests, and in a subgroup HRpQCT scans ($n = 34$).
Results
The participant median (range) age was 73 (51-88) years (56% women) with a median [IQR] prednisolone treatment duration of 12.5 [10.0 -17.8] months and an accumulated dose of 323 mg [217 – 481] six months before inclusion. $n = 42$ (36%) reported symptomatic GIA. Median (range) morning basal cortisol (nmol/l) was 258 (101 – 470) in the symptomatic GIA group vs 291 (135-497) in the group without symptomatic GIA, $P = 0.01$. Median [IQR] adult fractures were 1 [1; 2]. Four out of five received calcium/vitamin D, and 38% anti-osteoporotic medication (all bisphosphonates). Only 18% of patients did not meet criteria for (prophylactic) bisphosphonate treatment, defined by a T-score <1 in hip/lumbar spine and/or a diagnostic fracture. Sarcopenia, defined as appendicular lean mass index <7.26/5.45 kg/m^2 for men/women, was present in 18%. Stratifying for GIA symptoms, patients showed no differences in bone health, fractures, anti-osteoporotic treatment, comorbidity or HbA1c. Patients with GIA symptoms had lower ionized calcium (1.23 vs 1.25 nmol/l, p = 0.04), reduced grip strength (19.5 vs 28.5 kg, $P = 0.05$), and a longer Time Up and Go test duration (7.7 vs 6.7 s, $P = 0.03$). No differences in muscle/appendicular lean mass were observed, but patients with GIA symptoms had a higher fat percentage (41.2 vs 36.5%, $P = 0.02$) and larger waist circumference (99.1 vs 93.8 cm, $P = 0.03$). The results on muscle function and body composition remained significant after adjusting for age and gender.
Conclusions
1) The majority of long-term prednisolone users requires (prophylactic) osteoporosis treatment. 2) GIA symptoms are accompanied by impaired muscle function and increased abdominal fat. 3) We hypothesize that GIA symptoms are a component of the steroid withdrawal syndrome, which merits clinical attention.
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Peripheral cortisol concentration during adrenal vein sampling for primary aldosteronism

KarinZibar Tomšić[1], Ana Marija Alduk[2,3], Ivana Kraljevic[2,3], Tina Dusek[1] & Darko Kastelan[3]
[1]University Clinical Center Zagreb, Department of endocrinology, Zagreb, Croatia; [2]School of Medicine; [3]School of Medicine, Zagreb, Croatia

Background
Measurement of the peripheral cortisol concentration is necessary for calculating selectivity ratio (SR) based on which is AVS success evaluated.
Objective
The goal of this study was to assess the necessity for two peripheral cortisol measurements in sequential AVS, one after cannulation of the adrenal vein on one side, and the second after cannulation on the other side.
Methods
This retrospective study included 142 bilaterally successful AVS procedures in patients with primary aldosteronism. All procedures were performed by two experienced interventional radiologists. AVS was performed under continuous stimulation with adrenocorticotrophic hormone. Blood samples were taken sequentially, first from the right adrenal vein followed by the infrarenal segment of the IVC (time 1 = T1), then from the left adrenal vein followed by the infrarenal segment of the IVC (time 2 = T2). The AVS was considered technically successful if the SR (cortisol ratio of each adrenal vein to the IVC) was 5:1. The Wilcoxon paired test was used to assess differences.
Results
Median T1 and T2 cortisol concentrations were 743 (IQR 600-952) nmol/l and 760 (IQR 620-984) nmol/l, respectively ($P < 0.001$). Median T1 right SR was 30 (IQR 23-43), and T2 right SR was 29 (IQR 21-40), $P < 0.001$. Median T1 left SR was 15 (IQR 10-23), and T2 left SR was 14 (IQR 10-22), $P < 0.001$.
Conclusions
Although notable variations were observed in both absolute cortisol concentrations and SR at T1 and T2, these differences did not alter the overall conclusion regarding AVS accuracy in the patient group. Consequently, it might be considered that there is no imperative requirement for repetitive peripheral cortisol sampling during sequential AVS procedures under stimulation with adrenocorticotrophic hormone.

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Management of Giant Pheochromocytomas: A single tertiary center experience

Furnica Raluca[1], StefanMatei Constantinescu[1], Damien Gruson[2], Mourad Michel[3] & Dominique Maiter[1]
[1]Cliniques Universitaires Saint Luc, Endocrinology, Bruxelles, Belgium; [2]Cliniques Universitaires Saint Luc, Clinical Biochemistry, Bruxelles, Belgium; [3]Cliniques Universitaires Saint Luc, Abdominal surgery and transplantation department, Bruxelles, Belgium

Introduction
Giant pheochromocytomas (PCs) are adrenal tumors greater than 7 cm. The incidence and presentation of these large tumors is not well known, with only a few case reports published in literature. The preoperative and surgical management of giant PCs is also not well established.
Material and methods
A retrospective monocentric study at a tertiary center of 80 consecutive patients operated for a PC between 1988 and 2018.
Results
Among the 80 patients, 20 (25%) had a giant PC (mean tumor diameter of 9.9 cm). There was no difference in the clinical manifestations at diagnosis of these patients compared to patients with a smaller tumour. A significant proportion of patients with giant PC had hypertension (17/20) and half had diabetes. The diagnosis was made because of PC-related symptoms in half of the patients, mass symptoms in 5 patients (25%), during familial genetic screening in 2 (10%) and incidentally in only 1 case. Giant PCs presented higher levels of 24-hour urine metanephrines ($P = 0.028$) and normetanephrine ($P = 0.001$) compared with tumors of less than 7 cm. Interestingly, noradrenergic PCs were the largest tumors ($P < 0.01$). The rate of perioperative haemodynamic

($P=0.008$) and surgical complications ($P=0.032$) was influenced by tumor diameter. When comparing patients with preoperative alpha-blocker treatment, there was no difference in cumulative dose according to the tumor size. As expected, giant PCs were more likely to have an open surgery (17/20; 85% vs 14/60; 23%). Also, giant PCs presented a higher rate of recurrence ($P=0.039$) and malignant behaviour ($P<0.001$).
Conclusion
We show that giant PCs are usually symptomatic and their presentation is not different from average-sized PCs, but they have a higher rate of perioperative hemodynamic and surgical complications and exhibit a more aggressive phenotype, thus requiring multidisciplinary management in an expert center.

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Treatment outcomes in patients with recurrent adrenocortical carcinoma

Tamara Dojcinovic[1], KarinZibar Tomšić[2], IvanaDora Vodanović[2], Ivana Kraljevic[2,3], AnjaBarac Nekic[2], TanjaSkoric Polovina[2] & Darko Kastelan[2,3]
[1]University Clinical centre of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina; [2]University Hospital Center Zagreb, Zagreb, Croatia, Department of Endocrinology, Zagreb, Croatia; [3]School of Medicine, University of Zagreb, Zagreb, Croatia

Background
While a considerable body of literature exists detailing outcomes in patients with adrenocortical carcinoma (ACC), reports specifically addressing a cohort of patients with recurrent disease remain scarce. Therefore, the objective of this study was to evaluate treatment outcomes in patients with recurrent ACC.
Methods
In our cohort of 55 patients who underwent R0/Rx tumor resection between 2011 and 2022, 18 individuals (33%) exhibited recurrent disease and were consequently included in this study. Following disease recurrence, patients were treated with various modalities including surgery, mitotane, chemotherapy, locoregional therapy and radiotherapy. The main study outcomes were overall survival (OS) and progression free survival (PFS) following ACC recurrence.
Results
The median time from the initial surgery to ACC recurrence was 29 months (IQR 18–50), with three patients experiencing recurrence within 12 months post-surgery. Seven patients (39%) manifested local recurrence, while 11 patients (61%) developed distant metastases. Among those with distant metastases, seven exhibited lesions in a single organ, whereas four presented metastatic lesions in multiple organs. The median follow-up duration after tumor recurrence was 32 months (IQR 25–53). Regarding the treatment of ACC recurrence, 10 patients underwent a second surgery: surgery alone ($n=4$), surgery + mitotane ($n=4$), surgery + mitotane and chemotherapy ($n=1$) and surgery + radiotherapy and mitotane ($n=1$). Remaining patients were treated with chemotherapy ± mitotane ($n=4$) and locoregional therapy (microwave ablation (MWA), polyvynil alcohol (PVA) embolisation) ± chemotherapy ($n=3$). One patient chose not to proceed with further management and follow up. The median PFS was 17 (IQR 12-22) months while the median OS was not reached. Furthermore, the one, three and five-year OS rates were 94%, 68%, and 68%, respectively. In the multivariate model, increased mortality was associated with advanced age ($P=0.04$) and a shorter interval to ACC recurrence ($P=0.05$).
Conclusion
A significant proportion of patients with ACC recurrence experience disease progression or second recurrence, despite all treatment efforts. Nevertheless, by integrating diverse treatment modalities, many patients have the potential to attain long-term survival, underscoring the pivotal role of expert centers in their management.

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Congenital adrenal hyperplasia and myelolipomas: A case report

Ana Paola Leon Ocando, OliverQuintero Rodríguez, Selena Rodríguez Fernández, KevinDiaz Gorrin, ItziarAznar Ondoño & JudithLópez Fernández
Hospital Universitario de Canarias, Endocrinology and Nutrition, San Cristóbal de La Laguna, Spain

Introduction
Adrenal myelolipomas are benign and fatty tumors usually detected incidentally in imaging tests. Their prevalence increases in patients with CAH, probably because corticosteroid deficiency causes high ACTH levels that stimulate adrenal growth, although their effect on the growth of adrenal tumors is not yet well established.
Clinical case
A 41-year-old man with classic 21 OH deficiency, losing salt since he was 10 months old,with stable doses of corticosteroids for approximately 15 years, under follow-up in another center. He was referred to our hospital in June 2020 due to evidence of bilateral AI on spinal CT (requested for low back pain). In turn, he was referred to Urology who asked for an MRI that reported a heterogeneous solid mass of 11×9 cm in the left adrenal gland and a mass with similar characteristics measuring 7×4 cm in the right adrenal, the etiology of which was 'undetermined'. Functionality was ruled out and finally, it was decided to perform a left adrenalectomy by laparoscopic in September 2020, with a pathological diagnosis of myelolipoma. The clinical committee, given the stable growth of the contralateral mass and similar imaging characteristics, decided to follow up with clinical and imaging tests.
Discussion
According to the literature, in our case, these tumors were diagnosed in the 5th decade of life and were bilateral. Although CAH is associated with the development of adrenal myelolipomas, screening using images is currently not recommended in affected patients. On the other hand, the Spanish Society of Endocrinology and Nutrition recommends to determine levels of 17-OHP in cases of bilateral AI.
Conclusion
In the context of following up on CAH, it is advisable to conduct both analytical and clinical monitoring. However, it should be noted that the progressive growth of the adrenal glands and the development of myelolipomas are currently not established as criteria for assessing undertreatment, despite their potential correlation.

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Does 177Lu-DOTA-TATE works in metastatic cardiac paraganglioma?

Regina Medeiros[1], Ana Figueiredo[2], Tiago Silva[2] & Valeriano Leite[2]
[1]Hospital Divino Espírito Santo, P. Delgada, Serviço de Endocrinologia e Nutrição, Ponta Delgada, Portugal; [2]Instituto Português de Oncologia de Lisboa Francisco Gentil, Serviço de Endocrinologia, Lisboa, Portugal

Paraganglioma (PGL) are rare neuroendocrine tumors with an estimated prevalence of 1:6500, with cardiac PGL being even rarer. Although most PGL are benign, approximately 15–35% of PGLs have metastatic disease, with few effective treatment options. Novel therapeutic indications, such as 177Lu-DOTA-TATE for patients with PGL, has been investigated in several clinical trials. A 66-year-old woman was referred to Cardiology in 2011 due to an incidentaloma adjacent to the right atrium on a transthoracic echocardiogram, requested due to arterial hypertension. She underwent excision of the lesion, histology was compatible with paraganglioma, with no evidence of illness until 2021, when she began experiencing anterior chest pain, night sweats and fatigue. CT showed 2 suspicious nodules adjacent to the right superior vena cava (SVC) and a lesion causing extensive bone destruction of the right ischiopubic branch. All lesions show intense MIBG uptake. Analytically, increase (greater than 3× the upper limit) in norepinephrine, dopamine and normetanephrine in 24-hour urine and norepinephrine, dopamine and normetanephrine in plasma. A catecholamine-producing paraganglioma with bone metastasis was identified. Was referred to Endocrinology. Clinically with paroxysms of palpitations, sweating and high blood pressure and weight loss (6 kg in 1 month). She was subjected to alpha blocking. In 68Ga-DOTANOC PET, high-capture lesions: cervical in the carotid space on the right (SUV max 5.2), two mediastinal lesions adjacent to the right SVC (SUV max 89.5), bony in D3 (SUV max 133.7), L1 (SUV max 90.9), right ischiopubic branch (SUV max 118.8) and left pubic symphysis (SUV max 172.8). The genetic study revealed a pathogenic mutation in the SDHD gene. The patient was assumed to have no status for mediastinal surgery and underwent radiotherapy directed at the bone lesions (total dose of 30 Gy), with subsequent slow progression of all lesions, deciding to start therapy with 177Lu-DOTATATE. To date, she has undergone 4 PRRT therapies (total activity 800 mCi) with global clinical and imaging improvement, documented through both CT and PET. We report a rare silent paraganglioma adjacent to the right atrium. Having subsequently become productive and metastasized, leaving us with few treatment options. She responded well to PRRT, which went against the odds. The management of PGL is challenging due to the uncertain behavior during long-term follow-up, as demonstrated by our case.

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Cardiovascular risk in patients with primary hyperparathyroidism

Raluca Trifanescu[1,2], Maria Mohora[2], Iustin Toma[1,2], Ileana Nitu[2] & Catalina Poiana[1,2]

[1]'Carol Davila' University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania; [2]'C.I. Parhon' National Institute of Endocrinology, Bucharest, Romania

Background
PTH is a hormone with vascular and cardiovascular properties, involved in the expression of endothelial pro-atherosclerotic and pro-inflammatory parameters. Both hypercalcemic and normocalcemic primary hyperparathyroidism (PHPT) were associated with increased cardiovascular risk.
Patients and methods
84 patients (6M/78F) with PHPT, aged 58.9 ± 12.7 years, were retrospectively reviewed. Serum calcium levels, PTH and 25 OH vitamin D levels were measured. ECG was performed in all patients and echocardiography was performed in selected cases.
Results
Mean serum total calcium was 11.2 ± 1.2 mg/dl (range: 9.3–18.4); median PTH level was 158.4 pg/ml (range: 64.2–1982) and mean serum 25 OH vitamin D levels was 18.3 ± 9.1 ng/ml (range: 5.8–37.7). Mean body mass index was 27 ± 5.1 kg/m^2. Arterial hypertension was present in 48 patients (57.1%) in whom plasma metanephrines and normetanephrines were normal; 2 additional patients were prior operated for an adrenal paraganglioma (pheochromocytoma) and for an extra-adrenal paraganglioma, respectively. Chronic stable angina or resting ECG ischemic features were present in 23 patients (27.4%), arrhythmias in 12 patients (14.3%); on transthoracic echocardiography, aortic and mitral valve calcifications were present in 9 patients (10.7%). Impaired glucose metabolism was present in 15 patients (17.8%): type 2 diabetes mellitus in 8 patients (9.5%) and impaired glucose tolerance in 7 patients (8.33%).
Conclusions
cardiovascular involvement is frequent in PHPT patients. A proper screening should be done both in patients with hypercalcemic PHPT who will be referred to surgery and in patients with normocalcemic PHPT to assess cardiovascular risk and to weight potential benefits of surgery.

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β-estradiol contributes to sex differences in resilience to septic-induced cardiacdysfunction via GPER-1/PPARδ/NLRP3 signaling

Joseph Adu-Amankwaah, Lu Fu, Richard Mprah, Marie Louise Ndzie Noah, Zheng Gong & Hong Sun
Xuzhou Medical University, Xuzhou, China

Background and aim
Sepsis, a leading global cause of mortality, involves life threatening multi-organ failure triggered by a dysregulated host response to infection. Cardiac dysfunction significantly contributes to this failure, primarily influenced by septic-induced metabolic dysregulation. Clinical studies suggest a less favorable outcome for males in sepsis, potentially linked to hormonal disparities, which remains unclear. This study aimed to explore the sex-related cardiac mechanisms driving septic-induced mortality.
Methods and results
Here, we unveil that while sepsis induces dysfunction, metabolic dysregulation, oxidative stress, and apoptosis in the heart, these effects are notably more pronounced in males than females. Detailed mechanistic experiments employing ovariectomized mice, β-estradiol(E2) administration, GPER-1$^{+/+}$ (G protein-coupled estrogen receptor 1), and GPER-1$^{-/-}$ mice revealed that under lipopolysaccharide (LPS)-induced sepsis, E2 acting via GPER-1 enhances cardiac electrical activity, promotes PPARδ nuclear translocation, and subsequently ameliorates cardiac metabolism while mitigating oxidative stress and apoptosis in females. Furthermore, PPARδ specific activation using GW501516 in female GPER-1$^{-/-}$ mice reduced oxidative stress, ultimately decreasing NLRP3 expression in the heart. Remarkably, targeted GPER-1 activation using G1 in males mirrors these benefits, improving cardiac electrical activity and function and ultimately enhancing survival rates during LPS-induced sepsis. By employing NLRP3$^{+/+}$and NLRP3$^{-/-}$ mice, we demonstrated that the targeted GPER-1 activation mitigated injury, enhanced metabolism, and reduced cardiac apoptosis in the heart of male mice via the downregulation of NLRP3.
Conclusion
Our findings collectively illuminate the different sex-specific mechanisms influencing septic mortality, offering insights into physiological and pathological dimensions. From a pharmacological standpoint, this study introduces specific GPER-1 activation as a promising therapeutic intervention for males under septic conditions. These discoveries not only advance our understanding of sepsis regarding sex but also present a novel avenue for targeted interventions with potential translational impact.

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Glucocorticoid-induced adrenal insufficiency in patients with polymyalgia rheumatica and giant cell arteritis during long-term low-dose prednisolone treatment: Prediction based on indicators of exogenous hypercortisolism in the Double Edge Study

Nanna Thurmann Jørgensen[1,2], Jelena Stankovic[3,4], Anja Fenger Dreyer[5,6], Hajir Al-Jorani[5,6], Lise Sofie Bislev[3,4], Victor Brun Boesen[1], Stina Willemoes Borresen[1], Louise Lehmann Christensen[5,6], Ulla Feldt-Rasmussen[1], Dorte Glintborg[5,6], Tanja Fromberg Gorlen[2,7], Simon Bøggild Hansen[3,4], Merete Lund Hetland[2,7], Bente Jensen[8], Richard Christian Jensen[5], Marie Louise Lund[1], Paul M Stewart[9], Randi Tei[3,10], Marianne Andersen[5,6], Jens Otto Jørgensen[3,4] & Marianne Klose[1]
[1]Copenhagen University Hospital, Rigshospitalet, Department of Endocrinology and Metabolism, Centre of Cancer and Organ Diseases, Copenhagen, Denmark; [2]Faculty of Health and Clinical Sciences, Copenhagen University, Department of Clinical Medicine, Copenhagen, Denmark; [3]Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus, Denmark; [4]Aarhus University, Department of Clinical Medicine, Aarhus, Denmark; [5]Odense University Hospital, Department of Endocrinology and Metabolism, Odense, Denmark; [6]University of Southern Denmark, Department of Clinical Research, Odense, Denmark; [7]Copenhagen University Hospital, Rigshospitalet, Center of Rheumatology and Spine Diseases, Glostrup, Denmark; [8]Copenhagen University Hospital Bispebjerg and Frederiksberg, Center of Rheumatology and Spine Diseases, Frederiksberg, Denmark; [9]University of Leeds, Faculty of Medicine and Health, Leeds, UK; [10]Aarhus Universitetshospital, Endocrinology and Internal medicine, Aarhus N, Denmark

Background and aim
Identifying patients with glucocorticoid-induced adrenal insufficiency poses a challenge. We investigated whether factors associated with exogenous hypercortisolism (as a proxy of overall elevated glucocorticoid exposure) could predict the risk of glucocorticoid-induced adrenal insufficiency in patients with polymyalgia rheumatica and/or giant cell arteritis during long-term low-dose prednisolone treatment.
Material and methods
Baseline data analysis of a nationwide prospective study (Double Edge/-RESCUE, EudraCT:2021-002528-18) of 133 participants with polymyalgia rheumatica/giant cell arteritis treated with prednisolone for ≥12 weeks, with a current daily dose of ≤5 mg, 58 participants with adrenal insufficiency and 75 participants with normal adrenal function evaluated with a 250 µg ACTH test. The participants were evaluated for factors associated with exogenous hypercortisolism. These factors included present diagnoses of diabetes, hypertension, dyslipidaemia, and osteoporosis documented by medical history and study examinations. Study examinations included anthropometric data, blood pressure, bone mineral density assessed by dual-energy X-ray absorptiometry (DXA) scans, and blood tests for fasting glucose, haemoglobin A_{1c} (HbA_{1c}), and lipids. Apart from medical history, the paraclinical diagnosis of diabetes was defined as HbA_{1c} ≥48 mmol/mol and/or fasting glucose >7.0 mmol/l; hypertension was defined as systolic and diastolic blood pressure >140/>90 mmHg; dyslipidaemia was defined as total cholesterol >5.0 mmol/l and/or low-density lipoprotein cholesterol >3.0 mmol/l; and osteoporosis was defined as a T-score ≤−2.5. Adrenal insufficiency was defined as ACTH-stimulated cortisol <420 nmol/l (Liquid Chromatography Mass Spectrometry and/or Electrochemiluminescence immunoassay Roche Elecsys Cortisol II). Logistic regression models were used to identify predictor variables.
Results
The cumulative prednisolone dose over the past six months (OR 2.9[95% CI 1.3–6.5]) and female sex (2.8[1.1–6.4]) were associated with increased risk of adrenal insufficiency, whereas this was not the case for age (1.1[1.0–1.1]) and BMI (1.0[0.9–1.0]). Neither diabetes (0.8[0.3–2.0]), dyslipidaemia (0.8[0.4–1.9],), or hypertension (0.5[0.3–1.0]) were associated with increased risk of adrenal insufficiency. However, data suggest a 3-fold increased risk in patients with osteoporosis (2.9[1.4–6.1]), also after adjusting for age, sex, and BMI (all OR 2.2–2.7), but not after adjusting for the cumulative prednisolone dose (2.2[1.0–4.8]).
Conclusion
- Accumulated prednisolone dose may be a major predictor of adrenal insufficiency during prolonged low-dose prednisolone treatment.
- The risk of glucocorticoid-induced adrenal insufficiency is higher in females and is associated with osteoporosis.
- The data may aid in providing evidence-based risk stratification and prevention programmes for prednisolone-treated patients.

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P414

Aldosterone:metanephrine ratio better predicts laterality in patients with primary aldosteronism and mild autonomous cortisol co-secretion than aldosterone:cortisol ratio

Zin Htut[1], Aditi Sharma[2], Daniel Foran[3], Fausto Palazzo[1], Aimee Dimarco[1], Karim Meeran[1], Ali Alsafi[1] & Florian Wernig[1]
[1]Imperial College Healthcare NHS Trust, UK; [2]Barts Health NHS Trust, UK; [3]Imperial College London, UK

Introduction
Adrenal Venous Sampling (AVS) is considered the gold standard to identify surgically treatable primary aldosteronism (PA) subtypes. Current guidelines suggest using plasma cortisol concentrations to confirm successful adrenal vein (AV) cannulation and lateralisation, but cortisol co-secretion by adrenal adenomas can lead to diagnostic misinterpretation. Plasma metanephrines (MN) have a half-life of 3 to 6 min and are not affected by cortisol co-secretion, and therefore may offer a more precise and sensitive approach when used as an alternative analyte to cortisol to diagnose unilateral PA.
Aim
This study aims to demonstrate superiority of measuring MN over cortisol in patients with PA and mild autonomous cortisol co-secretion.
Methodology
We studied 132 patients undergoing unstimulated AVS in a tertiary referral centre carried out by a single operator between January 2018 to May 2023. Plasma samples for MN were collected from both AV and PV. Cannulation success was determined by using AV/PV cortisol >2 or AV/PV MN >12. Unilateral disease was confirmed by an aldosterone/cortisol ratio >2, aldosterone/MN ratio >5 and contralateral suppression by a ratio below 0.5 of that in PV.
Results
The cannulation success rate was 98%. Among 132 cases, 73 underwent overnight dexamethasone suppression testing, which identified 14 patients with mild autonomous cortisol co-secretion (cortisol >50 nmol/l [53–201] post dexamethasone) and low or suppressed baseline ACTH. AVS results were discordant in 4 out of 14 patients with mild autonomous cortisol co-secretion as well as in one patient with post-dexamethasone cortisol of 36 nmol/l, with aldosterone/cortisol suggesting bilateral disease and aldosterone/MN indicating unilateral disease. Four out of those 5 patients with discordant results underwent unilateral adrenalectomy and histological analysis confirmed an adrenocortical adenoma in all cases. One patient opted for medical therapy. All surgically treated patients achieved complete clinical and biochemical remission according to PASO criteria.

Table 1 Patient baseline characteristics

Total number	132
Male	60%
Age (years)	50.0 ± 10.3
MAP (mmHg)	116.0 ± 14.2
Potassium (mmol/l)	3.0 ± 0.48
T2DM (prevalence)	15%
Number of antihypertensives	2 (1-3)

Conclusion
This study provides a further important addition to the current literature demonstrating superiority of aldosterone/MN over aldosterone/cortisol to distinguish unilateral from bilateral disease in patients with PA and cortisol co-secretion undergoing unstimulated AVS.

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P415

Bilateral adrenal haemorrhage secondary to heparin induced thrombocytopenia- a rare cause and presentation of adrenal crisis

Veronica Chirila, Beas Bhattacharya & Alexandra Ward
Royal United Hospital Bath, Diabetes and Endocrinology, Bath, UK

Case history
We present the case of a 73 year old lady who was admitted following a neck of femur fracture after a fall. She had surgery performed with no major complications. During her inpatient stay, she unexpectedly became very unwell, complaining of abdominal pain, low grade pyrexia, tachycardia, tachypnoea, hypotension, nausea and vomiting (1). Initial management was as sepsis of unknown source.
Investigations
Bloods on admission (23/08/23): Hb 132 g/l, MCV 95.7 fl, Plt 219 10×9/l, WCC 11 10×9/l, **Na 135 mmol/l**, potassium 3.8 mmol/l, eGFR ml.min/1.73 m^2, LFTs normal, CRP 3, TSH 2.06. Bloods (31/08/23): Hb 104 g/l, MCV 94.4 fl, Plt: 38 10×9/l, WCC 12.3 10×9/l, neutrophils 9.7 10×9/l, lymphocytes 1.2 10×9/l, **Na 125 mmol/**l, potassium 3.3 mmol/l, eGFR>90, LFTs normal, albumin 28, CRP 226 mg/l; SST (November 2023): baseline cortisol: 15 nmol/l; 30 min: 109 nmol/l. US abdomen (30/08/23) was normal CT abdomen and pelvis (03/09/2023): **bilateral adrenal haemorrhage (BAH)** and partial left renal vein thrombosis; subcutaneous haematoma associated with left THR. CTPA (03/09/23): bilateral segmental and subsegmental emboli with segmental infarct in RLL.
Conclusion and discussions
Our patient had BAH secondary to HIT (heparin induced thrombocytopenia). Platelets dropped 8 days later after she was started on dalteparin and her HIT screening came back positive. We discuss a rare but serious presentation of adrenal crisis which can be potentially fatal, if clinical suspicion is not high, and non-infective causes of shock are not considered. This is very relevant post-surgery, after anti-coagulant use and any major trauma. Therefore, it is essential that it is considered as a differential particularly by specialities not used to managing hypoadrenalism. Radiologically findings can often be difficult and need expertise in abdominal radiology as often represent a mass and can be mistaken as adrenal neoplasm(3). There are two proposed mechanisms involved in the pathogenesis of idiopathic haemorrhages (2) stress and adrenal medullary venous thrombosis. Other causes of adrenal haemorrhage in pheochromocytoma, metastatic lesions and adrenocortical carcinoma, which then will need to be investigated involving adrenal MDT with endocrinologist.
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P416

Increased cardiovascular risk in patients with germline VHL gene alterations – a UKBIOBANK-based genomic study

Reut Halperin[1,2,3,] & Amit Tirosh[1,2,3,]
[1]Sheba, Endocrinology, diabetes and metabolism, Ramat Gan, Israel; [2]Sheba, ENTIRE Endocrine Neoplasia Translational Research Center, Ramat Gan, Israel; [3]Tel Aviv University, Medicine, Tel Aviv-Yafo, Israel

Introduction
Von Hippel-Lindau (VHL) is an autosomal dominant disease associated with increased risk for developing hemangioblastomas of the central nervous system and retina, renal cell carcinoma (RCC), pancreatic neuroendocrine tumors (PNET), adrenal pheochromocytomas and paraganglioma (PPGL). Loss of function *VHL* alterations lead to pseudohypoxia and, consequently, to angiogenesis and metabolic derangements (e.g., increased glucose uptake). Little is known about the systemic effects of *VHL* alterations on the cardiometabolic system.
Aim
Study whether *VHL* gene variants are associated with increased cardiometabolic risk.
Methods
Data were extracted from the UK Biobank database, including demographic and anthropometric parameters, medical history, and lab testing. Whole exome sequencing data were available for all patients, and a focused variant calling and annotation of the *VHL* gene region was performed on the DNA-nexus platform. A composite of major adverse cardiovascular events (MACE) per patient consisted of ischemic heart disease (IHD), cerebrovascular accident (CVA), and peripheral artery disease (PVD). *VHL* variant severity was sub-categorized into low (silent or missense), intermediate (in-frame insertion or deletion and 5′ UTR variants), and high-risk (nonsense or frameshift).
Results
Data from 460 430 participants were analyzed (45.8% males, age at inclusion 73.6 ± 8.1 years). IHD, CVA, and PVD rates were 11.5%, 3.0%, and 1.8%, respectively. Germline *VHL* variants were detected in 2594 participants (0.45%), with 2073 low- (242 silent, 1830 missense), 505 intermediate- (18 in-frame deletion and 23 in-frame insertion and 464 5′ UTR variants), and 16 high-risk (3 frameshift insertions, one frameshift deletion, and 12 nonsense) *VHL* variants. In the multivariable logistic regression analysis, harboring a high-risk *VHL* variant was associated with an 11-fold increased risk of MACE (odds ratio [OR] 11.1, 95% confidence interval 1.5–54.1, $P=0.006$), after adjustment for age at inclusion, age at diagnosis with cancer, sex, kidney function, c-reactive protein plasma levels, and diagnosis status with diabetes mellitus, hypertension, dyslipidemia, obesity, and RCC.
Conclusions and discussion
VHL gene alterations are associated with an increased cardiometabolic risk. Metabolic changes or enhanced drive for angiogenesis might contribute to this association. Further research is needed to verify these results and to assess a possible benefit from early intervention in this population.

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P417

Germline targeted next-generation sequencing in patients with adrenal incidentalomas

Erika Messina[1], Soraya Puglisi[1], Maria Scatolini[2], Pasquale Tomaiuolo[2], Anja Barač Nekić[3], Valentina Morelli[4], Ylenia Alessi[5], Karin Zibar Tomsic[3], Serena Palmieri[6], Francesco Ferraù[5], Enrico Grosso[2], Anna Pia[1], Giuseppe Reimondo[1], Iacopo Chiodini[7], Darko Kastelan[3] & Massimo Terzolo[1]
[1]Internal Medicine, Department of Clinical and Biological Sciences, San Luigi Hospital, University of Turin, Orbassano, Italy; [2]Molecular Oncology Laboratory, Fondazione Edo ed Elvo Tempia, Ponderano, Italy; [3]Department of Endocrinology, University Hospital Zagreb, Zagreb, Italy; [4]Unit for Bone Metabolism Diseases and Diabetes and Lab of Endocrine and Metabolic Research, IRCCS, Istituto Auxologico Italiano, Milan, Italy; [5]Department of Human Pathology G. Barresi, Endocrine Unit, University Hospital G. Martino, University of Messina, Messina, Italy; [6]Unit of Endocrinology, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Ca' Granda-Ospedale Maggiore Policlinico, Milan, Italy; [7]Department of Biotechnology and Translational Medicine, Unit of Endocrinology, Ospedale Niguarda Cà Granda, University of Milan, Milan, Italy

Background
The advances in next-generation sequencing (NGS) technologies and bioinformatic analysis have shed light on genetic alterations, either of germline or somatic origin, in many disorders, including adrenocortical diseases. However, our knowledge on genomic characteristics in benign adrenal tumors of serendipitous discovery (adrenal incidentalomas) remain scarce.The aim of this study was to understand the pathogenic role of germline variants in adrenal incidentalomas.
Methods
To identify disease-causing variants, in this multicenter study we performed targeted NGS of 191 patients with adrenal incidentalomas, using a custom panel of 21 genes potentially involved in the pathogenesis of adrenal tumors. Pathogenicity role of germline variants (GV) was assessed using ClinVar database or, in absence, using ACMG guidelines throw VarSome tool. Clinical and hormonal data were collected at diagnosis and at last follow-up visit. The median follow-up was 8.5 years (IQR 3–15 years).
Results
NGS analysis in 10 patients (5.2%) identified GV located in the following genes: ARMC5 ($n=3$), APC ($n=1$), CACNA1H ($n=2$), ZNRF3 ($n=2$), PDE11A ($n=1$), GNAS ($n=1$). We found two likely-pathogenic variants (LP) in ZNRF3 and GNAS genes and eight variants of suspicious pathogenicity (VUS/LP) in ARMC5, APC, CACNA11H, ZNRF3 and PDE11A genes. Two of the three patients with GV in ARMC5 gene had bilateral lesions at diagnosis and one of these developed hypertension during the follow-up despite the absence of cortisol autonomy. The patient with GV in APC gene did not present associated colon polyposis, significant changes of tumor characteristics and related comorbidities over time. None of the patients with GV in CACNA1H gene showed alterations in the aldosterone-renin ratio, whereas one was diagnosed with mild autonomous cortisol secretion and underwent adrenalectomy. Both patients with GV in ZNRF3 gene had unilateral adrenal lesions that did not changed their characteristics and developed hypertension during follow-up, despite the absence of mineralocorticoid and glucocorticoid excess. The patient with GV in PDE11A gene presented with unilateral lesions and hypertension, without significant changes of tumor characteristics and related comorbidities over time. A similar behavior was observed in the patient with a GV in GNAS gene (unilateral tumor, no significant radiological changes with time), who developed hypertension during follow-up.
Conclusion
GV with a pathogenic or potential pathogenic role were found in 5.2% of patients with benign adrenal incidentalomas. The small number of cases hampered the identification of a clear genotype-phenotype correlation; however, these data provide new insights for a better characterization of benign adrenal incidentalomas.

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P418

Appraisal of modified tests for the diagnosis and treatment of primary aldosteronism: A single endocrine center experience

Athina Markou[1], Gregory Kaltsas[2], Labrini Papanastasiou[1], Nikolaos Voulgaris[1], Aggeliki Gouli[1], Vaios Tsiavos[1], Christos Gravvanis[1], Ernestini Tyfoxylou[1], Sofia Vlachou[2], Chara Kapsali[1], Irini Giagourta[1], Theodora Kounadi[1], Kyriakos Vamvakidis[3], George Zografos[4], George Chrousos[5] & George Piaditis[6]
[1]General Hospital of Athens 'G. Gennimatas', Endocrinology, Athens, Greece; [2]Laiko Hospital, 1st Department of Propaedeutic Internal Medicine, Athina, Greece; [3]Henry Dunant, Department of Endocrine Surgery, Athina, Greece; [4]General Hospital of Athens "G. Gennimatas", Third Department of Surgery, Athens, Greece; [5]National and Kapodistrian University of Athens, University Research Institute of Maternal and Child Health and Precision Medicine, Athens, Greece; [6]Henry Dunant, Endocrinology, Athina, Greece

Introduction
Primary aldosteronism (PA), the most common endocrine cause of secondary hypertension, is generally underdiagnosed using current diagnostic tests.
Aim
To present our 14-year experience of prospective studies on the diagnosis, prevalence and treatment of PA.
Patients and methods
We studied 992 hypertensive patients and 278 age-, sex- and body mass index – matched controls (194 normotensive and 104 with essential hypertension), all with normal adrenal imaging. Participants underwent conventional confirmatory tests for PA modified by the addition of dexamethasone to exclude stress-induced aldosterone secretion including the Fludrocortisone Dex Suppression Test (FDST), the Dex Saline Infusion Test (DSIT) and the Dex Captopril Valsartan Test (DCVT). The normotensive controls underwent the FDST and the DSIT. Normal cut-offs of pre-FDST and pre-DSIT basal aldosterone to renin ratio (ARR) and post-FDST and post-DSIT aldosterone levels and ARR were calculated from this group of normotensive controls. Because the DCVT can only be applied to hypertensives, we used hypertensive individuals, in whom PA had been excluded by the FDST, as a control group for calculation of the normal cut-offs of pre-DCVT basal ARR and post-DCVT aldosterone levels and ARR. Hypertensive patients underwent the FDST, the DSIT and the DCVT. Failure to suppress aldosterone was demonstrated if the combination of post-test aldosterone levels and ARR were higher than the corresponding normal cut-offs for each test separately.
Results
Hypertensive patients of all three treatment groups had significantly higher blood pressure (BP) and lower serum potassium levels than their controls. Using the basal ARR, as a screening test, the prevalence of PA was 17.8%, but after applying the modified tests to all patients the prevalence of PA was 33.4%. Targeted treatment with Mineralocorticoid Receptor Antagonists was administered in 252 hypertensive patients with bilateral PA, with 188 (74.6%) obtaining a biochemical response (potassium >3.9 mmol/l, renin $>$ 7.5 mU/l) and a normalized BP ($<140/90$ mmHg). Forty-eight hypertensive patients with unilateral disease underwent laparoscopic adrenalectomy. Twenty-three of these had concomitant mild autonomous cortisol secretion. Postoperatively, three patients (6.2%) failed to suppress aldosterone, demonstrating a biochemical success rate of 94%.
Conclusion
Our modified methodology and the use of controls for each test separately (normotensives for FDST and DSIT and hypertensives for DCVT) for calculation of normal cut-offs of aldosterone suppression has never been reported before and significantly improves the sensitivity and specificity of the existing tests on the diagnosis of PA, allowing the detection of milder forms some with cortisol co-secretion.

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P419

Primary aldosteronism: Small molecule antagonists of mutant KCNJ5 potassium channels

Sanas Mir-Bashiri[1], Martina Tetti[2], Dennis Froebel[3], Dunja Reiss[1], Nicole Bechmann[3], Mirko Peitzsch[3], Graeme Eisenhofer[3], Martin Reincke[1] & Tracy Ann Williams[1]
[1]Klinikum der Universität München, Endocrine Research Unit, München, Germany; [2]University of Turin, Torino, Italy; [3]University Hospital Carl Gustav Carus Dresden, Dresden, Germany

Background
Primary aldosteronism (PA) is the most frequent cause of endocrine hypertension associated with excess aldosterone production from one or both adrenal glands. Somatic or germline mutations in the KCNJ5 potassium channel cause an imbalance in intracellular ion homeostasis. This ultimately drives aldosterone overproduction in some sporadic forms of PA and a familial form of the disease (familial hyperaldosteronism type 3). Our objective was to identify small molecule compounds that could be used in managing patients with PA driven by a *KCNJ5* mutation.
Methods
A virtual screening of $>$ 6 million low molecular weight compounds was used to identify candidate molecules potentially interacting with the KCNJ5 channel. Functional testing through WST-1 assays and flow cytometry was performed to quantify the inhibition of cell death mediated by high-level expression of KCNJ5 mutants in human adrenocortical cell lines (HAC15).

Results
In silico screening of the small molecule library identified 108 candidate molecules. One of these, referred to as C-81, was a spirocyclic molecule featuring an indene and pyrroloquinoline system that inhibited HAC15 cell death induced by mutant KCNJ5 overexpression by 34.95% (measured via flow cytometry, $P<0.001$). The effect of C-81 on different KCNJ5 mutations close to the channel pore was quantified by qPCR showing a 75% decrease in *CYP11B2* (aldosterone synthase) gene expression for KCNJ5 L168R mutations ($P<0.001$) and 91% decrease for T158A mutations ($P<0.001$). In contrast, C-81 only had a non-significant effect on *CYP11B2* gene expression levels in native HAC15 cells ($P=0.25$). Using a steady state system for *in vitro*evaluation of steroidogenic pathway dynamics, C-81 treatment resulted in up to a 50% reduction of aldosterone production.
Conclusion
C-81 is a candidate small molecule antagonist of mutated KCNJ5 which could have potential therapeutic use to decrease pathological aldosterone secretion in some sporadic and familial forms of PA.

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Different metabolic pathways associated with total cortisol exposure and the cortisol time profile: A randomized cross-over clinical trial

Johanna McQueen[1,2], Terence Garner[3], Dimitrios Chantzichristos[1,2], Hans Lennernäs[4], Stéphanie Espiard[5], Oskar Ragnarsson[1,2,6], Ragnhildur Bergthorsdottir[1,2], Stanko Skrtic[1], Adam Stevens[3] & Gudmundur Johannsson[1,2]
[1]Institute of Medicine at Sahlgrenska Academy, University of Gothenburg, Department of Internal Medicine and Clinical Nutrition, Gothenburg, Sweden; [2]Sahlgrenska University Hospital, Gothenburg, Endocrinology, Diabetology, and Metabolism,, Gothenburg, Sweden; [3]Division of Developmental Biology and Medicine, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK; [4]Uppsala University, Department of Pharmaceutical Biosciences, Uppsala, Sweden; [5]Lille University Hospital, Department of Endocrinology, Diabetology and Metabolism, Huriez Hospital, Lille, France; [6]Wallenberg Center for Molecular and Translational Medicine, University of Gothenburg, Gothenburg, Sweden

Context
Excess cortisol exposure and disruption of the circadian cortisol profile are both associated with adverse clinical outcome.
Objective
The aim of this study was to identify unique metabolites and metabolic pathways associated with total cortisol exposure and the cortisol time profile.
Design
A randomized, 12-week, two period, cross-over clinical trial.
Patients and interventions
Eighteen adults with primary adrenal insufficiency received the same daily dose of dual-release hydrocortisone (HC) tablets once-daily (OD) and conventional immediate-release HC tablets 3 times daily (TID) during 12 weeks each.
Main outcome measures
Total cortisol exposure was calculated by the area under the concentration-time curve from pharmacokinetic sampling over 24 h ($AUC_{0\text{-}24}$). The variability of the serum cortisol time profile was quantified by calculating the lag–1 autocorrelation (AUTO) from serum cortisol concentrations over 24-hours. Metabolomic analysis in serum and urine were performed using gas chromatography–mass spectrometry (GC–MS) and liquid chromatography-mass spectrometry (LC–MS), respectively. The relationship between total cortisol exposure, the variability of the cortisol time profile and metabolite expressions were assessed using a Bayesian generalized linear model.
Results
During TID, cortisol exposure was 20% higher and the variability of the cortisol time profile was larger, compared to OD. In total, 2406 metabolites were detected. 109 metabolites in serum and 21 in urine were uniquely correlated with total cortisol exposure. These metabolites were involved in arginine biosynthesis and alanine–aspartate–glutamate and tryptophan metabolism. Further, 40 metabolites in serum and 2 in urine were uniquely correlated with the cortisol profile variability. These metabolites were involved in primary bile acid biosynthesis and cysteine–methionine metabolism.
Conclusion
We identified different groups of metabolites and metabolic pathways that specifically correlated with total exposure of cortisol and cortisol profile variability, respectively. These findings suggest that total exposure and the time profile of serum cortisol have independent metabolic and regulatory effects in the human body.

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P421

A case of reversible Brugada syndrome with severe hypothyroidism

Shyam Seshadri[1], Raja Nata[1], Firas Hadaddin[1], Manoj Thomas[1] & Frankie Swords[2]
[1]The Queen Elizabeth Hospital Foundation NHS Trust, Department of Endocrinology, Kings Lynn, UK; [2]Norfolk and Norwich University Hospital, Department of Endocrinology, Norwich, UK

A 23-year-old gentleman with a 9-month history of extreme tiredness, muscle aches and pains, weight gain, cold intolerance and constipation presented to hospital with severe lethargy and dizziness and vacant episodes of increasing frequency. Initial examination revealed him to have a pulse rate of around 66 beats per minute. He was haemodynamically stable. A resting ECG showed an elevated ST segment of more than 2 mm with descent to an upward convexity to an inverted T wave especially prominent in the precordial leads in keeping with type 3 Brugada ECG pattern. The patient was in sinus rhythm with no symptoms of cardiac sounding chest pain. Further investigations revealed raised creatine kinase, deranged liver function in the form of isolated elevated alanine aminotransferase and acute kidney injury. Thyroid function revealed a markedly decreased FreeT4 of 1.6 pmol/l and TSH of greater than 150 miu/l. An echocardiogram showed good left ventricular function and no significant pericardial effusion. The patient was commenced on levothyroxine initially followed by low dose liothyronine. An ultrasound of his kidneys to probe his renal function was normal. An autoimmune screen turned out to be negative. Patient was hospitalised for further management. A 24-h ECG trace showed him to be in sinus rhythm throughout with no cardiac arrythmias. Patient's stay in hospital was uneventful and he was discharged after 1 week with further review in the endocrine, renal and cardiology outpatient clinics. Endocrine review a month later showed him to have improved with his symptoms though not completely well yet and he had lost the 6 kg which he had gained prior to his hospital admission. He had ongoing muscle aches and tiredness and did not feel mentally sharp. He was asked to wean off his liothyronine over 2 weeks while his levothyroxine was increased. Further cardiology review 3 weeks later showed improving ECG changes especially with settling ST elevation. The patient also had a nephrology review in 2 months which was satisfactory. The raised alanine aminotransferase and creatine kinase was thought to represent metabolic changes due to severe hypothyroidism. A specialist opinion at the inherited arrythmia clinic 8 months later showed resolved ECG changes with now no evidence of Brugada ECG pattern and patient was reassured and discharged. We report on a rare cardiac manifestation of severe hypothyroidism which fortunately was reversible on successful correction of his endocrine abnormality.

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P422

Undertreated and undiagnosed adrenal insufficiency as a premature cause of death in glucocorticoid users

Margret J Einarsdottir[1,2], Penelope Trimpou[1,2], Gudmundur Johannsson[1,2] & Oskar Ragnarsson[1,2,3]
[1]Sahlgrenska Academy, Gothenburg, Sweden; [2]Sahlgrenska Hospital, Gothenburg, Sweden; [3]Wallenberg Center for Molecular and Translational Medicine, Gothenburg, Sweden

Objective
Whether glucocorticoid (GC)-induced adrenal insufficiency may cause premature mortality in GC-users is not known. We conducted a retrospective cohort study to investigate if undiagnosed and undertreated GC-induced adrenal insufficiency is a contributor to premature death.
Methods
Information on dispensed prescriptions in West Sweden from 2007 to 2014 was obtained from the Swedish Prescribed Drug Register. Cause of death was collected from the Swedish Cause of Death Register. Of 223 211 patients who received oral GC prescriptions, 665 died from sepsis within 6 months from their last prescription. Three hundred of these, who had died in hospital, were randomly selected for further investigation. The medical records were initially reviewed by one investigator. Two additional investigators independently reviewed the medical records of those whose deaths were suspected to be caused by GC-induced adrenal insufficiency.
Results
Of 300 patients (121 females, 40%), 212 (75%) were prescribed GC treatment at admission. The mean age was 76 ± 11 years (range 30–99). Undiagnosed or undertreated GC-induced adrenal insufficiency was considered a probable contributor to death by at least two investigators in 11 (3.7%) patients. In 5 of these 11 cases, long-term GC therapy was abruptly discontinued during the hospitalization. Undiagnosed or undertreated GC-induced adrenal insufficiency

was considered a possible contributing factor to death in a further 36 (12%) patients.
Conclusion
GC-induced adrenal insufficiency is an important contributor to premature death in GC users. Increased awareness of adrenal insufficiency during intercurrent illness and following cessation of GC treatment is essential.

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P423

Baseline characteristics of adults with classic congenital adrenal hyperplasia enrolled in CAHtalyst, a phase 3 study of Crinecerfont, a corticotropin-releasing factor type 1 receptor antagonist

Richard Auchus[1], Oksana Hamidi[2], Rosario Pivonello[3], Irina Bancos[4], Selma Witchel[5], Andrea Isidori[6], Patrice Rodien[7,8], Umasuthan Srirangalingam[9], Florian Kiefer[10], Henrik Falhammar[11], Deborah Merke[12,13], Nicole Reisch[14], Julia Sturgeon[15], Eiry Roberts[15], Vivian Lin[15], Jean L Chan[15] & Robert Farber[15]
[1]University of Michigan Medical School, Ann Arbor, USA; [2]University of Texas Southwestern Medical Center, Department of Internal Medicine, Dallas, USA; [3]University of Naples Federico II, Napoli, Italy; [4]Mayo Clinic, Rochester, USA; [5]University of Pittsburgh School of Medicine, Pittsburgh, USA; [6]Sapienza University of Rome, Roma, Italy; [7]Mitovasc, Angers, France; [8]Angers University Hospital Center, Angers, France; [9]University of College London, London, UK; [10]Medical University of Vienna, Wien, Austria; [11]Karolinska Institute, Stockholm, Sweden; [12]NIH Clinical Center, Bethesda, USA; [13]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, USA; [14]Ludwig Maximilian University of Munich, München, Germany; [15]Neurocrine Biosciences, San Diego, USA

Objectives
To describe the baseline characteristics of individuals enrolled in CAHtalyst (NCT04490915), a randomized, double-blind, placebo-controlled, Phase 3 study evaluating the safety and efficacy of crinecerfont (a corticotropin-releasing factor type 1 receptor [CRF_1] antagonist) in adults with classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency (21-OHD).
Methods
The study included adults (age $\geq$18 years) with classic 21OHD. Key eligibility criteria included glucocorticoid dose $>$13 mg/m^2/day in hydrocortisone equivalents (HCe; conversion factors: 4$\times$ for predni[so]lone, 60$\times$ for dexamethasone) adjusted for body surface area (BSA) with stable dose for $\geq$1 month prior to screening, and normal or elevated androstenedione (A4). Baseline demographics and characteristics were summarized descriptively in all randomized participants.
Results
Of 182 enrolled participants, 51% were men and 90% were White. Mean ($\pm$s.d.) age was 30.8$\pm$9.9 years (range: 18–58 years), mean BSA was 1.8$\pm$0.2 m^2, and mean body mass index (BMI) was 29.8$\pm$7.0 kg/m^2 (with BMI $\geq$30 kg/m^2 in 47% of participants). The mean total daily glucocorticoid dose was 17.6$\pm$4.9 mg/m^2/day (32.3$\pm$9.3 mg/day) HCe, with 57% on hydrocortisone alone, 30% on a predniso(lo)ne-containing regimen, and 13% on a dexamethasone-containing regimen. In addition, 86% of participants were on fludrocortisone (mean dose: 136$\pm$72 µg/day). Mean ($\pm$s.d.) hormone concentrations prior to the morning glucocorticoid dose were as follows: adrenocorticotropic hormone, 264$\pm$317 pg/ml; 17-hydroxyprogesterone, 9467$\pm$8829 ng/dl; A4, 620$\pm$729 ng/dl; testosterone (T) in females, 86$\pm$85 ng/dl; A4/T in males, 2.2$\pm$2.4; follicle-stimulating hormone in males, 6.3$\pm$9.4 IU/l; and luteinizing hormone in males, 4.6$\pm$5.0 IU/l. Among the 90 females, 42 (47%) reported a history of hirsutism; of the 66 females of childbearing potential not on hormonal or intrauterine contraception, 35 (53%) reported a history of amenorrhea or menstrual irregularities. Among the 92 males, 44 (48%) reported a history of testicular adrenal rest tumors (TARTs) while 53 (58%) had evidence of TARTs by ultrasound prior to study entry. Comorbidities included osteopenia (15%), hypertension (10%), osteoporosis (5%), and diabetes mellitus (2%).
Conclusion
In a Phase 3 trial evaluating crinecerfont (a CRF_1 antagonist) in adults with classic 21OHD, clinical evidence of glucocorticoid and androgen excess (e.g., high prevalence of obesity, hirsutism [females], and TARTs [males]) were observed at baseline. Androgens and other steroid biomarkers were elevated despite treatment with supraphysiological doses of glucocorticoids. These findings emphasize the urgent need for novel glucocorticoid-sparing treatments for this chronic condition.

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P424

Diagnostic performance of dehydroepiandrosterone sulfate in predicting adrenal insufficiency

Ashley Han[1], Sara J Achenbach[2], Elizabeth J (Beth) Atkinson[2] & Irina Bancos[3]
[1]Mayo Clinic, Internal Medicine, Rochester, USA; [2]Mayo Clinic, Rochester, USA; [3]Mayo Clinic, Division of Endocrinology, Diabetes, Metabolism, and Nutrition, Rochester, USA

Background
Diagnosing adrenal insufficiency (AI) often requires complex multi-step testing which can be expensive and time consuming. In this study, we evaluated the diagnostic performance of baseline dehydroepiandrosterone sulfate (DHEAS) level in identifying patients with AI.
Methods
A single-center retrospective cohort study was performed of patients who underwent Cosyntropin stimulation testing (CST) between 2005 and 2023 and had a baseline DHEAS level obtained within 3 months of CST. Patients were excluded if they had congenital adrenal hyperplasia (CAH), oral estrogen use at the time of lab testing, were hospitalized within 1 month after CST, or died within 6 months after CST. AI was defined as post-CST peak cortisol $<$18 µg/dl and DHEAS level obtained closest to the time of CST was utilized. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were determined using a receiver operating characteristic (ROC) curve. Optimal cutpoint was determined to maximize both sensitivity and specificity. For further analysis, patients were stratified by gender and age; women $\geq$50 years old were assumed to be post-menopausal.
Results
Out of 1245 patients included in this study, 204 (16.4%) had an abnormal CST result. In these patients with AI, median DHEAS level was lower compared to patients without AI (21.2 vs 96.0 µg/dl, $P<0.001$). Similarly, patients with AI had a lower median baseline cortisol level than patients without AI (4.3 vs 8.0 µg/dl, $P<0.001$). Among all patients, baseline DHEAS level predicted an abnormal CST result with an accuracy rate of 73.7%. The optimal DHEAS cutoff point was determined to be 51 µg/dl with a sensitivity of 73.0%, specificity of 73.9%, PPV of 35.4%, and NPV of 93.3%. In our subgroup analysis, men had an optimal DHEAS cutpoint of 59.2 µg/dl with an accuracy rate of 72.2%, sensitivity 73.0%, specificity 72.0%, PPV 45.1%, and NPV 89.4%. While women $<$50 years old had an optimal DHEAS cutpoint of 63.9 µg/dl with an accuracy rate of 75.9%, sensitivity 75.9%, specificity 75.9%, PPV 29.2%, and NPV 96.0%, post-menopausal women had a lower optimal DHEAS cutpoint of 21.3 µg/dl with an accuracy rate of 71.1%, sensitivity 70.7%, specificity 71.2%, PPV 41.0%, and NPV 89.6%.
Conclusions
DHEAS is a valuable diagnostic test which can effectively rule out AI in many patients due to its high negative predictive value. For the majority of patients, a baseline DHEAS level $>$51 µg/dl makes a diagnosis of AI unlikely and additional dynamic testing may not be necessary.

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P425

Income and work loss in patients with Addison's disease in Sweden: A nationwide population-based study

Stavros Stergianos[1,2], Åsa Hallqvist Everhov[3,4], Jonas Söderling[3], Ragnhildur Bergthorsdottir[5,6], Jeanette Wahlberg[7], Olle Kämpe[1,8], Jakob Skov[2,9] & Sophie Bensing[1,2]
[1]Karolinska University Hospital, Department of Endocrinology, Stockholm, Sweden; [2]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [3]Karolinska Institutet, Clinical Epidemiology Division, Department of Medicine Solna, Stockholm, Sweden; [4]Karolinska Institutet, Department of Clinical Science and Education, Södersjukhuset, Stockholm, Sweden; [5]University of Gothenburg, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine at Sahlgrenska Academy, Gothenburg, Sweden; [6]Sahlgrenska University Hospital, Department of Endocrinology, Gothenburg, Sweden; [7]Örebro University, School of Medical Sciences, Faculty of Medicine and Health, Örebro, Sweden; [8]Karolinska Institutet, Department of Medicine (Solna), Center for Molecular Medicine, Stockholm, Sweden; [9]Karlstad Central Hospital, Department of Medicine, Karlstad, Sweden

Background
Previous studies have found reduced health-related quality of life and employability in patients with autoimmune Addison's disease (AAD). However, there are no large studies examining the economic cost of illness for the individual.

Objective
To study differences in income and work loss between patients with AAD and matched comparators.
Methods
In this cross-sectional study we linked the Swedish Addison Register and several Swedish national health registers to identify individuals of working age (18–64 years) with AAD and comparators from the general population, matched 1:5 by sex, age and region of residence. The study outcomes were taxable earnings, disposable income and mean annual days of work loss (sick leave or disability pension) during 2019. Quantile regression was used to calculate adjusted median differences in taxable earnings and disposable income (adjusted for age and sex), while linear regression was used to obtain adjusted mean differences in work loss days.
Results
We identified 1140 patients with AAD and 5700 comparators (51.6% female), with mean age 46.1 years. Type 1 diabetes was present in 15.7% of patients with AAD and 1.1% of the comparators. We found no significant difference in taxable earnings ($P=0.48$) or disposable income ($P=0.43$) between patients with AAD and their matched comparators. However, patients with AAD had significantly higher mean annual work loss, adjusted mean difference 14.4; 95% CI, 8.6–20.3 days, $P<0.001$. Subgroup analysis revealed that patients with short education (<9 years) or co-existence of type 1 diabetes had lower taxable earnings ($P=0.02$ and $P=0.006$), lower disposable income ($P=0.007$ and $P=0.02$) and higher mean annual work loss ($P=0.004$ and $P<0.001$).
Conclusion
Overall, patients with AAD have more work loss, but similar taxable earnings and disposable incomes compared to matched population comparators. One possible explanation is that the Swedish social welfare system partly compensates for the work loss financially. However, patients with AAD with lower levels of education or co-existent type 1 diabetes appear to be socioeconomically vulnerable.

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P426

Evaluation of quality of life by AddiQoL-30 compared to SF-36 in patients with previous long-term prednisolone treatment

Hajir Al-Jorani[1,2], Stina Willemoes Borresen[3], Lise Sofie Bislev[4,5], Richard Christian Jensen[1], Anja Fenger Dreyer[1,2], Simon Bøggild Hansen[4,5], Victor Brun Boesen[3], Louise Lehmann Christensen[1,2], Dorte Glintborg[1,2], Nanna Thurmann Jørgensen[3,6], Marianne Klose[3], Marie Louise Lund[3,6], Jelena Stankovic[4,5], Randi Tei[4,5], Ulla Feldt-Rasmussen[3,6], Jens Otto Jørgensen[4,5] & Marianne Andersen[1,2]
[1]Odense University Hospital, Department of Endocrinology, Odense, Denmark; [2]Research Unit OPEN, University of Southern Denmark, Department of Clinical Research, Odense, Denmark; [3]Copenhagen University Hospital, Rigshospitalet, Department of Endocrinology and Metabolism, Copenhagen, Denmark; [4]Aarhus University, Department of Clinical Medicine, Aarhus, Denmark; [5]Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus, Denmark; [6]Faculty of Health and Clinical Sciences, Copenhagen University, Department of Clinical Medicine, Copenhagen, Denmark

Background
Long-term prednisolone therapy may lead to subtle changes in circadian oscillations of the hypothalamic-pituitary-adrenal axis, which can affect quality of life of the patient. Low score of the Addison's disease-specific quality-of-life questionnaire (AddiQoL-30) could be a method to assess functional glucocorticoid-induced adrenal insufficiency.
Objective
To compare scores from AddiQoL-30 with generic Short Form (SF-36) questionnaire in patients terminating long-term prednisolone therapy.
Methods
This study is part of REPLACE, an ongoing multicenter, randomized, double-blinded placebo-controlled study, and sub-study of The Double Edge Study. We included 140 patients (72 women) with median age of 73 years, diagnosed with polymyalgia rheumatica and/or giant cell arteritis, where prednisolone was terminated during 2–12 weeks. AddiQoL-30 and SF-36 questionnaires as well as a clinical examination were carried out, and baseline standardized fasting cortisol levels were assessed. Multiple linear regression models were used to evaluate associations between AddiQoL-30 and SF-36.
Results
Patients with low AddiQoL-30 scores ($\leq$85) had significantly lower baseline cortisol levels ($P=0.03$) (abstract ID: 5059). In patients with low AddiQoL-30 scores, baseline cortisol showed positive association with the four SF-36 domains vitality, role limitations physical, social and physical functioning. The estimate for vitality in patients with AddiQoL-30 scores $\leq$85 was significantly different from patients with AddiQoL-30 scores >85 (P-interaction $=0.01$). In patients with AddiQoL-30 scores >85, associations between SF-36 and cortisol were not significant.
Conclusion
A low AddiQoL-30 score $\leq$85 may align with the SF-36, especially regarding the vitality dimension, in patients with previous long-term prednisolone use. The REPLACE sub-study (abstract ID: 4814) is still recruiting, and baseline and follow-up investigations of AddiQoL-30 and SF-36 questionnaires are ongoing.
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P427

First report of inclisiran utilization for hypercholesterolemia treatment in real-world clinical settings in a middle east population

Tanveer Ashraf[1], Sajid Iqbal[1], Hani Sabbour[2], Nader Lessan[1] & Adam Buckley[1]
[1]Imperial College London Diabetes Centre, Research Department, United Arab Emirates; [2]Imperial College London Diabetes Centre, Cardiology, Abu Dhabi, United Arab Emirates

Purpose
Inclisiran is the first small interfering RNA (siRNA)-based treatment approved to reduce pro-atherogenic lipoproteins in patients with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C). We report, to the best of our knowledge, the first evaluation of its effects in a Middle Eastern population.
Methods
Retrospective review of patients initiating inclisiran treatment at an outpatient Diabetology/Endocrinology and Cardiology Centre between May 2021 and December 2022. All individuals followed up for $\geq$90 days or with at least one lipid determination post-initiation were included. Participants were categorized into primary ($n=57$) and secondary prevention ($n=89$) groups according to previous ASCVD.
Results
Inclisiran was initiated in 146 individuals, mean $\pm$ S.D. age 54.8 $\pm$ 12.12 years, 82 (56.2%) males, 28 (19.2%) with FH diagnosis, 89 (61%) with Diabetes Mellitus (DM) and 35 (23.9%) with statin intolerance. Median follow-up was 137 (90–193) days. At 90 days, median (IQR) reductions in serum LDL-cholesterol (LDL-C), and triglycerides were respectively −37.9% (−9.5%; −51.2%), −12.0% (−9.8%; −40.5%) in primary prevention, and −54.1% (−17.1%; −71.4%), and −15.3% (−14%; −38.8%) in secondary prevention (all P-values < 0.001). LDL-C goals were attained in 110 (75.3%) patients. Non-attainment of LDL-C goal was attributed to system effect in 26 (72.2%), biological effect in 5 (13.9%), and discontinuation of treatment in 5 (13.9%) patients. Therapy was well tolerated.
Conclusion
To the best of our knowledge, this current study is the first from the Middle East and North Africa (MENA) region that reports the real-world efficacy and safety of inclisiran in a mixed-risk population of individuals with HeFH and other non-FH indications. Clinically meaningful and sustained reductions in pro-atherogenic lipids with good tolerability were observed after inclisiran initiation.
Keywords: Inclisiran, small interfering RNA (siRNA), Familial hypercholesterolemia, Atherosclerotic cardiovascular disease, Low-density lipoprotein cholesterol, Diabetes Mellitus, PCSK9-inhibitor.

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P428

Development and validation of LC–MS/MS assay for simultaneous determination of thirteen steroid hormones and two synthetic steroids in saliva: potential utility for pediatric population and beyond

Sandra R Dahl, Liv Hanne Bakke, Per Medboe Thorsby & Svetlana Zykova
Hormone Laboratory, Department of Medical Biochemistry, Oslo University Hospital, Oslo, Norway

Background
Saliva samples offer the possibility to obtain stress-free non-invasive samples, also for home-testing, especially useful when blood collection is either undesirable or difficult.
The aim of this work was to develop an LC–MS/MS method for the determination of clinically relevant steroid hormones cortisol, cortisone, 11-deoxycortisol, 21-deoxycortisol, 17OH-progesterone, aldosterone, corticosterone, deoxycorticosterone, betamethasone, dexamethasone, testosterone, androstenedione, DHEAS, DHEA and 17OH-pregnenolone. A special effort was made to adopt the method to neonatal population with respect to low sample volumes and multiplexing.
Results
Ten microliters were acceptable but 50 µl preferable sample volume for all the analytes. Cortisol, cortisone, aldosterone, 11-deoxycortisol, deoxycorticosterone, dexamethasone, betamethasone, 17OH-pregnenolone and DHEAS could be determined in as little as 2–5 µl saliva. Total analytical variation was $<15\%$, except for 17OH-progesterone, deoxycorticosterone, 17OH-pregnenolone, 21-deoxycortisol, androstenedione, DHEA and betamethasone, that could only be determined semi-quantitatively or qualitatively. The minimum turnaround time is 3–4 h. Recovery from the best-performing sample collection swab SalivaBio ranged from 83 to 127%. Aldosterone, cortisone and DHEA were more stable in saliva compared to serum when stored at ambient temperature for one week. Corticosterone and 17OH-progesterone needed immediate freezing.
Conclusion
The non-invasiveness, small saliva volume requirement, on-swab stability and analytical performance make the method relevant for both research and diagnostics, above all in the setting of neonatal intensive care unit.
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P429

Establishing cut-off values for late-night salivary cortisol and cortisone measured by LC–MS/MS in the diagnosis of endogenous hypercortisolism

Karlijn Koops[1,2,3], Peter H Bisschop[2,4], Annemieke C Heijboer[1,2,3,5] & Jacquelien Hillebrand[2,3]
[1]Amsterdam UMC location Vrije Universiteit Amsterdam, Department of Laboratory Medicine, Endocrine Laboratory, Amsterdam, Netherlands; [2]Amsterdam Gastroenterology, Endocrinology & Metabolism, Amsterdam, Netherlands; [3]Amsterdam UMC location University of Amsterdam, Department of Laboratory Medicine, Endocrine Laboratory, Amsterdam, Netherlands; [4]Amsterdam UMC location University of Amsterdam, Department of Endocrinology and Metabolism, Amsterdam, Netherlands; [5]Amsterdam Reproduction & Development Research Institute, Amsterdam, Netherlands

Background
Diagnosing endogenous Cushing's syndrome (CS) is often challenging because of the difficulty in interpreting results of dynamic endocrine tests. One of the recommended initial tests is the measurement of late-night salivary cortisol (LNSaCl). Some articles describe added value of late-night salivary cortisone (LNSaCn) measurements. However, published cut-off values of LNSaCl and LNSaCn vary widely between studies, which may be related to different experimental set-ups.
Aim
The aim of this study was to establish the cut-off values for LNSaCl and LNSaCn that differentiate between patients with and without endogenous hypercortisolism using LC–MS/MS.
Methods
The study included data from consecutive patients who underwent dynamic endocrine function tests to evaluate endogenous hypercortisolism at Amsterdam UMC between December 2015 and February 2022. The indications for testing included clinical suspicion, adrenal or pituitary incidentalomas, or evaluation in the context of genetic diseases. Endogenous hypercortisolism was diagnosed or excluded based on follow-up of more than 12 months, histology, symptom reduction, and the need for hydrocortisone supplementation postoperatively. Salivary samples were collected between 2200 and 2359 h on two consecutive days and analyzed for cortisol and cortisone using an in-house developed and well standardized liquid chromatography coupled to mass spectrometry method (LC–MS/MS). Data analysis was based on the lowest of the two LNSaCl and LNSaCn measurements. The test's diagnostic accuracy was evaluated using ROC curve analysis.
Results
Twenty-nine patients with endogenous CS (21 of pituitary and 8 of adrenal origin) and 497 patients without endogenous hypercortisolism were included. The median LNSaCl was 7.8 nmol/l (IQR: 8.5) for patients with CS ($n=25$ eligible measurements), and 1.0 nmol/l (IQR: 0.9) for patients without CS ($P=<0.001$, $n=430$ measurements). The median concentration of the LNSaCn measurements was 35.5 nmol/l (IQR: 30.8) for patients with CS ($n=16$ measurements), and 5.3 nmol/l (IQR: 4.5) for patients without CS ($n=311$ measurements, $P=<0.001$). For LNSaCl, a cut-off of 2.25 nmol/l provided the optimal diagnostic accuracy for endogenous hypercortisolism with a sensitivity of 96% and a specificity of 86% (positive predictive value (PPV) = 28.6%, negative predictive value (NPV) = 99.7%). For LNSaCn this was 15.5 nmol/l with a sensitivity of 93.8% and a specificity of 94.5% (PPV = 46.9%, NPV = 99.7%).
Conclusion
We established optimal cut-off values for cortisol and cortisone in saliva measured by LC–MS/MS. The cut-off of LNSaCn provided the highest accuracy. Using these cut-off values will add to the performance of screening for endogenous hypercortisolism and these can be used by other laboratories following method comparison.
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P430

Holistic nursing care in acromegaly: A case report

Nermin Olgun[1], Selda Çelik[2] & Merve Murat[2]
[1]Hasan Kalyoncu University, Şahinbey/Gaziantep, Türkiye; [2]Health Sciences University

Background
Acromegaly is an uncommon metabolic condition characterized by the excessive secretion of growth hormone after the closure of epiphyseal plates. The onset of acromegaly is gradual, and its progression is slow. Manifestations of elevated growth hormone levels may remain inconspicuous for an extended period. Clinical indications include enlarged jaw, swelling in the hands and feet, pronounced facial bones, roughened facial features, nasal enlargement, tongue enlargement, deepening of the voice, snoring, sleep apnea, skin thickening, and excessive and unpleasant sweating.
Objective
This nursing case report aims to describe the comprehensive care provided to a 64-year-old male diagnosed with acromegaly and other chronical health care problems, emphasizing the collaborative approach among healthcare professionals to address the unique challenges associated with health conditions.
Methods
The patient presented with characteristic features of acromegaly, including acral enlargement, facial changes, and visual disturbances. A multidisciplinary healthcare team, comprising endocrinologists, other specialties such as neurosurgeons, ophthalmologists, and nurses, collaborated to formulate and implement a tailored care plan. The nursing care focused on symptom management, psychoeducation, and emotional support.
Results
The nursing interventions encompassed monitoring and managing the patient's physical symptoms, such as pain and discomfort related to acral enlargement, as well as addressing psychosocial aspects such as body image concerns and emotional well-being. Education about medication adherence, self-care strategies, and the importance of regular follow-up appointments was integral to empowering the patient in managing his chronic conditions.
Conclusion
This case report illustrates the pivotal role of nursing care in the holistic management of acromegaly. By providing patient-centered care that addresses both physical and emotional aspects, nurses contribute significantly to enhancing the overall well-being and quality of life for individuals with acromegaly. The collaborative effort among healthcare professionals is essential in ensuring comprehensive and effective care for patients with this rare endocrine disorder.
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P431

Cognitive functions in patients with mild autonomous cortisol secretion: Is it related with the serum brain-derived neurotrophic factor level?

Tugba Barlas[1], Muhammed Aksu[2], Ethem Turgay Cerit[1], Mehmet Muhittin Yalcin[1], Mujde Akturk[1], Fusun Toruner[1], Ayhan Karakoc[1] & Altinova Alev[1]
[1]Gazi University Faculty of Medicine, Endocrinology and Metabolism, Ankara, Turkey; [2]Gazi University Faculty of Medicine, Department of Psychiatry and Behavioral Sciences, Ankara, Turkey

Context
The impact of abnormal cortisol secretion on cognitive functions in patients with mild autonomous cortisol secretion (MACS) remains uncertain.
Objective
To assess cognitive functions, determine serum brain-derived neurotrophic factor (BDNF) concentration in patients with MACS, and investigate the possible association between cognitive subdomains and BDNF after minimizing the impact of body mass index (BMI) and visceral adiposity.

Methods
We included 84 participants: 28 patients with MACS, 28 patients with nonfunctional adrenal adenoma (NFAA), and 28 control subjects matched for age, gender, BMI, visceral fat and educational level. The serum BDNF concentration of participants was measured. DSM-5-focused interviews and Montreal Cognitive Assessments (MoCA) were carried out by an experienced psychiatrist.
Results
Patients with MACS had a higher BDNF concentration than the NFAA ($P=0.001$), while that of patients with NFAA was lower than the controls ($P=0.044$). There was a positive correlation between BDNF concentration and BMI ($r=0.227$, $P=0.038$), waist circumference ($r=0.248$, $P=0.042$), abdominal fat ($r=0.248$, $P=0.038$), visceral fat ($r=0.272$, $P=0.023$), LDL concentration ($r=0.486$, $P<0.001$), whereas HDL concentration was negatively correlated with BDNF concentration ($r=-0.349$, $P=0.003$) in the whole group. Furthermore, there was a positive relationship between BDNF concentration and the largest adenoma diameter ($r=0.311$, $P=0.020$) and cortisol level after 1 mg overnight dexamethasone (DST) ($r=0.292$, $P=0.032$) in patients with adrenal adenoma (MACS and NFAA groups). BMI and cortisol level after 1 mg DST were found to be the parameters most associated with BDNF concentration in linear regression analysis. No significant difference was found in total MoCA scores between MACS and NFAA groups ($P=0.967$), whereas those were lower than the control group ($P=0.016$, $P=0.008$ respectively). When the cognitive subdomains were examined seperately, MACS group performed higher memory score than NFAA group, but lower language scores than both the NFAA and control groups ($P=0.024$, $P<0.001$). In the whole group, there was a positive correlation between BDNF concentration and memory ($r=0.337$, $P=0.002$). DST and language were also negatively correlated ($r=-0.355$, $P=0.008$), while DHEA-S level was positively correlated with attention ($r=0.310$, $P=0.043$), language ($r=0.303$, $P=0.048$), as well as visuospatial and executive functions ($r=0.317$, $P=0.038$) in the whole group.
Conclusion
Chronic low-grade hypercortisolism is associated with elevated BDNF concentrations, which might be a protective factor for memory function in patients with MACS compared to NFAA.

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P432

Role of ccfDNA-based biomarkers in classification of adrenocortical adenomas

Mengjie Xu[1,2], David S Tourigny[3], Juliane Lippert[4], Ana Crastin[1], Silke Appenzeller[5], Miriam Felicitas Asia[6], Oskar Podstawka[1], Yasir Elhassan[6], Kassiani Skordilis[7], Alessandro Prete[1] & Cristina L Ronchi[1]
[1]University of Birmingham, Institute of Metabolism and System Research, Birmingham, UK; [2]Taihe Hospital, Hubei University of Medicine, Department of Endocrinology, Shiyan, China; [3]University of Birmingham, School of Mathematics, Birmingham, UK; [4]University of Wuerzburg, Institute of Human Genetics, Wuerzburg, Germany; [5]University Hospital of Wuerzburg, Core Unit Bioinformatics, Comprehensive Cancer Center Mainfranken, Wuerzburg, Germany; [6]Queen Elizabeth Hospital Birmingham NHS Trust, Department of Endocrinology, Birmingham, UK; [7]Queen Elizabeth Hospital Birmingham NHS Trust, Department of Renal Histopathology, Birmingham, UK

Background
Adrenocortical adenomas (ACA) can be associated with different degrees of cortisol excess. Genetic alterations in the cAMP/PKA pathway are observed in up to 60% of cases with overt Cushing syndrome (CS-ACA) and 15% of cases with mild autonomous cortisol secretion (MACS-ACA), while variants in the gene coding for β-catenin (*CTNNB1*) are more frequent in MACS-ACA and non-functioning adrenal tumours (NFAT). We aimed to test whether somatic variants could be detected in circulating cell-free DNA (ccfDNA) from patients with adrenal CS or MACS and potentially contribute to management strategies.
Methods
We investigated 44 patients, including 17 with MACS-ACA, 9 with CS-ACA, 12 with aldosterone-producing adenomas (APA), and 6 with NFAT. A total of 23 healthy subjects (HS) were used as controls. ccfDNA was extracted from EDTA blood samples with commercially available kits and ccfDNA concentrations quantified with fluorimeter. Tumour-DNA (T-DNA) was isolated from paraffin embedded tissue samples in 14/44 cases. Matched ccfDNA/T-DNA were sequenced using a customized panel including 32 genes (Cell3™ Target by Informed Genomics) and Illumina platform. Leucocyte DNA was used to filter out germline variants using TNhyplotyper2 (Sentieon) with an additional orientation bias model to remove strand bias artefacts. Only variant candidates that passed stringent filters were retained (read depth greater than 10, variant allele frequency greater than 0.1 in ccfDNA/T-DNA and less than 0.02 in paired leucocyte DNA).
Results
Patients with ACA had higher total ccfDNA concentrations than HS (0.155 ± 0.147 vs 0.052 ± 0.048 ng/μl, $P<0.001$), with CS-ACA showing the highest ccfDNA levels (0.267 ± 0.143 ng/μl, $P<0.005$ *vs* HS). ccfDNA concentrations did not correlate with age, sex, and maximum tumor diameter, but there was a trend toward a positive correlation with cortisol levels after overnight dexamethasone suppression test ($P=0.0641$, $R=0.29$). At T-DNA level, somatic variants were identified in 50% of ACA (i.e., *PRKACA* in 2/6 CS-ACA, *CTNNB1* in 2/4 MACS-ACA and 1/6 CS-ACA, and *KCNJ5* in 2/4 APA). Somatic mutations were not detected in any of the investigated ccfDNA samples.
Conclusions
Total ccfDNA concentrations are higher in patients with adrenal CS, likely due to an impact of the excessive circulating cortisol levels. Despite the presence of somatic variants in 50% of tumor samples from our ACA cohort, we did not detect any at ccfDNA level. Therefore, this approach appears ineffective for pre-operative evaluation of genetic alterations and clinical decision making.

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P433

Prediction of endogenous mineralocorticoid receptor activity by depressor effects of mineralocorticoid receptor antagonists in patients with primary aldosteronism

Makiko Ikemoto, Satoshi Morimoto & Ichihara Atsuhiro
Tokyo Women's Medical University, Department of Internal Medicine, Japan

Objective
Patients with primary aldosteronism have an increased risk of developing cardiovascular disease. The response to mineralocorticoid receptor antagonists (MRAs) varies among individuals, indicating diverse mineralocorticoid receptor activities in these patients. This study explored the factors linked to the efficacy of blood pressure reduction through MRAs in patients with primary aldosteronism.
Methods
We retrospectively investigated patients with primary aldosteronism who were newly administered MRA and had no changes in other antihypertensive medications during a 6-month treatment period. We assessed age, estimated daily salt intake, body fat percentage, clinic blood pressure, electrolytes in urine, eGFR, HbA1c, plasma renin activity, and plasma aldosterone concentration. The association between the reduction in blood pressure and patient characteristics before and after undergoing treatment with MRAs was examined. The blood pressure-lowering effect of MRAs was defined as the decrease in systolic BP (ΔsBP) divided by the spironolactone-equivalent dose of MRA at 3 and 6 months (ΔsBP 3M and ΔsBP 6M). The MRA dosage was based on the equivalent spironolactone dosage, with 100 mg spironolactone equal to 100 mg eplerenone or 5 mg esaxerenone.
Results
We examined the relationship between the reduction in blood pressure and patient characteristics in a group of 41 patients with primary aldosteronism (24 males, mean age 55 ± 13 years, including 34 patients diagnosed with bilateral primary aldosteronism) before and after undergoing treatment with MRAs. Significant reductions in office blood pressure were observed 3 and 6 months after treatment initiation. Single correlation analyses showed that the urinary chloride-to-potassium ratio displayed the strongest positive association with blood pressure reduction, surpassing plasma aldosterone concentration, plasma renin activity, and urinary sodium-to-potassium ratio, at 3 and 6 months. Multiple correlation analyses revealed a consistent and independent positive correlation between the urinary chloride-to-potassium ratio and blood pressure reduction at 3 and 6 months. The optimal threshold for the urinary chloride-to-potassium ratio with respect to its ability to lower blood pressure, was determined as 3.18. These results imply that the urinary chloride-to-potassium ratio may be independently associated with the effectiveness of blood pressure reduction facilitated by mineralocorticoid receptor antagonists.
Conclusion
The urinary chloride-to-potassium ratio could potentially serve as a valuable predictor of the effectiveness of MRAs and function as an indicator of endogenous mineralocorticoid receptor activity in patients with primary aldosteronism. Further investigation is needed to determine if similar associations exist in essential hypertension.

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Even a nonfunctional adrenal incidentaloma carries a higher metabolic disease risk: Cross-sectional controlled study

Hyo-Jeong Kim[1], Kyong Yeun Jung[1] & Kil-Young Kwon[2]
[1]Nowon Eulji Medical Center, Eulji University, Department of Internal Medicine, Seoul, Republic of South Korea; [2]Nowon Eulji Medical Center, Eulji University, Department of Family Medicine, Seoul, Republic of South Korea

Background
Although metabolic syndrome was prevalent in patients with autonomous cortisol secretion, there are limited data for those with nonfunctioning adrenal incidentaloma (NFAI). This study aimed to compare metabolic features and body composition of patients with NFAI to referent subjects without adrenal mass.
Methods
This study included 141 patients with biochemically confirmed NFAI and 1:3 age and sex matched controls without adrenal incidentaloma ($n=420$) among subjects who underwent both abdominal computed tomography and dual-energy X-ray absorptiometry (DEXA) at a Eulji healthcare center in 2013-2020. Among 141 patients with NFAI, 48 patients underwent DEXA, so we evaluated body composition of these patients compared to 1:3 age, sex and underlying metabolic disease matched controls ($n=143$).
Results
Mean age was 56.5 ± 12.0 years and 52% were women in 141 patients with NFAI. The NFAI group had a higher body mass index compared to control group (25.1 ± 4.1 vs 24.1 ± 3.4 kg/m^2, $P=0.011$). Age, sex and BMI adjusted logistic regression showed significantly higher odds ratios (ORs) for diabetes, hypertension and dyslipidemia in NFAI (OR [95% confidence interval], 2.33 [1.45–3.74], 1.92 [1.22–3.03] and 2.26 [1.48–3.45], respectively. The body fat index (8.0 ± 0.3 vs 7.1 ± 0.1 kg/m^2, $P=0.027$) and total fat mass (20.7 ± 0.5 vs 18.5 ± 0.3 kg, $P=0.005$) were higher and skeletal muscle index was lower (6.4 ± 0.1 vs 6.7 ± 0.1 kg/m^2, $P=0.042$) in NFAI group compared to control.
Conclusion
Patients with NFAI were associated with higher risk for diabetes, hypertension and dyslipidemia and demonstrated abnormal body composition. Even a non-functioning hormone status may impact metabolic feature in patients with adrenal incidentaloma.

Keywords: nonfunctioning adrenal incidentaloma, metabolic syndrome, body composition

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Performance of plasma cortisol at 1600 hours for the diagnosis of Cushing syndrome

Hippolyte Dupuis[1], Merlen Emilie[1], Elices Diez Julien[2], Balaye Pierre[2], Cortet Christine[1], Jannin Arnaud[1], Do Cao Christine[1], Douillard Claire[1], Ramdane Nassima[3], Soudan Benoit[4], Marie-Christine Vantyghem[1] & Stéphanie Espiard[1]
[1]Lille University Hospital, Department of Endocrinology, Diabetology and Metabolism, Lille, France; [2]Lille University Hospital, Include – INtegration Center of the Lille University hospital for Data Exploration, Lille, France; [3]Lille University hospital, Department of statistics and data management, Lille, France; [4]Lille University Hospital, Biology Department, Lille, France

Introduction
Guidelines recommend using first-line tests, including 24-hour urine-free cortisol (UFC), overnight 1-mg dexamethasone suppression test (DST), and late-night salivary cortisol (LNSC) for the positive diagnosis of hypercortisolism. Unfortunately, LNSC access is constrained in certain institutions, requiring, as an alternative, hospitalization for midnight plasmatic cortisol (F00h) measurement. This study explores the diagnostic potential of afternoon plasma cortisol (F16h), aligning with the contemporary shift toward outpatient care.
Materials and methods
Patients assessed for suspicion of Cushing's syndrome at a single center from September 2017 to Jully 2021. Plasma cortisol at 8h (F8h), 16h (F16h), and midnight (F00h), DST, and UFC performed in a single center were extracted via the Integration Center of the Lille University Hospital for Data Exploration. Two endocrinologists reviewed electronic patient's medical files to establish the positive diagnosis of CS. Patients with interfering treatment, including oestrogen therapy, and patients assessed for adrenal incidentalomas or recurrence of Cushing's disease were excluded.
Results
Among 1922 cortisol cycles, 589 patients (41.3% women, mean age 50.7 ± 16.30 years) were included, with 49 (8.3%) diagnosed with CS. There were no significant differences between age and sex between patients with CS (CS group) and patients without CS (no-CS group). The F00h, F16h, 24h-UFC and DST were significantly higher in the CS group compared to the no-CS group (F00h: 8.60 µg/dl [5.60–11.50] vs 2.65 µg/dl [1.70 to 4.10], $P<0.001$; F16h: 10.80 µg/dl [8.40–14] vs 6.40 µg/dl [4.70–8.60], $P<0.001$; UFC: 71 µg/24h [38.4–116] vs 30 µg/24h [21–45], $P<0.001$; DST: 4.4 µg/dl [3 to 9.3] vs 1 µg/dl[1–1.3], $P<0.001$). F16h significantly correlated with DST, 24h-UFC and F00h in both groups, with a stronger correlation in the CS group. The area under the ROC curve (AUC) for the F16h did not differ from UFC yet its sensitivity was higher using the optimal diagnostic threshold. The AUC for the F16h was significantly lower than that for F00h and DST. The optimal cut-off of the F16h was 7.9 µg/dl, achieving 83.7% sensitivity and 67.4% specificity.
Discussion
If LNSC should remain the first-line test for evaluating the circadian rhythm of cortisol, when not available, the F16h could be an interesting alternative for diagnosing hypercortisolism in an ambulatory setting. Further studies are required to assess its variability and confirm its utility in different situations, with a specific focus on evaluating recurrences of Cushing's disease.

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Different modes of cell death induced by chemotherapeutic agents in treatment resistant and sensitive models of adrenocortical carcinoma

Sarah Feely[1], Nathan Mullen[1], Cong Hong[1], Constanze Hantel[2], William Rainey[3] & Michael Dennedy[1]
[1]Discipline of Pharmacology and Therapeutics, School of Medicine, Galway, Ireland; [2]Department of Medicine IV, University Hospital, Ludwig Maximillan University of Munich, Munich, Germany; [3]Department of Molecular and Integrative Physiology, University of Michigan, Ann Arbor, USA

Adrenocortical carcinoma (ACC) is a rare aggressive cancer with poor survival. Adjuvant mitotane is the only approved drug for treatment of ACC. It improves survival but its use is limited by poor tolerability and drug resistance. For metastatic ACC, combination chemotherapy, using mitotane and etoposide, doxorubicin, and cisplatin improves survival, but efficacy is limited. Better understating the cytotoxic mechanisms of mitotane offers potential to develop improved therapeutic options for ACC. To investigate the underlying mechanisms in vitro, human ACC cells (HAC15 and H295R), in monolayer cell culture were treated with increasing concentrations of mitotane. Cell death was evaluated at 6 and 24 h using flow cytometry analysis of Annexin V and Sytox Blue. This was complemented by Incucyte ® Live-Cell Analysis System imaging of annexin V and Sytox Blue staining. Expression of the markers of apoptosis, cleaved caspase 3, and necroptosis, phosphorylated MLKL and RIPK1 was measured at 6 and 24 h. Mitotane significantly reduced the viability of H295R cells at 6 and 24 h at the therapeutic concentration of 50 µM ($P>0.0001$), thereby demonstrating treatment-sensitivity. In HAC15 cells, a supratherapeutic dose of 200 µM was needed to significantly reduce viability ($P>0.05$) at 24 h, indicating resistance to mitotane treatment at therapeutic concentrations. There was increasing Annexin V fluorescence with increasing mitotane concentration in H295R and HAC15 cells ar 6 and 24 h without higher coinciding staining with Sytox Blue. Video analysis demonstrated these findings. Cleaved caspase 3 expression was associated with mitotane-induced cell death in H295R cells at 6 and 24 h, indicating apoptosis. HAC15 cells demonstrated cleaved caspase 3 expression only at the highest concentration of mitotane exposure (600 µM) at 6 h, without appreciable expression at 24 h. Phosphorylated-MLKL and RIPK1 expression was seen in controls and all mitotane doses in both cell lines at both timepoints, indicating necroptosis. In this study, H295R cells, representing a treatment-sensitive model of Mitotane undergo both apoptotic and necroptotic cell death at 6 and 24 h of mitotane exposure. In contrast, HAC15 cells, demonstrated relative treatment resistance to mitotane, and undergo necroptotic cell death only. These results highlight the importance of understanding and targeting non-apoptotic and necroptotic cell death pathways, particularly when evaluating mechanisms of treatment resistance in ACC. Given the difference in the mechanism of cell death in treatment-sensitive and treatment-resistant cells, further exploration of necroptosis is necessary to better understand how ACC cells may manifest treatment resistance.

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Adrenocortical activity in patients with vasovagal syncope

Barbora Bačkorová[1], Zora Lazúrová[2], Monika Lukáčová[3], Peter Mitro[3] & Ivica Lazúrová[1]
[1]Louis Pasteur University Hospital, 1st Department of Internal Medicine, Košice, Slovakia; [2]Louis Pasteur University Hospital, 4th Department of Internal Medicine, Košice, Slovakia; [3]East Slovak Institute of Cardiovascular Diseases, 1st Department of Cardiology, Košice, Slovakia

Background
Syncope is a transient loss of consciousness resulting from cerebral hypoperfusion. Despite the extensive efforts by the scientific community over decades, the pathophysiology remains unclear. Although syncope itself is a reversible, short-lasting, benign condition, it negatively impacts quality of life. Vasovagal syncope (VVS) is a form of orthostatic intolerance (OI). Its clinical signs such as dizziness and hypotension may mimic symptoms of adrenal insufficiency. The objective of this study was to evaluate the adrenal gland function in patients with vasovagal syncope after stimulation with synthetic ACTH.
Methods and results
The study involved 42 participants (33 females and 9 males, aged 22–82 years, median 51 years), including 27 patients diagnosed with vasovagal syncope using the head-up tilt (HUT) test. The control group consisted of 15 healthy individuals with no history of syncope. Serum cortisol and aldosterone concentrations were measured under basal conditions and at 30 and 60 min after intramuscular ACTH stimulation. Patients with VVS had significantly higher cortisol levels at baseline (441 ± 143 vs 331 ± 84.7 nmol/l, $P = 0.01$), at 30 min (802 ± 143 vs 686 ± 105 nmol/l, $P = 0.009$) and at 60 min (931 ± 141 nmol/l vs 793 ± 147 nmol/l, $P = 0.005$) after ACTH administration (Synacthen 250 μg). Plasma aldosterone increased after ACTH stimulation, but did not show significant differences between the two studied groups. There were no significant differences in measured hormones between males and females. Furthermore, there was also no significant correlation between cortisol levels and systolic or diastolic blood pressure or heart rate.
Conclusion
Patients diagnosed with VVS have higher cortisol levels both at baseline and after ACTH stimulation. This finding indicates that individuals with VVS have a hyperactivated adrenal cortex potentially as a response to the orthostatic stress induced by syncope, which acts as a stressful stimulus on the autonomic nervous system.
Key words: orthostatic intolerance, vasovagal syncope, adrenal cortex, cortisol, aldosterone

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A service review of phaeochromocytoma management at the regional adrenal referral centre

Hina Aslam[1], Katherine Alington[1], Ma'en Al-Mrayat[1], Diane Bray[1], C Richard W Lockyer[2] & Jana Bujanova[1]
[1]University Hospital Southampton NHS Foundation Trust, Department of Diabetes and Endocrinology, Southampton, UK; [2]University Hospital Southampton NHS Foundation Trust, Department of Urology, Southampton, UK

Aims
The aim of this project was to conduct a service review of ph*a*eochromocytoma management and to benchmark local practice against national guidelines and recommendations defined in the 'Getting It Right First Time' (GIRFT) national report.
Methods
Electronic patient records were searched for patients referred to our centre, within our catchment area and from peripheral centres, with phaeochromocytoma between 2017 to February 2023. Data on their presentation, treatment, perioperative complications and follow-up were collected.
Results
Forty patients were identified during this period (average 6.5 patients/year). 21 (52.5%) of patients were referred from peripheral centres and 19 were internal referrals. Twenty-three (57.5%) presented incidentally, 11 (27.5%) with typical symptoms and 6 (15%) identified on surveillance of genetic syndromes. Twenty-five (65%) had tumour size between 2 and 6 cm and 5 (12.5%) >6 cm. Ninety-five percent were discussed at the adrenal multidisciplinary team meeting (MDT). 30 (75%) had adrenalectomy (80% laparoscopic, 20% open), 8 were managed conservatively, one received MIBG therapy for metastatic disease and one had no follow-up data. None of those managed conservatively were hospitalised for reasons related to their phaeochromocytoma during period covered by this review. Ninety-five percent of patients received preoperative medical preparation, with twice as many patients treated with doxazosin (57.5%) than phenoxybenzamine (27.5%). 57% received concomitant beta-blocker. Most achieved blood pressure (86%) and heart rate (93%) targets preoperatively. Sixty-seven percent of surgically treated patients, had uneventful intraoperative period, 33% experienced haemodynamic instability, mainly labile BP and intraoperative hypotension. 43% had a postoperative haemodynamic complication, mostly hypotension requiring inotrope support. 45% receiving phenoxybenzamine preoperatively experienced intraoperative complication versus 33% of those on doxazosin. 45% receiving phenoxybenzamine experienced postoperative complication versus 40% receiving doxazosin. 19 (63%) had a PASS score included in their histology report (PASS < 4 in 14 and PASS > 4 in 5 patients). 83% of patients had metanephrines performed 12 weeks postoperatively, whilst only 47% of patients had postoperative surveillance imaging at 3–6 months. 63% underwent annual metanephrines screening. 63% of surgically treated patients were offered genetic testing.
Discussion
Our review showed effective collaborative working of the adrenal MDT with peripheral centres. Doxazosin performed slightly better in terms of risk of peri/postoperative complications and was better tolerated. We identified developmental opportunities for perioperative and follow-up phaeochromocytoma pathways led by a specialist endocrine nurse with an independent prescriber qualification. We also identified a need for a standardised postoperative follow-up across the peripheral hospitals including consideration of genetic testing.
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NFAT and risk of dementia

Hadis Mirzaei[1,2,3,3], Jekaterina Patrova[1], Buster Mannheimer[4], Jonatan Lindh[5] & Henrik Falhammar[6,7]
[1]Department of Endocrinology, Södersjukhuset, Stockholm, Sweden; [2], [3]Karolinska Institute, Department of Clinical Science and Education, stockholm, Sweden; [4]Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden; [5]Department of Laboratory Medicine, Division of Clinical Pharmacology, Karolinska Institutet, Stockholm, Sweden, stockholm, Sweden; [6]Karolinska Institutet, Department of Endocrinology, stockholm, Sweden; [7]Karolinska Institute, Stokcholm, Sweden

Importance
It is not known if non-functional adrenal tumors (NFATs) are associated with dementia.
Objective
To analyze incidence and prevalence of dementia in individuals with NFAT.
Design, setting and participants
A national retrospective register-based study in patients with NFAT diagnosed in Sweden 2005–2019 and controls without adrenal tumors followed until death or end of 2019 was conducted. Individuals with a diagnosis of adrenal hormonal excess or previous malignancy were excluded.
Exposures
NFAT diagnosis.
Main outcomes and measures
Main study outcomes were prevalence and incidence of dementia, after adjustment for sex, age and comorbidities. Secondary outcomes were Alzheimer's and vascular dementia.
Results
Among 20390 cases, 12 120 (59.4%) were women, and the median (IQR) age was 66 (57; 73) years. Among 125 392 controls, 69 994 (55.8%) were women, and the median (IQR) age was 66 (57; 73) years. Previous dementia was less common in patients diagnosed with NFAT compared to controls (odds ratio (OR) 0.59, 95% CI 0.50–0.69, adjusted OR 0.47, 95% CI 0.56). We obtained similar results för Alzheimer's dementia (odds ratio (OR) 0.48, 95% CI 0.38–0.62 adjusted OR 0.44, 95% CI 0.34–0.57). Vascular dementia were also less common in patients with NFAT compared to controls (odds ratio (OR) 0.71, 95% CI 0.52–0.94, adjusted OR 0.48, 95% CI 0.35–0.64). During the follow-up period (5.4years (IQR 2.5–8.8)) dementia incidence was similar in patients with NFAT and controls (hazard ratio (HR) 1.06, 95% CI 0.97–1.15, adjusted HR 1.06). For Alzheimer's and vascular dementia the incidences were also similar between patients with NFAT and controls (HR 0.86, 95% CI 0.73–1. 00, adjusted HR 0.94, 95% CI 0.8–1.1 and HR 1.29, 95% CI 1.08–1.53, adjusted HR 1.13 (95%CI 0.95–1.35)).
Conclusions and relevance
NFAT was not associated with increased risk for all-cause dementia, Alzheimer's or vascular dementia.
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The challenges of adrenal incidentaloma evaluation in dialysis patients

Mihaela Florea, Stefana Bilha, Viviana Popa, Irina Puscasu, Alexandru Florescu, Anca Matei, Letitia Leustean & Cristina Preda
'Grigore T. Popa' University of Medicine and Pharmacy Iasi, Endocrinology, Iasi, Romania

Introduction
Chronic kidney disease (CKD) is associated with alterations in endogenous glucocorticoid regulation through various mechanisms: longer plasma cortisol half-life, reduced renal cortisol clearance, loss of 11b-HSD type 2 activity in the kidney contributing to an elevated cortisol/cortisone ratio, less effective hepatic metabolism of cortisol and, finally, hyperactivation of the hypothalamus-pituitary-adrenal axis due to acidosis, chronic stress, and inflammation.
Case report
We present the case of a 63-year-old woman, with cardiovascular, renal, and gastrointestinal comorbidities (arterial hypertension, heart failure, end-stage chronic kidney disease undergoing hemodialysis for 5 years, chronic hepatitis C) that was referred to the Endocrinology Department for uncontrolled blood pressure (220 mmHg) and an incidentally discovered right adrenal mass of 22/11 mm, with radiological features suggestive of adenoma. Clinical examination revealed a BMI of 33.9 kg/m^2, blood pressure of 160/80 mmHg, pale, dehydrated skin and anuria. Hormonal evaluation revealed normal 0800 h ACTH (21.5 pg/ml) and cortisol levels (19.8 µg/dl), normal free plasma metanephrine levels, elevated late-night salivary cortisol (LNSC):85.1 nmol/l (reference range, <11.3) and lack of suppression of serum cortisol on 1 mg, 2×2 mg and 8 mg dexamethasone suppression tests. DHEAS levels were in the low-normal range. Despite biological tests suggesting autonomous cortisol secretion, the patient did not exhibit glucose and lipid metabolism abnormalities (normal plasma glucose, HbA1c, lipid profile), therefore periodic follow-up was recommended. At one-year follow-up, biochemical testing showed a normal LNSC (8.5 nmol/l), normal 0800 h ACTH and cortisol and lack of adequate suppression after 8 mg overnight dexamethasone suppression (cortisol level of 5.79 µg/dl). Follow-up adrenal CT scan didn't show any significant changes. In the absence of significant metabolic disturbances and considering the limitations of hypercortisolism assessment in CKD, we opted for periodical follow-up.
Discussions
One particular feature of investigating adrenal incidentalomas in dialysis patients is the difficulty to distinguish autonomous cortisol secretion from the impact of chronic kidney disease on cortisol metabolism. False-positive results may occur at screening investigations for hypercortisolism, such as late-night salivary cortisol or low-dose dexamethasone tests. In our case, a repeated value of LNSC within the normal range was not in favor of a definitive diagnosis of Cushing syndrome. More so, metabolic complications, such as dyslipidemia and glycemic abnormalities, were lacking. In such patients, clinical and biological follow-up and evaluation of comorbidities potentially attributable to cortisol excess (diabetes mellitus, dyslipidemia, osteoporosis) is recommended.

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Association between endothelial dysfunction and androgen levels in men with coronary artery disease

Shafaat Talib[1], Pooja Alipuria[2] & Atush Alipuria[3]
[1]MGM Medical College & Hospital, Internal Medicine, Aurangabad, India; [2]Yashoda Super Speciality MediCentre, Karkardooma, Internal Medicine, New Delhi, India; [3]Yashoda Super Speciality Hospital, Ghaziabad, India

Background
The available literature is meagre on relationship of Androgen levels in Coronary Artery Disease (CAD).
Objective
The current study analyzes the androgen levels (Total Testosterone, Free Testosterone, and Dehydroepiandrosterone sulfate (DHEA-S)) in relation to endothelial dysfunction and graded coronary artery disease.
Design
Serum androgen levels were measured in 112 angiographically proven, stable CAD male subjects, who were assessed by flow mediated dilatation (FMD) of brachial artery using angiodefender device. Estimation of DHEA-S & Total Testosterone (TT) were carried out by electrochemiluminescent immunoassay and Free Testosterone (FT) by enzyme linked immunosorbent assay. Pearson Correlation, t-Test and multivariate analysis were applied for the analysis of risk factors of coronary artery disease. The Mann–Whitney *U* test and Kruskal Wallis test were applied with 95% confidence interval wherever necessary. Probability value of less than 0.05 was considered statistically significant.
Results
In our study, FMD provides the information on the extent and the severity of CAD ($P<0.0001$).The low serum total testosterone level though correlates with cardiovascular risk factors but do not correspond to the severity of CAD viz. single, double and triple vessel disease. Multivariate analysis was applied to analyze the correlation of risk factors of CAD with Model A and B as dealt in methodology. The multivariate results revealed Model A was significant predictor of Dheas and total testosterone values of the patient, whereas the other model was statistically inconclusive. The results also showed significant association between androgen levels and endothelial dysfunction, wherein age being a confounding independent parameter.
Conclusion
It is concluded that age adjusted androgen levels remained confounding factor in atherogenesis, hence also a cardiovascular risk factor of CAD. The subject needs more focus with larger group of patients.

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Premature Adrenarche and metabolic dysfunction – a systematic review and meta-analysis

Wogud Ben Said[1,2,3], Ioannis Lempesis[3], Silvia Fernandez Garcia[3], Shakila Thangaratinam[2,3], Wiebke Arlt[4] & Jan Idkowiak[1,2,3]
[1]Birmingham Women's and Children's NHS Foundation Trust, Department of Endocrinology and Diabetes, Birmingham; [2]Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners.University of Birmingham, Birmingham, UK; [3]University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, UK; [4]MRC London Institute of Medical Sciences (New building), London, UK

Background
Androgen excess frequently manifests in pre-pubertal children as premature adrenarche (PA). PA is characterised by the development of pubic and axillary hair, adult-type body odour in girls <8yrs and in boys <9yrs. PA may be a forerunner condition of polycystic ovary syndrome (PCOS), a complex metabolic disorder characterised by androgen excess. It is well established that women with PCOS have high risk of insulin resistance and frequently develop type 2 diabetes, dyslipidaemia, hypertension, and fatty liver disease. Importantly, androgens are identified as independent drivers to accelerate metabolic risk in PCOS. Whilst the link between PCOS and metabolic risk is well established, there is paucity of data on the risk for children with PA to develop metabolic dysfunction.
Objective
We conducted a systematic review and meta-analysis on metabolic disturbances in children with PA.
Methods
Published cross-sectional case/control studies were identified using Medline, Embase and Cochrane Library. Key outcome measures: Mean difference in anthropometric measures (height SDS, BMI SDS), indices of glucose metabolism (fasting insulin/glucose, HOMA-IR, HbA1c) and measures of lipid metabolism in children with PA compared to healthy controls.
Results
From 4640 records identified via electronic databases, 25 cross-sectional studies were selected, reporting on 823 children with PA and 707 healthy controls. Height SDS (mean difference [MD] 0.66; 95% confidence interval [CI_{95}] 0.36–0.95; $I^2=79\%$) and weight SDS (MD: 0.63; CI_{95} 0.33 −0.93; $I^2=53\%$) were significantly higher in PA group. These findings persist with subgroup analysis by PA definition, sensitivity analysis for gender and risk of bias assessment. PA children also have higher fasting insulin levels than controls (MD: 15.04; CI_{95} 5.27–24.81 pmol/l; $I^2=91\%$). Fasting glucose levels, HOMA-IR, mean serum glucose, mean serum insulin and HbA1c did not differ between PA and controls. Total cholesterol, LDL, HDL and VLDL were similar in both groups.
Conclusion
Our systematic review and meta-analysis with a pooled sample of more than 800 children with PA revealed higher fasting insulin levels but no other significant metabolic disturbances. However, we observed statistical and methodological heterogeneity. A unified approach in the assessment of metabolic risk in children with idiopathic early-onset androgen excess is needed, as well as long-term follow-up studies to identify children who might be at higher risk of developing metabolic dysfunction and PCOS.

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Calcium and Bone

P33

Elevated serum uric acid in asymptomatic primary hyperparathyroidism: a biomarker of disease severity?

Matteo Malagrinò, Nicolò Bisceglia, Giulia Vandi, Anna Piazza, Uberto Pagotto & Guido Zavatta
Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Bologna

Context
Numerous studies propose a potential role of PTH in uric acid (UA) metabolism, particularly through its impact on the ABCG2 transporter, which is responsible for UA excretion in the intestines and kidneys. Another suggested mechanism involves increased tubular reabsorption of UA due to hypercalcemia-induced extracellular volume contraction. Elevated UA levels constitute a well-established risk factor for cardiovascular disease, nephrolithiasis, and chronic kidney disease – conditions prevalent in individuals with primary hyperparathyroidism (PHPT). Despite current international guidelines not advocating routine UA-level measurements in PHPT, addressing hyperuricemia could potentially safeguard renal and cardiovascular health in these patients.
Objective
To assess UA levels in patients with PHPT.
Design
Case-control study.
Setting
Academic, outpatient.
Patients
From February 2021 to December 2023, we consecutively evaluated 206 women with classical hypercalcemic asymptomatic PHPT. These underwent comprehensive assessments, including blood and urinary analysis, dual-energy X-ray absorptiometry (DXA), and renal ultrasound. From this group, 116 patients with thorough testing, including UA measurement, were selected. Of these, patients with known interfering drugs (e.g. diuretics) or drugs affecting PTH or serum calcium (bisphosphonates, denosumab, and cinacalcet) were excluded, obtaining a final cohort of 59 patients. Women without primary or secondary hyperparathyroidism enrolled during the same period ($n=251$), without interfering medications, and with full mineral, serum UA, and DXA evaluation were used as controls.
Results
Both groups had similar age, BMI, and blood creatinine levels, but showed significant differences in biochemical and densitometric parameters as expected. UA level proved notably higher in PHPT patients than controls (5.0 mg/dl vs 4.6 mg/dl, $P=0.015$). Correlation analyses unveiled an inverse relationship between elevated UA and reduced eGFR ($\rho=-0.809$, $P<0.001$), and a positive correlation emerged with PTH levels ($\rho=0.217$, $P<0.001$). Univariate analysis in PHPT individuals identified significant associations of UA levels with eGFR ($P=0.012$), and serum calcium levels ($P=0.007$). Instead, in the control group, UA levels showed significant associations with BMI ($P<0.001$) and eGFR ($P<0.001$), but not with serum calcium levels ($P=0.725$). In a logistic multinomial regression model, hyperuricemia was predicted by higher BMI (OR = 1.087, CI:1.005–1.167, $P=0.037$), serum creatinine (OR = 67.949, CI:6.745–684.535), and serum calcium (OR = 2.371, CI:1.348–4.172, $P=0.003$), regardless of age, PTH levels or diagnosis of PHPT.
Conclusions
Asymptomatic PHPT is associated with elevated serum uric acid, which seems dependent on the degree of hypercalcemia and renal dysfunction, irrespective of PTH levels. Further studies are needed to determine if uric acid levels might have an impact on the clinical management of PHPT.

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Extensive scalp calcification in pseudohypoparathyroidism type 1A: A case report and genetic insight

Ho-Cheol Kang & HeeKyung Kim
Chonnam National University – Hwasun Campus, Internal Medicine, Hwasun, Republic of South Korea

Subcutaneous ossifications (SCO) represent a recognized manifestation of pseudohypoparathyroidism type 1A (PHP1A) and pseudopseudohypoparathyroidism (PPHP), posing significant morbidity to affected individuals. This report details the case of a 37-year-old woman with PHP1A with extensive scalp calcifications, an unusual and unexpected finding. The patient presented with multiple firm skin nodules on the right knee and dorsum of both hands. Having been diagnosed with hypothyroidism and hypocalcemia five years prior, she was receiving levothyroxine (50 μg/day), alfacalcidol (1 μg/day), and calcium carbonate (1 g/day). Despite a stature of 148 cm and displaying typical Albright hereditary osteodystrophy (AHO) features, she maintained regular menstrual cycles. Genetic analysis identified a c.85C>T mutation in the GNAS, confirming the suspicion of PHP1A. To assess extraskeletal calcifications (ESO), a brain CT scan was conducted, revealing basal ganglial calcifications and unexpectedly extensive scalp SCO. Notably, the patient remained asymptomatic with regard to these calcifications. A skin biopsy from a knee nodule confirmed osteoma cutis. Subsequently, the patient's identical twin daughter, born three years later, exhibited hypocalcemia and seizures, leading to the identification of PHP1A. Genetic testing revealed a shared GNAS mutation in both the patient and her daughters. This case aligns with previous observations suggesting that patients with frameshift and nonsense mutations in GNAS tend to manifest more severe SCO compared to those with missense mutations. The identification of SCO in conjunction with AHO phenotypes underscores the importance of GNAS mutation analysis, not only for diagnostic purposes but also for facilitating genetic counseling. This emphasizes the need for a comprehensive approach in managing patients with SCO and AHO phenotypes, ensuring a more accurate diagnosis and informed genetic guidance.

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P35

Utility of 18F-choline PET-CT in the localization of adenomas in primary hyperparathyroidism

Elena Martínez Silla, Migueluesada Charneco, Javier García Sánchez, Raúl Rodríguez Juárez, Juan Luis Delgado Montoya & Pablo José López-Ibarra Lozano
San Cecilio Clinical University Hospital, Endocrinology and Nutrition, Granada, Spain

Objective
The definitive treatment of primary hyperparathyroidism (PPH) is the removal of the affected gland(s). However, its localization can be complicated. The usefulness of 18F-Choline PET-CT versus classical techniques is unknown. The aim of this study was to evaluate the results of 18F-Choline PET-CT in the detection of hyperfunctioning parathyroid tissue with respect to conventional imaging tests and to analyze the relationship between its findings and the levels of calcium and parathyroid hormone (PTH) prior to surgery.
Material and methods
Retrospective observational study of a sample of 30 patients with PPH candidates for surgery, assessed in consultation between 2020-2023, who underwent 18F-Choline PET-CT after negative or discordant conventional localization tests.
Results
Twenty-two females and 8 males were studied. Mean age: 55.6±12.1 years. Surgical criteria were: osteopenia/osteoporosis (73.3%), renal lithiasis (53.3%), serum calcium (50%), age (33.3%), elevated calciuria (20%) and glomerular filtration rate (3.5%). Eighty percent met 2 or more surgical criteria. Parathyroid ultrasound and/or MIBI scintigraphy had been performed in 96.7% of patients, with a concordance with 18F-choline PET-CT results of 40% and 17.2%, respectively. Parathyroid 4D-CT was performed in 19 patients, with a concordance with PET-CT results of 36.8%. In 100% of the sample the 18F-choline PET-CT was positive, with the most frequent localization being the right lower gland (36.7%). Ectopic gland was reported in 10%. The mean diameter of the lesions on PET-CT was 12.58 mm. 15 patients had already undergone surgery, and parathyroid adenoma was found in 13 of them and parathyroid hyperplasia in the remaining 2. There was 100% concordance between the PET-CT findings and the anatomical location of the hyperfunctioning gland in the pathological anatomy study. No association was found between serum PTH and/or calcium levels with the diameter of the lesion on PET-CT or with its weight on anatomic pathology.
Conclusions
18F-Choline PET-CT was useful in cases where ultrasound, scintigraphy or CT-4D had negative or discordant results. It presents a high detection rate of parathyroid hyperfunction and concordance with the surgical location of the affected gland. In addition, it offers benefits in the planning of surgery in patients in whom a good preoperative localization of the lesion was not achieved and in patients with persistent or recurrent PPH.

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P36

Impact of parathyroidectomy on calcium metabolism, bone mineral density and trabecular bone score in patients with non-syndromic primary hyperparathyroidism

Efstratios Kardalas, Georgia Ntali, Panagiotis Mouxtouris, Aglaia Papachristou & Marinella Tzanela
Evangelismos General Hospital, Department of Endocrinology 'D. IKKOS', Diabetes Center European and National Center of Excellence for Rare Endocrine Diseases, Greece

Background/aim
Primary hyperparathyroidism (pHPT) is a relatively common endocrine disorder, which is associated with severe disruption of calcium metabolism and deterioration of bone density and quality. Our study aimed at examining the effect of parathyroidectomy on bone mineral density (BMD), T-Score in both the femoral neck (FN) and the lumbar spine (LS) and on trabecular bone score (TBS).
Materials and methods
A cohort of 280 adult patients (195 males and 85 females), diagnosed with non-syndromic pHPT (from 1998 to 2023), who underwent parathyroidectomy and were followed-up post-surgically in our endocrine center, was retrospectively evaluated. Demographic, clinical and laboratory data of these patients at the time of diagnosis of pHPT and 1 year after parathyroidectomy were evaluated.
Results
Mean age and body mass index of the patients at diagnosis were 54.1 years and 28.6 kg/m^2 respectively. Mean PTH and corrected serum calcium values decreased significantly 1 year after parathyroidectomy (PTH: 65.3 ± 44.3 vs 307.5 ± 284.9 ng/l, $P<0.01$; corr Ca: 9.2 ± 0.6 vs 11.9 ± 1.8 mg/dl, $P=0.014$, respectively). BMD values were dramatically increased 12 months after parathyroidectomy in both the FN and the LS (LS BMD: 0.792 ± 0.133 vs 0.731 ± 0.105, $P < 0.01$, FN BMD: 0.611 ± 0.123 vs 0.544 ± 0.110, $P=0.022$ respectively). The same positive observation applied in case of T-Score values in both sites post-parathyroidectomy (LS T-score: -1.3 ± 0.9 vs -2.2 ± 1.3, $P<0.01$; FN T score: -1.5 ± 0.6 vs -2.3 ± 0.9, $P=0.016$). Interestingly, pre-operative PTH values were found to be moderately and inversely associated with the post-operative BMD and T-Score values in both the LS ($r=-0.44$, $P=0.013$; and $r=-0.56$, $P=0.022$ respectively) and the FN ($r=-0.52$, $P=0.018$; and $r=-0.58$, $P=0.015$ respectively). Finally, the evaluation with TBS pre- and post-operatively identified no significant alterations (TBS pre- and post-operatively: 1.23 ± 0.12 vs 1.25 ± 0.15, $P=0.37$).
Conclusions
The results of our study indicate that the surgical treatment of pHPT can potentially lead to significant improvement of BMD and T-Score values already after 1-year time. Nonetheless, higher biochemical severity of pHPT could be associated to limited recovery of bone metabolism post-surgically. Unfortunately, bone microarchitecture seems to remain relatively unaffected from the parathyroidectomy, thus possibly indicating irreversible effects of pHPT on bone structural integrity. Further long-term study and evaluation of the impact of parathyroidectomy on bone metabolism and quality of patients with pHPT is needed.

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P37

Intrathyroidal parathyroid adenoma: Two case reports

Anca Maria Andrei[1], Andreea Manole[1], Alicia Ungureanu[1], Delia Varlan[1], Ramona Dobre[1,2], Iulia Burcea[1,2] & Catalina Poiana[1,2]
[1]'C.I.Parhon' National Institute of Endocrinology, Bucharest, Romania; [2]'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania

Introduction
The basis of treatment of primary hyperparathyroidism (pHPT) is parathyroidectomy of the responsible lesion, and thus, preoperative localization is important. Ectopic parathyroid adenomas are rare, and they can be accounted for persistent or recurrent hyperparathyroidism. An intrathyroidal parathyroid adenoma (IPA) is an ectopic variant where the adenoma is either partly (>50%) or completely enveloped by the thyroid gland. The incidence of IPAs ranges from 0.7% to 6%. We herein report two cases of primary hyperparathyroidism due to intrathyroidal parathyroid adenomas (IPA).
Case presentation
The first patient, a 60-years-old woman, was referred to our clinic for hypercalcemia. She was not experiencing any symptoms of hypercalcemia. The laboratory investigations showed an elevated serum calcium level of 12 mg/dl (normal range: 8.5–10.2) and parathyroid hormone level of 148.3 pg/ml (normal range: 15–45). The anterior cervical ultrasound revealed an intense hypoechoic, homogenous, with well-defined margins mass of 17/15 mm localized in the right thyroid lobe. A fine needle aspiration with PTH washout was performed indicating a PTH level of 2213 pg/ml. She underwent surgery and postoperative levels of calcium and PTH normalized. The histopathological evaluation confirmed the diagnosis of parathyroid adenoma. The second patient, a 30-year-old male, with history of autosomal dominant tubulointerstitial kidney disease and renal transplant, was admitted for a routinely endocrinological check−up. His laboratory results showed a serum calcium level of 11.5 mg/dl and a parathyroid hormone level of 200.5 pg/ml (normal range: 15–45). A homogenous, clear borderline, hypoechoic mass of 21.5/5.6 mm located in the left thyroid lobe was found at the neck ultrasound. The ^{99}mTc−estamibi scintigraphy did not find images suggestive of parathyroid adenomas, but fine needle aspiration with PTH washout from the intrathyroidal nodule revealed a PTH of 1215 pg/ml, which confirmed the parathyroid origin of the nodule. He is scheduled to undergo a left hemithyroidectomy.
Conclusion
It is difficult to make a definitive diagnosis of IPA before surgery, although the accuracy of diagnosis of IPA can be increased by combining various techniques, such as imaging and fine needle aspiration biopsy. The optimum technique likely depends on a variety of patients, surgeons, and center-dependent factors. The presented cases had completely enveloped parathyroid adenomas, one was cured after surgery and the other will undergo the same treatment. A thorough search for other adenomas and at other ectopic sites before thyroid lobectomy is associated with higher success rates.

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P38

Hypoparathyroidism following thyroid surgery: Risk factors and the role of early postsurgical PTH determination

Tânia Matos[1], Daniela Dias[1], Catarina Silvestre[1], Filipa Serra[1], Pedro Marques[1,2], Carlos Leichsenring[3], Nuno Pinheiro[3] & Inês Sapinho[1]
[1]Hospital CUF Descobertas, Endocrinology, Portugal; [2]Universidade Católica Portuguesa, Faculdade de Medicina, Portugal; [3]Hospital CUF Descobertas, General surgery, Portugal

Introduction
Hypoparathyroidism is one of the most common complications following thyroidectomy and it is associated with significant morbidity. It usually occurs within the first 48 h after thyroid surgery, however hypocalcemia symptoms may only begin up to 64 h after surgery. Therefore, early detection of hypoparathyroidism is essential to a secure postsurgery discharge.
Objectives
We aimed to evaluate the potential risk factors for postsurgical hypoparathyroidism and to determine the role of early determination of serum parathyroid hormone (PTH) following thyroid surgery to predict the occurrence of postsurgical hypoparathyroidism.
Methods
Retrospective analysis of patients submitted to thyroid surgery between August/22 and July/23 at Hospital CUF Descobertas, Lisbon. Serum PTH and calcium levels were determined 6 hours postoperatively. Hypoparathyroidism was defined as an inappropriately low PTH level (PTH normal range 18.5–88 pg/ml) in the context of hypocalcemia (calcium normal range 8.5–10.1 mg/dl), and it was classified as definitive if persisted longer than 6 months. Patients with a follow-up <6 months and with pre-operative abnomal phospho-calcium metabolism were excluded.
Results
We included 76 patients, 82% female ($n=62$), with an average age of $52 \pm$ 12years (23–75). 74 patients were submitted to thyroidectomy (lymph node dissection: 7 unilateral, 2 bilateral and 2 central) and 2 to thyroidectomy completion. Thyroid cancer was present in 24 patients (32%). Nineteen patients developed hypoparathyroidism (25%): 14 transient (18%) and 5 definitive (7%). These patients had lower early postoperative PTH levels (5.6 ± 3.8 vs $21.3 \pm$ 16.4 pg/mL, $P<0.001$), lower postoperative calcium levels (8.3 ± 1.1 vs $8.7 \pm$ 0.5 mg/dL, $P=0.026$) and had incidental parathyroidectomy more frequently (66.7% vs 19.4%, $P=0.002$). There were no significant differences among patients with or without postsurgical hypoparathyroidism regarding sex, age, type of thyroid disease (benign or malignant), neither on surgery type (with or without lymph node dissection). ROC-curve analysis revealed a good accuracy for PTH levels measured 6 hours after surgery to rule out the late occurrence of transient or definitive hypoparathyroidism (AUC 0.908 (CI 95% 0,832-0,983)). In all patients with postoperative PTH levels below 4pg/mL hypoparathyroidism was confirmed (29% of these corresponding to definite hypoparathyroidism), while for 6h-postoperative PTH levels above 18.75 pg/ml transient or definitive hypoparathyroidism has never occurred.
Conclusion
Early postsurgical PTH levels represent a simple and useful tool for a rapid evaluation of hypoparathyroidism risk following thyroid surgery. It allows for

selective and appropriate calcium and vitamin D supplementation, preventing symptomatic hypocalcemia and reducing delays on hospital discharge.

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P39

Co-morbidities in adults with hereditary hypophosphatemia compared to controls – a retrospective Danish register study

Signe Beck-Nielsen[1], Ulla Ege Johansen[2], Rikke Faergemann Hansen[2], Jennifer Gleisner[3] & Angela Williams[4]
[1]Aarhus University Hospital, Aarhus, Denmark; [2]Signum Life Science Aps, København, Denmark; [3]Kyowa Kirin AB, Sweden; [4]Kyowa Kirin International, HEOR, Marlow, UK

Background
Hereditary hypophosphatemia (HH) are rare diseases, characterized by excessive renal phosphate wasting and inappropriately low 1,25-dihydroxy-vitamin D causing hypophosphatemia. In children, the disease manifests as rickets and osteomalacia, in adults osteomalacia.
Aim
The study aims to describe the co-morbidities more prevalent in adults (18y+) with HH and the median age at first diagnosis compared to controls.
Methods
The case population was identified in the Danish National Patient Register based on five diagnostic codes referring to rickets or hypophosphatemia. A journal audit was performed based on all cases identified in Region of Midt Jutland and on available medical files from the remaining four regions in Denmark to verify the diagnosis of HH based on predefined diagnostic criteria. The background population (control) matched by gender, birth year and month, was randomly selected using the Danish Civil Registration System matching fifty controls to each adult with HH. Data on co-morbidities were retrieved from the Danish National Patient Register.
Results
The dataset comprised 98 adults with HH matched with 4.893 controls. Arthrosis was significantly more prevalent in adults with HH compared to controls ($P<0.001$) and first diagnosed at a significantly earlier median age (37.5y vs 55.5y, $P<0.001$). Knee prosthesis and osteotomy were significantly more prevalent in adults with HH ($P<0.001$ both); although younger in age at first registered contact, it was not significant. Hyperparathyroidism, renal failure, and hypertension were more prevalent in adults with HH ($P<0.001$, $P<0.001$, and $P=0.002$, respectively), also being diagnosed significantly earlier in adults with HH (median age 35.0y vs 62.0y, $P=0.010$; 40.5y vs 62.0y, $P=0.027$; and 41.5y vs 58.0y, $P=0.027$, respectively) compared to controls. Chiari I malformation, spinal stenosis, hearing loss, obesity and diseases of pulp and periapical tissues were more prevalent in adults with HH compared to controls ($P<0.001$, $P<0.001$, $P<0.001$, $P=0.002$ and $P=0.001$ respectively), but with no difference in age at presentation. Depressive episode(s) were of similar prevalence, but the median age at presentation was younger for adults with HH (26.0y vs 34.0y [$P=0.008$]).
Conclusion
This retrospective analysis revealed a significantly higher prevalence of co-morbidities already well-known in adults with HH, identifying that in some cases a first contact was at a significantly earlier age compared to controls. Clinicians taking care of adults with HH need to be aware of co-morbidities occurring at an earlier age to identify and initiate correcting actions to limit progression of morbidities in adults with HH.

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P40

Comparative effects of vitamin D supplementation on serum calciotropic hormone profile, in orthodox nuns with hypovitaminosis d in different regions of greece, versus intermittent fasting and western diet in lay women

Spyridon Karras[1,2], Neoklis Georgopoulos[3], Zadalla Mouslech[2], Georgios Koukoulis[4], Filotas Talidis[5], Stefan Pilz[6] & Martin Hewison[7]
[1]Thessaloniki, Aristotle University Medical School, Thessaloniki, Greece; [2]Thessaloniki, Greece; [3]Patras, Greece; [4]Larissa, Greece; [5]Kastoria, Greece; [6]Graz, Austria; [7]Birmingham, UK

Introduction
Greek Orthodox monasteries due to their sartorial habits, comprise a population with high prevalence of hypovitaminosis D. Intermittent religious fasting is adopted by this population, as well as from a large part of general lay Greek population. Comparative effects of vitamin D supplementation and intermittent fasting on vitamin D equilibrium and calciotropic profiles remain scarce.
Aim
To comparatively evaluate effects of vitamin D supplementation in two different forms (drops and pills at 2.500 IU daily) in Orthodox nuns from different regions of Greece, versus Orthodox fasting and Western diet patterns in women from general population on vitamin D and calcium homeostasis.
Methods
Two groups of 25 women from two Orthodox monasteries in Northern Greece (Groups A and B) and two groups of 25 healthy women (Groups C and D) were included. During enrollment a detailed recording of demographic, dietary habits and anthropometric characteristics (via bioimpedance) was conducted. We evaluated calciotropic profiles [Calcium-Ca, Albumin, Parathyroid hormone-PTH, 25(OH)D] at baseline and after 12 weeks. Groups A and B received vitamin D supplementation with 2.500 international units of cholecalciferol daily (in the form of drops - Group A- and tablets - Group B). Groups C and D adopted a dietary pattern of Orthodox intermittent fasting [daily feeding window (1000 h–1800 h)] (Group C) and a diet based on the recommendations of the American Heart Association (AHA) for the management of overweight and obesity in adults (Group D).
Results
All groups were comparable at baseline for calcium, PTH and 25(OH)D concentrations. All groups demonstrated significant increases of 25(OH)D [Group A (21.68 vs 31.05 ng/ml),(Group B 25.78 vs 38.35 ng/ml),(Group C 17.31 vs 24.32 ng/ml),(Group D 17.62 vs 24.12 ng/ml), with no significant between group differences. PTH concentrations decreased significantly in Group C (42.18 vs 25.89) pg/ml and Group D (34.22 vs 17.68) pg/ml, whereas PTH changes in groups A and B were non-significant after 12 weeks of supplementation compared to baseline, with no effects of anthropometric measures of body fat,as well as type of supplementation.
Conclusions
Intermittent fasting and AHA dietary patterns were equally effective with equal moderate doses of vitamin D supplementation in improving vitamin D status, in different groups of Greek nuns and lat women.

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P41

Frequency and causes of hypophosphatemia in internal medicine patients

Lisa Hübener[1], Christian Haas[2] & Birgit Harbeck[3]
[1]University of Lübeck, Lübeck, Germany; [2]University Hospital of Marburg, Department of Nephrology, Marburg, Germany; [3]University Hospital of Hamburg, Department of Medicine III, Hamburg, Germany

Background
Hypophosphatemia is of relevant clinical importance, especially in its severe form. Hypophosphatemia occurs when serum phosphate levels are below 0.84 mmol/l. It can be divided into a mild form (serum phosphate between 0.5 and 0.83 mmol/l), a moderate form (serum phosphate between 0.3 and 0.5 mmol/l) and a severe form (serum phosphate <0.3 mmol/l). Approximately 2.2 to 3.1% of hospitalized patients not requiring intensive care are affected (Brunelli et al., 2007). There are multiple causes such as chronic alcohol consumption, parenteral nutrition or sepsis. However, it has been observed that a mostly mild form of hypophosphatemia often occurs in routine laboratory controls. Aim of the study was to assess the frequency of subtypes of hypophosphatemia and to identify their causes.
Methods
In a retrospective analysis between March 2014 and March 2016, laboratory values from a total of $n=34103$ patients were collected and statistically evaluated. The parameters tested were phosphate, calcium, alkaline phosphatase, creatinine and albumin.
Results
A very high prevalence of hypophosphatemia (23.9%) was demonstrated. The mild form is by far the most common, while the severe form is, as expected, rare. In numbers: the mild form of hypophosphatemia occured in 21.3% ($n=7920$) of all patients, the moderate form in 2.1% ($n=705$) and the severe form in 0.5% ($n=165$) of patients. The further results were obtained using correlation matrixes. According to initial findings, hypophosphatemia may not occur when creatinine

levels are elevated. In the severe form hypophosphatemia can be associated with hypocalcemia.

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P42

Unveiling unique clinical phenotypes of hip fracture patients and the temporal association with cardiovascular events in Hong Kong and the United Kingdom: A retrospective study

Ching-Lung Cheung[1], Warrington Hsu[1], Xiaowen Zhang[1], Chor-Wing Sing[1], Kathryn Tan[1], Ian Wong[1] & Wallis Lau[2]
[1]The University of Hong Kong, Pok Fu Lam, Hong Kong; [2]University College London, London, UK

Major adverse cardiac events (MACE) are the leading cause of death among hip fracture patients. This study aimed to: (1) identify hip fracture subphenotypes using LCA and (2) evaluate the prognosis of the hip fracture subphenotypes on CVE-related outcomes in two extensive hip fracture cohorts from Hong Kong (HK CDARS; $n=78,417$) and the United Kingdom (UK THIN; $n=27,948$), employing both the conventional cohort (between-individual comparison) design and the self-controlled case series (SCCS; within-individual comparison) design. The latent class analysis (LCA) revealed three distinct clusters in the HK cohort: Cluster 1 had cerebrovascular and hypertensive diseases, hyperlipidemia, and diabetes; Cluster 2 had congestive heart failure; Cluster 3 consisted of relatively healthy patients. In the UK THIN dataset, Cluster 1 consisted of a high prevalence of CVE including coronary heart disease, congestive heart failure, and arrhythmia and conduction disorders, and with a higher prevalence of most clinical conditions studied when compared with the relatively healthy Cluster 2. In the HK cohort, the risk of 180-day all-cause mortality and MACE were significantly higher in Clusters 1 (all-cause mortality: HR 1.35, 95% CI 1.28 to 1.42; MACE: HR 1.97, 95% CI 1.83 to 2.12) and Cluster 2 (all-cause mortality: HR 2.22, 95% CI 2.10 to 2.34; MACE: HR 4.06, 95% CI 3.78 to 4.35) compared to Cluster 3. For the secondary outcomes, both Clusters 1 and 2 were associated with a higher number of hospital visits, A&E visits, and total length of hospital stays in the 180-day period after hip fracture. In the between-individual analysis, an immediate risk of overall MACE was observed in the Clusters 1 and 2 in the HK cohort, using the relatively healthy cluster as the reference. SCCS analysis (the within-individual analysis) showed a significantly elevated risk of MACE within 60 days post-hip fracture. Similar associations were observed in the UK cohort in all analyses. In conclusion, this study identified distinct subphenotypes of hip fracture in both the Hong Kong and UK older adult populations using LCA. Temporal associations with MACE were observed in all hip fracture patient clusters. Notably, heart failure consistently emerged as a key characteristic associated with poor prognosis in hip fracture patients. Personalised care of hip fracture patients, considering their specific subphenotypes, is required to prevent MACE.

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P43

The association between the 'time to first fracture' and imminent fracture risk – data from the FRISBEE cohort

Jeroen M.K. de Filette[1], Alexia Charles[2], Amélie Bellanger[2], Iconaru Laura[1], Felicia Baleanu[1], Murielle Surquin[3], Bergmann Pierre[2,4] & Jean-Jacques Body[1,2,3]
[1]CHU Brugmann, Endocrinology, Bruxelles, Belgium; [2]CHU Brugmann, Laboratoire de Recherche Translationnelle, Bruxelles, Belgium; [3]CHU Brugmann, Internal Medicine, Bruxelles, Belgium; [4]CHU Brugmann, Nuclear Medicine, Bruxelles, Belgium

Background
Risk factors for fragility fractures were assessed in several prediction models (e.g. FRAX®, Garvan, FRISBEE, …). The predictors of a shorter 'time to first fracture' and its impact on imminent fracture risk, however, remain to be determined.
Methods
The concept of 'time to first fracture' between inclusion in the FRISBEE cohort ('Fracture RIsk Brussels Epidemiological Enquiry'; 3560 postmenopausal women; median follow-up time of 10.1 ± 2 years) and first fragility fracture was studied. Subjects with validated fractures were divided into 3 groups: first fracture $<$ 2 years, 2-5 years, and >5 years after inclusion. Cox proportional hazard modeling using uni- and multivariate analysis was performed to evaluate factors associated with first fracture risk in these groups. Furthermore, the association between a short 'time to first fracture' as a risk factor for imminent fractures was analyzed. Differences between groups were evaluated by chi^2-test.
Results
Classical risk factors (age, prior fracture, fall history and low BMD) were associated with first fracture in all groups. Previous glucocorticoid use and rheumatoid arthritis (RA) were predictors for early fracture (<2 years), consistent with the concept of very high risk. The 'time to first fracture' was not an independent risk factor for subsequent imminent fractures as FRAX® at baseline was significantly different between groups. Imminent fractures were similar in subjects with/without osteoporosis treatment (16.3 vs 15.5%) despite a higher estimated 10-year risk of fragility fracture in those treated, suggesting that treatment was efficient.
Conclusion
Among the risk factors considered, only previous glucocorticoid use and RA were specific predictors for early fracture. The 'time to first fracture' was not an independent risk factor for imminent fractures. Patients with a first osteoporotic fracture should thus be considered at very high risk for re-fracture, independent of the 'time to first fracture'.

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P44

Risk of sarcopenia can predict quality of life in Primary Hyperparathyroidism

Christina Manani[1], Georgios Tzikos[2] & Theodosios S Papavramidis[2]
[1]Aristotle University of Thessaloniki, 1st Propedeutic Department of Surgery, AHEPA University Hospital, Thessaloniki, Greece; [2]Aristotle University of Thessaloniki, 1st Propedeutic Department of Surgery, AHEPA University Hospital

Background
A specific self-administered health-related quality of life questionnaire for sarcopenia, the sarcopenia and Quality of life (SarQol®) has been recently developed. The questionnaire is composed of 55 items and organized into seven domains of quality of life. The Pasieka Quality of life questionnaire (PAS-Qol) is a specific self-administered quality of life questionnaire that has been developed for patients with primary hyperparathyroidism. The questionnaire has been developed as an assessment tool to find out how primary hyperparathyroidism affected patients' lifestyle and wellbeing. Many of these symptoms develop insidiously and are not easily recognized. If you have primary hyperparathyroidism and your score is over 200 then you are likely to be symptomatic and affected by the disorder. Sarcopenia and low quality of life are widely found among patients suffering from primary hyperparathyroidism.
Aim This study aims to verify whether risk of sarcopenia can predict quality of life in patients with primary hyperparathyroidism.
Methods
The study included both men and women diagnosed with primary hyperparathyroidism and community-dwelling adults with no known hyperparathyroidism disorder. Both groups were assessed with the SarQol questionnaire, and the hyperparathyroidism group was also assessed with the PAS-Qol questionnaire.
Results
Of the 100 included individuals 80% were women with a mean age of 63.8years. Increased age is associated with a lower quality of life (<-1.160, $P<0.001$) in the community-dwelling adults, and gender, with females as the reference is also a significant negative predictor (-11.323, $P=.010$).Neither age ($B=4.845$, $P=.219$) nor gender ($B=-37.816$, $P=0.685$) significantly predicted quality of life in hyperparathyroidism group using the PAS-Qol scale. The mean overall scores of the SarQol scale for patients of the normal group was 72.6 (s.d. = 14.9) and for the hyperparathyroidism group 63.7 (s.d. = 15.1). There was a statistically significant difference ($P=0.006$), suggesting that individuals with hyperparathyroidism generally had lower quality of life scores compared to those without the condition. Between the quality-of-life scores as assessed by the SarQol scale and the PAS-Qol scale there is a significant negative correlation suggesting that as the SarQol score increases PAS-Qol score tends to decline in primary hyperparathyroidism (negative correlation -0.444^{**}, $P=0.001$).
Conclusion
The study highlights the potential interconnectedness between these two conditions, sarcopenia and primary hyperparathyroidism, and their impact on patients' overall well-being. The study emphasizes the need for comprehensive management strategies addressing both sarcopenia and hyperparathyroidism to enhance patients' quality of life.

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Education, and early retirement in patients with hereditary hypophosphatemia compared to controls – a retrospective Danish register study

Signe Beck-Nielsen[1], Ulla Ege Johansen[2], Rikke Faergemann Hansen[2], Jennifer Gleisner[3] & Angela Williams[4]
[1]Aarhus University Hospital, Centre for Rare Diseases, Aarhus, Denmark; [2]Signum Life Science Aps, København, Denmark; [3]Kyowa Kirin AB, Sweden; [4]Kyowa Kirin International, HEOR, Marlow, UK

Background
Hereditary hypophosphatemia (HH) are rare diseases, characterized by excessive renal phosphate wasting and inappropriately low 1,25-dihydroxy-vitamin D causing hypophosphatemia. In children, the disease manifests as rickets and osteomalacia, in adults osteomalacia. Complications from the disease appear with increasing age, in adults characterized by pain, arthrosis, persisting deformities of long bones if not corrected during childhood causing compromised functions of daily living and decreased health-related quality of life.
Aim
In this study, we aimed to investigate if patients with HH achieved the same educational level as the background population and if the ability to work with increasing age was comparable.
Methods
The case population was identified in the Danish National Patient Register based on five diagnosis codes referring to rickets or hypophosphatemia. A journal audit was performed based on all cases identified in Region of Midt Jutland and on available medical files from the remaining four regions in Denmark to verify the diagnosis of HH based on predefined diagnostic criteria. The background population (control) matched by gender, birth year and month, was randomly selected using the Danish Civil Registration System matching fifty controls to each patient with HH. Data on highest educational attainment and employment information were retrieved from the Educational Register and the Ministry of Employments database, respectively.
Results
The dataset comprised 120 patients with HH matched with 6000 controls. We found no difference in the highest obtained educational level between patients with HH compared to controls. A significantly lower proportion of patients with HH aged 40–49y were employed compared to controls ($P=0.012$), and a significantly larger proportion aged 30-49y were in flexible job, in rehabilitation or on flexible benefits compared with controls ($P<0.05$). From age 60+y, a significantly larger proportion of controls were unemployed ($P<0.001$). There was no difference in early retirement in age groups 18–29y, but from age 30–59y, a significantly larger proportion of patients with HH were early retired ($P<0.05$). The mean age at early retirement was 38.7y for patients with HH compared to 45.1y for controls (Δ 6.4y, $P=0.015$).
Conclusion
Patients with HH achieved a comparable educational level compared with the background population, but a significantly larger proportion of patients with HH had the need for a flexible job, rehabilitation or flexible benefits in addition to early retirement. There is a need for identifying and addressing the possible causes for well-educated patients with HH leaving working life too early.

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P246

A rare cause of bone pain: Fibrodysplasia ossificans progressiva

Gökçen Nailer Ertuna[1], Feride Pınar Altay[1], Fatih Gürbüz[2], Abbas Ali Tam[3], Didem Ozdemir[3], Oya Topaloglu[3], Reyhan Ersoy[3] & Bekir Cakir[3]
[1]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yıldırım Beyazıt University Faculty of Medicine, Pediatric Endocrinology, Ankara, Turkey; [3]Ankara Yıldırım Beyazıt University Faculty of Medicine, Endocrinology and Metabolism, Ankara, Turkey

Introduction
Fibrodysplasia ossificans progressiva (FOP), also known as stone man disease, is a rare connective tissue disorder with a prevalence of 1 in 2 million. It is caused by a mutation in ACVR1 gene, usually sporadic and sometimes with autosomal dominant (AD) inheritance. These patients are normal at birth except for the short great toes and hallux valgus. Over time soft tissues such as ligaments, skeletal muscles or tendons ossify. Diaphragm, tongue, extraocular and cardiac muscles are spared.
Clinical case
A 32-year-old female with severe bone pain and hip contracture applied to our clinic. In her history, at age 8 she was admitted to hospital due to lump on her back. The biopsy result of the lesion was reported as fibrotic fat tissue and she was discharged. Two years later at age 10 she was admitted to hospital again due to protrusion and pain in the area where the biopsy was taken. The second biopsy taken from the left thoracic wall was reported as heterotopic endochondral ossification. Further examination of the case for FOP was recommended. Genetic testing could not be done due to the family's financial difficulties. Over the years, painful swellings continued to develop in various regions. When the patient's daughter was 5 years old, the same painful swellings began to occur. This time genetic testing was done on both. Mutation was detected positive for ACVR1 gene for both. (NM_001105.5, c.617G>A (p.R206H) (p.Arg206Pro) (Heterozygote)). During our examination, many painful ossification areas were detected in different regions such as the back, dorsum of foot and chest wall. In addition, contracture of the left hip joint occurred in external rotation and abduction. She also had short big toes and hallux valgus. No abnormalities were detected in laboratory tests. In plain radiographs, pseudoexostoses were seen in various parts such as left sided thoracic wall, left iliopsoas muscle and adductor magnus muscle. Also, monophalangic great toes were noted (Figure 1). Since there was no treatment to prevent the progression of the disease, we administered ibuprofen for symptomatic treatment and glucocorticoid to use during painful flare-ups.
Conclusion
FOP is a rare disease that reduces quality and duration of life. Where heterotopic ossification is detected clinically or radiologically, FOP should be kept in mind. Since it can be inherited AD, genetic testing and counseling should be provided in case of clinical suspicion.

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P247

More potent antiresorptive effect of denosumab versus zoledronate in osteoporotic postmenopausal women with primary hyperparathyroidism

Katarina Mlekus Kozamernik[1,2], Luka Ležaić[2,3], Marko Hočevar[2,4] & Tomaž Kocjan[1,2]
[1]UMC Ljubljana, Endocrinology, Ljubljana; [2]Faculty of medicine, University of Ljubljana, Ljubljana; [3]UMC Ljubljana, Department of nuclear medicine, Ljubljana; [4]Institute of Oncology, Department of Surgical Oncology, Ljubljana

Introduction
Primary hyperparathyroidism (PHPT) is a state of increased bone turnover that can result in secondary osteoporosis. Antiresorptive treatment can be used to preserve bone mineral density (BMD). We compared the impact of zoledronate and denosumab on bone-related biochemical parameters.
Methods
We analyzed interim data from our ongoing randomized trial on osteoporotic postmenopausal women with PHPT who are being treated with either zoledronate 5 mg i.v. once a year (ZOL group) or with denosumab 60 mg s.c. every six months (DMAB group) (ClinicalTrials.gov Identifier NCT04085419). Here, we compare the serum calcium levels (S-Ca), intact parathyroid hormone (iPTH), and bone turnover markers at baseline and 3 months after the start of the treatment.
Results
We enrolled 40 female patients with a mean age of 73.0 (7.8 s.d.) years and 22.6 (10.0) years from menopause with a BMI of 27.77 (5.1) kg/m^2 and with osteoporosis: BMD at a lumbar spine (LS) 0.833 (0.134), total hip (TH) 0.736 (0.117), femoral neck (FN) 0.624 (0.084), distal third radius (1/3R) 0.494 (0.069) g/cm^2 and trabecular bone score (TBS) 1.190 (0.127). After randomization, 20 women received zoledronate (ZOL group) and 20 denosumab (DMAB group). Three months (3M) after the treatment, there was a statistically significant decrease of serum calcium (S-Ca) in both groups (DMAB: baseline S-Ca 2.72 (0.16) vs 3M S-Ca 2.65 (0.18) mmol/l; $P=0.045$, ZOL: baseline S-Ca 2.72 (0.1) vs 3M S-Ca 2.64 (0.12) mmol/l; $P<0.01$). No significant difference in S-Ca decrease between the groups was detected. Similarly, there was a significant increase in iPTH levels in both groups but no statistically significant difference between the groups: (DMAB Δ iPTH 61.91 (126.93) vs ZOL Δ iPHT 30.24 (56.84) ng/l; $P=0.31$). Bone turnover markers decreased significantly in both groups with greater decline of CTX and bone-specific alkaline phosphatase (BAP) in DMAB group (DMAB Δ CTX 0.952 (0.639) vs ZOL Δ CTX 0.556 (0.439) µg/l; $P=0.03$ and DMAB Δ BAP 19.92 (8.51) vs ZOL Δ BAP 12.99 (9.3) µg/l; $P=0.03$). The apparent numerical difference in P1NP was not statistically significant: DMAB Δ P1NP 75.45 (33.87) vs ZOL Δ P1NP 55.12 (32.52) µg/l; $P=0.06$.
Conclusion
Within the first three months of treatment, our data show a greater reduction in bone turnover markers in the DMAB group than in the ZOL group. S-Ca decreased, and iPTH increased in both groups without significant differences between the groups.

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P248

Comparison of fractional excretion of calcium from different urine samples in the differentiation between primary hyperparathyroidism and familial hypocalciuric hypercalcemia

Markus Koster[1], Siegenthaler Martin[1,2] & Bilz Stefan[1]
[1]Kantonsspital St. Gallen, Division of Endocrinology and Diabetes, St. Gallen, Switzerland; [2]Charité Universitätsmedizin Berlin, Department of Endocrinology and Metabolic Disease, Berlin, Germany

Background
Calculation of the fractional excretion of calcium (FECa) from 24-hour (24h) urine collections is recommended to identify patients with suspected familial hypocalciuric hypercalcemia (FHH) during the work-up of primary hyperparathyroidism (pHPT). The current study was designed to test whether calculating the FECa or calcium-to-creatinin clearance obtained from 24h urine specimen can be substituted by results obtained from second morning or spontaneous void urine samples.
Methods
Ninety-one patients subsequently referred for the workup of PTH-dependent hypercalcemia (albumin-corrected and/or ionized calcium $\geq$ 2.6/1.3 mmol/l, PTH $\geq$ 30 ng/l, 25-OH vitamin D3 $\geq$ 50 nmol/l) were included and provided two independent 24h urine collections (groups D1 and D2), one second morning urine (MU) and one spontaneous void urine sample (SU). FECa (%) was calculated from paired blood and urine samples. Patients with a FECa $<$1% were categorized as suspicious for FHH (sFHH), the remaining considered to have pHPT. Descriptive statistics (median, IQR), Kruskal Wallis and McMemar tests were used to test whether FECa results or the proportion of sFHH patients were different across the four urine collections.
Results
The median FECa in the 4 samples were D1: 2.1% (1.2, 2.7), D2: 2.2% (1.6, 2.8), MU: 1.6% (1.0, 2.4) and SU: 2.1% (1.2, 2.7). FECa derived from the MU was significantly lower when compared to D1 and D2 ($P=0.04$ and <0.001, respectively). The proportion of patients assigned to the sFHH category were D1: 0.23 (95%CI 0.14–0.32), D2: 0.10 (95%CI 0.03–0.16), MU: 0.24 (95%CI 0.15–0.33), SU: 0.21 (95%CI 0.13–0.30). The proportions of patients assigned to sFHH were significantly different between D1 and D2 ($P=0.027$), D2 and MU ($P=0.006$) and D2 and SU ($P=0.027$). 7/91 subjects had a FECa $<$1% in all samples and 3 of them received a genetically confirmed diagnosis of FHH.
Conclusion
Considering the inherent variability of FECa derived from 24h urine collections using spontaneous void urine samples may be an adequate alternative to identify patients with possible FHH. Based on our preliminary data, we hypothesize that repeated testing of FECa in spontaneous void urine samples rather than relying on single 24h urine collection may aid to reduce the number of patients in whom genetic testing is required to rule out FHH.

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P249

Burosumab treatment for FGF23-related hypophoshatemia in an adult patient with severe fibrous dysplasia in McCune-Albright syndrome

Maria Stelmachowska-Banaś[1], Karolina Cylke-Falkowska[1], Wojciech Zgliczyński[1] & Waldemar Misiorowski[1]
[1]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland

Background
McCune Albright syndrome (MAS) is a rare mosaic genetic disorder affecting 1/100 000 to 1/1 000 000 of the population. It arises from a somatic gain-of-function mutation in GNAS gene. The clinical picture is complex and includes fibrous dysplasia (FD), café-au-lait spots, precocious puberty and other hyperactive endocrinopathies. The degree of FGF23 overproduction is correlated with FD severity, and frank hypophosphatemia occurs only in patients with extensive skeletal involvement, resulting in frequent fractures, pain, increased propensity for deformities, and muscle weakness. Burosumab is a monoclonal antibody that targets FGF23, indicated for the treatment of hypophosphatemic rickets and tumor-induced osteomalacia caused by overproduction of FGF23. To date, there is no evidence on the effectiveness and safety of burosumab treatment in adults with FD/MAS.
Case presentation
A 27-year-old male with MAS was under the care of the Endocrinology Department for persistent hypophosphatemia despite treatment with oral phosphate supplements and alfacalcidol. MAS was diagnosed at the age of 6 years and his medical history included precocious puberty, multiple fractures, skeletal deformities, muscle weakness and exacerbated skeletal pain due to severe FD. The patient was diagnosed with GH excess at the age of 22 years and has been treated with pasireotide 40 mg every 4 weeks i.m. with normalization of IGF-1 level for age and sex. Because of persistent hypophosphatemia (serum phosphate 0.38 mmol/l) resulting from FGF23 excess (serum FGF23 495kRU/L normal $<$100), bone pain and frequent fractures, the treatment with burosumab has been attempted (1 mg/kg body weight s.c. every 4 weeks). Over the 10-month course of treatment, the patient reported improved general well-being, reduced bone pain and increased muscle strength. Normalization of serum phosphate 0.87 mmol/l, PTH 51.6 pg/ml and significant reduction in alkaline phosphatase levels from 1022.2 U/l to 592.6 U/l were achieved. No adverse effects of the short-term therapy were observed.
Conclusions
This is the first reported case of burosumab treatment in an adult patient with FGF23-related hypophosphatemia in MAS. In our case, positive effects of the therapy were observed, both in terms of the patient's reported well-being and in terms of calcium-phosphate balance and bone markers. However, a longer follow-up in a larger group of adult patients with MAS seems necessary.

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Cystic parathyroid adenomas – a rare case of primary hyperparathyroidism: Two case reports

Katja Veraguth[1], Walter Kolb[2], Ole Maas[3] & Stefan Bilz[1]
[1]Kantonsspital St.Gallen, Klinik für Endokrinologie, Diabetologie, Osteologie und Stoffwechselerkrankungen, St. Gallen, Switzerland; [2]Kantonsspital St.Gallen, Klinik für Allgemein-, Viszeral-, Endokrin- und Transplantationschirurgie, St. Gallen, Switzerland; [3]Kantonsspital St. Gallen, Klinik für Radiologie und Nuklearmedizin, St. Gallen, Switzerland

Less than 0.5% of parathyroid lesions are cysts out of which only 10–20% are endocrine active. Depending on their localisation, the most frequent symptom of a parathyroid cyst (PC) is neck mass (41.7%) with possible compressive symptoms. Women are more frequently affected and tend to have hormone-inactive PCs. Men tend to have endocrine-active PCs. The best diagnostic approach is still under debate as PCs are relatively rare.
Case report 1
A 68-year-old man was referred by the rheumatologists for primary hyperparathyroidism, which had been diagnosed as part of the extended investigations for CPPD arthritis. His history revealed recurrent kidney stones, chronic kidney disease and osteopenia (T-score minimal -2.0 s.d.) as possible associated secondary diseases. There were no local complaints or compression symptoms. The albumin-corrected calcium was 2.8 mmol/l and the PTH was 200 mmol/l. Ultrasonography showed a large cystic lesion (58 mm) caudal to the left lobe of the thyroid gland. The cyst fluid obtained by fine needle aspiration was hemorrhagic and contained high concentrations of PTH (305 000 ng/l). Intraoperatively, most of the cyst was retrosternal and could be removed intact. Histopathologically, the specimen weighed 28 g and could be clearly assigned to a cystic parathyroid adenoma.
Case report 2
A 74-year-old female patient was diagnosed with primary hyperparathyroidism as part of a search for secondary causes of osteoporosis (T-score minimal -4.5 s.d.). The serum calcium was 2.7 mmol/l, the PTH was 177 mmol/l. Sonography revealed a predominantly cystic mass with solid margins (max. 37 mm) in the area of the caudal right lobe of the thyroid gland, which could not be clearly differentiated from the thyroid gland. The choline PET/CT showed a choline-enriched lesion with strong margins dorsally adjacent to the right lobe of the thyroid gland. The findings could be surgically resected and histopathologically corresponded to a 5 g cystic parathyroid adenoma. A low normal PTH was measured in both patients on the 1st day postoperatively, the Calcium normalized in the following investigations.
Conclusion
The diagnosis of cystic parathyroid adenomas can be made by imaging or fine needle aspiration. To date, the diagnostic value of Tc-99m MIBI SPECT/CT in primary hyperparthyroidism caused by cystic parathyroid adenomas is unclear (no data for choline PET), and minimally invasive FNA appears to be very useful for the diagnosis and differentiation of other neck cysts due to the highly elevated PTH level in both endocrine active and inactive PCs, what is very characteristic.

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P251

Age-associated changes of fast-twitch skeletal muscle fibers in male rats

Branko Filipović[1], Branka Šošić-Jurjević[1], Svetlana Trifunovć[1], Natasa Ristic[1], Milica Manojlović-Stojanoski[1], Nataša Nestorović[1] & Vladimir Ajdžanović[1]

[1]University of Belgrade, Institute for Biological Research "Siniša Stanković", National Institute of Republic of Serbia, Citology, Belgrade, Serbia

Aging process is accompanied by structural and functional changes in different organs including bone and muscle tissues. Between these tissues there is a mutual interaction mediated by endocrine factors such as the peptide hormone osteocalcin, produced by osteoblasts. Since the skeletal muscles is composed of two basic fiber types, slow-twitch (type I) and fast-twitch (type II), the aim of this study was to examine the age-related changes in rat fast-twitch skeletal muscle fibers using morphometrical, immunohistochemical and biochemical analysis. Experimental animals included three age group of male Wistar rats: young adult (3-months old), middle-aged (16-months old) and old (24-months old). For immunohistochemical characterization of fast myosin heavy chains (MHC-fast) in skeletal muscle fibers, anti-fast myosin skeletal heavy chain served as primary antibody. Morphometric analysis of muscle fibers was performed using Olympus microscope (BX-51), equipped with a microcator, a motorised stage and a CCD video camera, and controlled by the newCAST stereological software package. Blood serum was used for determination of serum osteocalcin (OC) and testosterone (T) concentrations. Morphometric analysis of fast-twitch muscle fibers, in gastrocnemius muscle cross-sections, showed a significant reduction in mean MHC-fast fiber perimeter (MHC-fast FP) by 15% ($P<0.01$) and 10% ($P<0.05$) in old rats compared to the young adult and middle-aged rats, respectively. The value of MHC-fast fiber cross-sectional area (MHC-fast FCSA) was markedly reduced by 27% ($P<0.01$) and 19% ($P<0.05$) in the old rats, related to young adult and middle-aged groups, respectively. The MHC-fast fiber minimal Feret's diameter (MHC-fast FMFD) in old rats decreased by 17% ($P<0.01$) when compared to young adult. Evaluation of the biochemical parameters showed a significant reduction in serum OC concentration by 61% ($P<0.0001$) and 63% ($P<0.0001$), when the middle-aged and old rats were compared to the younger animals. Serum T was significantly lower by 26% ($P<0.05$) and 56% ($P<0.0001$) in the middle-aged and old groups respectively, compared to young adults. The reduction of serum T measured 40% ($P<0.01$) when old rats were compared to middle-aged animals. These findings indicate age-related changes in the morphometric parameters of fast-twitch muscle fibers, as a consequence of their size reduction in the rat gastrocnemius. This is supported by the decline in serum levels of osteocalcin and testosterone, which may contribute to the reduction of their muscle anabolic effects in old age.

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Role of variants of uncertain significance in determining bone fragility or low bone mineral density in adults: A multicenter study

Silvia Carrara[1], Silvia Vai[2], Alessandra Mihalich[3], Anna Di Blasio[3], Emanuela Ponti[3], Gregorio Guabello[4], Vito Guarnieri[5], Stella Pigni[6], Andrea Lania[6], Gherardo Mazziotti[6] & Sabrina Corbetta[7]
[1]Bone Metabolism Disorders and Diabetes Unit, IRCCS Istituto Auxologico Italiano, Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [2]Bone Metabolism Disorders and Diabetes Unit, IRCCS Istituto Auxologico Italiano, Milan, Italy; [3]IRCCS Istituto Auxologico Italiano, Medical Genetic Laboratory, Cusano Milanino, Italy; [4]IRCCS Ospedale Galeazzi Sant'Ambrogio, Ambulatorio Metabolismo Osseo, Milan, Italy; [5]Fondazione IRCCS Casa Sollievo della Sofferenza, Division of Medical Genetics, San Giovanni Rotondo (Foggia), Italy; [6]Endocrinology, Diabetology and Medical Andrology Unit, IRCCS Humanitas Research Hospital, Department of Biomedical Sciences, Humanitas University of Milan, Rozzano (Milan), Italy; [7]Bone Metabolism Disorders and Diabetes Unit, IRCCS Istituto Auxologico Italiano, Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy

Osteoporosis causes bone fragility usually affecting the elderly. Genetic susceptibility plays a crucial role in determining the risk of fragility fractures and is involved in early-onset osteoporosis. When fragility fractures or low bone mineral density (BMD) occur in young adults without evident secondary osteoporosis, an underlying monogenetic bone disease should be assessed. The list of genes related to low BMD and their mutations is increasing. Nevertheless, little is known about the role of Variants of Uncertain Significance (VUS). We retrospectively evaluated 65 adult patients undergoing Next Generation Sequencing analysis for osteogenesis imperfecta/lowBMD panel including the following genes: COL1A1, COL1A2, BMP1, CRTAP, FKBP10, IFITM5, P3H1, PLOD2, PLS3, PPIB, SERPINF1, SERPINH1, WNT1, LRP5. The indication for genetic analysis was prompted by multiple fragility fractures or low BMD in premenopausal/perimenopausal women and in men aged less than 55 years, in the absence of a clear phenotype of monogenetic bone disease and after exclusion of secondary causes of osteoporosis. Gene variants were detected in 37 (57%) out of 65 enrolled patients: 3 patients, mean aged 47.3 years, had pathogenic mutations in COL1A1 and COL1A2, therefore being diagnosed with osteogenesis imperfecta. They denied dental diseases, while two of them had moderate-severe scoliosis and hearing loss, and one reported ligament laxity; each reported a mean of 5 fractures, more commonly appendicular. One patient had densitometric osteoporosis. The remaining 34 patients harboured VUS: they did not significantly differ from wild-type patients regarding age, sex, age at first fracture, presence of low BMD and circulating markers of mineral metabolism and C-terminal telopeptide. Of note, though the prevalences of dental disease and hearing loss were similar, VUS patients had more commonly a family history of fragility fractures (56.2 versus 24.0%, $P=0.015$), and a higher number of axial fractures (2.9 versus 1.0%, $P=0.01$), whereas the number of appendicular fractures was comparable with wild-type subjects. Moreover, moderate-severe scoliosis showed a trend to be more common in the VUS group (20.6 versus 3.6%, $P=0.087$), and the median levels of alkaline phosphatase and its bone isoenzyme were higher in VUS patients (81.8 versus 55.0 U/l, $P=0.01$; 20.3 versus 9.8 µg/l; $P=0.02$, respectively). In conclusion, VUS in low BMD related genes may associate with a family history of fragility fractures, moderate-severe scoliosis, high number of axial fractures and relatively high bone turnover. These findings suggest the need to extend genetic diagnosis and to investigate the role of VUS.

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P253

Alterations in phosphate metabolism in patients with Klinefelter's syndrome

Rita Indirli[1,2], Valeria Lanzi[1,2], Iulia Petria[1,2], Giovanna Mantovani[1,2] & Emanuele Ferrante[1]
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [2]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy

Background
Patients with Klinefelter's syndrome (KS) present a high prevalence of osteopenia, osteoporosis and fragility fractures. Several factors may contribute to skeletal fragility, e.g. hypogonadism, derangements in vitamin D metabolism, reduced testicular secretion of Insulin-like Factor 3. However, phosphate metabolism has never been investigated.
Methods
A retrospective analysis was conducted to investigate prevalence and characteristics of hypophosphatemia (HypoP, serum phosphate $\leq$2.7 mg/dl) among adult KS patients followed-up at a tertiary endocrinology center in Milan, Italy. Among 100 patients, 86 had at least one phosphate assessment and were included in the analysis. HypoP was defined as recurrent/persistent if confirmed in $\geq$2 assessments. Moreover, 36 KS patients (age 32 [26–43] years) were consecutively enrolled in a cross-sectional study and compared to 32 male healthy controls (age 29 [26–40], $P=0.49$). Blood and urine parameters of phosphate metabolism, including tubular resorption of phosphate (TmP/GFR), were assessed in both groups. Hip, femoral neck and lumbar spine bone mineral density (BMD) was evaluated in KS patients by dual-energy X-ray absorptiometry.
Results
In the retrospective analysis, 20 out of 86 (23%) patients presented mild-moderate HypoP in at least one assessment. HypoP was recurrent/persistent in 9 patients (10%). No apparent causes of HypoP were identified. Patients with HypoP were older (43 [40–53] vs 31 [26–46] years, $P<0.001$) and had a greater phosphate urinary loss (TmP/GFR 3 [2.7-3.7] vs 2.4 [2.2-2.9] mg/dl, $P=0.002$) than patients with normal phosphate, but prevalence of low BMD was similar (5/21 vs 14/66, $P=0.9$). In the cross-sectional study, KS patients displayed lower testosterone concentrations than controls (4.8 [3.4–5.6] vs 5.1 [4.6–7.2] ng/ml, $P=0.03$), but comparable levels of phosphate (3.4 [0.7] vs 3.6 [0.6], $P=0.18$), 25OH-vitamin-D, parathyroid hormone and alkaline phosphatase. HypoP was observed in 7/36 KS (19%) and 3/32 controls (9%, not-significant). However, KS patients displayed a statistical trend for greater urinary phosphate excretion (TmP/GFR 2.9 [2.6–3.3] vs 3.3 [2.9–3.8], $P=0.07$). Phosphate metabolism parameters were not associated to testosterone concentrations or BMD. TmP/GFR correlated inversely with 25OH-vitamin-D ($r=-0.34$, $P=0.046$).
Conclusion
Persistent/recurrent, unexplained hypoP can be observed in 10% of KS patients. In KS a trend to increased urinary phosphate excretion is observed. However, these mild derangements in phosphate metabolism are not associated with BMD. Interestingly, the finding that phosphate urinary excretion is associated with 25OH-vitamin-D may suggest a role for FGF-23. This phosphatonin, indeed, inhibits both renal 1alpha-hydroxilaton of 25OH-vitamin-D and tubular resorption of phosphate, and should be evaluated in further studies.

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P254

Hypocalcemia after hyperthyroidism surgical treatment: Besides iatrogenic hypoparathyroidism

José Vicente Rocha[1], Marta Vaz Lopes[1], Mariana de Severino[1], Carolina Peixe[1], Ana Gomes[1], Maria Inês Alexandre[1] & Maria João Bugalho[1]
[1]ULS Santa Maria, Endocrinology, Diabetes and Metabolism, Lisboa, Portugal

Introduction
Hypocalcemia is a possible complication of thyroid surgery, usually assumed in the context of iatrogenic hypoparathyroidism. On the other hand, Hungry Bone Syndrome (HBS) is a complication classically described after surgical correction of primary hyperparathyroidism. It is characterized by hypocalcemia with normal or elevated PTH values (usually accompanied by hypophosphatemia and hypomagnesemia) and occurs consequently to a compensatory bone formation after a period of increased resorption. As increase bone resorption is present in hyperthyroidism, HBS can also follow hyperthyroidism surgery.
Methods
We retrospectively reviewed patients submitted to hyperthyroidism surgery in our center between 2020 and 2023. Exclusion criteria included concomitant hyperparathyroidism, bisphosphonate treatment, or previous therapy with radioactive iodine. Patients were subdivided into 2 subgroups; those who developed HBS (HBS+) and those who did not (HBS-). A comparative analysis including demographic, clinical and laboratory data was performed.
Results
A total of 98 patients were included. Thirteen patients underwent lobectomy (corresponding to toxic adenomas) and the remaining total thyroidectomy. The median age was 51 ± 14 years, 85% were female patients ($n=83$). Thirty-five out of forty-seven patients (74%) who developed hypocalcemia (calcium <8,4 mg/dl) had normal or high PTH values (HBS+). Subgroups were similar for age at diagnosis, hyperthyroidism duration, medical treatment duration, initial values of TRABs (in patients with Graves' disease), calcium, phosphorus and alkaline phosphatase. HBS + patients had higher fT4 (3.29 vs 2.6 ng/dl, $P=0{,}06$), ft3 (12.16 vs 10.78 ng/dl, $P=0.29$), and PTH (63 vs 48 pg/ml, $P=0.037$, $n=25$). Moreover, HBS+ patients needed higher doses of tiamazol (13 mg vs 9 mg, $P=0{,}014$).
Conclusion
In the current study, postoperative hypocalcemia was a common occurrence with most cases corresponding to HBS. Among those with hypoparathyroidism, there was recovery of hypocalcemia likely to correspond to transient hypoparathyroidism. Maximum needed tiamazol dosages and pre-operative PTH values were significantly different between HBS + and HBS- patients, suggesting that more severe hyperthyroidism is associated with HBS development.

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Evaluating novel bone biomarkers (FGF2, lipocalin, sclerostin) in patients with tumor induced osteomalaî ia (TIO) and acromegaly

Sofia Gronskaia[1], Zamira Zuraeva[1], Larisa Nikankina[1] & Zhanna Belaya[1]
[1]Endocrinology Research Centre, Moscow, Russian Federation

Background
Bone tissue is a non-classical endocrine organ, which controls phosphate metabolism through production of fibroblast growth factor 23 (FGF-23) mainly by osteocytes. Recent studies have demonstrated that specific proteins involved in paracrine regulation of bone remodeling can be measured in serum samples and may be involved in human metabolism.
Aims
To evaluate serum biomarkers related to endocrine and paracrine function of bone tissue in patients with phosphate metabolism disturbances such as FGF-23 hyperproduction in patients with tumor induced osteomalacia (TIO) or FGF-23 resistance due to acromegaly.
Materials and methods
This is a case-control study. Fasting serum samples were taken between 0800 and1000 h from patients with TIO, acromegaly and age- sex-matched healthy volunteers and stored at −40°C. Commercially available kits for enzyme-linked immunosorbent assay (ELISA) were used to determine the serum levels of iFGF-23 (Biomedica BI-20700), cFGF-23 (Biomedica BI-20702), FGF2 (R&DDFB50), lipocalin (Biovendor RD191102200R) and sclerostin (Biomedica BI-20492). Insulin-like growth factor-1 (IGF-1) was measured by immunochemiluminescence assays (Mediagnost E20). Non-parametric tests (the Kruskal-Wallis test and the Mann-Whitney test) were used to assess the differences between the groups of patients. One-way ANOVA and Bonferroni criterion were utilized to assess the differences between groups.
Results
We enrolled 71 subjects (mean age 48 ± 12 years): 23 patients suffered from TIO (group 1), 24 patients with acromegaly (group 2) and 24 matched healthy controls (group 3) with no differences among the groups in sex and age ($P=0.328$, 0.959 respectively). Patients with TIO had significantly higher iFGF-23 serum (median 86 [28;736]) and cFGF-23 (5 [3;14]) as compared to the other groups ($P=0{,}003$, $P<0{,}001$). Phosphorus (Pi) serum levels in subjects with TIO were significantly lower as compared to the other groups (median 0.49 [0.46;0.53] ($P<0.001$)). Patients with acromegaly had higher Pi - 1.4 [1.3; 1.6] ($P<0.001$) and IGF1 - 780 [650;810] ($P<0.001$) vs control. Nevertheless, we did not find statistically significant differences in the measured biomarkers: FGF2 ($P=0.38$), Lipocalin ($P=0.16$), sclerostin ($P=0.12$) within the three investigated groups.
Conclusion
TIO and acromegaly are associated with phosphate metabolism disturbances with no detected changes in the serum levels of FGF2, lipocalin or sclerostin.

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P256

The association of vasomotor symptoms with fracture risk and bone mineral density in postmenopausal women: a systematic review and meta-analysis of observational studies

Panagiotis Anagnostis[1,1], Konstantinos Lallas[2], Anna Pappa[1], Georgios Avgeris[1], Kristina Beta[1], Dimitrios Damakis[1], Eirini Fountoukidou[1], Maria Zidrou[1], Irene Lambrinoudaki[3] & Dimitrios Goulis[1]
[1]Aristotle University of Thessaloniki, 1st Department of Obstetrics and Gynecology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Aristotle University of Thessaloniki, Department of Medical Oncology, School of Medicine, Thessaloniki, Greece; [3]National and Kapodistrian University of Athens, 2nd Department of Obstetrics and Gynecology, Athens, Greece

Purpose
Vasomotor symptoms (VMS) adversely affect postmenopausal quality of life. However, their impact on bone health has not been elucidated. This study aimed to systematically review and meta-analyze the evidence regarding the association of VMS with fracture risk and bone mineral density (BMD) in peri- and postmenopausal women.
Methods
A literature search was conducted in PubMed, Scopus and Cochrane databases until 31 August 2023. Fracture, low BMD (osteoporosis/osteopenia) and mean change in lumbar spine (LS) and femoral neck (FN) BMD were assessed. The results are presented as odds ratio (OR) and mean difference (MD), respectively, with a 95% confidence interval (95% CI). The I2 index quantified heterogeneity.
Results
Twenty studies were included in the qualitative and 12 in the quantitative analysis ($n=49\,659$). No difference in fracture risk between women with and without VMS was found ($n=5$, OR 1.04, 95% CI 0.93–1.16, I2 16%). However, VMS were associated with low BMD (n=5, OR 1.54, 95% CI 1.42–1.67, I2 0%). Patients with VMS had lower LS BMD than those without VMS (MD -0.019 g/cm^2, 95% CI -0.03 to -0.008, I2 85.2%). In contrast, there was no difference in FN BMD between groups (MD -0.010 g/cm^2, 95% CI -0.021 to 0.001, I2 78.2%). These results were independent of VMS severity, age and study design. When the analysis was confined to studies that excluded menopausal hormone therapy use, the association with BMD remained significant.
Conclusions
The presence of VMS compromises bone health in postmenopausal women, since it is associated with low BMD.

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22q11.2 deletion syndrome diagnosed in the context of seizure and hypocalcemia in adulthood

Maria Galani[1], Grigoris Effraimidis[1,2], Ioannis Gkountios[1], Eleni Georgiou[1], Anastasia-Konstantina Sakali[1], Dimitra Pappa[1], Eleftheria Barmpa[1], Nektarios Adamopoulos[1] & Alexandra Bargiota[1,2]
[1]Larissa General University Hospital, Department of Endocrinology and Metabolic Disorders, Larissa, Greece; [2]University of Thessaly, School of Health Sciences, Faculty of Medicine, Larissa, Greece

Introduction
The 22q11.2 deletion syndrome (22q11.2DS) caused by a microdeletion of the 22q11.2 region of chromosome 22 is the most common deletion in humans causing a variety of disorders, including DiGeorge syndrome (OMIM #188400), velocardiofacial syndrome (OMIM #192430) and distal chromosome 22q11.2 deletion syndrome (OMIM #611867). Most individuals diagnosed with this condition are identified in early childhood and the diagnosis in adults is uncommon. It is characterized by a specific facial phenotype, and structural and functional abnormalities in the cardiac and endocrine systems.
Case
A 42-year-old female was admitted in the emergency room due to loss of consciousness followed by grand mal epileptic seizure. Prior to the episode the patient felt dizziness and nausea. Clinical examination revealed postural hypotension, systolic murmur 1-2/6, strabismus, dental deformities, and numbness of the upper limps, while Chvostec and Trousseau's sign were not present. Chest X-ray showed an increased cardiothoracic index and no electrocardiographic or echocardiographic abnormalities were found. Laboratory tests revealed primary hypoparathyroidism with total calcium 5.1 mg/dl [ref. range: 8.8–10.4], phosphorus 5.76 mg/dl [2.5–4.5], parathyroid hormone 6.8 pg/ml [15–65] and 25(OH)D3 11.5 ng/ml. On admission she was treated with IV calcium gluconate and fluids, and during hospitalization she was started on oral calcium, magnesium, alfacalcidol and cholecalciferol. The patient had a history of epilepsy on systematic medication since childhood. She displayed a mild intellectual disability, speech sound disorders and history of anxiety and psychosis. She had slight facial dysmorphia (long face, hypertelorism, ear helix folded) and normal stature and had performed surgical extraction of the majority of her teeth, due to jaw malocclusion and enamel hypoplasia. No history of cervical surgery or irradiation, heart disease or recurrent infections was reported. Basal ganglia calcification was shown in brain CT. Taken into consideration the patient's history, facial features and clinical and biochemical (primary hypoparathyroidism) manifestations, 22q11.2DS was suspected. Fluorescence in-situ hybridization (FISH) revealed deletion of 22q11.2 (46,XX.ish del(22)(q11.2)(D22S75 -), confirming the diagnosis.
Discussion
We report the case of an adult woman diagnosed with 22q11.2DS at the age of 42 in the context of syncope and seizures due to severe hypocalcaemia, highlighting the need for clinicians to be aware of the manifestations of the syndrome in adults, as well as the role of endocrinologists in the correct diagnosis and treatment of these patients. Confirmation of the diagnosis allows the initiation of appropriate treatment and multidisciplinary follow-up.

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Hyperostosis frontalis interna – a case of Morgagni–Stewart–Morel syndrome

Vlad Radulescu[1], Anastasia Stanescu[1], Cristina Stancu[1] & Corin Badiu[1,2]
[1]C.I. Parhon National Institute of Endocrinology, BucureŞti, Romania; [2]Carol Davila University of Medicine and Pharmacy, BucureŞti, Romania

Introduction
Morgagni–Stewart–Morel syndrome is defined as the absolute presence of hyperostosis *frontalis interna*, associated with metabolic, endocrine, and neuropsychiatric disorders. There are very few cases reported in the literature and some experts do not even recognize it but the exact etiology of the syndrome remains unclear; some theories relate to estrogen dysfunction, obesity and leptin dysfunction, and genetic alterations.
Case report
We present the case of a 33 year old, Caucasian woman, referred to us for frontal cranial hyperostosis associated with intense, invalidating headaches with nausea, vomiting, tremor and palpitations. She was seen by the neurology department that confirmed the frontal cranial hyperostosis with CT and MRI imaging. She was already in treatment with Tramadol 150 mg 4 times a day, Carbamazepine 200 mg twice a day, Metamizole 400 mg + Caffeine 60 mg + Drotaverine 40 mg three times a day, Sumatriptan one administration when needed. From the patient's history we note a lost pregnancy due to oligohydramnios at 30 weeks, allergic bronchitis, left micropolycystic ovary and secondary amenorrhea for 2 years at the moment of her presentation in our clinic. The clinical exam showed an altered general state due to constant multidrug resistant headache, photophobia, hyperemic face, grade II obesity (BMI = 39 kg/m^2), acanthosis nigricans in the nucal area, accelerated intestinal movements, normal blood pressure and pulse with no other modifications. She had hypercolesterolemia, HbA1c = 6.1% and an insufficient status of vitamin D3 = 17.2 ng/ml, with no other modified parameters on lab work. The bone resorbtion and formation markers were in the normal range. As far the treatment is concerned, we had to choose between neurosurgery of the frontal bone to reduce the frontal hyperostosis or to find a medical approach, to stop the bone formation process. We decided to administer one vial of zolendronic acid 4 mg/5 ml, with benefit in pain reduction and mild flu-like syndrome 24 h after administration. Six months later, the patient comes for a check-up and we note a BMI = 32.08 kg/m^2, a significant decrease in the headaches intensity with a significant reduced use of pain medication, no more tremors, normal menstrual cycles and a CT that showed stationary frontal hyperostosis.
Discussion
Morgagni–Stewart–Morel syndrome is a rare entity, mostly diagnosed on the clinical setting, with speculative theories about its pathogenesis. Its management is usually symptomatic, but in this particular case we needed a more specific approach as the use of the pain medication was very high and the quality of life was severely affected.

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P445

Clinical characterization of a cohort of patients with multiple endocrine neoplasia syndrome type 1 (MEN1): role of the MEN1 gene mutation on the phenotypic expression of the syndrome

Laura Pierotti[1], Elena Pardi[1], Chiara Sardella[2], Simone/////Della Valentina[1], Anna Dal Lago[1], Paolo Piaggi[3], Fausto Bogazzi[2], Maria Adelaide Caligo[4] & Filomena Cetani[2]
[1]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University of Pisa, Unit of Endocrinology, Pisa, Italy; [3]University of Pisa, Department of Information Engineering, Pisa, Italy; [4]University of Pisa, Laboratory of Molecular Genetics, Pisa, Italy

The clinical diagnosis of MEN1 is established when a proband manifests at least two of the manifestations of the triad (Primary Hyperparathyroidism (PHPT), Pituitary adenoma, Gastroenteropancreatic Neuroendocrine Tumor (GEP-NET)). Typically, it is a familial disease (F-MEN1), while in about 10% of cases the disease is sporadic. In sporadic forms (S-MEN1), up to 70% of patients may exhibit a negative genetic analysis (*MEN1*-negative). These patients seem to have distinct features compared to those who carry *MEN1* mutation (*MEN1*-positive). This study aims to assess the clinical phenotype of *MEN1*-negative and *MEN1*-positive patients in terms of endocrine and non-endocrine manifestations and survival. This is a retrospective study including 187 patients (105 index cases and 82 relatives) with S-MEN1 and F-MEN1 followed at our clinic from January 1993 to January 2023. One hundred-forty (75%) were *MEN1*-positive and 47 (25%) MEN1 negative. The median observation time was 120 months (IQR 60-190) for *MEN1*-positive and 122 months (IQR 75-178) for *MEN1*-negative. *MEN1*-positive exhibited a significantly lower mean age of onset of PHPT (36.3 + 14.2 vs 49.5 + 13 years; $P < 0.00001$), pituitary adenoma (36.2 + 13.5 vs 44.2 + 14.4 years; $P = 0.006$), and GEP-NET (39.7 + 13 vs 47.8 + 11 years; $P = 0.008$). None of the *MEN1*-negative patients had GEP-NET before 30 years. *MEN1*-positive patients also displayed a significantly lower age of onset of the first (36 + 14.3 vs 46 + 14.8 years; $P < 0.0001$), second (39.7 + 14.1 vs 50.2 + 13.1 years; $P < 0.0001$), and third (42 + 14 vs 54.4 + 11.4 years; $P = 0.001$) endocrine manifestations. A higher prevalence of GEP-NET was found in *MEN1*-positive than *MEN1*-negative (61% vs 29%; $P = 0.02$). Additionally, none of the *MEN1*-negative presented metastatic GEP-NET (0% vs 16%; $P < 0.001$). Although no difference in the median number of manifestations was observed between the two groups ($P = 0.06$), *MEN1*-positive exhibited a greater distribution of the number of manifestations compared to *MEN1*-negative (1 to 6 vs 2 to 4, respectively; $P = 0.005$). *MEN1*-positive had a higher prevalence of lipomas ($P = 0.01$) and angiofibromas ($P = 0.01$) compared to *MEN1*-negative. No difference in survival rate was found between the two cohorts. However, in *MEN1*-negative patients none died for MEN1-related causes, whereas in *MEN1*-positive 7 patients died for MEN1-related causes. The overall findings suggest that *MEN1*-negative patients exhibit a less aggressive phenotype than *MEN1*-positive. Consequently, they may benefit from a less intensive follow-up. This underscores the need to update the MEN1 guidelines to differentiate the diagnostic and therapeutic workout in *MEN1*-negative and MEN1-positive.

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P446

Investigating the etiology of non-surgical hypoparathyroidism: insights from a sponsored genetic testing program

Michael Mannstadt[1], Claudio Marelli[2], Ananth Sridhar[3], Lyndsay Smith[3], Mary Scott Roberts[3], Scott Adler[3] & Arun Mathew[3]
[1]Massachusetts General Hospital and Harvard Medical School, Endocrine Unit, Boston, USA; [2]BridgeBio Pharma Inc., Sestri Levante, Italy; [3]Calcilytix Therapeutics Inc., San Francisco, USA

Hypoparathyroidism is a rare endocrine disorder characterized by inadequate production of parathyroid hormone to maintain normal blood calcium levels. Hypoparathyroidism is most frequently caused by damage to or removal of the parathyroid glands but can also be associated with genetic etiologies. Genetic forms of hypoparathyroidism can present as isolated or as part of a syndrome and include disorders of parathyroid gland formation, parathyroid hormone secretion, and damage to the parathyroid gland through autoimmunity. A sponsored genetic testing program in the United States was made available for patients with suspected genetic hypoparathyroidism who met program eligibility criteria and included those with an idiopathic diagnosis. The next-generation sequencing panel leveraging a whole exome backbone with copy number variant detection has evolved to include 26 genes known to be associated with hypoparathyroidism: *ACADM*, *AIRE*, *ATP1A1*, *CASR*, *CHD7*, *CLDN16*, *CLDN19*, *CNNM2*, *DHCR7*, *EGF*, *FAM111A*, *FXYD2*, *GATA3*, *GCM2*, *GNA11*, *HADHA*, *HADHB*, *KCNA1*, *NEBL*, *PTH*, *SEMA3E*, *SLC12A3*, *SOX3*, *TBCE*, *TBX1* and *TRPM6*. A total of 169 samples over a 2-year period were tested from participants with a mean±SD age of 23.4±20.4 (range 0-81). With the multi-gene panel, 77 variants were identified in 64 individuals (37.9%) which have been classified as pathogenic, likely pathogenic, and variants of uncertain significance. In order of frequency, the number of individuals with detected variants are as follows: *CASR* 56.3% (36/64), *AIRE* 12.5% (8/64), *TBX1* 9.38% (6/64), *GATA3* 7.8% (5/64), *GNA11* 6.25% (4/64), *CHD7* 3.13% (2/64), *FAM111A* 3.13% (2/64), *PTH* 3.13% (2/64), *ACADM* 1.6% (1/64), *GCM2* 1.6% (1/64), *HADHB* 1.6% (1/64) and *TBCE* 1.6% (1/64). Of note, 5 individuals had variants identified in more than 1 gene. Within this group of participants, the most frequent genetic form of hypoparathyroidism was found to be autosomal dominant hypocalcemia type 1 (ADH1), caused by gain-of-function mutations in the *CASR* gene (21.3%; 36/169). An ongoing global Phase 3 study is investigating an oral calcilytic that functions as a negative allosteric modulator of the calcium-sensing receptor, potentially the first targeted treatment for ADH1, which affected over half of individuals with identified variants. Genetic testing should be considered for all patients with non-surgical hypoparathyroidism as identified variants in known genes can inform medical management of patients. Genetic testing may uncover the underlying etiology of nonsurgical hypoparathyroidism and can help confirm clinical diagnosis, guide medical treatment, identify affected family members, and assist in determining eligibility for participation in clinical studies.

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P447

Optimal strategies for vitamin D supplementation in the management of severe vitamin D deficiency

Ashraf Soliman, Fawzia Alyafei, Nada Alaaraj, Noor Hamed & Shayma Mohamed
Hamad General Hospital, Pediatric Endocrinology, Doha, Qatar

Introduction
The uncertainty surrounding the optimal dose to rectify severe vitamin D deficiency (VDD) necessitates further investigation.
Aim
To review and analyze various vitamin D (VD) supplementation doses, durations, and their effects on 25-hydroxyvitamin D (25OHD) levels, along with their biochemical and clinical outcomes, in the management of VDD.
Methods
We reviewed intervention studies targeting VDD from databases (PubMed, Google Scholar, ResearchGate, and Scopus, focusing on studies published after 2010.
Results
Twenty-two studies were reviewed. Comparing different regimens, VD3 showed superiority over VD2 in doses of 1600 IU and 50 000 IU once daily and once monthly, respectively, at the conclusion of a year. For adults, the widely adopted 'loading dose' approach (50 000 IU VD orally once weekly for 2–3 months) indicated a minimum cumulative dose of 600 000 IU for achieving an end-of-treatment 25OHD level exceeding 30 ng/ml. The average daily dose for significant serum 25OHD increase was 4707 IU/day for a large adult population. A predictive equation for VD dosage suggested that the required dose = [(8.52 – Desired change in serum 25OHD level) + (0.074 × Age) - (0.20 × BMI) + (1.74 × Albumin concentration) - (0.62 × Starting serum 25OHD concentration)] / (−0.002). Another simplified equation for adults proposed a loading dose formula: IU = 40 × (75 nmol/l – serum 25OHD) × body weight. Two prospective studies involving infants and adolescents who received intramuscular cholecalciferol injections (10 000 IU/kg) demonstrated significant improvements in biochemical and clinical outcomes, with most achieving serum 25OHD levels ≥ 20 ng/ml three months post-injection. In older women, a daily oral dose of 50 000 IU calciferol for ten days elevated 25OHD from 8 ng/ml to 21 ng/ml. Patients treated with cumulative doses of 100 000, 150 000, and 200 000 IU displayed corresponding increases in mean serum 25OHD levels. Reviews of 49 and 76 trials indicated an increase of 2 ng/ml per 100 IU/d of ingested VD and an average rise of 0.78 ng/ml per 40 IU of VD3 supplement daily, respectively. In a study with sixty adolescents, those receiving 300 000 IU VD3 followed by 50 000 IU monthly, or 100 000 IU every three months had higher 25OHD levels (30 ng/ml) than those receiving 50 000 IU every three months or 100 000 IU every three months (15 ng/ml).
Summary
Utilizing a megadose oral or intramuscular loading regimen of VD (300 000 IU, 10 000 IU/kg) followed by daily doses of 1000–2000IU or 50 000IU monthly seems effective for managing severe VDD.

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Formation of new bone lesions in an adult patient with fibrous dysplasia/McCune–Albright syndrome over 19 years and the effect of postoperative hypoparathyroidism on bone turnover markers – case report

Katerina Zajickova[1] & Josef Vcelak[2]
[1]Institute of Endocrinology, Clinical endocrinology, Prague 1, Czech Republic; [2]Institute of Endocrinology, Molecular endocrinology, Prague 1, Czech Republic

Introduction
Fibrous dysplasia (FD) is a rare mosaic disorder originating from the activating mutation in the gene encoding the alpha subunit of the Gs stimulatory protein (*GNAS*) in multipotent skeletal stem cells that cannot differentiate into bone-forming osteoblasts. FD is thought to be a self-limited disease with a peak of activity in childhood and a waning of activity in adulthood.
Case presentation
We report a 39-year-old woman with mild polyostotic FD and precocious puberty in her history. At the age of 31, the patient underwent total thyroidectomy for papillary thyroid cancer, complicated by postoperative permanent hypoparathyroidism. The ^{18}F- NaF PET/CT, carried out to monitor skeletal activity, showed several new skeletal lesions that were not documented on the original PET/CT with ^{18}F-fluorodeoxyglucose performed 19 years ago when FD was diagnosed. Four new lesions were localized in the ribs, two in the vertebrae and one in the symphysis, with corresponding changes in the CT image characteristic of FD. The patient had no clinical evidence of fractures and the thyroid cancer was in remission at the time of the scan. In contrast to polyostotic FD, osteocalcin, alkaline phosphatase and collagen beta crosslaps, which reflect bone remodeling and should correlate with disease extent, were within normal ranges in our patient. The only exception was procollagen 1 N-terminal propeptide (P1NP), which was consistently 3–4 times higher (mean value of P1NP in years 2021–2023: 219.2 ng/ml, normal values 15.3–58.8 ng/ml).
Conclusion
The present case documents the evolution of new skeletal lesions on ^{18}F-NaF PET/CT imaging in an adult patient with mild FD/ McCune-Albright syndrome and shows that the skeletal burden in FD may not be completely stable in adulthood. Furthermore, concomitant postoperative hypoparathyroidism modulates the patient's bone turnover and may highlight a possible role of parathyroid hormone in skeletal involvement in FD. Supported by MH CZ - DRO (Institute of Endocrinology – EÚ, 00023761).

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The incidence of fractures in cancer patients initiating immune check-point inhibitors

Ruth Karov, Eugene Feigin, Etty Osher, Yona Greenman & Vanessa Rouach
Tel aviv Souraski medical center, Institute of Endocrinology, Diabetes, Metabolism and Hypertension

Introduction
Immune check-point inhibitors (ICI) can cause adverse events in many organs due to the activation of T-cells. Data on the effect of ICI on bones and incidence of fracture is still scarce.

Aim
To quantify the rate of osteoporotic fracture before and after the use of ICI in cancer patients.
Methods
We retrospectively retrieved pertinent data of all patients who were treated with ICI between 2015 and 2023 at the Tel-Aviv Souraski Medical Center. Healthcare administrative databases were assessed for the presence of fracture diagnostic codes in the year prior to and up to two years after ICI initiation. Fracture rate was stratified based on the time-period before and after ICI initiation.
Results
The study cohort consisted of 1349 ICI users. The mean age was 67.7 (10.9) years, 58% were male, 35.5% were active smokers, 18% were diabetics, mean BMI was 25.7 (6.8) and mean Charlson Comorbidity Index was 4.2 (2.3). Most patients were treated with an anti-PD-1 agent (82.1%), for 17.6% it was the only therapy. The fracture rate in the year prior to ICI initiation was 8.9 per 1000 patient-years. The fracture rate in the year after ICI initiation was 12 per 1000 patient-years. The fracture rate in the second year after ICI initiation was 18.9 per 1000 patient-years. In the first and second years after ICI treatment initiation, incidence rates of fractures were higher compared to the last year prior ICI treatment, IRR = 1.34 (95% 0.64–2.85) and IRR = 2.13 (95% 1.02–4.41), respectively. Only 12.5% of the patients who sustained a fracture received an antiresorptive treatment.
Conclusions
Fracture risk may be increased in cancer patients after initiation of ICI. Prospective studies monitoring BMD in addition to fracture rate are needed. An effort should be made to identify patients at risk for fractures and offer adequate therapy.

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P450

A pharmacoeconomic analysis from Italian guidelines for the management of sporadic primary hyperparathyroidism

Roberto Attanasio[1], Irene Samperi[2], Alessandro Scoppola[3], Agostino Paoletta[4], Roberto Novizio[5], Fabio Vescini[6], Giorgio Borretta[7], Iacopo Chiodini[8], Enrico Papini[9], Agnese Persichetti[10], Michele Basile[11], Marco Boniardi[12], Marina Carotti[13], Elena Castellano[7], Cristiana Cipriani[14], Cristina Eller-Vainicher[15], Sandro Giannini[16], Maurizio Iacobone[17], Antonio/////Stefano Salcuni[6], Federica Saponaro[18], Stefano Spiezia[19], Annibale Versari[20], Guido Zavatta[21], Zuzana Mitrova[22], Alexia Giovannazzi[23], Rosella Saulle[22], Simona Vecchi[22], Debora Antonini[11], Giorgio Calò[24], Filomena Cetani[25], Luisella Cianferotti[26], Sabrina Corbetta[27], Maria Luisa De Rimini[28], Alberto Falchetti[29], Giovanni Iannetti[30], Stefano Laureti[31], Celestino/////Pio Lombardi[32], Bruno Madeo[33], Claudio Marcocci[25], Sandro Mazzaferro[34], Vittorio Miele[35], Salvatore Minisola[36], Andrea Palermo[37], Jessica Pepe[13], Laura Tonzar[11], Alfredo Scillitani[38], Franco Grimaldi[39], Renato Cozzi[40] & Roberto Attanasio[1]
[1]AME Scientific Committee, Milan, Italy; [2]SSD of Diabetology and Metabolic Diseases - Azienda Sanitaria Locale Novara, Novara, Italy; [3]Endocrinology, Ospedale Santo Spirito, rome, Italy; [4]Endocrinology,, ULSS6 Euganea, Padua, Italy; [5]Endocrinology and Metabolism, Agostino Gemelli University Polyclinic (IRCCS), Catholic University of the Sacred Heart, Rome, Italy; [6]Endocrinology Unit, Azienda Sanitaria-Universitaria Friuli Centrale, P.O. Santa Maria della Misericordia, Udine, Italy; [7]Department of Endocrinology, Diabetes and Metabolism, Ospedale Santa Croce and Carle Hospital, Cuneo, Italy; [8]Endocrinology Department, ASST Grande Ospedale Metropolitano di Niguarda, Milan, Italy; [9]Endocrinology, ospedale Regina Apostolorum, Rome, Italy; [10]Department of Human Sciences and Promotion of the Quality of Life, San Raffaele Roma Open University, Rome, Italy; [11]High School of Economy and Management of Health Systems, Catholic University of Sacred Heart, Rome, Italy; [12]General Oncologic and Mini-invasive Surgery Department, ASST Grande Ospedale Metropolitano di Niguarda, Mialn, Italy; [13]Department of Radiology, AOU delle Marche, Ancona, Università Politecnica delle Marche, Ancona, Italy; [14]Department of Clinical, Internal, Anesthesiological and Cardiovascular Sciences, Sapienza University of Rome, Rome, Italy; [15]Endocrinology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [16]Clinica Medica 1, Department of Medicine, University of Padova, Padua, Italy; [17]Endocrine Surgery Unit, Department of Surgery, Oncology and Gastroenterology, University of Padova, Padua, Italy; [18]Department of Surgical, Medical, and Molecular Pathology and Critical Care Medicine, University Pisa, pisa, Italy; [19]Department of Endocrine and Ultrasound-Guided Surgery, Ospedale del Mare, Naples, naples, Italy; [20]Nuclear Medicine, Azienda Unità Sanitaria Locale–IRCCS di Reggio Emilia, Reggio Emilia, Italy; [21]Division of Endocrinology and Diabetes Prevention and Care, IRCCS AOU di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, bologna, Italy; [22]Department of Epidemiology, Lazio Region Health Service, Rome, Italy; [23]Azienda Provinciale per i Servizi Sanitari della Provincia Autonoma di Trento, Trento, Italy; [24]SIUEC President, Department of Surgical Sciences, University of Cagliari, Cagliari, Italy; [25]Endocrine Unit 2, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [26]Bone Metabolic Diseases Unit, Department of Experimental, Clinical and Biomedical Sciences, University of Florence, AOU Careggi, Florence, Italy; [27]Bone Metabolism and Diabetes, IRCCS Istituto Auxologico Italiano, Milan, Italy; [28]AIMN President, Nuclear Medicine Unit, AORN Ospedali dei Colli, Naples, Naples, Italy; [29]Laboratory of Experimental Clinical Research on Bone Metabolism, Istituto Auxologico Italiano IRCCS, Milan, Italy; [30]SIUMB President, Ultrasound Unit, S. Spirito Hospital, Pescara, Italy; [31]General Practitioner, USL Umbria 1, Perugia, Italy; [32]Endocrine Surgery, Ospedale Gemelli, Rome, Italy; [33]Unit of Endocrinology, Department of Medical Specialties, Ospedale Civile di Baggiovara, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy; [34]Nephrology Unit at Policlinico Umberto I Hospital and Department of Translation and Precision Medicine, Sapienza University of Rome, Rome, Italy; [35]Department of Emergency Radiology, Careggi University Hospital, Florence, Italy; [36]UOC Medicina Interna A, Malattie Metaboliche dell'Osso, Ambulatorio Osteoporosi e Osteopatie Fragilizzanti, Sapienza University of Rome, Rome, Italy; [37]Unit of Thyroid and Bone-Metabolic Diseases, Fondazione Policlinico Universitario Campus Bio-Medico, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy; [38]Unit of Endocrinology, Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, San Giovanni Rotondo, Italy; [39]AME past President, Udine, Italy; [40]AME president, Milan, Italy

Background
Primary hyperparathyroidism (PHPT) is the third most common endocrine disease and the most frequent cause of hypercalcemia in outpatients with an estimated incidence of 20/100 000/year and prevalence in the general population of 0.1%–0.4%. Parathyroidectomy (PTX) is the only treatment that can achieve PHPT cure but a few medications can be used to control calcium levels, bone and kidney impairment.
Aims
1) To assess costs associated with the different treatment options for PHPT (PTX, cinacalcet, bisphosphonates, denosumab, and thiazides); 2) To assess the cost-utility profile of the alternatives to inform the policy making; 3) To provide comprehensive recommendations for the most cost-utility and efficient approaches to managing PHPT in the Italian healthcare setting.
Method
A systematic literature review and a survey among the panel were performed to address drivers that contribute to each therapeutic option. Economic analysis was carried out with Activity Based Costing methodology.
Results
The estimated cost of PTX arm amounts to an average of € 4588. This amount includes: diagnostic assessment, surgery, post-operative follow-up, indirect costs for patient and caregiver, and costs due to the acute and chronic post-operative complications (added for the fraction of patients undergoing those complications). Taking into account the expected additional costs in the first year for the complementary services, the total expenditure is € 5714. In the case of non-surgical policy, the estimated annual cost is a mean € 197 and € 953 for surveillance and drug treatments (including cost of drugs and follow-up in the proportion of patients treated with each drug), respectively. As surgery for sporadic PHPT is performed at a mean age of 55 years, the residual time horizon points to about 30 years. The estimated cost for the same 30-year time horizon amounts to € 28 590 for the patients followed up with medications and to € 5910 for surveillance alone (Table 1).

Approach	Annual cost	30-year cost
Surgery	€ 5116	€ 5116
Surveillance	€ 197	€ 5910
Medication	€ 953	€ 28 590

Conclusions
Despite limitations of this analysis, we can believe that the 30-year excess costs for patients who are managed pharmacologically in comparison to those who are surgically treated is € 23 474 (28 590 – 5116). If we assume that at least 10% of patients currently treated pharmacologically (estimated to be near 1500 in Italy) could be switched to surgical strategy, we can estimate an annual saving for National Health System exceeding € 3 500 000 (23 474 × 150 = 3 521 100).

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P451

Bone responsiveness in PTH resistance syndromes: preliminary data of a single centre retrospective study

Giulia Del Sindaco[1,2], Angela Pagnano[1,2], Arianna Cremaschi[2] & Giovanna Mantovani[1,2]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Ern Bond, Milan, Italy

Inactivating PTH/PTHrP signaling disorders (iPPSDs, historically named pseudohypoparathyroidism (PHP)) are primarily characterized by end-organ resistance to parathormone (PTH), which leads to hypocalcemia, hyperphosphatemia and elevated PTH levels. The extent to which bone is responsive to PTH in these patients remains controversial. Until now, variable bone phenotypes have been associated to different subtypes of iPPSDs and increased concentrations of bone turnover markers (BTMs) are described. Persistently elevated PTH levels may cause bone abnormalities similar to what observed in hyperparathyroidism (osteitis fibrosa and rickets). Moreover, data about bone mineral density (BMD) are sparse and report both normal, increased or decreased values. Aim of the present study is to characterize bone metabolism in a cohort of iPPSD patients. We collected data about BMD, vertebral morphometry and BTMs to describe bone abnormalities, aiming to investigate whether there is a relationship with PTH levels or iPPSD subtype. We enrolled 21 patients (62% females, mean age 39.6±11.3 years) diagnosed with iPPSDs and regularly followed-up at our Centre. Six patients were diagnosed with iPPSD2/PHP1A (28.6%), 13 patients with iPPSD3/PHP1B (61.8%), 1 patient with iPPSD4/Acrodysostosis type 1 and 1 patient had no detected mutations. In our cohort PTH levels show significant positive correlation with both CTX and bone alkaline phosphatase (bALP) levels (CTX: $r=0.482$, $P=0.02$; bALP: r=0.508, $P=0.02$). Bone turnover markers were not significantly different between iPPSD2/PHP1A and iPPSD3/PHP1B patients. As for BMD values, mean lumbar, femoral neck and total hip scores were 1.083± 0.18, 0.856±0.18 and 0.968±0.18 g/cm^2 respectively, with no significant difference between iPPSD2/PHP1A and iPPSD3/PHP1B patients. One patient (5%) was diagnosed with osteoporosis and one patient with osteopenia according to Z and T-scores respectively, as expected for age and sex. Fractures were described in 2 patients with pre-existing comorbidities. As for vertebral morphometry, we described rickets-like signs in 39% (7/18) of patients, with no difference among various iPPSD subtypes. It is worth report one patient affected by iPPSD3/PHP1B, who presented PTH > 1000 pg/ml at diagnosis with concomitant cystic bone lesions (compatible with brown tumors/osteitis fibrosa cystica) at multiple sites. In conclusion, our study confirms previous reported data about bone metabolism and phenotypes in iPPSDs. According to BTMs and skeletal remodeling, bone seems to be responsive to PTH in both iPPSD2/PHP1A and iPPSD3/PHP1B. Although these are preliminary data that we are expanding through comparative studies, they could have clinical impact on management, suggesting to control PTH levels on optimal range to avoid negative impact on bone.

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P452

Clustering of clinical and biochemical data for defining primary hyperparathyroidism 'phenotypes' and predicting parathyroid imaging results

Karolina Kucharczyk[1], Anna Drynda[1], Jacek Podlewski[2], Malgorzata Trofimiuk-Muldner[3] & Alicja Hubalewska-Dydejczyk[3]
[1]Jagiellonian University Medical College, Students' Scientific Group at the Department of Endocrinology, Krakow, Poland; [2]Dover Fueling Solutions, Krakow, Poland; [3]Jagiellonian University Medical College, Department of Endocrinology, Krakow, Poland

Introduction
Primary hyperparathyroidism (PHPT) is a prevalent endocrinopathy typically identified through biochemical testing. PHPT is characterized by hypercalcemia accompanied by increased or inappropriately normal plasma parathyroid hormone (PTH) concentrations. Preoperative imaging is conducted when surgery is indicated to pinpoint parathyroid adenomas. MIBI scintigraphy is highly specific and sensitive in diagnosing PHPT, with a higher adenoma detection rate demonstrated for patients with larger lesions or higher blood calcium concentrations. The study aimed to investigate the relationship between the results of biochemical tests and clinical manifestations (PHPT 'phenotype') and the rate of positive results of parathyroid [99mTc]Tc-Sestamibi scintigraphy.
Materials and methods
This was a retrospective study of patients suspected of PHPT who underwent parathyroid [99mTc]Tc-Sestamibi SPECT/CT scintigraphy between 2010 and 2022. Patients' cluster analysis was conducted based on PTH, serum calcium (Ca), and phosphate (Pi) concentrations to find distinct patterns in these parameters. Furthermore, we compared the distributions of additional patients' attributes, including gender, lesion size, serum vitamin D, ALP concentrations, urinary calcium, urolithiasis prevalence, as well as parathyroid scintigraphy results.
Results
Five hundred and thirteen patients were divided into 5 clusters using different algorithms. Finally, clusters from K-means methods were selected based on statistical metrics and expert interpretation. Those were organized in ascending order of positive scintigraphy results, with Cluster 5 reaching a 79.5% positivity rate and median values of PTH – 315.5 pmol/l, Ca – 2.96 mmol/l, and Pi – 0.7 mmol/l. As the proportion of positive imaging outcomes declined, median PTH and calcium concentrations decreased while phosphate concentrations increased. In Cluster 1, with 30% of positive imaging results, medians were as follows: PTH – 79.06 pmol/l, Ca – 2.55 mmol/l and Pi – 1.1 mmol/l. A comparative analysis of various clinical and biochemical parameters revealed statistically significant differences between clusters. Patients from Clusters with a higher frequency of positive scintigraphy were significantly more likely to be males, vitamin D deficient, with higher ALP concentrations, diagnosed with urolithiasis, and harbouring larger lesions.
Conclusions
PHPT 'phenotypes' correlated with disease severity are evidently linked to parathyroid scintigraphy detection rate. Therefore, it is crucial to know that false-negative imaging is more likely in PHPT patients with minor deviations in laboratory tests. Judicious assessment of biochemical and clinical features may limit the number of redundant parathyroid scintigraphies and, in consequence, reduce healthcare costs and unnecessary radiation exposure.

Keywords: primary hyperparathyroidism, imaging, scintigraphy, biochemistry
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P453

Mild hyponatremia is not associated with degradation of trabecular bone microarchitecture despite bone mass loss

Fabio Bioletto, Michela Sibilla, Alessandro Maria Berton, Nunzia Prencipe, Emanuele Varaldo, Federica Maiorino, Daniela Cuboni, Alessia Pusterla, Valentina Gasco, Silvia Grottoli, Ezio Ghigo, Emanuela Arvat, Massimo Procopio & Marco Barale
University of Turin, Department of Medical Sciences, Turin, Italy

Context
Hyponatremia is associated with an increased risk of osteoporosis and fractures, and in recent years increasing evidence is accumulating in favor of a likely causal relationship between hyponatremia and bone loss. In rat models, the induction of hyponatremia enhances osteoclast activation and bone catabolism. In humans, the correction of hyponatremia by tolvaptan or SGLT2-inhibitors has a favorable effect on bone turnover markers, possibly due to an interplay both with osteoblast and osteoclast activation. The impact of hyponatremia on non-invasive indices of bone quality, however, is unknown.
Objective
To evaluate whether trabecular bone microarchitecture, assessed non-invasively by trabecular bone score (TBS), is altered in patients with hyponatremia.
Methods
We conducted a cross-sectional analysis of the 2005–2008 cycles of the National Health and Nutrition Examination Survey (NHANES), in which TBS measurement was performed. The main outcome measures were TBS values and bone mineral density (BMD) T-scores at the lumbar spine, total hip and femoral neck.
Results
A total of 4204 subjects aged 50 years or older were included (4041 normonatremic, 163 hyponatremic). The mean serum sodium value in hyponatremic patients was 132.6±2.1 mmol/l, with sodium levels in the range of mild hyponatremia (130–134 mmol/l) in 90.8% of cases. Univariate analyses did not show any difference in TBS between patients with and without hyponatremia (1.308±0.145 vs 1.311±0.141, $P=0.806$). Hyponatremic subjects had lower BMD T-score at total hip (−0.70±1.46 vs −0.13±1.32, $P<0.001$) and femoral neck (−1.11±1.26 vs −0.72±1.14, $P=0.004$), while no difference was observed at lumbar spine (−0.27±1.63 vs −0.31±1.51, $P=0.772$). After adjustment for relevant confounders (i.e.: age, sex, ethnicity, smoking, body mass index, 25-hydroxyvitaminD, diabetes, chronic kidney disease, use of loop, thiazide or potassium-sparing diuretics, history of chronic glucocorticoid treatment), hyponatremia was confirmed as an independent predictor of lower BMD T-score at the total hip ($\beta=-0.20$, 95%CI:[−0.39,−0.02], $P=0.029$), while the significance was lost at the femoral neck ($P=0.308$). The lack of association between hyponatremia and lumbar spine BMD ($P=0.236$) or TBS ($P=0.346$) was confirmed.

Conclusions
This study confirms that hyponatremia is associated with a reduced bone density, particularly at the total hip. On the other hand, no significant impact on trabecular bone microarchitecture, evaluated by TBS, was found. The lack of prospective data does not allow to assess the prognostic role of these parameters as predictors of incident fractures, but the available evidence may suggest, differently from other forms of secondary osteoporosis, a possible limited added value of TBS in this setting.

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P454

The clinical presentation of primary hyperparathyroidism: effects of obesity and vitamin D deficiency

Vit Zikan[1,2], Jan Hrdlicka[3], Judita Klímová[4], Václav Hána Jr[1], Monika Wagnerova[5], Petr Libánský[6], Dana Michalska[1], Renata Vlasakova[1] & Ivan Raska Jr[1]
[1]General University Hospital in Prague, Department of Internal Medicine 3, Prague, Czech Republic; [2]General University Hospital, Internal Medicine 3, Prague, Czech Republic; [3]General University Hospital in Prague, Department of Radiology, Prague, Czech Republic; [4]Military University Hospital in Prague, Department of Internal Medicine, Prague, Czech Republic; [5]General University Hospital in Prague, Department of Radiology and Institute of Nuclear Medicine, Prague, Czech Republic; [6]Motol University Hospital in Prague, Department of Surgery III, Prague, Czech Republic

Our understanding of modifiable risk factors for developing primary hyperparathyroidism (PHPT) may support interventions to prevent the development of the disease or reduce its severity and deepen our insights into its pathogenesis. Obesity has been associated with elevated serum parathyroid hormone (PTH) in the general population and may also alter the clinical presentation in patients with PHPT.
Objectives
The objectives of the study were to compare the clinical, radiological and biochemical presentation of obese vs nonobese PHPT patients and to assess the impact of obesity and vitamin D deficiency on the presentation of PHPT.
Methods
Calcium metabolism and bone turnover markers (BTMs) S-CTX and PINP were analysed. Bone mineral density (BMD) and body composition was assessed by dual-energy X-ray absorptiometry (DXA). Clinical fractures were assessed from medical records.
Results
One hundred forty-four PHPT patients (79% postmenopausal women) were included in this analysis. Sixty-three percent of patients fulfilled the criteria for asymptomatic PHPT (84 patients with classic PHPT and 11 patients were normocalcemic, NHPT). Obesity was diagnosed in 64% of NHPT patients and in 44% of PHPT. The obese patients showed higher BMD in total and femoral neck and a lower rate of osteoporosis (41.8% vs 60.7%); however higher prevalence of clinical vertebral fractures was observed in obese women (9% vs 3.6%). Regarding the BTMs, it was found to be significantly lower values in women with obesity ($P < 0.05$); however, the comparison of those with severe deficient (<25 nmol/l; 18.8%) vs replete (≥ 75 nmol/l; 15%) 25OHD demonstrated more severe PHPT as reflected by significantly higher PTH, Ca and BTMs. Conclusions: In PHPT and NHPT patients, obesity is a protective factor for hip BMD; however, our findings of higher number of vertebral fractures in obese women suggest that BMD does not adequately assess the risk for vertebral fractures. Severe vitamin D deficiency may increase PTH and bone loss.

Keywords: primary hyperparathyroidism, obesity, osteoporosis, vitamin D deficiency
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Diabetes, Obesity, Metabolism and Nutrition

P45

The impact of diabetes mellitus on morbidity and mortality in patients with covid-19 pneumonia. retrospective study

Elona Xhardo Hysenbelli[1,1], Bledar Hysenbelli[2], Sofiela Telo[3] & Dorina Ylli[4]
[1]Sushn, Internal Medicine, Tirana, Albania; [2]Qsut, Emergency Care Department, Tirana, Albania; [3]Sushn, Epidemiologu and Statistics, Tirana, Albania; [4]Qsut, Endocrinology, Tirana, Albania

Background
The relationship between diabetes and COVID-19 is known to be bidirectional. Diabetes Mellitus (DM) and hyperglycemia are important risk factors for poor outcomes in hospitalized patients with coronavirus disease 2019 (COVID-19) pneumonia.
Objective
This study aimed to evaluate the impact of glycemic control pre- and after admission, on outcomes of hospitalised patients with COVID-19 pneumonia.
Methods
A total of 400 hospitalized patients with confirmed COVID-19-pneumonia during the interval 2020-2021 in e tertiary Hospital Center in Albania were included in the present study. Diabetic patients were classified in two groups, new onset and pre-existing diabetes. The outcomes were compared with non-DM patients with COVID-19 pneumonia. At the same time we analysed how mean glucose during the hospitalization period could influence final outcomes regarding in-hospital case fatality and in-hospital adverse events.
Results
Overall, 400 hospitalizations with confirmed COVID-19 pneumonia were documented. COVID-19 patients with DM demonstrated an aggravated comorbidity profile, with a higher Charlson comorbidity index. Risk for acute respiratory distress syndrome (96% CI: 1.57–1.64), $P<0.001$), non-invasive ventilation (95% CI: 1.43–1.57), $P<0.001$ and mechanical ventilation (95% CI: 1.39–1.48), $P<0.001$ were increased in DM patients. DM was an independent risk factor for in-hospital complications like major cardiac events, acute kidney failure, and in-hospital mortality (OR: 1.24 (95% CI: 1.25–1.31), $P<0.001$) Severe hyperglycemia (mean blood glucose $>$ 250 mg/dl) on second day of hospitalization was associated with high mortality compared with patients with mean blood glucose around 140 mg/dl. In-hospital hypoglycemia events (blood glucose $<$ 70 mg/dl) was also associated with increased mortality.
Conclusion
In patients with COVID-19-pneumonia, DM is a important risk factor for adverse events and fatality. Severe hyperglycemia and hypoglycemia events after admission were both strong predictors of poor outcomes. Diabetics patients with COVID-19 are a vulnerable group that requires intense medical care and need to be strictly monitored during hospitalization.

Keywords: Diabetes mellitus, COVID-19-pneumonia, in-hospital complications, intensive care.
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P46

Obesity in women with polycystic ovary syndrome –an individual participant data meta-analysis of well characterised, unselected populations

Johanna Melin[1], Ricardo Azziz[2], Larisa Suturina[3], Xiaomiao Zhao[4], Alessandra Gambineri[5], Fahimeh Tehrani[6], Bulent Yildiz[7], Jin Ju Kim[8], Christian Makwe[9], Helena Teede[10] & Anju Joham[1]
[1], Monash Centre for Health Research and Implementation, Faculty of Medicine, Nursing and Health Sciences, Clayton, Australia; [2]University of Alabama at Birmingham, Department of Obstetrics and Gynecology, School of Medicine, United States; [3]Scientific Center for Family Health and Human Reproduction, Department of Reproductive Health Protection, Russian Federation; [4]Sun yat-sen University, Department of Reproductive Endocrinology and Infertility, Guangdong, China; [5]University of Bologna, Italy, Department of Medical and Surgical science –DIMEC endocrinology Unit, Bologna, Italy; [6]Shahid Beheshti University of Medical Sciences, Reproductive endocrinology Research Center, Research Institute for Endocrine Sciences, Tehran, Iran; [7]Hacettepe University of Medicine, Division of Endocrinology and Metabolism, Ankara, Turkey; [8]Division of Reproductive Endocrinology, DeparHealthcare System Gangnam Center, Seoul National University Hospital, Division of Reproductive Endocrinology, Department of Obstetrics and Gynecology, Seoul, Korea, Rep. of South; [9]University of Lagos, Department of Obstetrics and Gynecology, Lagos, Nigeria; [10]Monash University, Monash Centre for Health Research and Implementation, Faculty of Medicine, Nursing and Health Sciences, Melbourne, Australia

Objective
For women with polycystic ovary syndrome (PCOS) weight gain and obesity exacerbate insulin resistance and increase the risk of type 2 diabetes and cardiometabolic diseases. The PCOS Phenotype in Unselected Populations (P-PUP) study includes individual participant data (IPD) from eleven well characterised, multiethnic and unselected populations globally. The aim of this study was to assess risk of obesity in women with and without PCOS according to ethnicity and age.

Methods
The dataset consisted of 9,930 unselected women, aged 15 to 60 years from Italy, Turkey, China, Iran, South Korea, United States of America, Russia and Nigeria. The women were categorized into those with PCOS (10.7%) and without PCOS (89.3%) according to Rotterdam criteria or National Institutes of Health Criteria (NIH). Multiple logistic regression was used to estimate odd ratios (ORs) with 95% confidence intervals (CI) for obesity (BMI >30 kg/m^2) comparing women with and without PCOS, adjusting for age and ethnicity. We performed sub-analyses according to ethnicity and age.
Results
Obesity was more common in women with PCOS (17.9%), compared to women without PCOS (14.4%) (aOR 1.6, 95% CI 1.3-1.9). We observed significant differences in the prevalence of obesity according to ethnic groups, being lowest for Asian (3.8%), followed by Middle Eastern (24.1%), Caucasian (29.1%) and Black women (33.8%). After adjusting for age, compared to Asian women with PCOS, the odds for obesity were higher for Middle Eastern women (aOR 6.3, 95% CI 3.6-11.9), Caucasians (aOR 9.5, 95% CI 4.8-18.9) and Black women (aOR 10.3, 95% CI 5.0-21.5) with PCOS. The risk for obesity in women with PCOS increased with age, being 14.5% for women aged 15-39 years and 48.6% for women aged 40-60 years (aOR 4.0, 95% CI 2.6-6.2).
Conclusion
In a large, unselected, multiethnic population obesity was more common in women with PCOS compared to women without PCOS. We observed significant differences in obesity by ethnicity, with Asian women with PCOS having the lowest odds and Middle Eastern, Caucasian and Black women all having higher odds for obesity. Compared to younger individuals with PCOS, those aged 40 to 60 years had a 4-fold risk for obesity.

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P47

Demographics and baseline characteristics of patients with charcot foot: a multi-center cohort analysis

Edward Jude[1], Christos Siafarikas[2], Robert Bem[3], Javier LaFontaine[4], Marie-France Kong[5], Tsvetalina Tankova[6], Pappachan Joseph[7], Ashu Rastogi[8] & Nicolaas Tentolouris[2]
[1]Tameside and Glossop Integrated Care NHS Foundation Trust, Ashton Under Lyne, United Kingdom; [2]National and Kapodistrian University of Athens, Athens, Greece; [3]Institute of Clinical and Experimental Medicine, Czech Republic; [4]utrgv school of podiatric medicine, San Antonio, United States; [5]leicester general hospita; l, leicester, United Kingdom; [6]medical universty of sofia, sofia, Bulgaria; [7]lancashire teaching hospitals, Preston, United Kingdom; [8]Postgraduate institute of Medical Education and Research, Chandigarh, India

Aims
Charcot foot (CF) is a rare complication of T2DM, progressively leads to bone deformities of the lower extremities. The aim of this study was to record baseline characteristics of patients with CF.
Patients and methods
A multicenter retrospective cohort study ($n=774$), including all patients diagnosed with CF from eight Diabetic Foot Clinics in 6 countries between 01/01/1996 and 31/12/2022, was performed. Data regarding duration and complications of DM, anthropometric, clinical and laboratory parameters were obtained from the medical records.
Results
Mean age of patients was 56.5 ± 10.7 years and the mean age at CF diagnosis was 54.5 ± 11.7 years, 70.5% were men. T2DM was more prevalent (83.2%), the mean duration of DM at diagnosis was 17.3 years and median glycated hemoglobin was 8% (Interquartile range-IQR 6.8-9.3%) at diagnosis of CF. Regarding anthropometric features, mean height, weight and body mass index (BMI) were 169.40 ± 16.5 cm, 84.4 ± 21.0 kg, 28.97 ± 7.8 kg/m^2, respectively. Most of the patients had hypertension (74.5%), quarter of them were active or ex-smokers (25.2%) or alcohol users (23.3) and previous medical history comprised of peripheral artery disease (19.7%), coronary artery disease (17.5%) or stroke (5.4%). Neuropathy was the most prevalent (89%) amongst the microvascular complications followed by retinopathy (60%) and nephropathy (45%). A foot ulcer was present in about half of the patients (48.5%) while CF was equally distributed between feet (right foot 49%-left foot 44%-bilateral 6.5%) and majority of them were in midfoot (65%), forefoot 18%, hindfoot 13.9% and multiple joint involvement (2.6%). Patients with type 1DM in comparison with those with T2DM were diagnosed with CF at younger age (46.9 ± 11.0 vs 57.9 ± 10.2 years, $P<0.001$), had lower BMI (26.6 ± 6.0 vs 29.5 ± 8.0 kg/m^2, $P=0.001$) and longer diabetes duration [median (IQ): 29.0 (21.0-38.0) vs 14.0 (8.0-20.0) years, $P<0.001$]. No differences were found between T1D and T2DM in HbA1c. No significant gender differences were found in terms of age at CF diagnosis, BMI or HbA1c; however, the duration of DM at CF diagnosis was lower in men vs women 15.0 (1.0-22.0) vs 17.0 (10.0-25.0) years, $P=0.037$].
Conclusion
This is the largest cohort of patients with CF globally. CF is predominant in males, occurs in people with long-standing DM, is often accompanied by microvascular complications, half of patients have foot ulcers at CF diagnosis, affects equally both feet, and the more frequent location is in the midfoot. Further studies are needed to look at outcomes and mortality.

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P48

Screening for gestational diabetes in the first trimester: the impact of fasting blood glucose in maternal and foetal health

Ana Carreira[1], Sofia Lopes[1], Kristina Hundarova[2], Antonio Lobo[2], Maria Céu Almeida[2], Luísa Ruas[1], Sandra Paiva[1], Miguel Melo[1] & Isabel Paiva[1]
[1]Hospitais da Universidade de Coimbra, Unidade Local de Saú de de Coimbra, Endocrinology, Diabetes and Metabolism, Coimbra, Portugal; [2]Hospitais da Universidade de Coimbra, Unidade Local de Saú de de Coimbra, Obstetrics, Coimbra, Portugal

Introduction
Screening for gestational diabetes (GD) in the first trimester using fasting plasma glucose (FPG) ≥92 mg/dl is routinely performed in several countries. However, evidence on the benefits and harms of early universal screening, as well as the optimal cut-off of FPG, is conflicting. This results in lack of standardised screening and treatment approaches for GD worldwide.
Aims
o compare the use of pharmacological treatment and pregnancy outcomes in GD diagnosed in the first and second trimesters, as well as between different levels of FPG in the first trimester.
Materials and methods
Retrospective cohort study of singleton pregnancies with GD that were followed in a tertiary centre (2016-2020). Cases of first-trimester-diagnosed GD were divided in 3 groups according to their FPG level (G1: 92-94 mg/dl, G2: 95-100 mg/dl, G3: >100 mg/dl). All women received guidance on lifestyle behavior changes. Neonatal morbidity included respiratory distress syndrome, hypoglycaemia and/or hyperbilirubinaemia.
Results
1498 pregnancies were analysed, with mean maternal age of 34.0 ± 5.4 years and pregestational BMI of 27.1 ± 5.9 kg/m^2 48.8% diagnosed in the first trimester. Compared to second-trimester, first-trimester GD showed a greater need for pharmacological treatment (43.0% vs 26.4%, $P<0,001$) and earlier start of insulin treatment (19.7 ± 7.1 vs 30.9 ± 3.1 weeks, $P<0.001$); with no differences in pregnancy outcomes. FPG in the first-trimester-diagnosed GD was 92-94 mg/dl in 46.0%, 95-100 mg/dl in 36.8% and >100 mg/dl in 17.2%. Pregestational BMI was superior in G3 (28.5 ± 6.8 vs 26.8 ± 6.0 kg/m^2, $P=0.007$). Adjusting for BMI, the risk of neonatal morbidity was reduced by 39.2% in G1 (CI: 0.39-0.92) and the risk of preterm birth was 2.0 times higher in G3 (CI: 1.1-3.7), compared to the remaining. There were no differences on the risk of large or small for gestational age, macrosomia or caesarean delivery between groups. The need for pharmacological treatment was inferior in G1 ($P=0.002$), and increased progressively across groups (36.9% $<$ 40.9% $<$ 63.5%). In multivariate analysis, the odd for requiring pharmacological treatment increased 6.0% per 1 mg/dl of FPG (CI: 1.02-1.10), 7.9% per year of maternal age (CI: 1.03-1.13) and 11.9% per 1 kg/m^2 of BMI (CI: 1.08-1.16), and was 80.6% higher in women with previous GD (CI: 1.07-3.06). Pharmacological treatment showed no association with pregnancy outcomes.
Conclusion
Screening in the first trimester was essential for the early diagnosis and treatment of a large proportion of GD. Women diagnosed by FPG of 92-94 mg/dl showed a lower risk of neonatal morbidity and a lesser need for pharmacological intervention, but suffered no evident harm from ongoing monitoring and treatment.

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P49

Overweight and obesity in survivors of childhood cancer

Miriam Helin[1], Inna Zaslavsky-Paltiel[2], Michal Ben Ami[1,3], Eve Stern[1,3], Liat Lerner[4] & Dalit Modan[1,3]
[1]Tel Aviv University, Faculty of Medicine, Tel Aviv, Israel; [2]Chaim Sheba Medical Center, Gertner Institute for epidemiology and health policy resaerch, Ramat Gan, Israel; [3]The Edmond and Lily Safra Children' s Hospital, Chaim Sheba Medical Center, Pediatric Endocrinology and Diabates, Ramat Gan, Israel; [4]Faculty of Medicine, Tel Aviv University, School of Public Health

Background
Multiple studies demonstrated increased incidence of obesity, as well as associated morbidity, such as the metabolic syndrome and cardiovascular disease, in childhood cancer survivors (CCS). Still, data regarding the rates and the timeline of obesity as well as of specific risk factors are inconsistent.
Aim
To evaluate the rate of overweight and obesity in CCS, to characterize longitudinal changes in weight status, and to identify predictors of obesity in this population.
Methods
A retrospective cohort study, comprising of all patients followed at the endocrine late effects of childhood cancer clinic between 1.1.2000 –31.12.2020, diagnosed between the ages of 0-18 years, with follow-up of at least one year following completion of anti-cancer treatment. Pertinent data were abstracted from the patients' medical charts.
Results
The final study cohort included 820 CCS (males:473, 57.7%). The mean age at the time of oncological diagnosis was 7.1 ± 5.1 years, with a median follow-up of 5.5 years from diagnosis. At their last clinic visit, 15.6% of survivors were overweight and 11.1% of them were obese. Compared to the general population, we observed higher rates of overweight and obesity in CCS males aged 2-6 years (33% vs 14%, $P<0.001$), in males aged 6-12 years (38% vs 19%, $P<0.001$) and in females aged 6-12 years (35% vs 21%, $P<0.001$). Multivariate analysis identified weight status at the time of diagnosis ($P<0.001$), and endocrine dysfunctions (OR = 1.46, 95%CI 1.08-1.98, $P=0.01$), as independent predictors of overweight and obesity. The highest rates of overweight and obesity were observed 3-5 years after diagnosis (OR = 1.3, 95% CI 1.11-1.53, $P=0.001$). Diagnosis between the ages 10-14 years, was associated with lower odds of overweight and obesity at the end of follow up compared to diagnosis at an age younger than three years (OR 0.51, 95% CI 0.32-0.83, $P<0.01$). There was no association between weight status at the last visit and gender or type of oncological disease. There was a significant increase in BMI-SDS up to 5 years after diagnosis (0.067 ± 0.033, $P=0.04$), followed by a decrease in BMI-SDS with a later follow up of 5-10 years (-0.11 ± 0.037, $P=0.002$), and more than 10 years after diagnosis (-0.25 ± 0.055, $P<0.001$).
Conclusion
Weight status at diagnosis, endocrine deficiencies, and length of follow-up were identified as predictors of overweight and obesity in CCS. Our results may help in identifying at-risk patients and in designing appropriate targeted interventions that might decrease obesity and related morbidity in CCS.

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P50

Post-lifestyle modification program changes in betatrophin and FGF21 levels among arab adolescents with varying levels of adiposity

Mona Alenazi[1], Shaun Sabico[1] & Nasser Al-Daghri[1]
[1]King Saud university, Biochemistry, Riyadh, Saudi Arabia

Background and Aim
Betatrophin has been observed to play an important role in regulating lipid and glucose metabolism, at least in adults. FGF21 is one of the members of endocrine arm of FGF family and its actions as a glucose and lipids metabolism regulator. FGF21 is rapidly emerging as an attractive target in the treatment of metabolic syndrome and type 2 diabetes. They may serve as both risk factors and biomarkers of chronic metabolic disorders. This study aimed to investigate the changes in betatrophin and FGF21 levels in Arab adolescents with varying levels of BMI and glycemia after a 12-month lifestyle modification program.
Methods
A total of 218 children and adolescents (Male = 106, Female = 112) aged 13-17 years were included and stratified based on baseline BMI [normal ($n=45$, overweight ($n=77$ and obese ($n=96$] before undergoing a 12-month intervention program. Anthropometric and fasting blood samples were taken at baseline and after 12 months of intervention. Glycemic and lipid profiles were measured routinely. Betatrophin and FGF21 were assessed using commercially available assays.
Results
At baseline, obese adolescents had a higher betatrophin level [0.7 ng/ml (0.4–1.3), $P=0.032$]. Follow-up BMI was significantly lower in the obese ($P<0.001$) and overweight ($P=0.018$) groups. However, in obesity adolescents, betatrophin levels and BMI were significantly lower after 12-month lifestyle intervention [0.5 ng/ml (0.1–1.1), $P=0.032$; 33.1 ± 7.5), $P<0.001$ respectively] and FGF21 was significantly higher in prediabetic and obesity subjects [194.4 (103.4 - 295.4), $P=0.017$; 208.0 (115.8 - 362.0), $P=0.003$ respectively]. Follow-up lipid profile and insulin were significantly higher in all obese participants ($P<0.05$). Finally, betatrophin levels of those who achieved 5% weight loss ($n=25$) showed no significant difference after follow-up ($P=0.59$).
Conclusion
Changes significantly in FGF21 and betatrophin after lifestyle modification program. An increase in FGF21 and a decrease in betatrophin were associated with clinical characteristics related to the adrenergic and lipolytic responses to a healthy lifestyle.

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P51

A single nucleotide polymorphism in the EGF gene is associated with glycemic control in type two diabetes mellitus patients

Mahmoud Alfaqih[1], Jannat Maraqah[2] & Ebaa Ababneh[3]
[1]Arabian Gulf University, Biochemistry, Manama, Bahrain; [2]Jordan University of Science and Technology, Physiology and Biochemistry, Irbid, Jordan; [3]University of Central Florida, Burnett School of Biomedical Sciences, Orlando, United States

Background
Poor glycemic control in patients with type two diabetes mellitus (T2DM) is a strong risk risk factor for the development of complications and is associated with increased mortality. A growing body of evidence has demonstrated a role of the epidermal growth factor (EGF) in glucose homeostasis. The EGF contributes to the function, survival and proliferation of the β cells of the pancreas. The EGF also influences the action of insulin via the modulation of insulin receptor expression and downstream signaling pathways. The collective effect of these actions regulates glucose uptake, utilization and sensitivity to insulin. Given the above, it is conceivable that the EGF could also be associated with glycemic control in T2DM patients. Variations in the *EGF* gene, including single nucleotide polymorphisms (SNPs), could affect the level of the coded EGF protein. Hence, this investigation tested the association of rs4444903 SNP in the *EGF* gene, EGF protein and *EGF* mRNA levels with glycemic control.
Methods
In this case-control study, a total of 330 patients with T2DM were recruited. Cases were patients with poor glycemic control and controls were patients with good glycemic control. Blood samples were collected for DNA extraction and measurement of the EGF protein. An enzyme-linked immunosorbent assay (ELISA) was used to quantify levels of the EGF. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used to determine *EGF* rs4444903 genotype. An additional set of 42 patients per group was recruited to determine *EGF* mRNA expression in peripheral monocytes. mRNA levels were quantified using qPCR.
Results
Patients with poor glycemic control had significantly lower levels of EGF compared to controls ($P<0.05$). GA genotype of rs4444903 was significantly more frequent among the poor glycemic control group ($P<0.05$). Multivariate regression analysis confirmed this association and showed that EGF levels significantly lowered the risk of poor glycemic control (OR = 0.99, 95%CI:0.98-0.99, $P<0.001$). In this analysis, the GA genotype was associated with an increased risk of poor glycemic control (OR = 1.96, 95%CI:1.02-3.57, $P=0.04$). Cases had a markedly reduced expression of *EGF* mRNA (60% of the expression levels observed in the controls).
Conclusion
This study revealed the association between EGF genetic variation, protein and mRNA expression with glycemic control. Future studies should provide more insights into the molecular mechanism(s) of this association and the role of the EGF in the management of poor glycemic in T2DM.]

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P52

First trimester fasting glycaemia ≥ 92 mg/dl and risk of gestational diabetes in the 24-28th week ogtt

Catarina Cidade-Rodrigues[1], Vania Benido[1], Catarina Chaves[1], Bruna Silva[1], Ana Saavedra[1], Alexandra Araujo[1], Claudia Machado[1],

Catarina Pereira[1], Vania Gomes[1], Odete Figueiredo[2], Anabela Melo[2], Anabela Ferreira[2], Mariana Martinho[3], Ana Morgado[2], Margarida Almeida[1], Maria Ceu Almeida[4] & Filipe Cunha[1]
[1]Centro Hospitalar do Tamega e Sousa, Endocrinology, Portugal; [2]Centro Hospitalar do Tamega e Sousa, Gynecology and Obstetrics, Portugal; [3]Centro Hospitalar de Vila Nova de Gaia/Espinho, Endocrinology, Portugal; [4]Centro Hospitalar Universitário de Coimbra, Gynecology and Obstetrics, Portugal

Introduction
Gestational diabetes (GD) is defined as a glucose intolerance firstly recognized during pregnancy and it is the severity of hyperglycaemia which is relevant to maternal and foetal risks. The American Diabetes Association (ADA) recommends screening before 15 weeks of gestation for women at risk, using standard diagnostic criteria, and defines early abnormal glucose metabolism as fasting glucose 110-125 mg/dl or HbA1c 5.9-6.4%. However, the benefit of treating women with early pregnancy detected GD has not been well established, and one third of untreated women showed normal results when retested at 24-28 weeks.
Objectives
We aimed to study the prevalence of GD diagnosis in the 2nd trimester OGTT in women who had 1st trimester glycaemia (FTG) between 92-125 mg/dl and were not pharmacologically treated.
Materials and Methods
Retrospective study using a convenience sample of women from the Portuguese national GD registry who had a FTG between 92-125 mg/dl and had passed unnoticed until the realization of the 24-28th week OGTT and had received no pharmacological treatment. We excluded women without data on known GD risk factors. The primary endpoint was a positive 24-28th week OGTT according to the WHO diagnostic criteria. Women with GD diagnosis by the OGTT and those without GD criteria were compared. A multivariate logistic regression analysis was used to study predictors of GD by the 24-28th week OGTT: the variables included were FTG and those with known association with GD.
Results
We studied 225 women with a median age of 34 (30-37) years and median BMI of 28.3 (24.2-32.4). Forty-eight (21.3%) women had normal results in the 24-28th week OGTT. Women with abnormal OGTT results were older [34 (31-38), 32 (29-35), $P=0.02$], and had higher BMI [29.3 (24.4-33.6) kg/m^2 vs 27.4 (23.1-30.3) kg/m^2, $P=0.05$]. There were no differences between groups concerning T2D family history, previous GD, previous miscarriage, presence of chronic hypertension, or FTG levels. Women with GD in the OGTT were more likely to use insulin or metformin for the remainder of the pregnancy. In the multivariate logistic regression analysis, age $>$ 35 years and BMI(per 1 kg/m^2) associated with diagnosis of GD on the OGTT with an OR (95% CI) of 2.34 (1.04-5.31), $P=0.04$, and 1.07 (1.00-1.14), $P=0.047$, respectively, independently of FTG levels, T2D family history, or previous GD.
Conclusion
More than 20% of women with FTG between 92-125 mg/dl had a normal 24-28th week OGTT. Older age and higher BMI were associated with increased risk of abnormal OGTT.

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P53

Impact of gestational diabetes and its management on the nutritional balance and quality of life of a population of tunisian women

Chaima Arfa[1], Chaima Jemai[1], Wafa Ben Brahim[1], Mouna Djebbi[1], Achwak Mehrez[1], Yasmine Fakhfekh[1], Yosra Htira[1], Zohra Hadj Ali[1] & Faika Ben Mami[1]
[1]National Institute of Nutrition of Tunis, C

Introduction
Gestational diabetes mellitus (GDM) is the most common endocrinopathy in pregnancy. Its management is based on hygienic and dietary measures associated, if needed, with insulintherapy. Therapeutic goals must be quickly reached in order to limit complications. GDM has some therapeutic and progressive particularities which could alter the quality of life of patients. The aim of our study was to evaluate the nutritional intake of a population of women with GDM and to assess its impact on their quality of life.
Methods
This was a cross-sectional study, carried out at the research unit on diabetes and pregnancy (UR17SPO2) of department C of the national institute of nutrition of Tunis. We included 40 women with gestational diabetes, defined according to ADA 2023. The data collection was carried out using an interview, anthropometric measurements, a dietary survey, and a pre-established questionnaire assessing the impact of GDM on patients'quality of life.
Results
The mean age was 33.6$\pm$5.54 years. The average pre-gestational BMI was 27.67$\pm$4.93 kg/m^2. The average energy intake was 2019.08$\pm$330.9 kcal/d. The majority of patients (95%) had a hypoglucidic diet ($<$5 g/kg/d). 55% of Women had protein intake below recommended requirements. All the population had a hyperlipid diet ($>$1 g/kg/d). The average ratio w6/w3 was 18.64$\pm$5.83. We noted insufficient intakes of iron, iodine, calcium, zinc, vitamin D, vitamin B9 and vitamin B12. The average fiber intake was 26.54$\pm$6.15 g/d. Most women appreciated the personalized therapeutic education. Following the diet was difficult for 62.5% of patients. 87.5% made diet deviations. Family support was essential for diabetes self-management. The quality life of 77.5% of patients was affected by GDM. Thus, women do not arrive always express their emotions towards the practitioner which can lead to stress or guilt.
Conclusion
Psychological care should be proposed to patients with GDM in order to manage the psychological impact of the disease and improve the quality of life of patients.

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P54

Diabetes and covid-19: factors involved in the occurrence of complications and death: about 60 cases

Marwa Sassioui[1], Saloua Elamari[1], Soukaina Laidi[1] & Marouan Fatima[1]
[1]Cheikh Khalifa Bin Zayd Al Nahyan Hospital - University Mohamed VI of Health Sciences, Casablanca, Morocco

Introduction
Coronavirus 2019 (COVID-19) is a potentially fatal infection caused by the acute respiratory syndrome virus coronavirus-2. Diabetes is one of the most distinct comorbidities of COVID-19. Our study describes the clinical characteristics of diabetic patients with COVID-19 to identify factors predictive of the occurrence of complications and death in these patients.
Materials and methods
This was a retrospective, monocentric study that included diabetic patients with Covid-19 referred to Mohamed VI International University Hospital from January 01 to December 21, 2021. We performed a multivariate analysis to quantify risk and identify significant predictive factors for complications and death.
Results
Our study included 60 patients. The sample was 63.33% male, with a median age of 67 years. At least one complication was present in 41.67% of patients, including death in 21.7% of subjects in the series. In univariate analysis, variables that were associated with the risk of complications occurring were: male gender, overweight or obesity, heart failure, otolaryngological signs, high percentageé of lung lesions on CT scan, low glomerular filtration rate and mean daily blood glucose $>$2.5g/l; while protective factors were insulin treatment and high saturation. Only male gender (OR: 28.55; $P=0.005$), overweight and obesityé (OR: 9.48; $P=0.025$), hyperleukocytosis (OR: 8.98; $P=0.038$) and blood glucose levels in the first 4 days persisted as a predictor of the occurrence of complications and death.
Conclusion
Male diabetic patients with high BMI admitted with hyperleukocytosis and persistent high blood glucose levels during hospitalization are more unlikely to progress to more severe COVID-19 and have a poor prognosis.

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P55

Adult sitosterolemia in singapore: a case report

Mark Poh[1,2] & Abel Chen[1]
[1]Tan Tock Seng Hospital, Endocrinology, Singapore, Singapore; [2]Tan Tock Seng Hospital, Singapore

Introduction
Sitosterolemia is a rare lipid disorder characterised by excessive accumulation of phytosterols in the body. There are fewer than 110 cases worldwide, and to our knowledge, there are no reported cases of adult Sitosterolemia from South-East Asia. We report our experience in diagnosing a middle-aged Chinese lady from Singapore with Sitosterolemia.
Case Report
A 45-year-old Chinese lady was referred to the Endocrinology clinic in Oct 2022 by her General Practitioner for possible Familial Hypercholesterolemia (FH). She had first noticed tendon xanthomata on her two children (5-year old daughter; 3-year old son) and brought them for review at another pediatric institution.

Investigations for her children revealed very elevated Total Cholesterol (TC) levels (daughter 16 mmol/l; son 8 mmol/l) and Low Density Lipoprotein (LDL) levels, raising the suspicion for FH. Our patient is a non-smoker who consumes a low-fat diet and engages in weekly yoga sessions and runs. She is in a non-consanguinous marriage and does not have a family history of early cardiovascular events or deaths. The father of her 2 children does not have hyperlipidemia. She does not have tendon xanthomata or corneal arcus on examination. She does not have diabetes mellitus, hypertension, thyroid or kidney disorders. She was previously on atorvastatin 10 mg ON, which was increased to atorvastatin 20 mg ON after her first consult with our Endocrinology clinic in October 2022. However, her LDL remained elevated at 4.5 mmol/l and therapy was switched to rosuvastatin 20 mg ON in December 2022. Her LDL remained high at 4.8 mmol/l when rechecked in April 2023 despite compliance to rosuvastatin. She was counselled for and underwent genetic testing for FH. Around this time, the patient's daughter was found to have elevated plant sterol levels at another institution. We hence switched our patient to ezetimibe 10 mg ON while awaiting the results of her own genetic testing. There was a marked improvement in her LDL levels to 1.9 mmol/l 3 months after switching to ezetimibe monotherapy. Molecular genetic analysis later revealed that she was heterozygous for a variant of the ABCG5 gene c.1166G> A (p.R389H). This variant gene has been implicated in sitosterolemia in which there is a defective ATP-binding cassette transporter leading to decreased gut transport and excretion of plant sterols.

Conclusion

This case illustrates the importance of considering sitosterolemia as a differential apart from familial or polygenic hypercholesterolemia in patients with hyperlipidemia as this would greatly impact subsequent management.

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P56

Strength-endurance training and liraglutide treatment: impact on metabolic parameters in middle-aged ovariectomized female rats

Branka Šošić-Jurjević[1], Svetlana Trifunovć[1], Dragana Vlahović[1], Ivona Gizdović[1], Natasa Ristic[1], Ljiljana Marina[2] & Branko Filipović[1]
[1]Institute for biological research "Siniš Stanković " - National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia; [2]National Centre for Infertility and Endocrinology of Gender, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Exercise training and liraglutide have been shown to be effective in promoting weight loss, improving glycemic control, and regulating blood lipid levels, especially in animal models and patients with obesity and diabetes. However, their combined effects on body composition, glucose, and lipid metabolism in healthy aging models have not been studied yet. In this study, we used apparently healthy middle-aged (16-month-old) female Wistar rats that underwent ovariectomy (Ovx) to mimic human menopause. The Ovx was performed under isoflurane anesthesia (3%) with ketoprofen analgesia (5 mg/day). Two weeks after the surgery, the Ovx rats were randomly assigned to four groups: sedentary control (SC; received 0.3 ml/day normal saline subcutaneously), liraglutide (L; received 0.3ml Saxenda ®, Novo Nordisk A/S, Denmark, at a dose of 0.186 mg/kg body mass/day subcutaneously), exercise strength-endurance training (E; ladder-climbing with 25-50% body weight load 3 times/week), and liraglutide + exercise (L+E) groups. The treatment lasted for seven weeks, with an additional two weeks of adaptation to exercise or liraglutide treatment. Compared to the sedentary control group, the L+E group showed the most significant weight loss ($P<0.05$) and reduction in relative retroperitoneal adipose tissue weight (g/100g body mass). The relative weight of the slow-twitch soleus muscle increased ($P<0.05$) in the L+E group, while the relative weight of the mixed (fast/slow)-twitch gastrocnemius muscle remained unchanged. The serum glucose area under the curve (AUC) following the intraperitoneal glucose tolerance test was lower only in the E group. Conversely, liraglutide treatment mainly contributed to the reduction of total cholesterol, triglycerides, and non-high density lipoprotein (HDL) concentrations in serum compared to exercise alone, which was similar to the effects of the combined E + L treatment. Our findings suggest that in apparently healthy middle-aged Ovx rats, the combination of liraglutide treatment and exercise had the most significant synergistic effects on weight loss, reduction of adipose tissue, soleus muscle activation and improvement in body composition. The improved lipid profiles were mainly due to liraglutide treatment, while exercise alone enhanced glycemic control, indicating their diverse impacts on metabolic parameters in this model.

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P57

The association of metabolic dysfunction-associated steatotic liver disease (masld) and metabolic syndrome with cardiovascular outcomes: a nationwide study

Sohyun Cho[1], Rosa Oh[1], Seohyun Kim[2], Ji Yoon Kim[1], You-Bin Lee[1], Sang-Man Jin[1], Kyu Yeon Hur[1], Gyuri Kim[1] & Jae Hyeon Kim[1]
[1]Samsung Medical center, Sungkyunkwan University School of Medicine, Department of Medicine, Seoul, Korea, Rep. of South; [2]Samsung Advanced Institute for Health Sciences and Technology, Sungkyunkwan University, Department of Clinical Research Design and Evaluation, Seoul, Korea, Rep. of South

Background

Metabolic Dysfunction-Associated Steatotic Liver Disease(MASLD) is considered a potential independent risk factor for cardiovascular disease(CVD) as it shares a common risk factor with CVD. We investigated the association with cardiovascular risk according to the metabolic risk factors in patients with MASLD.

Methods

This nationwide study included 1,710,144 individuals aged 40–79 years who underwent health check-ups between 2009 and 2012 in Korea. We excluded previous CVD history, those with viral hepatitis, those who died before follow-up investigation, and missing data. Participants were categorized into no steatotic liver disease(SLD), MASLD, MASLD with increased alcohol intake(MetALD), and alcohol-related liver disease(ALD) and the combination of the presence or absence of risk factor of metabolic syndrome(MetS). Hepatic steatosis was defined as the fatty liver index (FLI) $\geq$30. MASLD was defined as the presence of at least one of cardiometabolic risk factors: 1) Waist circumference $\geq$90 cm in men and $\geq$85 cm in women or body mass index$\geq$23 kg/m^2; 2) Blood pressure $\geq$130/85 mmHg or specific drug treatment; 3) Triglyceride $\geq$150 mg/dl or specific drug treatment; 4) High-density lipoprotein cholesterol $\leq$40 mg/dl for men and $\leq$50 mg/dl for women; 5) Fasting blood glucose levels $\geq$100 mg/dl or specific drug treatment. The primary outcome was a hospitalization due to CVD and CVD-related mortality. Hospitalization due to CVD was defined as the ICD-10 codes of I21-23, I50, I63. CVD-related mortality was defined as heart disease (I00-99). Cox analyses were used to analyze the association between metabolic dysfunction and MASLD and CVD.

Results

The study population consists of a total of 785.132 participants. There were 370.207 male (47.2%) and 414,529 female (52.8%). During a median 8.6 years of follow up, 46,391 (5.9%) hospitalization, 6,802 (0.9%) CVD-related mortality were detected. When no SLD/risk factor(-) were set as the reference group, in no SLD (FLI <30), the more metabolic risk factors, the higher the adjusted hazard ratio (aHR) in hospitalization and CVD-related mortality. In the FLI $\geq$30 (SLD), the hospitalization risk and CVD-related mortality was higher than the reference group. Even within the MASLD, the more metabolic risk factors, the higher the aHR, and the highest aHR in the ALD (aHR, 1.86; 95% CI,1.70–2.03) in hospitalization of CVD.

Conclusion

MASLD independently increases CVD-related outcomes, and the importance of MASLD is more emphasized when accompanied by metabolic syndrome. And both MASLD and significant alcohol consumption increased CVD-related outcome.

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P58

Biometric and metabolic changes at one-year follow-up in patients with obesity and steatotic liver disease undergoing endoscopic sleeve gastroplasty-endosleeve (apollo method)

Diego Schwarzstein[1], Lissette Batista[1], Patricia Gonçalves[1], Luis Yip[1], Leoniana Bustillos[1], Mar Bacardit[1], Cristina Colomer[1] & Josep Merlo[1]
[1]Clínica ServiDigest, Obesity Unit, Barcelona, Spain

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD, formerly called non-alcoholic fatty liver disease, NAFLD) is a leading cause of chronic liver disease, affecting 25% adult population worlwide. Its most advanced form is the metabolic dysfunction-associated steatohepatitis, or MASH which may progress to cirrhosis. It has no approved pharmacotherapy yet, and weight reduction is an important therapeutic option. Few studies have evaluated the effect of Endoscopic Sleeve Gastroplasty (ESG) on comorbidities in patients with obesity and MASLD.

Aims

To evaluate the evolution of metabolic comorbidities, weight changes and technique's safety in patients with obesity and MASLD undergoing ESG.

Material and Methods
We performed retrospective-descriptive analysis in 32 patients with MASLD and Obesity undergoing ESG between 2016-2022. We evaluated the evolution of analytical and anthropometric parameters, and metabolic comorbidities with 1-year follow-up.
Results
72% of the patients were women, mean age 44 +/- 8.5 years. Mean baseline BMI (body mass index) was 39 +/- 5.47 kg/m^2, most of them type II obesity (57%). 11 patients (36%) had steatosis grade I, 11 (36%) grade II and 10 (28%) grade III. There were 7 patients with hypertension (HT) (28%), 2 with diabetes (8.7%), 6 with pre-diabetes (26%), 10 with dyslipidemia (47.6%) and 3 with severe Obstructive Sleep Apnoea (OSA) (17%). At 1-year follow-up, there was resolution of HT in 3 patients (*P*; 0.003), of prediabetes in all cases (*P*; 0.000), of dyslipidemia in 6 cases (*P* 0.361) and of OSA in 1 case (*P*; 0.020). We found a significant decrease in basal glycemia (*P*; 0.025), glycosylated hemoglobin (*P*; 0.046) and triglycerides (*P*; 0.013). There were significant differences in % TWL (total weight loss) mainly at month 6 of treatment: 18.7% TWL (*P*; 0.004). We observed good correlation between % TWL, age and BMI. 84% of patients completed the endocrinology/nutrition visits. There were no complications in the studied population.
Conclusions
ESG can be considered an effective and safe option in patients with obesity and MASLD, with a positive impact on excess weight and the evolution of associated metabolic comorbidities.

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P59

Cardiac changes in obese patients following bariatric surgery

David Verissimo[1], Joana Vinhais[1], Catarina Ivo[1], Pedro Daniel[2], Bruno Stuart[2], Ana Cláudia Martins[1], Joao Silva[1], Dolores Passos[1], Luis Lopes[1], J Jácome Castro[1] & Mafalda Marcelino[1]
[1]Armed Forces Hospital, Department of Endocrinology, Lisboa, Portugal; [2]Armed Forces Hospital, Department of Cardiology, Lisboa, Portugal

Introduction
Obesity is a chronic disease whose association with increased cardiovascular morbidity and mortality, including heart failure, is well established. Not only is obesity intricately connected with an increased prevalence of concurrent risk factors, such as coronary artery disease, hypertension, diabetes mellitus, and obstructive sleep apnea, but it also exerts a direct impact on myocardial structure and pump performance. Over time, prolonged obesity fosters cardiac remodeling, marked by left ventricle hypertrophy, cardiac fibrosis, and diastolic dysfunction, culminating in the progression to manifest heart failure. The intricate interplay between obesity and cardiovascular health is underscored by these structural and functional alterations in the heart. Bariatric surgery emerges as a highly effective intervention for obesity, exhibiting a remarkable remission rate of associated comorbidities, including cardiac dysfunction. Notably, gastric bypass surgery has demonstrated significant benefits in the reversal of left ventricle remodeling, preservation of both left and right ventricle function, along concomitant weight loss.
Material and methods
Prospective study comparing pre- and post-surgical echocardiograms of 38 obese patients submitted to bariatric surgery.
Results
After 21 [16-30] months, BMI, waist circumference, and fat mass percentage decreased by 31.7% ($P<0.001$), 20.9% ($P<0.001$) and 41.8%, ($P<0.001$), respectively, with remission of Diabetes *mellitus*, dyslipidemia, and obstructive sleep apnea of 82.4% ($P<0.001$), 36.1% ($P<0.001$) and 48.5%, ($P<0.001$). We observed a reduction in ventricular hypertrophy (mainly eccentric) from 36.4% to 13.2%, $P=0.004$, due to a reduction in left ventricle mass/heigh$^{2.7}$ (-13.9%, $P<0.001$), septal wall thickness (-10.9%, $P<0.001$), posterior wall thickness (-7.3%, $P=0.007$), and relative wall thicknesses (-6.5%, $P=0.017$), without a significant volumetric change. Changes in both BMI and abdominal circumference were associated with the described shifts in septal wall thickness ($r=0.415$, $P<0.001$ and 0.428, $P<0.001$), posterior wall thickness ($r=0.314$, $P=0.006$ and r=0.377, $P=0.001$), and left ventricle mass/heigh$^{2.7}$ ($r=0.336$, $P=0.003$ and r=0.309, $P=0.007$). No association was observed between fat mass percentage. There were no significant differences in left ventricle function (ejection fraction, fractional shortening, nor cardiac output). Despite an improvement in E/A of 25.4% ($P=0.005$), there was no difference in the prevalence of diastolic disfunction (31.6% vs 28.9%, $P=1.000$).
Conclusions
Weight loss following bariatric surgery had a positive effect in left ventricle remodeling, a hallmark of obesity-related cardiomyopathy.

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P60

Predicting liver fibrosis using artificial intelligence in obese patiens

Rona Penso[1,1], Natalia Perez[1], Pilar Matias[1], Antonio Torres[1], Andres Sanchez-Pernaute[1], Candela García[1], Irene Crespo[1], Lorea Herraiz[1], Maria Elena Mendoza[1] & Miguel Angel Rubio[1]
[1], Madrid, Spain

Introduction
The prevalence of hepatic steatosis in people with obesity is very high. However, what is relevant is to detect those patients with associated fibrosis. The aim of the present study was to predict by artificial intelligence (AI) using clinical-analytical parameters, the presence of liver fibrosis in the biopsy performed during bariatric surgery (BS) of patients with obesity.
Subjects and methodology
Cross-sectional study of patients with obesity undergoing BS (2010-2018) who had liver biopsy (after informed consent) during the intervention. Patients with other liver diseases were excluded. Heat MAP was used initially to filter clinical and analytical variables with more association with the Target (fibrosis), subsequently the sample was randomly divided into 2 groups, 75% to train the AI models: Gradient-boosting, LGBM and xgboost. The remaining 25% to test efficacy and reduce overfitting. Sensitivity, specificity and accuracy were calculated using the best AI model.
Results
362 patients (68.8% women), aged 47 [39-47] years, and BMI 42 [38-46] kg/m^2. Comorbidities: arterial hypertension 49.5%, Dyslipemia 46% and Type2 Diabetes (Dm^2) 42%. Biopsies: 83.5% showed steatosis, 18% some degree of fibrosis (10.7%, 3.1% and 4.3% grades 1,2 and 3 respectively). It was observed in the heat map that the variables abdominal perimeter, Hypertension, Dm^2, Insulin, daily amount of alcohol ingested, Albumin, HBA1c, HOMA-IR index, C-peptide, HDLc, GOT, GPT and GGT, are more related to fibrosis. Gradient-boosting was the model that provided the best overall results. Among the variables finally used by the model, those with the greatest weight were GOT and HDLc, followed by GGT, HbA1c, Insulin, GPT, Albumin, amount of alcohol ingested, history of Dm^2 and HOMA-IR index. In the 25% of patients reserved for the accuracy test of the best model, it was observed that only 7.1% presented fibrosis in the biopsy, and the model predicted fibrosis in 12.5%, with only 1 false negative case. Finally, a Sensitivity:0.75, specificity:0.93 and accuracy of:0.827 was achieved.
Conclusions
The Gradient-Boosting model is highly used in medical studies since it can automatically identify more complex data structures, such as nonlinearity and diverse interactions; it has allowed to predict in previous studies cardiovascular events, delirium, sepsis, among o thers. In our sample it showed excellent specificity and good accuracy, which implies that its use in the clinic practice could avoid many liver biopsies, given the few false negatives it presents. This accuracy could even be improved with further training of the model

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P61

Evaluation of the digital support tool gro health W8Buddy as part of tier 3 weight management service

Farah Abdelhameed[1], Petra Hanson[1,2], Mohammed Sahir[1], Nick Parsons[3], Arjun Panesar[4], Michaela de la Fosse[4], Charlotte Summers[4], Amit Kaura[5], Harpal Randeva[1,2] & Thomas M Barber[1,2]
[1]University Hospital Coventry & Warwickshire NHS Trust, United Kingdom; [2]Warwick Medical School, University of Warwick, United Kingdom; [3]University of Warwick, United Kingdom; [4]DDM Health, United Kingdom; [5]Imperial College London, United Kingdom

Introduction
The escalating prevalence of obesity worldwide increases the risk of chronic diseases and diminishes life expectancy with growing economic burden necessitating intervention. The existing tiered approach to weight management, particularly specialist Tier 3 services, falls short of meeting the population's needs. The emergence of digital health tools, while promising, lacks exploration in specialized NHS weight management services (WMS).
Methods
This was a service evaluation study to evaluate the effectiveness and clinical impact of the W8Buddy digital support tool as part of a specialist WMS. W8buddy was collaboratively developed September 2022 with input from patients and clinical teams. It is a personalized platform, offering users a tailored weight management plan to empower individuals or caregivers to cultivate the necessary attitudes, knowledge, and skills to self-manage their health. All patients accessing the service were offered W8buddy and everyone received standard of care regardless of whether they used the digital tool. No financial incentives were given for using W8Buddy.

Results
Complete data was available for 226 patients (118 users, 108 non-users). W8buddy users, predominantly female (80%) and Caucasian, had a mean age of 42years, while non-users averaged 48years ($P=0.01$). Co-morbidity frequencies were comparable. Users had significantly higher baseline weight (135 kg vs 123 kg, $P=0.003$) and BMI (48 kg/m^2 vs 45 kg/m^2, $P=0.009$). During follow-up (3 months for users, 6 months for non-users), 28% ($n=220/783$) activated the tool by June 2023, of which 93% ($n=205/220$) actively engaged with the platform. W8Buddy demonstrated a substantial impact on absolute weight loss (β -1.16, SE 0.40, $P=0.004$) compared to standard care alone. Time using W8Buddy was a crucial predictor of weight loss ($P=0.05$), with a 0.74 kg monthly loss compared to standard care (β -0.74, 95%CI (-1.28, -0.21), $P=0.007$). W8buddy users with type 2 diabetes (T2DM) experienced a significant HbA1c reduction (59.8 mmol/mol to 51.2 mmol/mol, $P=0.018$) compared to non-users with T2DM. Optional surveys included satisfaction with life, PHQ8, Karolinska scale, and quality of life score (EQ5D5L). W8Buddy users showed significant improvement across all psychological outcomes ($P<0.001$) during follow-up.
Conclusion
W8Buddy demonstrated significant improvements in clinical and psychological outcomes for users. These findings suggest that digital tools can complement traditional services and promote patient empowerment. Future research should explore the key beneficial aspects of the tool for users and strategies to boost activation and engagement rates. Endorsed by National Institute for Health and Care Excellence (NICE) guidelines, W8Buddy holds promise for improved weight management and glycaemic control within specialized WMS.

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Advanced hybrid closed-loop therapy in adults with type 1 diabetes: outcomes in a real-world setting

Elena Pérez Galende[1], Gema Gonzalez Fernandez[1], Pablo Lozano Martínez[1], Clara Fernández Rivera[1], Marta Dolz Lopez[1], Cesar Jesus Avellaned Fabon[2] & Maria Orosia Bandres Nivela[1,2]
[1]Lozano Blesa Clinical Hospital, Endocrinology, Zaragoza, Spain; [2]Lozano Blesa Clinical Hospital, Zaragoza, Spain

Introduction
In the past few years, advances in technology applied to diabetes have significantly changed the type 1 diabetes management. However, only a minority of patients with type 1 diabetes achieves the recommended glycemic goals. Advanced Hybrid Closed-Loop (AHCL) systems, which combine continuous glucose monitoring (CGM) with a continuous subcutaneous insulin infusion (CSII) pump and a control algorithm, improve glycemic control and patient-reported outcomes, such as satisfaction.
Objectives
To evaluate the glycemic control in real life with the different AHCL systems, as well as the differences between them and the degree of patient satisfaction with the treatment.
Material and methods
A prospective observational study was carried out with adults with type 1 diabetes who started treatment with an AHCL system at our Hospital. Data on glycemic control were collected, in terms of HbA1c and CGM glucometric parameters, as well as data related to treatment satisfaction at baseline and at 6 months. In addition, glucometric parameters were also collected one month after the start of therapy.
Results
A total of 40 patients were included (27 started Minimed 780G, 6 Tandem Control-IQ and 7 DIABELOOP DBLG1 patients). They had a mean age of 39.9 ± 14.3 years, the majority were women (67.5%), with a mean duration of diabetes of 26.9 ± 12.4 years. In the total cohort, after 6 months of treatment, HbA1c was reduced from 7.26 ± 0.91% to 6.98 ± 0.76% ($P=0.002$), as well as the TIR increased from 65 (IQR 56 -71) % to 77.5 (IQR 71-85) % ($P=0.0003$). It was observed that a TIR of 75 (72-84) % was reached one month after starting treatment ($P<0.0001$). The percentage of patients who achieved optimal control after therapy increased from 17.5% to 75% ($P<0.0001$). At 6 months after the start of therapy, no significant differences in glycemic control were observed between the systems, however, Minimed 780G was the only system that improved HbA1c (from 7.35 ± 0.91 to 7.07 ± 0.84) ($P=0.03$) as well as the TIR (65 (IQR 56-71) to 79.5 (IQR 71-82.25) ($P<0.0001$). According to the DTSQ-c and DTSQ-s, the change of treatment to an AHCL system was satisfactory and there was a significant improvement in satisfaction after 6 months of therapy ($P<0.0001$), with no significant differences between the different systems.
Conclusion
After 6 months of treatment with AHCL systems, significant improvements were observed, both in glycemic results and those related to patient satisfaction, with no between-group differences.

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Association of MMP-2 gene polymorphisms with diabetic retinopathy in tunisian population

Sameh Sarray[1,2], Ben Lamine Laila[3], Dallal Meriem[3], Intissar Ezzid[4] & Touhami Mahjoub[3]
[1]Arabian Gulf University, Medical Biochemistry, Manama, Bahrain; [2]Faculty of Sciences, University Tunis El Manar, Biochemistry, Tunis, Tunisia; [3]Faculty of Pharmacy of Monastir, University of Monastir, Monastir, Tunisia, Laboratory of Human Genome and Multifactorial Diseases (LR12ES07), Monastir, Tunisia; [4]Higher Institute of Biotechnology of Monastir, Monastir, Tunisia

Aims
Few studies investigated the association of genetic difference in metalloproteinase-2 (MMP-2) gene with diabetic retinopathy but with mixed outcome. The aim of the study is to investigate the association between a set of MMP-2 genetic variants and the risk of diabetic retinopathy in an Arab Tunisian population with type 2 diabetes.
Subjects and Methods
A retrospective case-control study involving 779 type 2 diabetes patients with or without diabetic retinopathy was conducted. A total of four MMP-2 SNPs (rs243865 (C/T), rs243864 (T/G), rs243866 (G/T) and rs2285053 (C/T)) were selected for this study, based on their established MAF (>5%) in Caucasians, and association with DR. Genotyping of MMP-2 variants was performed by real time PCR. Replicated blinded quality control samples were included to evaluate reproducibility of the genotyping procedure; concordance was >99%.
Results
The minor allele frequency (MAF) of the rs243864 MMP-2 variant was significantly higher among diabetic retinopathy patients. Setting homozygous wild type genotype carrier as reference, the rs243864T/G allele was associated with increased risk of diabetic retinopathy under the dominant, recessive, and additive models which persisted when key covariates were controlled for, while a reduced risk of diabetic retinopathy progression was seen after adjustment between non-proliferative and proliferative diabetic patients. Furthermore, the heterozygous genotype GT of the rs243866 variant is positively associated with the risk of proliferative diabetic retinopathy in the additive model. A limited linkage disequilibrium (LD) was revealed between the four-matrix metalloproteinase-2 variants. Four-loci haplotype analysis identified GCTC, TTTC, and GCTT haplotypes to be positively associated with the risk of diabetic retinopathy.
Conclusion
MMP-2 constitutes an at-risk locus of risk of DR, and for the first time, we found an association in an Arab Tunisian population where the MMP-2 gene variant rs243864 (–790T/G) and rs243866 (-1575G/T) are linked with the risk of DR development and progression.

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Metabolic and cardio-renal benefits of SGLT2- inhibitors in diabetic patients

Ergita Nelaj[1], Julinda Feracaku[2], Kei Xhixhabesi[1] & Irida Kecaj[1]
[1]University Hospital Center, Internal Medicine, Tirana, Albania; [2]Regional Hospital of Gjirokatra " Omer Nishani", Albania

Introduction
Diabetes mellitus (DM) increases the risk of any form of cardiovascular (CVD) and renal disease. Their identification is important for a further careful monitoring and treatment in all aspects. Sodium-glucose cotransporter-2 inhibitors (SGLT2i) have been associated with a remarkable reduction of cardiovascular and renal mortality, lower hospitalization rates for heart failure and lower progression of renal damage and albuminuria. Our study aim to assess SGLT2i effects on both cardio- and renal protection in diabetic patients.
Material and Methods
Were included elderly patients (>65 years) with T2DM, divided in two groups, one group treated with iSGLT2, and the other without. Data were collected at the beginning of treatment, 3, 6, 9 and 12 months after. HbA1C, BMI, GFR and renal

parameters, uric acid, NTproBNP, echocardiography, PAS and PAD values, were evaluated in every meetings, in both groups.
Results
Included in total 298 elderly diabetic patients. At 198 of them dapagliflozin 10 mg, was initiated. After 12 months, HbA1c, weight, systolic blood pressure, NTproBNP, uric acid, albuminuria, were lower in group with dapagliflozin versus the other group without it, and estimated glomerular filtration rate was higher (75.3 –87.19mL/min/1.73m^2; $P<0.005$). Follow up in patients with SGLT2i showed a significant decrease in left ventricular end-diastolic dimension (LV-EDD) (62.86 mm to 54.85 mm; $P<0.001$) and improvement in LV-EF. The SGLT2i-induced improvements in cardiac function were more prominent in HF patients than those without HF.
Conclusion
SGLT2i (Dapagliflozin) showed metabolic benefits in patients with T2D with clinically significant reductions in HbA1c, blood pressure, weight, uric acid, and NTproBNP. Cardiovascular and renal benefits were shown, also. So, SGLT2i has a significant effect in both, cardio- and renal protection in diabetic patients.

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The effect of dynamics in fasting glucose level on the risk of chronic kidney disease and ESRD: a nationwide cohort study

Haein Hwang[1], Heesung Kim[1], Seon Mee Kang[1] & Eun-Hee Cho[1]
[1]Kangwon National University Hospital, Internal Medicine, Chuncheon, Korea, Rep. of South

Background
Diabetes and renal disease are global burden with increasing prevalence, respectively. Moreover, they are closely related because diabetic nephropathy itself is well known serious complication of diabetes. However, the significance of decreasing fasting blood glucose on the risk of renal complications remains unclear. We identified the effect of chanes in fasting serum glucose level without diabetes mellitus on the renal complication in Korean adults.
Methods
We analyzed the data from retrospective cohort of Korean National Health Insurance Service-Health Screening (NHIS-HealS). In total, 267.176 Korean adults aged over 40 years measured change in serum fasting glucose level without diabetes at baseline according to the criteria of impaired and diabetic fasting glucose status: normal fasting glucose (NFG, fasting glucose: <100 mg/dl), impaired fasting glucose (IFG, fasting glucose: 100.0–125.9 mg/dl), and diabetic fasting glucose (DFG, fasting glucose: ≥ 126.0 mg/dl). ComparedCox proportional hazard regression model was used to obtain the hazards ratio (HR) with 95% confidence interval (CI) for the incidence of CKD and ESRD. Individuals, selected among national health examination participants in first in 2002–2003 and second in 2004–2005, underwent follow-up evaluations until 2019.
Results
In this report, we describe the protective effect of early glucose recovery on the risk of CKD and ESRD development. In comparison with participants with persistant DFG, participants with recovery from DFG to NFG had an decreased risk of CKD(HR [95% CI]: 0.76 [0.59-0.97], $P=0.025$) and ESRD(HR [95% CI]: 0.64 [0.39-1.07], $P=0.089$).
Conclusions
Early recovery of NFG in individuals with DFG is associated with decreased risk of development of Chronic Kidney Disease and End Stage Renal Disease.

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Is type 1 diabetes a risk factor for insulin resistance in young adults?

Samir Mkaouer[1], Zeineb Rekaya[1], Yazidi Meriem[1], Kamoun Elyes[1], Khessairi Nadia[1], Oueslati Ibtissem[1], Chaker Fatma[1] & Chihaoui Melika[1]
[1]La Rabta university hospital, Endocrinology department, tunis, Tunisia

Introduction
Insulin resistance is classically a feature of type 2 diabetes mellitus (T2D). It may also develop among patients with type 1 diabetes (T1D) increasing the risk of cardiovascular mortality. Metabolic syndrome (MS) reflects a state of IR. The aim of this study was to assess the frequency of MS in a population of young adults with T1D and compare it to healthy controls.
Methods
We conducted a case control study including 68 T1D patients and 68 healthy controls matched for age, gender, and body mass index (BMI). The study subjects were young adults, aged between 18 and 45 years. Subjects with other autoimmune, inflammatory, or neoplastic diseases, as well as those with renal failure, were not included. Each patient and each control underwent a physical examination (anthropometric parameters and blood pressure) and a fasting biological sample collection for the measurement of fasting blood glucose, HbA1c, and lipid parameters. MS was diagnosed according to the International Federation of Diabetes (IDF) criteria.
Results
The study population consisted of 58 men (42.6%) and 78 women (57.4%). The mean age was 29.4$\pm$7.23 years. The mean BMI was 24.9$\pm$3.9 Kg/m^2 for T1D patients and 25.0$\pm$4.1 for controls ($P=0.823$). The median duration of diabetes was 11 years (IQR: 4.2 –17.0). The HbA1c median was 8.5% (IQR: 7.7-10.8) in patients with T1D and 5.0% (IQR: 4.9-5.1) in controls ($P<0.001$). Three T1D patients and one healthy control had hypertension ($P=0,31$). Android obesity was observed in 44.6% of the T1D patients and in 47% of the controls ($P=0,731$). Low HDLc levels were observed in 36.4% of the T1D patients and in 38.1% of the controls ($P=0.839$). High triglyceride levels were observed in 13.4% of the T1D patients and in 7.4% of the controls ($P=0,247$). MS was observed in 14 T1D patients (20.6%) and 6 controls (8.8%) ($P=0.053$).
Conclusion
The prevalence of MS in the patients with T1D in our study was similar to that found in a recent meta-analysis (19.8% [13.6-26.8%]). However, the metabolic profile of the T1D patients and controls was comparable, suggesting that T1D is not a risk factor for MS and insulin resistance in young adults.

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Prevalence and predictive factors of sleep apnoea in type 2 diabetic patients

Meriem Adel[1], Rayene Ben mohamed[1], Marwa Chiboub[1], Lina Ghram[1], Hajer Kandara[1], Manel Jemel[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technology, Endocrinology, Tunis

Introduction
Obstructive sleep apnoea (OSA) is common in people with type 2 diabetes mellitus (T2DM), with prevalence ranging from 20-50% and up to 85% in obese T2DM. However, OSA remains largely undiagnosed due to the high cost of testing and limited availability of sleep clinics, particularly in developing countries. The aim of this study is to determine the prevalence of type 2 diabetic patients at high risk of OSA and to identify factors associated with OSA in this population.
Methods
A cross-sectional study was conducted on 130 patients with T2DM who were hospitalized in the Endocrinology Department of the National Institute of Nutrition and Food Technology in Tunis. The inclusion criteria were patients aged 30 years or older with T2DM diagnosed for at least 2 years. The study excluded patients with known OSA, any endocrinopathy that could be the cause of OSA, acute respiratory failure, acute or chronic bronchopneumonia, or bronchopulmonary tumour pathology. Screening for OSA was conducted using the Berlin questionnaire and the ApneaLink sleep screening device.
Results
The mean age of the patients was 59.37$\pm$7.80 years, with a female predominance (63.1%). Hypertension was present in 68% of cases. The mean BMI of the patients was 30.53$\pm$5.16 kg/m^2. The mean waist circumference was 101.23$\pm$13.3 cm. Fat distribution was android in 96.34% of women and 52% of men. The mean neck circumference was 39.51$\pm$3.11 cm. The mean duration of diabetes was 12.54$\pm$7.81 years. The mean HbA1c was 11.15$\pm$1.82%. According to the Berlin questionnaire, 62.3% of the population were at high risk of OSA, and according to the Apnealink device, 61% had an AHI $\geq$ 5/h and 20% an AHI $\geq$ 15/h. The factors associated with high risk of OSA in our study were: Age ($P=0.036$), female gender ($P=0.011$) and BMI ($P=0.013$) especially android fat distribution ($P=0.03$), high fasting glucose ($P=0.046$), hypercholesterolaemia ($P=0.013$) and diabetic nephropathy ($P=0.010$). In terms of functional signs, snoring ($P=0.024$), insomnia ($P=0.048$), chronic fatigue ($P=0.011$) and memory problems ($P=0.017$) were also associated with a high risk of OSAHS. Multivariate analysis showed a positive and statistically significant association with a high risk of OSAS for: female sex ($P=0.045$), fasting plasma glucose ($P=0.038$)) and diabetic nephropathy ($P=0.012$)
Conclusion
OSA is often associated with T2DM. Systematic screening for OSA in these patients is essential, especially in the presence of android obesity and poorly controlled diabetes.

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Analysis of autoimmunity to the insulin-receptor in diabetes mellitus

Thilo Samson Chillon[1], Kamil Demircan[1], Sabrina Asaad[1], Waldemar Minich[1] & Lutz Schomburg[1]
[1]Institute of Experimental Endocrinology, Charité- Universitätsmedizin Berlin

Introduction
Diabetes mellitus (DM) is a complex chronic metabolic disease characterized by elevated blood glucose levels due to insulin resistance and the failure of pancreatic beta cells to compensate. T2D and its complications have reached epidemic proportions worldwide over the past four decades [1]. A very rare condition known as Type B Insulin Resistance (TBIR) is characterized by severe insulin resistance and the presence of circulating autoantibodies (autoAb) directed against the insulin receptor (InsR). TBIR usually manifests in adulthood and is associated with a high risk of mortality. Insulin receptor autoAb are associated with higher fasting insulin levels in patients with TBIR [2]. Current methods for the diagnosis of TBIR have several limitations, most importantly they cannot be used for routine applications or for the analysis of large sample cohorts. There for it has been suggested that Type 1 Diabetes (T1D) and T2D patients with severe insulin resistance may be underdiagnosed of InsR-autoAb.
Objectivee
The pilot study aimed to determine the prevalence of InsR-autoAb in healthy controls and patients with DM.
Subjects and Methods
An in-house developed and validated fluorescence immunoprecipitation assay [2] was used to quantify InsR autoAb in sera from a small commercial cohort of ($n=443$ participants, including ($n=296$ self-reported healthy subjects, ($n=111$ T2D patients, and ($n=36$ patients with T1D.
Results
The group of T2D subjects showed an InsR autoAb prevalence of 4.5% compared to 0% in T1D and 2% in healthy subjects. In a more rigorous analysis using a stricter cut-off of BI >20, the prevalence in the T2D group is 2.7% compared to 0% in healthy subjects.
Conclusion
The pilot study supports the hypothesis that there are patients with T2D with undiagnosed InsR autoAb. None of the T1D patients showed InsR autoAb, suggesting that this is associated with acquired insulin resistance rather than insulin deficiency. This raises the question of the clinical relevance of these autoAb in the pathogenesis, which needs to be tested in sufficiently large prospective clinical trials.
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The correlation between heart failure and diabetic kidney disease in individuals diagnosed with type 2 diabetes mellitus

Yanina Rebrova[1], Yana Saienko[1], Borys Mankovsky[2] & Ievgen Marushko[1]
[1]Ukrainian Children's Cardiac Center, Kyiv, Ukraine; [2]Dmitry F. Chebotarev Institute of Gerontology of the National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine

Background
Agrowing body of evidence suggests that type 2 diabetes mellitus (T2DM) may contribute to the the development and deterioration of heart failure (HF) with either reduced or preserved ejection fraction. On the other hand, diabetic kidney disease (DKD) is associated with a high risk and worse outcomes of HF. However, the relationship between DKD and various types of HF hasn't been fully investigated. The aim of this study was to assess the association between the signs of DKD and different types of HF in patients with T2DM.
Methods
Three groups of patients with T2DM were examined. The first group included 20 patients with T2DM and no HF. (age - 62.6±10.0 years, mean diabetes duration - 3.9±2.5 years, HbA1c - 7.0±1.2%, creatinine - 99.0±19.0 μ mol/l, estimated glomerular filtration rate (eGFR) - 64.0±16.0 ml/min/1.73m^2, albumin/creatinine ratio (ACR) - 25.0±21.0 mg/g, ejection fraction (EF) - 58.0±4.0%.(data are presented as mean±SD). The second group included 15 patients with T2DM and HF with reduced EF (HFrEF). (age 66.0±7.0 years, mean diabetes duration - 4.0±2.0 years, HbA1c - 6.9±0.7%, creatinine - 122.0±26.0 μ mol/l, eGFR - 48.0±9.0 mL/min/1.73m^2, ACR - 76.0±73.0 mg/g, EF - 34.0±10.0%). The third group included 15 patients with T2DM and HF with preserved EF (HFprEF). (age - 67.0±9.0 years, mean diabetes duration - 5.0±2.0 years, HbA1c - 7.0±2.0%, creatinine - 130.0±52.0 μ mol/l, eGFR - 48.0±18.0 mL/min/1.73m^2, ACR - 115.0±110.0 mg/g, EF -55.0±3.0%). The ACR in urine and eGFR were recorded and compared among these three groups using Student's t-test.
Results
We found that the eGFR levels were significantly lower in patients with T2DM and HFprEF compared to patients without HF and patients with HFrEF (48.0±18.0; 64.0±16.0; 48.0±9.0, –respectively, $P<0.05$). Also the ACR was significantly higher in patients with T2DM and HFprEF compared to patients without HF and patients with HFrEF (115.0±110.0; 25.0±21.0; 76.0±73.0, –respectively, $P<0.05$)
Conclusion
We found that the signs of DKD were the most pronounced in the group of patients with T2DM and HFprEF, which could suggest an important role of DKD in the pathogenesis of HFpEF in patients with T2DM.

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The sodium plunge: a world-record dip with a happy ending

Mohsin Mukhtar[1], Irbaz Nazir[1], Ghazanfar Rana[2] & Aftab Mirza[1]
[1]St. Luke's General Hospital, Endocrinology, Kilkenny, Ireland; [2]University Hospital Waterford, Cardiology, Waterford, Ireland

Severe or profound hyponatremia, defined by a serum sodium level below 125 mmol/l[5], presents a critical challenge with potential grave neurological consequences. We present a case of a middle-aged woman in her late 50s with a history of depression, bipolar affective disorder, chronic gastritis and hyperlipidaemia presented to the acute medical assessment unit with a five-day history of severe vomiting, profuse diarrhoea, generalized weakness and multiple falls in the last 3 day and exhibited an extraordinary serum sodium level of 94 mmol/l, which we believe to be the lowest ever recorded in reported literature[1], with a successful outcome. The underlying causes included a combination of diarrhoea, vomiting, and medication, ultimately resulting in hypovolemic hyponatremia and **SIADH**. Another intriguing aspect of this case is the lack of any neurological symptoms even at this low serum sodium level. Rapid and meticulous management was initiated, involving the cessation of the escitalopram and olanzapine, intravenous fluid replacement with isotonic saline, with a target correction of serum sodium no more than 10meq/day and frequent neurological monitoring. There was close monitoring of serum electrolytes, every 6 hours. The approach aimed to correct the electrolyte imbalance while preventing rapid sodium correction and associated complications The favourable outcome following meticulous management underscores the importance of individualized care and comprehensive understanding of the complex interactions underlying electrolyte imbalances.
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P71

Causal associations between adiposity markers and nuclear magnetic resonance spectroscopy-measured lipids in plasma: a mendelian randomisation study in 110,000 mexican adults

Beryl Lin[1,2], Diego Aguilar Ramirez[1], Jesus Alegre-Diaz[3,4], Natalie Staplin[1,5], William G Herrington[1,5], Paulina Baca[3,4], Carlos González Carballo[3,4], Raul Ramirez-Reyes[3,4], Fernando Rivas[3,4], Louisa Gnatiuc-Friedrichs[1,5], Michael Hill[1,5], Fredrik Romer[1,5], Jason Torres[1,5], Eirini Trichia[1,5], Rachel Wade[1,5], Regeneron Genetics Center[6], Rory Collins[1], Jonathan Emberson[1,5], Jaime Berumen[3,4], Pablo Kuri-Morales[4,7] & Roberto Tapia-Conyer[4]

[1]Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health (NDPH), University of Oxford, Oxford, United Kingdom; [2]Faculty of Medicine and Health, University of Sydney, Sydney, Australia; [3]Experimental Research Unit from the Faculty of Medicine, National Autonomous University of Mexico, Mexico City, Mexico; [4]School of Medicine, National Autonomous University of Mexico, Mexico City, Mexico; [5]MRC Population Health Research Unit, Nuffield Department of Population Health (NDPH), University of Oxford, Oxford; [6]Regeneron Genetics Center, Tarrytown, New york, United States; [7]Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, Mexico

Background
The genotyped Mexico City Prospective Study (MCPS) cohort enables the causal effects of adiposity on lipids to be explored in an overweight Hispanic population with scarce statin use.
Methods
MCPS participants aged 35-84 years, with baseline nuclear magnetic resonance measurements of blood lipids, and not using lipid-lowering therapy at recruitment were included. Using the Mendelian randomisation one-sample ratio method, univariable and multivariable models with genetic scores for body-mass index (BMI) and waist-hip-ratio (WHR) as instruments estimated the unadjusted and mutually-adjusted effects of BMI and WHR on six nuclear magnetic resonance spectroscopy-measured plasma lipids: total cholesterol; low-density lipoprotein cholesterol (LDL-C); high-density lipoprotein cholesterol (HDL-C); triglycerides; apolipoprotein A1; apolipoprotein B. Interactions by age, sex and diabetes were explored.
Results
Among 110,669 included participants (mean age 52 years), mean (SD) BMI and WHR were 29.0 (4.9) kg/m^2 and 0.90 (0.07), respectively. Each 5 kg/m^2 higher genetically-predicted BMI (772 SNPs, 3.0% variation) was associated with 0.19SD higher triglycerides (95% CI 0.15-0.22), 0.14SD lower HDL-C (0.11-0.18), 0.11SD lower LDL-C (0.07-0.15), 0.06SD lower apolipoprotein A1 (0.02-0.09) and 0.03SD lower apolipoprotein B (-0.01-0.07). By contrast, each 0.075 unit higher genetically-predicted WHR (398 SNPs, 0.9% variation) was associated with 0.66SD higher triglycerides (0.57-0.74), 0.29SD lower HDL-C (0.21-0.37), 0.13SD lower LDL-C (0.05-0.20), 0.04SD lower apolipoprotein A1 (-0.03-0.12) and 0.10SD higher apolipoprotein B (0.03-0.18). Overall, higher BMI was associated with 0.09SD lower total cholesterol (0.05-0.12) and WHR was associated with 0.04SD lower total cholesterol (-0.03-0.12). Adjustment of BMI for WHR (or vice versa) had little impact on the effect size estimates. Associations were similar in men and women and irrespective of history of diabetes, but for several lipid indices the associations varied significantly depending on age. In particular, associations of BMI and WHR with triglycerides were substantially stronger at younger than at older ages.
Conclusion
In Mexican adults not on lipid-lowering therapy, genetically-predicted general and particularly central adiposity are associated with substantially higher triglycerides but moderately lower cholesterol levels. Triglycerides may be a more important lipid mediator of adiposity-associated atherosclerosis in this population than cholesterol.

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P72

Metabolic and renal benefits of using sodium-glucose cotransporter type 2 inhibitors in patients with type 1 diabetes mellitus and continuous subcutaneous insulin infusion

Paloma Perez Lopez[1], Beatriz Torres Torres[1], Esther Delgado Garcia[1], Emilia Gomez Hoyos[1], Gonzalo Diaz Soto[1], Maria de la O Nieto de la Marca[1], Ana Ortolábuigues[1] & Daniel De Luis Roman[1]
[1]Hospital Clinico Universitario de Valladolid, Endocrinology and Nutrition, Valladolid, Spain

Ntroduction and Aim
The use of sodium-glucose cotransporter type 2 (SGLT-2) inhibitors has importantly improved the management of patients with type 2 diabetes mellitus. The aim of the present study was to evaluate the renal and metabolic effects after one year of SGLT-2 use in a cohort of patients with type 1 diabetes mellitus (T1D) treated with continuous subcutaneous insulin infusion (CSII).
Methods
Retrospective observational study in adult patients with T1D under treatment with CSII who started SGLT-2 in a tertiary hospital. Clinical, metabolic and glycometric parameters of Continuous Glucose Monitoring (CGM), including the Time in Tight Range (TTR) and the Glycemia Risk Index (GRI) were obtained at baseline and at 6 and 12 months of follow-up, as well as the existence of complications derived from the use of SGLT-2.
Results
18 patients were selected (55.6% female) with a mean age of 41.5 [39-48] years and 20 [11.8-29] years of T1D evolution were evaluated. Initially 22.2% met criteria for diabetic nephropathy. After 12 months of treatment, there was an increase in Time in range 70-180 mg/dl (TIR) (63.0 [53.0-74.0] vs 78.0[66.0-85.0]%; $P<0.01$) and a decrease in GRI (39.2[28.4-43.8] vs 20.0[14.2-33.2]; $P<0.05$), Time above 180 mg/dl (TAR) (31.5[20.5-39.5] vs 21.0[13.3-30.3]%; $P<0.05$) and Coefficient of Variation (CV) (34.8[32.8-38.4] vs 31.5[29.1-36.7]%; $P<0.05$), as well as a trend towards better TTR (45.0[32.5-57.5] vs 51.0[38.3-59.8]%; $P=$ns). No changes were observed in time below 70 mg/dl (TBR) (2.0[1.0-4.8] vs 2.0[1.0-2.8]%; $P=$ns) or in glycosylated hemoglobin A1c (7.3[6.6-7.8] vs 7.1[6.6-7.6]%; $P=$ns). In terms of renal parameters, at 12 months of treatment, a decrease in albuminuria (AlbU) was observed (11.5[3.8-107.9] vs 7.8[3.1-13.6]mg/l; $P<0.01$) as well as an increase in serum urea levels (34.0[27.8-36.3] vs 43.0[33.0-51.0]mg/dl, $P<0.05$], with no worsening of creatinine levels (0.9[0.8-1.0] vs 1.0[0.8-1.0]mg/dl, $P=$ns]. At 6 months follow-up, albumin-creatinine ratio (ACR) levels decreased in 2 patients with initial ACR > 300 mg/g: 1 achieved ACR less than 30 mg/dl (29.6 mg/g), and 1 less than 300 mg/dl (161 mg/g). Treatment with SGLT-2 was withdrawn in 3 patients (17.3%): 1 case due to gestational desire and 2 because of genitourinary infections. No case of ketoacidosis was documented during follow-up.
Conclusion
The use of SGLT-2 in patients with T1D under treatment with CSII led to an increase in TIR, with a significant decrease in GRI, TAR and CV, as well as improvement in renal parameters (AlbU, ACR), without the presence of serious complications during follow-up. The use of SGLT-2 may be a good therapeutic alternative in patients with T1D treated with CSII.

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P73

Vitamin b12 deficit mimics diabetic polyneuropathy in patients taking metformin

Anna Alieva[1] & Kamila Kenjaeva[2]
[1]Republican Specialized Scientific-and-Practical Medical Centre of Endocrinology, Intensive Care Unit, Tashkent, Uzbekistan; [2]Mirzo Ulug'bek shoh ko'chasi 56, Intensive Care Unit, Toshkent, Uzbekistan

Introduction
Prolonged use of Metformin is associated with the development of vitamin B12 deficiency. The aim of our study was to investigate the relationship of clinical manifestations similar to diabetic polyneuropathy with vitamin B12 levels in patients with type 2 diabetes mellitus.
Materials and methods
We examined 35 patients with type 2 diabetes taking Metformin. Mean age 55.9±11.5 years, mean diabetes duration 9.2±7.7 years. All patients were tested for diabetic polyneuropathy (DPN). The level of vitamin B12 was determined by the chemiluminescence immunoassay method.
Results
There was a trend towards a decrease in the level of vitamin B12 in persons with reduced sensitivity compared to persons with preserved sensitivity: 243.85±117.8 versus 336.66±98.3 pg/ml for pain sensitivity; 299.1±84.3 versus 326.9±121.2 pg/ml for tactile sensitivity; 297.0±175.2 versus 357.0±134.9 pg/ml for temperature sensitivity; 117.8±73.3 pg/ml for persons with vibration sensitivity from 0 to 3 points versus 522.5±188.2 pg/ml for persons with vibration sensitivity from 4 to 6 points ($P<0.05$). Also, among persons with a decrease in tendon reflexes, the level of vitamin B12 was lower (197.0±78.5 pg/ml) compared to persons with preserved reflexes (316.2±117.1 pg/ml).
Conclusion
The presence of clinical manifestations of polyneuropathy was associated with a decrease in the level of vitamin B12 in the blood in patients with type 2 diabetes mellitus taking Metformin, a significant decrease in the level of vitamin B12 was shown in patients with reduced vibration sensitivity. Patients with clinical manifestations of diabetic polyneuropathy should measure vitamin B12 levels.

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P74

Gestational diabetes: what is the evolution in the postpartum period, those on a hygienic diet, versus on insulin therapy?

Rakia Bachir Moctar[1], Bensbaa Salma[1], Nassim Essaba Haraj[1], El Aziz Siham[1] & Asma Chadli[1]

[1]CHU Ibn Rochd, Casablanca, Morocco, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Casablanca, Morocco

Introduction
Gestational diabetes or gestational diabetes is an increase in blood sugar levels that appears during pregnancy and disappears after delivery. It has an impact on the health of both mother and child.
Our objective
was to detect predisposing factors for remission in patients followed for gestational diabetes after delivery on a hygienic diet, versus on insulin therapy.
Patients and Methods
Our work is a case-control study including 182 patients with gestational diabetes followed at the Endocrinology-Diabetology department between January 2016 and January 2022. Diabetes is screened in the postpartum period at 6 to 8 weeks by HGPO75 g, divided into two groups: G1 (Diabetes has disappeared after pregnancy) and G2 (Diabetes has persisted after pregnancy). To do this work, we used SPSS software.
Results
The study included 182 patients, 46.18%, Diabetes disappeared after pregnancy (G1) and remained more or less on a hygienic-dietary diet with a good clinical course, G2, Diabetes persisted after pregnancy 52.12%, and are on insulin therapy. A pre-pregnancy BMI (<25 kg/m^2) of 25.4% (G1) and 29.8% (G2), P ($=0.06$). A mean post-pregnancy GAJ of 0.94 g/I(G1), 1.8 g/I(G2), a mean pregnancy weight gain of 0.27 kg/Sa(G1), 0.39 kg/Sa (G2), P(0.08), a hypertension of 12.3%(G1), 21.9% (G2), P(0.8), and a lost follow-up of 1.12%(G1), 1.1% (G2), with a good remission for patients doing physical activity, with a normal BMI and a normal HbA1C.
Discussion and Conclusion
Remissions are not uncommon in our patients, with a good balance of diabetes and good weight monitoring. It is therefore essential to screen for them and also to look for those lost to follow-up.

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P75

Effect of alcohol-induced hypoglycemia on myocardial perfusion

Nodira Alikhanova[1], Charos Musakhanova[1], Nozimakhon Nazarova[1], Feruza Takhirova[1], Lola Abboskhujaeva[1], Gulzoda Akramova[1], Munavvara Shakirova[1], Doniyor Nurmukhammedov[1], Lutfulla Usmanov[1] & Farrukh Almuradov[1]
[1]Republican Specialized Scientific and Practical Medical Center of Endocrinology Named after Academician Y.Kh. Turakulov, Diabetology, Tashkent

Background and Aims
When alcohol abuse and diabetes are combined, the consequences can be unpredictable and cause a double whammy, since both conditions cause similar pathological effects, in particular negative effects on the cardiovascular system.
Methods
The patient is 49 years old, male. Height 175 cm, weight 95 kg. BMI 31.02 kg/m^2. T2D was diagnosed 10 years ago. At the beginning of the disease, he took oral hypoglycemic drugs (can't remember their names). For 5 years, he has been taking medium- and short-acting human insulin. Poor control glycemia and bread units. BP has been increasing for 5 years and at the time of examination, he took Telmisartan 80 mg once daily. Diagnosed with type 2 diabetes mellitus in the decompensation stage. Complication: Diabetic nephropathy, CKD 1. Hypertension, stage 1 arterial hypertension. In addition to routine tests to diagnose CKD, we performed carotid-femoral sphygmography (SphygmoCor XCEL, AtCor) to assess pulse wave velocity (PWV) and Myocardial perfusion imaging using SPECT - AnyScan® SC - Mediso with technetium-99m sestamibi before and after 6-month follow-up. To evaluate summed score of perfusion during rest (SRS), computer software is used to evaluate perfusion isotope activity in each segment compared to the volume of radiopharmaceutical accumulation, set as 100%, in 17 segments of the polar map. the decrease in the accumulation of the radiopharmaceutical was translated into a point scale: 0 points - 70% and more, 1 point - 69-50%, 2 points - 49-30%, 3 points - 29-10%, 4 points - 9 and below%.
Results
Results of first laboratory examination: HbA1C - 11.2%, fasting blood sugar - 10.8 mmol/l. Instrumental examination ECG unchanged. PWV 14,70 m/s. SRS - 0 points, average perfusion indicator (API) - $84.95 \pm 7.3\%$. The patient was prescribed to take dapagliflozin 10 mg 1 tablet once daily for 6months. During the re-appointment the patient complained of general weakness. Body weight 96 kg, TVI 31.34 kg/m^2. HbA1C - 9.4%, fasting blood sugar - 13.4 mmol/l. The patient underwent re- sphygmography and SPECT examination. PWV 14,70 m/s. SRS –9 points, API - $74.0 \pm 23.2\%$. Despite the decrease in vascular stiffness according to the results of Sphygmocore, a decrease in myocardial perfusion was noted. The patient admitted that he had been abusing alcohol for the past few months and had frequent nocturnal hypoglycemia
Conclusion
Despite a decrease in vascular stiffness during treatment with dapagliflozin, a decrease in myocardial perfusion was noted due to alcohol-induced hypoglycemic conditions.

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P76

Association between low vitamin d level and depressive symptoms

Nana Kvinikadze[1], Mariam Tkeshelashvili[1], Claytan Monis[1], Nanditha Narendran Geetha[1] & Elene Pestvenidze[1]
[1]Tbilisi State Medical University, USMD program, T'bilisi, Georgia

Background
Depression has a multifaceted nature that is influenced by genetics, molecular mechanisms, and environmental stress. Vitamin D is involved in the development of depression, impacting neurotransmitters and neurological function when deficient, therefore it can be seen as a part of the discourse around depression, as well as preventing, treating and managing the same.
Aim
The aim of this study is to assess the relationship between low Vitamin D level and depressive symptoms in adult patients.
Methods
This prospective cohort study focuses on Vitamin D deficient adults. Family doctors conducted self-report surveys, covering demographics, medical history, Vitamin D levels, and the PHQ-9 questionnaire. Follow-up was done after one month using the same questionnaire. The study analyzed data using Prism, employing descriptive statistics, paired t-tests, Fisher's exact test and Pearson correlation analysis.
Results
The study involves 43 participants (4 excluded). Paired T-test revealed a significant decline ($P=0.0018$) in depression symptoms with vitamin D supplementation. By Subgroup analyses females ($P=0.0093$), age (18-25) ($P=0.0317$), unmarried ($P=0.0216$) and moderate workplace stress ($P=0.0176$) demonstrated significant decline in PHQ-9 scores with supplementation. Pearson correlation analysis between vitamin D levels and depression symptoms yielded to a nonsignificant result ($P=0.5887$). Fisher's exact test found no significant link ($P=0.4121$) between severities of vitamin D deficiency and depression symptoms.
Conclusion
This study supports Vitamin D's role in mitigating depressive symptoms. Significant declines were observed with supplementation, particularly among females, those aged 18-25, unmarried individuals, and those with moderate workplace stress. However, no link was found between severities of vitamin D deficiency and depressive symptoms. These findings suggest that vitamin D is involved in pathogenesis of depression and even though there is no direct correlation its supplementation alleviates the depressive symptoms.

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P77

The prognostic significance of antinuclear antibodies in metabolic steatopathy: a cross-sectional study

Ahmed Mohamed Nefzi[1], Bouchabou Bochra[1], El Mouldi yosr[1], Nakhli Abdelwahab[1], Hemdani Nesrine[1], Benzarti Zeineb[1], Ben Nejma Houda[1] & Ennaifer Rym[1]
[1]Hôpital Mongi Slim, Hepato-gastroenterology, Marsa, Tunisia

Introduction
The pathophysiology of metabolic steatopathy remains complex, prompting numerous inquiries to date. While the isolated presence of antinuclear antibodies (ANA) has been reported in this pathology, their prognostic relevance has not been adequately investigated. The objectives of our study were to:
- Examine the prevalence of antinuclear antibodies during metabolic steatopathy.
- Investigate the prognostic significance of ANA in metabolic steatopathy.
Patients and Methods
This was a single-center, cross-sectional, descriptive study encompassing all patients diagnosed with metabolic steatopathy from March 2021 to December 2022. Patients diagnosed with connectivitis and autoimmune hepatitis were excluded. Clinical data (age, medical history, anthropometric measurements, and blood pressure) were collected. A laboratory assessment (metabolic and hepatic profiles, viral serologies for hepatitis B and C) was conducted, along with the detection of antinuclear antibodies. Liver fibrosis evaluation employed transient elastography (Fibroscan), and cardiovascular risk assessment utilized the GLOBORISK score.
Results
The study population comprised 104 patients with a mean age of 54.51 ± 10.2 years and a gender ratio of 0.52. Histories of type 2 diabetes, hypertension, and dyslipidemia were noted in 41.3%, 44.2%, and 30.8% of patients, respectively. ANA were positive in 13.5% of patients ($n = 14$) with titers ranging from 1/80 to 1/400. No significant differences were observed in basic demographic data based on ANA positivity. Regarding biological data, thrombocytopenia was more frequently observed in ANA-positive patients (35.7% versus 5.5%) ($P = 0.038$). Liver elasticity was higher in patients with positive ANA (8.7 kPa versus 6.9 kPa), although not statistically significant ($P = 0.327$). Cardiovascular risk assessment did not show an elevated risk in ANA-positive patients ($P = 0.207$).
Conclusion
Our study suggests that ANA positivity during metabolic steatopathy is not uncommon. However, it appears to be an epiphenomenon without substantial prognostic implications. Larger studies with better-matched groups are required to confirm this hypothesis.

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P78

Testosterone replacement therapy improves metabolic parameters in obese men with testosterone deficiency: a meta-analysis and systematic review

Yaoxia Liu[1], Tao Wang[2], Yerong Yu[3] & Min Zhang[1]
[1]Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China., Geriatric Endocrinology, Chengdu, China; [2]West China Second University Hospital, Sichuan University., Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, China; [3]West China School of Medicine/ West China Hospital of Sichuan University., Endocrinology and Metabolism., Chengdu, China

Objective
This systematic review aimed to assess the efficacy and safety of testosterone replacement therapy (TRT) in obese men with testosterone deficiency through the analysis of randomized controlled trials (RCTs).
Materials and Methods
A comprehensive computer-based search was conducted in Cochrane Library, PubMed, Embase, Web of Science, Scopus, Open SIGLE database, China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP database, and China Biology Medicine (CBM) database to identify RCTs involving obese men with testosterone deficiency treated with TRT.
Results
A total of 10 RCTs, all published in English, were included in this study, involving 665 subjects at baseline. Meta-analysis demonstrated that, compared to the control group, TRT resulted in a decrease in body mass index (BMI) by 0.57 kg/m^2 (MD = -0.57, 95% CI: -0.94 to -0.20, $P = 0.002$), a reduction in waist circumference by 2.78 cm (MD = -2.78, 95% CI: -4.86 to -0.70, $P = 0.009$), an increase in lean body mass by 1.96 kg (MD = 1.96, 95% CI: 0.30 to 3.61, $P = 0.027$), a decrease in fasting blood glucose by 0.53 mmol/l (MD = -0.88, 95% CI: -0.88 to -0.19, $P = 0.020$), a decrease in HOMA-IR by 1.89 (MD = -1.89, 95% CI: -3.11 to -0.65, $P = 0.003$), a decrease in HbA1c by 0.52% (MD = -0.52, 95% CI: -0.82 to -0.22, $P = 0.0006$), and a decrease in triglycerides by 0.22 mmol/l (MD = -0.22, 95% CI: -0.36 to -0.07, $P = 0.003$). There were no statistically significant differences in body weight, body fat mass, non-fat body mass, total cholesterol (TC), LDL cholesterol (LDL-C), and HDL cholesterol (HDL-C) between the groups. SBP and DBP did not significantly increase after TRT compared to the control group. However, TRT was associated with a statistically significant increase in hematocrit (HCT) by 3.19% (MD = 3.19, 95% CI: 2.14 to 4.24, $P < 0.00001$). The impact of TRT on PSA levels could not be conclusively determined.
Conclusion
The meta-analysis of randomized controlled trials suggests that testosterone replacement therapy in obese men with testosterone deficiency can improve metabolic parameters. TRT leads to reductions in BMI, waist circumference, and triglycerides, while increasing lean body mass and improving insulin resistance. There is no significant effect on blood pressure, but there is a risk of increased hematocrit. In clinical practice, it is recommended to carefully consider the indications for TRT and closely monitor cardiovascular risks.

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P79

Serum Oxytocin predicts body dysmorphic concerns and ketosis occurrence in patients withobesity on a VLCKD

Rebecca Rossetti[1], Rossella Tozzi[1], Davide Masi[1], Maria Ignazia Curreli[1], Sabrina Basciani[1], Maria Elena Spoltore[1], Elena Gangitano[1], Paola Nevi[1], Orietta Gandini[1], Vittoria Strinati[1], Maria Chiara Massari[1], Mikiko Watanabe[1], Stefania Mariani[1], Lucio Gnessi[1] & Carla Lubrano[1]
[1]Sapienza University of Rome, Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Roma, Italy

Introduction
Obesity is a chronic neurometabolic disorder with complex psychological aspects. Patients with obesity often suffer from eating disorders and altered body image perception and show increased plasma concentrations of oxytocin (OT).
Objective and Design
This pilot study investigates the interplay between psychological factors, OT levels, and very-low-calorie ketogenic diet (VLCKD)-induced weight loss. We collected data from patients with overweight or obesity undergoing VLCKD, assessing anthropometrics, metabolism, psychometrics, and OT levels at baseline (t0) and after 45 days of diet (t1). The psychometric analysis involved the Ritvo Autism Asperger Diagnostic Scale-Revised (RAADS-R), the Body Uneasiness Test (BUT), and the Twenty-item Toronto Alexithymia Scale (TAS 20).
Results
Forty-seven participants (28 females) were enrolled, exhibiting a mean baseline BMI of 35.88 ± 4.37 kg/m^2 and a serum OT concentration of 1163.74 ± 410.08 pg/ml at t0. Following VLCKD intervention, significant alterations in anthropometric, biochemical, and body composition parameters were evident at t1. Notably, a substantial average weight loss of -8.8 kg and a significant reduction in mean BMI to 32.76 kg/m^2 ($P < 0.001$) were observed. Additionally, a remarkable decline in OT levels to 734.35 ± 203.35 pg/ml was recorded ($P < 0.001$). Correlation analyses revealed associations between baseline OT levels and body weight ($r = 0.35$, $P < 0.05$), BMI ($r = 0.39$, $P < 0.05$), total fat mass ($r = 0.35$, $P < 0.05$), trunk fat ($r = 0.33$, $P < 0.05$), and android fat distribution ($r = 0.43$, $P < 0.05$). Psychometric evaluations unveiled pathological BUT Global Severity Index (BUT-GSI) in 39% of participants, with OT exhibiting a direct association with BUT-GSI ($r = 0.416$, $P < 0.05$). Moreover, baseline OT levels correlated with weight loss and BMI ($P < 0.005$). A linear relationship emerged between the reduction in OT levels (t0-t1) and BMI decline. Baseline OT also correlated directly with t1 plasma ketone bodies, remaining significant after adjustments ($P = 0.02$). Furthermore, the ROC curve highlighted the predictive capacity of baseline OT levels (>1034 pg/ml) for ketosis occurrence at t1, with 100% sensitivity and 60.7% specificity (AUC 0.819, $P < 0.001$). Multivariate analyses revealed the female sex was negatively associated with BUT-GSI, while OT at t0 displayed a positive correlation. OT at t1 indicated a trend but did not achieve statistical significance.
Conclusion
This investigation underscores the complex interplay among psychological parameters, circulating OT levels, and VLCKD-induced weight loss, highlighting baseline OT as a potential predictive marker for diet-induced ketosis and weight reduction in obesity.

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P80

Resting metabolic rate in children with obesity: a predictor of metabolic syndrome

Amalia Ioana Arhire[1,2], Papuc Teodora[2], Miruna Sinziana Chiper[2] & Boroghina Steluta[3,4]
[1]Kilostop Junior, Endocrinology, Diabetes and Nutrition Department, Bucharest, Romania; [2]Elias Hospital, Endocrinology, Diabetes and Nutrition Department, Bucuresti, Romania; [3]Kilostop Junior, Endocrinology, Diabetes and Nutrition Department, Bucuresti, Romania; [4]Fundeni Clinical Institute, Gastroenterology, Bucharest, Romania

Introduction
The prevalence of obesity and metabolic syndrome among children is rising alarmingly worldwide, so the need is high for an objective and easily manageable predictor, in order to control obesity's impact on health. Childhood weight gain results from an imbalance between energy expenditure and energy intake, where the intake surpasses the energy requirements, including metabolic rate and growth. Physical inactivity impacts growth and muscle formation and can lead to pediatric obesity through low resting metabolic rate. We studied the correlation between the resting metabolic rate, LDL-cholesterol and waist circumference on a group of children with obesity in order to emphasize the importance of metabolic syndrome screening, especially in children with high percentage of body fat and low resting metabolic rate.
Materials and method
We conducted a retrospective correlational study on 168 children from the southern part of Romania, who were patients in our nutrition clinic from 2020-2021, with the age median 12, BMI median 27.2 kg/m^2, obesity degree median 143%, 89 male/79 female. We used indirect calorimetry to measure the resting metabolic rate.
Results and conclusion
77 of our patients have LDL-cholesterol values over 100 mg/dl (45.83%) and 103 of them have their waist circumference over the 95th percentile (61.3%). The percentage from the predicted resting metabolic rate negatively correlates with the LDL-cholesterol values (r=-0.18, p value=0.019) and with waist circumference (r=-0.192, p value=0.013). Thus, as resting metabolic rates values decrease, waist circumference and LDL-cholesterol values increase, leading to metabolic syndrome. Recognizing the impact of resting metabolic rate on weight gain during childhood is crucial as these children are more predisposed to metabolic complications. A more intensive lifestyle intervention with focus on diet but also physical activity is needed on these patients to prevent obesity and other complications of metabolic syndrome.
Keywords: pediatric obesity, LDL-cholesterol, waist circumference, metabolic syndrome, resting metabolic rate

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P81

Sleep quality in adults with type 2 diabetes mellitus: a tunisian study

Sana Khamassi[1], Emna Bornaz[1], Haifa Abdesselem[1], Dorra Ben salem[1], Kamilia Ounaissa[1] & Chiraz Amrouche[1]
[1]National Institute of Nutrition, Outpatient Department and Functional Explorations, Tunis, Tunisia

Introduction
Diabetes mellitus, evolving as a silent epidemic, is a chronic metabolic disease associated with high morbidity and mortality among the patients. In addition to its micro and macrovascular complications as well as its impact on quality of life, evidence has shown that patients with diabetes mellitus are prone to poor sleep quality [1]. This study aims to evaluate the sleep quality (SQ) in patients with type 2 diabetes mellitus (T2DM) and to determine possible factors that may alter the SQ of these patients.
Methods
A cross-sectional study was conducted in 100 adults with T2DM. Patients' demographic and anthropometric characteristics, diabetes related complications and biological parameters were collected. SQ was evaluated using the Pittsburgh sleep quality index (PSQI) in its arabic-validated version. The total PSQI score was obtained by adding seven scores corresponding to seven subcomponents of sleep quality, ranging between 0 and 21. PSQI score >5 indicates significant sleep disturbance and categorizes the subjects as poor sleepers.
Results
Mean age was 54.45$\pm$7.13 years with female predominance (72%). Mean diabetes duration was 12.67$\pm$7.35 years, mean glycated hemoglobin was 9.69$\pm$2.02 % and mean BMI was 29.49$\pm$4.97 Kg/m^2. Half of our sample was obese (49%). Twenty two percent of patients used oral glucose-lowering drugs (OGLDs), mostly sulfonylureas (87,5%), while 78% used insulin. Within the insulin user subgroup, 67% were prescribed metformin, and 12% were on iSGLT2. Retinopathy, nephropathy and peripheral neuropathy were found, respectively in 40%, 22% and 27% of patients. Mean DN4 score was 1.82$\pm$1.65. Mean ALT and AST levels were 20.73$\pm$7.90 UI/l and 20.72$\pm$7.08 UI/l, respectively. The mean PSQI score was 7.89$\pm$3.69 with extremes ranging from 1 to 15 and 69% of our patients had poor sleep quality. Patients with poor SQ had significantly higher prevalence of mild retinopathy (87.5% vs 12.5%; P=0.049) and peripheral neuropathy (86.4% vs 13.6%; P=0.034). Additionally, a significant disturbance of sleep was higher among patients using sulfonylureas (90% vs 10%; P=0.021). Patients with poor SQ had higher DN4 score (2.06$\pm$1.74 vs 1.17$\pm$1.21; P=0.017), higher ALT levels (21.93$\pm$8.04 UI/l vs 17.70$\pm$5.94 UI/l; P=0.016) and AST levels (21.86$\pm$7.89 UI/l vs 17.96$\pm$4.61; P=0.021).
Conclusion
highlights the high occurrence of poor sleep quality among patients with type 2 diabetes mellitus (T2DM), particularly in the presence of microvascular complications. These results underscore the importance of advocating for screening this disorder in this population
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Maaori and pacific-specific diabetes protective crebrf r457q variant alters glucocorticoid receptor activity

Kate Lee[1,2], Sanaz Vakili[1] & Peter Shepherd[1,2]
[1]University of Auckland, [1]Maurice Wilkins Centre

Type 2 diabetes (T2D) is a debilitating, multifactorial disease with a complex mix of genetic and environmental pathomechanisms. For this reason, effective treatment of T2D requires a varied arsenal of therapeutic strategies and indeed, it is an excellent candidate for precision medicine. Essential for this, we need a more detailed understanding of the genetic drivers and how these differ between individuals. There is an ever-intensifying global effort to identify genetic associations with diabetes and their mechanisms; however, these efforts mostly exclude indigenous populations which have been shown to have unique genetic variants and often higher rates of T2D. In New Zealand/Aotearoa we have indigenous Māori population as well as a large population of Pacific peoples and we are exploring unique variants associated with diabetes and metabolic disease with a focus on enabling precision medicine. A coding SNP (p.Arg457Gln) in the Creb3 regulatory factor (CREBRF) gene, found in ~25% of M?ori and peoples of the Pacific islands, is associated with a large increase in BMI, yet paradoxically, it is also associated with an approximately 50% reduction in the incidence of type-2 diabetes and gestational diabetes [Minster et al 2016, Krishnan et al 2020]. The mechanisms by which the variant drives diabetes protection remains unknown and CREBRF itself was only identified in 2008 [Audas et al 2008]. To date, CREBRF has been shown to regulate cAMP response element binding proteins (CREB3 and CREBL2) that are ubiquitously expressed and have roles in several key cellular processes including ER/Golgi stress and cell metabolism. CREBRF has also been shown to regulate glucocorticoid receptor (GR) signalling [Penney et al 2018, Martyn et al 2012]. We have characterised 20-month-old mice carrying the variant and show there are differences in body composition that manifest at this age and in males this is accompanied by lower myostatin levels [Lee et al 2022]. We have also shown the variant to alter GR transcriptional activity in vitro and in vivo. This includes differential responses of GR-mediated genes such as Dusp1 and Hsd11b1. Despite this, the mice show no overall changes in cortisol nor ATCH, no difference in response to dexamethasone suppression test and no difference in acute restraint test. This differential regulation of GR activity has the potential to explain diabetes protection in carriers of the variant and inform effective therapeutic approaches in non-carriers and therefore we are further exploring impacts on islet, adipose and muscle function.

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P83

Expression of pro-inflammatory cytokines and fibrinogen in human diabetic nephropathy

Maha Maqsood, Saima Sharif, Saira Rafaqat & Shagufta Naz
Lahore College for Women University, Lahore, Zoology, Lahore, Pakistan

Background
Diabetic nephropathy (DN) is a micro-chronic diabetic complication brought on by changes in metabolism and hemodynamics. Inflammatory cytokines, generally

IL-1β, IL-6 and IL-18 are linked in the development and advancement of DN. They act as pleiotropic polypeptides regulating inflammatory and immune responses through actions on cells. Fibrinogen is the liver-synthesized protein, with different functions and responses to both acute and chronic stimuli.
Aim
The aim of this research work is to find the relationship of IL-1β, IL-6, IL-18 and fibrinogen in the advancement of diabetic nephropathy.
Methods
This cross sectional study was conducted on 1152 subjects selected from different cities (Lahore, Gujranwala, Multan, Islamabad, Karachi and Gharro) of Pakistan. The enrolled subjects were categorized into control group (n=384), diabetes mellitus group (DM) (n=384) and diabetic nephropathy group (DN) (n=384). The serum concentration of IL-1β, IL-6, IL-18 and fibrinogen were determined by enzyme-linked immunosorbent assay (ELISA). The expression analysis of IL-1β, IL-6, IL-18 and fibrinogen were performed by Real Time PCR.
Results
The significant increased level of serum IL-6 (56.01 pg/ml), IL-1β (36.93 pg/ml) and decreased level of IL-18 (132.61pg/ml) and Fibrinogen (11.93 pg/ml) was observed in DN subjects as compared to control and DM subjects. The expression profile of IL-6 were increased by more than thirty three fold (n-fold = ∼ 33.3) and expression of IL-1β increased by more than eleven fold (n-fold = ∼ 11.76) in DN group. The decreased expression of IL-18 (n-fold = ∼ 1.92) and fibrinogen (n-fold = ∼ 12.03) was observed in DN group as compared to DM and control group. The uric acid, creatinine, blood sugar and GFR highly correlated with inflammatory cytokines that showed the disease severity. The predictive model by linear regression analysis concluded that age, serum creatinine, blood sugar and expression of IL-6 plays an essential role in the progression of DN. An inverse relationship between fibrinogen and blood sugar was observed in DN subjects. Differences in serum levels of IL-1β, IL-6, IL-18 and fibrinogen was observed among population of selected cities.
Conclusion
The present study implicates that among pro-inflammatory cytokines, Il-6 is an important predictor of DN progression in Pakistani population. The significant variation was observed in the expression of IL-1β, IL-6, IL-18 & fibrinogen in Lahore, Gujranwala, Multan, Islamabad, Karachi and Gharro that screen the variation in different races of Pakistan.

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P84

Cognitive disorders in elderly with type 2 diabetes

Maryam Cheikhrouhou, Kamilia Ounaissa, Abir El Amri, Nesine Dhieb, Dorra Ben Salem, Emna Bornaz, Haifa Abdesslem, Chiraz Amrouche
National Nutrition Institute, Department of Nutritional Diseases D, Tunisia

Introduction
Cognitive disorders are common in the elderly population. Diabetes accelerates cognitive deterioration in this population. We aimed to estimate the frequency of cognitive disorders in elderly diabetics ubjects.
Methods
This was a cross-sectional study including200 elderly diabetic patients. Cognitive function was assessed using the Mini Mental State Examination (MMSE) score. Participants having a score below 26 were considered cognitively impaired.
Results
Median HbA1C was 8.66%. The median MMSE score was 26 (IIQ= [23-27]). A score <26 was recorded in 28.5% of patients. We noted that cognitive impairment was more frequent in women ($p<0.001$) and that it increased with age (p=0.034). thus, cognitive disorders were found in 22.1% of patients aged between 70 and 75, 53.3% of patients aged between 75 and 80, and 44.4% of patients aged over 80. Patients with cognitive impairment, hadmore frequently a poor glycemic control (70.2% vs 51.1% $p<0.001$) and a higher frequency of mild and sever hypoglycemia (43.9% vs 27.3% p=0.023), than those without cognitive disorders.
Conclusion
Cognitive disorders are common among older diabetics. Systematic screening and optimization of treatment are essential in these patients.

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P85

Mauriac syndrome in adolescents: A clinical entity that still exists

Marwa Sassioui, Saloua ELAMARI, Soukaina LAIDI & Marouan Fatima
Cheikh khalifa bin zayd al nahyan Hospital - University Mohamed VI of health sciences, casablanca , Morocco

Introduction
Mauriac syndrome is a rare pathology characterized by the presence in an unbalanced type 1 diabetic (T1DM) of delayed stature-weight and puberty, and hepatomegaly with disturbance of the liver balance. We report a case of Mauriac syndrome in a young diabetic to recall the syndrom, as well as the diagnostic criteria.
Medical observation
This was a 17-year-old patient, type 1 diabetic since the age of 2, with recurrent ketoacidosis. Admitted to the endocrinology department post ketoacidosis. On clinical examination, abdominal distension was noted, with a liver arrow greater than 12 cm. Height 136 cm (-4 DS) and weight 30 kg. The pubertal stage according to Tanner's classification was P2G2. Biology revealed poorly balanced diabetes (HbA1c 12%) and moderate cytolysis. Viral serologies and immunological work-up were negative; thyroid work-up was normal. Abdominal ultrasound showed hepatomegaly (hepatic arrow FH: 17cm) homogeneous and hyperechoic. Liver biopsy concluded glycogenic overload.
Conclusion
Mauriac syndrome was first described by Mauriac in 1930, in children with type 1 diabetes mellitus presenting with stunted growth and puberty, hepatomegaly and elevated transaminases. Differential diagnoses include toxic causes, viral hepatitis, Wilson's disease, autoimmune hepatitis, celiac disease and minor glycogenosis. Paraclinical investigations confirm clinical suspicion and establish the diagnosis. The gold standard is liver biopsy, to rule out autoimmune hepatitis. Balanced diabetes allows normalization of liver function and recovery of growth and puberty.

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P86

Testosterone levels in men with type 2 diabetes: impact of statins and dyslipidemia

Anis Grassa[1], Manel Jemel[1], salma salhi[1], Brahim Khalfa[1], Asma Krir[2], Ahlem Benhmid[2], Marwa Chiboub[1], Radhouane Gharbi[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technologies, Zouheir Kallel, [2]Pasteur Institute of Tunis

Introduction
Hypogonadism (HG), a condition characterized by insufficient testosterone levels, is a prevalent concern in men with Type 2 Diabetes (T2D). Simultaneously, the use of statins and the presence of dyslipidemia are common aspects of the medical management of individuals with T2D. This study investigates the intricate relationship between HG, statin therapy, and dyslipidemia in men with T2D, aiming to unravel potential correlations and shed light on the complex health dynamics within this population.
Methods
This is a cross-sectional study that included 250 male patients aged 40 to 65 diagnosed with T2D, recruited from outpatient clinics. All patients underwent lipid and hormonal assessments. HG was considered in the presence of specific criteria: Total Testosterone (TT) levels below 231 ng/dL, Free Testosterone (FT) levels below 6.5 ng/dL, or Bioavailable Testosterone (BT) levels below 150 ng/dL.
Results
The median age of our cohort was 58 years, with an interquartile range of [52.7-62], spanning from 40 to 65 years. Regarding blood lipids, the average levels of total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDLc) were 4.14 ± 0.96 mmol/L, 1.44 ± 0.89 mmol/L, and 1.03 ± 0.22 mmol/L, respectively. Dyslipidemia was noted in 72.3% of patients, predominantly marked by hypoHDLemia (55.7%) followed by hypertriglyceridemia (27.7%). Additionally, 12.8% of patients exhibited hypercholesterolemia . Notably, 69.2% of participants were under statin therapy. Concerning TT levels, The average level was 438.8 ± 172.1 ng/dL. No significant difference was observed between the statin group (434.0 ± 158.2 ng/dL) and the non-statin group (453.6 ± 201.2 ng/dL) (p=0.414). The analysis of HG prevalence between the statin (69.7%) and non-statin groups (71.1%) did not reveal a significant difference (p=0.829).
Conclusion
These findings suggest that in the studied cohort of men with T2D, dyslipidemia and statin therapy did not significantly impact total testosterone levels or the prevalence of hypogonadism. Further research may be warranted to explore additional factors influencing hormonal health in this population.

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P87

Investigation of anti-diabetic effects of various extracts of Jatropha tanjorensis in BRIN-BD11 clonal pancreatic beta cells

Simren Kaur Heer[1], Opeolu Ojo[1,2], Ayokunle Benjamin Falana[1], Adaeze Enebuse[3], Mojisola Adie[1] & Iyiola Tella[3,4]
[1]University of Wolverhampton, Faculty of Science and Engineering, [2]IRiD Biosciences, Stoke-on-Trent, [3]Modibbo Adama University, Department of Forestry and Wildlife Management, Yola, Nigeria, [4]First Technical University, Faculty of Natural and Applied Sciences, Ibadan, Nigeria

Aim
Beneficial effects of Jatropha tanjorensis (J. tanjorensis) extracts in African traditional medicinal practices for the management of type 2 diabetes have been reported. However, mechanisms through which these extracts exert their anti-diabetic actions have not been widely studied.
Methods and materials
Effects of various aqueous extracts of root, leaf, and bark J. tanjorensis (0-1000 μg/ml) on insulin-release, cytotoxicity and cell viability were investigated using BRIN-BD11 cells. Effects of leaf extracts (100 μg/ml) on glucose-stimulated insulin secretion and changes in insulinotropic actions in the presence of known modulators as well as the absence of extracellular calcium were also assessed.
Results
J. tanjorensis extracts stimulated insulin secretion from BRIN-BD11 cells at concentrations $\geq$0.1 μg/ml for leaf (1.7-fold, $P<0.001$), 1 μg/ml for bark (2-fold, $P<0.05$) and 10 μg/ml for root (1.8-fold, $P<0.05$) extracts. These insulin-releasing effects were not associated with significant release of lactate dehydrogenase at concentrations $\leq$100 μg/ml for leaf, 100 çg/ml for bark and 100 μg/ml for root extracts. Effects of the leaf extracts were inhibited by diazoxide (51%, $P<0.01$), verapamil (29%, P0.05) and in the absence of intracellular calcium (41%, $P<0.01$). However, effects of the extract were enhanced by KCl (2.3-fold, $P<0.01$. Improved intracellular calcium concentration were observed in cells treated with the leaf extracts of J. tanjorensis (2.4-fold, P0.01).
Conclusion
The results confirm insulinotropic actions of J. tanjorensis extracts and suggest that the KATP-dependent pathway may be involved in the mechanism of action.

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P212

NGO project on status report on pediatric diabetes in developing countries

S Pal[1] & T Roy[1]
[1]SFCCP NGO, Med, meerut, India

Issues
In developing nations diagnosis of diabetes brings mental-trauma/depression in family. Focused treatment for pediatric age-group is unavailable in developing-countries. 26% of diagnosed diabetics are children's. Adequately trained physicians/Nurses in issues of pediatric-diabetes provide continuity of care, relief from depression and smooth transition from diagnosis to treatment. Qualitative collaborative relationship between these makes diabetics life bearable. Our NGO-project highlights significance of relationship between nurses and diabetic-children in community clinic setup of rural India. For Diabetes, its assumed that depression is inevitable sequel to diagnosis. Retrospective analysis of past studies shows—counselling improves QOL & attitude towards diabetes-treatment.
Aims
To describe care issues in diabetic-children's. Observe/modify nature of relationship between nurse and child. To evolve comprehensive treatment plan for patients and families.
Methods
A retrospective analysis of data base from 7 rural health-clinics. Specialized therapy/support to pediatric-age-group not available at any centre. Total 117 children's [4-13 years] diagnosed with diabetes. 23 had additional endocrine/-metabolic problems. Nursing/medical care plan analyzed. No specialized trained personal in rural/tribal India. Opinion/needs from patients families collected on feedback questionnaire. Then we trained 10 nurses & 2 physicians for handling pediatric cases [4 weeks training].
Results
out of 117, 41 discontinued Rx due to improper counseling/guidance. 3 died. Patient/family's feedback highlights: Better access to newer drugs-delivery-systems, psychosocial support, follow-up-plan. Nurses/physician be sensitized in pediatric care-issues. Main issues of concern were: [1] illness and coping with their feelings. [2] Initial impact of diagnosis and a search for solution? Expectations for future life & its quality? [3] Concerns of cost of RX [4] Availability of proper follow-up centers in rural areas of developing nations.
Conclusion
Multifaceted Relationship between physician/nurse and Diabetics children's is crucial. This relationship provides better continuity of treatment. We show concerns/difficulties while working in Asian set-up to experts/seniors at ECE congress

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P257

Real-world comparison of real-time continuous glucose monitoring and intermittently scanned continuous glucose monitoring in glycemic control among individuals with type 1 diabetes: a nationwide cohort study

Ji Yoon Kim[1], Seohyun Kim[2], Rosa Oh[1], So Hyun Cho[1] & Jae Hyeon Kim[1]
[1]Samsung Medical Center, Medicine, Seoul, Korea, Rep. of South; [2]Sungkyunkwan University, Clinical Research Design and Evaluation, Seoul, Korea, Rep. of South

Aim
There is little real-world evidence comparing the effectiveness of real-time continuous glucose monitoring (rtCGM) and intermittently-scanned continuous glucose monitoring (isCGM) in glycemic control, with a large population and long-term follow-up. This study aimed to compare the association of rtCGM and isCGM with glycemic control in individuals with type 1 diabetes (T1D) in a real-world setting.
Methods
From the Korean National Health Insurance Service Cohort (2016–2022), individuals with T1D managed by intensive insulin therapy were followed up for 2 years at 3-month intervals since the initiation of CGM. The HbA1c and coefficient of variation (CV) of rtCGM and isCGM users were compared using an independent two-sample t-test and a linear mixed model.
Results
A total of 4,333 and 6,257 individuals were included in the HbA1c and CV analyses, respectively. Overall, a significant reduction in HbA1c levels was observed after 3 months of receiving CGM, and the effect remained durable for 2 years. A greater reduction in HbA1c levels was observed with rtCGM compared to isCGM (P for between-group difference <0.05 in both children and adults). The mean HbA1c level decreased from 8.9% at baseline to 7.1% at 24 months in rtCGM users, whereas it decreased from 8.6% to 7.5% in isCGM users. The greater reduction in HbA1c with rtCGM remained significant after adjusting for the baseline characteristics of users. CV also decreased more with rtCGM than with isCGM.
Conclusion
In this large nationwide cohort study, the use of rtCGM was associated with a greater improvement in glycemic control including HbA1c reduction than the use of isCGM in individuals with T1D.

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P258

Unraveling the role of the upper small intestine microbiome in metabolic diseases: insight on new potential therapeutic interventions

Eugeni Belda[1], Emilie Steinbach[1], Rohia Alili[1], Solia Adriouch[1], Davide Masi[2], Emavieve Colas[1], Charlène Dauriat[3], Gianfranco Donatelli[4], Jean-Loup Doumont[4], Laurent Genser[1], Flavien Jacques[1], Melissa Kordahi[3], Véronique Pelloux[1], Harry Sokol[5], Paul Taillandier[1], Thierry Tuszunski[4], Benoit Chassaing[3], Tiphaine Le Roy[1] & Karine Clément[1]
[1]Sorbonne Université, Inserm, Nutrition and Obesities: Systemic Approaches (NutriOmics) Research Unit, Paris, France; [2]Sapienza University of Rome, Experimental Medicine, Roma, Italy; [3]Université de Paris, Inserm U1016, Team ' Mucosal microbiota in chronic inflammatory diseases', Cnrs Umr 8104, Paris, France; [4]Hôpital privédes Peupliers - Ramsay Générale de Santé, Paris, France; [5]Sorbonne Université, Inserm Umrs-938, Centre de Recherche Saint-Antoine, Crsa, AP-HP, Paris, France; Paris Center for Microbiome Medicine, Fédération Hospitalo-Universitaire, Paris, France; INRAE, UMR1319 Micalis & AgroParisTech, Jouy en Josas, France

Introduction
While extensive research on the fecal microbiome (FM) has already underscored the gut microbiome's role in metabolic diseases, it is imperative to recognize its limitations in depicting the entire gastrointestinal tract. Each segment of the tract harbors unique conditions shaping microbial ecosystems, necessitating exploration

beyond the FM. The upper small intestine (USI) significantly impacts nutrient digestion and absorption, hinting at its microbiome's potential influence on the regulation of host metabolism. In a recent systematic review of the literature, we pointed out that studies on the C57BL/6 murine strain fed a high-fat diet showed a causal connection between the USI microbiome (USIM) and metabolism. However, research on individuals with obesity remains scarce and conflicting, and comparative studies between different gastrointestinal niches in patients with obesity are lacking.
Materials and Methods
This pilot study employed Shotgun Illumina sequencing to conduct metagenomic analysis of the USI, FM, and oral microbiome (OM) in both candidates for metabolic surgery ($n=15$) and healthy controls ($n=15$).
Results
USIM exhibited lower gene richness than OM and FM ($P<0.0001$). Compositionally, USIM resembled OM more than FM but exhibited significant differences from FM. Multivariate permutational analysis revealed that body composition and corpulence variables accounted for variance in USIM and its associated metabolome composition, showing a negative correlation with metagenomic richness. Comparison between groups with and without obesity within each ecosystem unveiled greater metagenomic richness in the USI of patients with obesity ($P=0.037$). This group also displayed a lower relative abundance of Proteobacteria ($P<0.001$), notably Neisseriaceae ($P<0.0001$), in the USIM.
Conclusion
Our study underscores the significance of studying the proximal gut microbiota to unravel intricate connections between gut microbiota composition and metabolic health. These insights provide a foundation for potential therapeutic interventions targeting the proximal gut microbiome in managing metabolic diseases.

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P259

The development of cardiovascular disease or cancer is correlated with higher FIB-4 in patients with T2DM

Katerina Stefanaki[1], Dimitrios Karagiannakis[2], Petrea Foteini[3], Panagiota Zacharaki[1], Alexandra Giannou[3], Olympia Michalopoulou[1], Paraskevi Kazakou[1], Theodora Psaltopoulou[1], Vasiliki Vasileiou[3] & Stavroula Paschou[1]
[1]Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece., Endocrine Unit and Diabetes Center, Department of Clinical Therapeutics, Athens, Greece; [2]Laiko General Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, Academic Department of Gastroenterology; [3]Alexandra Hospital, Athens, Greece., Department of Endocrinology

Introduction
Metabolic dysfunction-associated steatotic liver disease (MASLD) is a common feature of type 2 diabetes mellitus (T2DM). Liver fibrosis has been associated with an increased risk of cardiovascular diseases (CVD).
Aim
To investigate whether the fibrosis 4 index (FIB-4), a non-invasive marker of liver fibrosis, is associated with CVD or cancer in patients with T2DM.
Methods
Two hundred and nine consecutive T2DM patients were retrospectively evaluated. The mean time from the diagnosis to the first visit to our diabetes center was 9.83 ± 8.6 years (median: 8.2 years; IQR: 12).
Results
One hundred and thirty-two (63.2%) patients were male and 77 (36.8%) were female. The mean age, body mass index (BMI), glycated hemoglobin (HbA1c), and FIB-4 were 64.3 ± 11 years, 30.5 ± 5.8 kg/m^2, 7.8 ± 2, and 1.15 ± 0.5, respectively. One hundred and fifty (71.8%) patients had FIB-4 <1.3, and 59 (28.2%) had FIB-4 >1.3. Patients with CVD at the first visit were significantly older compared to patients without CVD (68.9 ± 8.4 vs 62.9 ± 11.4, respectively; $P<0.001$), while they had substantially higher FIB-4 (1.26 ± 0.54 vs 1.08 ± 0.51, respectively; $P=0.007$). Patients with cancer of any type at the first visit were older (68.2 ± 9.5 vs 64.4 ± 10.9 years, $P=0.098$), having significantly higher FIB-4 (1.37 ± 0.6 vs 1.1 ± 0.5, $P=0.004$) compared to those without cancer. A significant correlation was revealed between FIB-4$>$ 1.3 and the presence of CVD (χ 2=4.92, $P=0.027$) or the presence of cancer (χ 2=7.603, $P=0.006$), respectively. In the multivariate analysis, the presence of CVD was found to be independently associated with sex (male: OR 0.261, 95% CI 0.095-0.717; $P=$ 0.009), age (OR 1.057, 95% CI 1.008- 1.108; $P=$ 0.021), and hypertension (OR 6.146, 95% CI 2.442-15.471; $P<0.001$).
Conclusion
T2DM patients who develop CVD or cancer are older with higher FIB-4. Older female patients with a history of hypertension are at a higher risk of developing CVD.

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P260

The influence of finerenone on renal function in patients with type 2 diabetes

Yanina Rebrova[1], Yana Saienko[1], Borys Mankovsky[2] & Ievgen Marushko[1]
[1]Ukrainian Children's Cardiac Center, Cardiometabolic Disease, Kyiv, Ukraine; [2]Dmitry F. Chebotarev Institute of Gerontology of the National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine

Background
Chronic kidney disease develops in approximately 40% of patients with type 2 diabetes mellitus (T2DM) and significantly increases the risk of mortality and cardiovascular morbidity. Finerenone, a novel nonsteroidal mineralocorticoid receptor antagonist, has demonstrated a significant impact on renal function by reducing proteinuria and preserving glomerular filtration rate in patients with chronic kidney disease. However, the influence of finerenone on kidney function in the different patients populations requires the further investigation. Therefore, the aim of our study was to investigate the influence of treatment with finerenone on kidney function in patients with chronic kidney disease with and without T2DM.
Methods
Two groups of patients were examined. The first group included 45 patients with T2DM who were taking finerenone. Their age was 63.0 ± 6.0 years, duration of diabetes - 7.0 ± 4.0 years, HbA1c was 7.6 ± 2.2%, creatinine level -115.6 ± 3.78 μ mol/l, estimated glomerular filtration rate (eGFR) -50.95 ± 1.56 ml/min/1.73m^2, and the urinary albumin-to-creatinine ratio (UACR) -43.08 ± 10.84 mg/g % (data are presented as mean$\pm$SD). The second group consisted of 40 patients without type 2 diabetes but with chronic kidney disease (CKD) who were taking finerenone. Their age was $54,0\pm4,0$ years, HbA1c -5.1 ± 0.9%, creatinine level -84.73 ± 2.01 μ mol/l, eGFR -83.60 ± 1.86 ml/min/1.73 m^2, and UACR -25.14 ± 4.18 mg/g. To compare the effect of finerenone on eGFR and UACR, we used one-way analysis of variance (ANOVA) and Student's t-test.
Results
In patients with diabetes, the increase in eGFR under the influence of the drug does not significantly differ between groups with and without diabetes (54.41 ± 1.77 ml/min/1.73 m^2; 86.75 ± 1.69 ml/min/1.73 m^2, –respectively, $P<0.05$). The decrease in UACR under the influence of the drug does not significantly differ between groups with and without diabetes, but there is a tendency toward a more pronounced effect in patients without diabetes (42.42 ± 10.68 mg/g; 21.32 ± 4.38 mg/g,–respectively, $P<0.05$).
Conclusion
We found that finerenone positively affects kidney function in patients with and without T2M. The administration of finerenone has been associated with a decrease in urinary albumin excretion and a slowing of the progression of kidney disease, highlighting its potential as a therapeutic option for managing renal complications.

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P261

Familial partial lipodystrophy:genetic and clinical data from a greek referral center

Aikaterini Kountouri[1], Emmanouil Korakas[1], Eirini Maratou[2], Ignatios Ikonomidis[3], Konstantinos Balampanis[1], Loukia Pliouta[1], Stavros Liatis[4], Nikolaos Tentolouris[4], Panagiotis Toulas[5], Foteini Kousathana[1], Christoforos Giatzakis[6], George Dimitriadis[7] & Vaia Lambadiari[1]
[1]Attikon University Hospital, Second Department of Internal Medicine, Chaidari, Greece; [2]Attikon University Hospital, Department of Clinical Biochemistry, Chaidari, Greece; [3]Attikon University Hospital, Second Cardiology Department, Chaidari, Greece; [4]Laiko Hospital, First Department of Propaedeutic and Internal Medicine, Athens, Greece; [5]Bioiatriki Healthcare Group, Athens, Greece; [6]DNAbiolab, Cretan Center for Research and Development of Applications on Genetics and Molecular Biology, Heraklion, Greece; [7]Sector of Medicine, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Background
Familial partial lipodystrophy (FPLD) is a rare syndrome in which a patient's phenotype is not dependent merely on the specific genetic mutation, but also on a combination of other demographic, environmental and genetic factors. In this report, we present a large cohort of novel mutation in FPLD patients from a large referral center in Greece and we investigate the possible relationship between the genetic variations detected and their phenotype and the effect of metreleptin treatment in eligible FPLD patients.

Methods
This is a prospective observational study in a Greek referral center, included patients who fulfilled the clinical criteria of FPLD. A genetic analysis was conducted, which included sequence and deletion/duplication analyses of the LMNA and PPRARG genes. Anthropometric parameters and laboratory examinations were evaluated. The treatment responses of patients who received treatment with metreleptin were evaluated at 3 and 12 months.
Results
Overall, 39 patients were included in the study. The mean ± SD age was 47.59 ± 10.13 years, and 30 patients were female (76.9%). All the patients presented lipoatrophy in lower limbs, 59% in upper limbs and 66.7% in gluteal area. 97.4% displayed fat deposition in the abdomen, 46.2% in the trunk, 56.4% in the face and 35.9% in the neck. 76.9% presented acanthosis nigricans while 12.8% displayed muscular hypertrophy. Regarding the comorbidities related to lipodystrophy phenotype, 66.7% suffered from diabetes mellitus, thirty 76.9% presented dyslipidemia, 61.5% had hypertension, 56.4% had NASH or NAFLD and six 5.4% suffered from heart diseases. 33.3% of females met the criteria for PCOS. Genetic testing for did not result in any of the already known pathogenic mutations, but it revealed three likely pathogenic mutations, along with various changes in other exons and introns, especially in introns 7 and 10, whose pathogenicity and the subsequent role in the patients' phenotype remains unclear. Treatment with metreleptin in eligible FPLD patients significantly improved indices of glycemic and lipidemic control, and the benefit was sustained after 12 months.
Conclusion
We have shown the presence of mutations both in exons, which are different from the ones which already have an established association with the disease, and in introns, which might also contribute to the final amino acid products and the phenotype of the patient. The sustainable and favorable results of metreleptin treatment in FPLD patients were confirmed, and they are independent from any baseline parameters.

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P262

Exploring the metabolic and cellular/molecular benefits of mediterranean and a low-fat diet in the revertion of obesity and diabetes in mice

Andre Sarmento-Cabral[1,2,3,4], António Montero-Hidalgo[1,2,3,4], Jesús Pérez-Gómez[1,2,3,4], Andrea Martínez Vara[1,2,3,4], José Lopez-Miranda[4,5,6,7], Elena M Yubero-Serrano[4,5,6], Manuel D. Gahete[2,3,4,8] & Raul M. Luque[1,2,3,4]
[1]Maimónides Institute of Biomedical Research of Córdoba (IMIBIC), GC27 OncObesity and Metabolism, Cordoba, Spain; [2]University of Córdoba, Department of Cell Biology, Physiology and Immunology, Cordoba, Spain; [3]Reina Sofí a University Hospital (HURS), Cordoba, Spain; [4]CIBER Pathophysiology of Obesity and Nutrition (CIBERobn), Cordoba, Spain; [5]Maimónides Institute of Biomedical Research of Córdoba (IMIBIC), GC09 Nutrigenomics. Metabolic Syndrome, Cordoba, Spain; [6]Reina Sofí a University Hospital, Lipids and Atherosclerosis Unit, Department of Internal Medicine, Cordoba, Spain; [7]University of Córdoba, Department of Medical and Surgical Sciences, Cordoba, Spain; [8]Maimónides Institute of Biomedical Research of Córdoba (IMIBIC), GC30 Molecular Hepatology, Cordoba, Spain

Obesity (OB) and type-2 diabetes (T2D) are chronic endocrine-metabolic diseases, associated to insulin-resistance (IR), that represent capital health problems. Fortunately, both pathologies are, at least, partially reversible by dietary interventions, but the potential metabolic, molecular, cellular factors and mechanisms that might be involved in the total/partial reversion of OB/IR/T2D by dietary interventions are poorly known. Thus, in this work, we aimed evaluate the impact of Mediterranean-diet (MedD) and a low-fat-diet (LFD) on the reversion of OB/IR/T2D, and the associated metabolic/cellular/molecular alterations in key tissues [e.g. visceral adipose tissue (VAT) and liver]. To that end, 8-weeks old littermate-male-mice were fed a high-fat diet [HFD; 60% fat (54.2% lard + 5.6% soybean oil)] to develop OB/IR, or a control-diet [17.4% fat (soybean oil), (n = 12] for 14-weeks. Then, HFD group mice (with OB/IR) were divided into 3 groups with different diet interventions for additional 13-weeks: i) maintained with the same HFD (n = 12); ii) shifted to MedD [35% fat: 21.7% MUFA (extra virgin olive-oil), 5.9% PUFA (4.9% corn-oil + 1% fish-oil), and 6.9% SFA (butter); (n = 18]; or, iii) shifted to a LFD [30.1% fat: 12.7% MUFA (extra virgin olive oil), 6.8% PUFA (5.7% corn-oil + 1.1% fish-oils) and 9.7% SFA (butter); (n = 18], while the control-diet group continued with the same diet for a total of 27 weeks. Before and after diet intervention, body-status (weight and composition), glucose homeostasis, indirect calorimetry, and activity as well as plasma insulin, leptin, ghrelin, and ALT were measured. Finally, alterations in the expression of inflammasome- and proliferation-related genes were measured in VAT and liver. As main results, we could observe that both MedD and LFD significantly reversed the OB/IR/metabolic-status induced by HFD (i.e. decreased body/tissue weights, body fat mass, VAT adipocytes area, liver triglyceride content, and proliferation-related genes expression in VAT and liver; improved glucose/insulin tolerance; reestablished respiratory exchange ratio, energy expenditure and activity; recovered plasma insulin/-leptin/ghrelin/ALT levels), close to the levels found in the control-diet group. Additionally, MedD/lFD reduced inflammasome-related genes expression vs HFD group in VAT. However, this inflammatory profile was only reverted in the liver of MedD, but not LFD, group vs HFD-group. All toghether, we can conclude that MedD and LFD intervention successfully reverted OB/IR/metabolic-status, but the molecular fingerprints associated to this beneficial effects at the VAT and liver are distinct.
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Risk of type 2 diabetes in 99,892 nordic women with polycystic ovary syndrome and 446,055 controls: national cohort study from Denmark, Finland and Sweden

Dorte Glintborg[1,2], Meri-Maija Ollila[3], Jens-Jakob Møller[4], Paula Pesonen[3], Sofia Persson[5], Evangelia Elenis[5], Katrine Rubin[1,6], Mika Gissler[7,8,9], Marianne Andersen[1], Inger Sundström-Poromaa[5] & Terhi Piltonen[3]
[1]Odense University Hospital, Odense, Denmark; [2]University of Southern Denmark, Odense, Denmark; [3]Oulu University Hospital, Oulu, Finland; [4]Odense University Hospital, OPEN, Odense, Denmark; [5]Uppsala University Hospital, Sweden; [6]University of Southern Denmark, OPEN research unit, Odense, Denmark; [7]Helsinki, Department of Knowledge Brokers, THL Finnish Institute for Health and Welfare, Helsinki, Finland, Helsinki, Finland; [8]Region Stockholm, Academic Primary Health Care Centre, Sweden; [9]Karolinska Institute, Department of Molecular Medicine and Surgery, Sweden

Background
The risk of type 2 diabetes (T2D) in PCOS is associated with BMI, but prospective data regarding risk of T2D in PCOS are limited. We investigated prospective risk of T2D in Nordic women with PCOS compared to controls.
Methods
National register-based study in women with PCOS and age-matched controls originating from Denmark (PCOS Denmark, (n = 27,016, controls, (n = 133,994), Finland (PCOS Finland, (n = 20,467, controls, (n = 58,051), and Sweden (PCOS Sweden, (n = 52,409, controls, (n = 254,010). The main study outcome was T2D occurring after PCOS diagnosis. T2D was defined according to ICD-10 diagnosis codes and/or filled medicine prescriptions. Cox regression analyses were adjusted for BMI and length of education.
Findings
The median age at cohort entry was 28 years in PCOS Denmark, Finland and Sweden with median follow-up time (interquartile range) in women with PCOS of 8.5 (4.0; 14.8), 9.8 (5.1; 15.1), and 6.0 (2.0; 10.0) years, respectively. The crude hazard ratio (HR, 95% CI) for T2D in women with PCOS was 4.28 (3.98 –4.60) in Denmark, 3.40 (3.11 - 3.74) in Finland and 5.68 (5.20 –6.21) in Sweden. In adjusted regression analyses, BMI $\geq$ 30 vs $<$ 25 kg/m^2 was associated with 7.6- to 11.3-fold risk of T2D. In a combined meta-analysis (PCOS, (n = 99,892, controls, (n = 446,055), the crude HR for T2D in PCOS was 4.64 (3.40 –5.87) and adjusted HR 2.92 (2.32 –3.51).
Interpretation
Diagnosis of PCOS and BMI $\geq$30 kg/m^2 represented a high-risk phenotype for prospective risk of T2D across Nordic countries.

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Comparison of metabolic and immunological profile of 2 types of familial partial lipodystrophy syndromes (PLIN1 and LMNA)

Dupuis Hippolyte[1], Stienne Lucie[1], Lion Georges[2], Pigny Pascal[2] & Marie-Christine Vantyghem[1,3]
[1]Hospital Center University De Lille, Endocrinology-Diabetology-Metabolism-Nutrition, Lille, France; [2]Hospital Center University De Lille, Nuclear Medicine, Lille, France; [3]Lille University Hospital, competence center for rare endocrine diseases Firendo Prisis, Lille, France

Familial Partial Lipodystrophy Syndromes (FPLD) are rare diseases characterized by partial lack of subcutaneous fat resulting in a severe metabolic

syndrome and cardiovascular complications. Besides premature cell senescence, 2 main mechanisms are involved in FPLD: impaired adipocyte differentiation and lipid droplet, corresponding to two of the main causes of FPLD: *LMNA*-related FPLD2 and *PLIN*-related FPLD4. The objective of this study was to compare the clinical, metabolic and immuno-hematological profile of these 2 types of FPLD.
Methods
The study was conducted in the frame of a prospective cohort (NCT0178428) aiming to characterize different types of fat disorders associated with a variable degree of insulin resistance from lean control subjects to obese patients and lipodystrophy syndromes in a university hospital. Clinical (sex, age), metabolic (HbA1c, fasting blood glucose and C-peptide, triglycerides, liver enzymes, leptin, CRP), % of fat mass (DEXA), intra&total abdominal fat and % of liver steatosis (MRI) were recorded. Four groups of patients (20 lean and 20 non-diabetic obese patients, 26 R482-*LMNA*-mutated patients and 8 *PLIN1*-linked FPLD patients were compared with the Mann-Whitney test, whereas correlation studies were done with the Pearson test.
Results
The 2 FPLD groups (FPLD2 and FPLD4) showed higher BMI, intraabdominal fat, HbA1c, triglycerides, ALAT, fatty liver, and eosinophils than the lean controls, but FPLD2 and FPLD4 groups only differed by a significantly lower leptin level in the FPLD4 group. Compared to lean controls, leukocytes & neutrophils were increased, and NK cells decreased, in the FPLD2 group. Basophils levels were increased in the FPLD4 group compared to lean, but also obese subjects. Basophils were the cell subtype the most often correlated positively with metabolic (HbA1c, FBG, triglycerides) and liver (ALAT, steatosis %) parameters, and negatively with the % of body fat mass and leptin levels.
Conclusion
This is the first report comparing the clinical and biological phenotype, including immune-hematological profile, of FPLD patients, especially the rare FPLD4 patients, to lean and obese control groups. Although the controverses on the pathogenicity of *PLIN1* variants, the phenotype of FPLD4 was similar to FPLD2, with however a less severe lipoatrophy as suggested by a lower leptin level. In addition, despite the small size of the groups, we found variations of NK and basophils cells, key cells involved in Th2 response, suggesting the potential interest of targeting basophil activation with treatments such as omalizumab, benlizumab, in the field of these rare orphan diseases.

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Clinical outcomes of patients with diabetic foot ulcer treated with dalbavancin in the outpatient setting

Sarah Lawless[1], Elias Eltoum[1], Emily Madden[1], Avril Clancy[1], Ana Rueda[1], Carole Doherty[2], Siobhan Bacon[1] & Catherine McHugh[1]
[1]Sligo University Hospital, Department of Diabetes, Endocrinology and Metabolism, Ireland; [2]Sligo University Hospital, Department of Pharmacy, Ireland

Aims
The primary aim of this retrospective study was to examine clinical outcomes of patients with diabetic foot ulcer (DFU) and/or osteomyelitis (OM) who attended day services at Sligo University Hospital (SUH) for dalbavancin between November 2020 and August 2023. The secondary aim was to perform a cost analysis of the use of dalbavancin.
Methods
Clinical information was obtained from the Prowellness electronic patient record and laboratory results were extracted from the SUH information system.
Results
In total, data from 42 patients who received dalbavancin was collected. 37(90.2%) patients have T2DM, 9(24.3%) of which are insulin dependent, and 4(12.9%) patients carry a diagnoses of T1DM. Mean duration of diabetes is 16.1 years. Average HbA1c was 61.2 mmol/mol. We have follow up podiatry data on 34 of these patients, unfortunately, 8 patients either transferred care to another hospital or did not attend follow up clinics. 26 (76.47%) achieved remission with no active foot disease, 10 (38.5%) of these patients suffered another diabetic foot ulcer at a different site(s) post resolution. 18 of these patients have been discharged to community podiatry. Prior to the availability of dalbavancin, patients with DFU were admitted as inpatients for treatment as out-patient antimicrobial therapy (OPAT) is limited in our area. A cost analysis was performed comparing inpatient admission and outpatient treatment with dalbavancin. The average length of stay for an inpatient with diabetes in Ireland is 8+/-13 days. The Health Service Executive advised in 2019, that the cost of a hospital bed is € 878 per night. Therefore, the average cost of an admission is approximately € 7024. The current cost of a course of a complete course of dalbavancin is € 3852.
Conclusion
Patients treated with dalbavancin for DFU have had good clinical outcomes to date while avoiding inpatient admission. There is significant cost savings using this approach.

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MAFLD and type 2 diabetes: is dual therapy an effective option?

Giovanni Ragozzino[1], Igea Martina Madonna[1] & Edi Mattera[2]
[1]University of Campania, Environmental Biological and Pharmaceutical Sciences and Technologies, Caserta; [2]University of Campania, Precision Medicine, Naples

Background and Aims
Metabolic dysfunction-associated fatty liver disease (MAFLD) is a diagnosis of inclusion relying on a set of metabolic risk factors and the presence of hepatic steatosisis; viscerl obesity, insulin resistance, type 2 diabetes (T2D) may often coexist in MAFLD patients. MAFLD is present in up to 80%f of T2D patients. Pioglidazone, a peroxisome proliferator-activated receptor agonist reduce hepatic/visceral fat (HVF) and improve necroinflammation in liver. Dulaglutide, a weekly glucagon-like peptide-1 (GLP-1) receptor agonist, significantly reduces liver fatty content (LFC) and improves GGT levels in NAFLD. Aim of this study was to evaluate dual treatment (pioglidazone plus dulaglutide) vs pioglidazone alone in recruited MAFLD/T2D patients.
Method
MAFLD was assessed using ultrasound-fatty liver index that allows to grade steatosis severity (US-FLI score ≥ 3) and liver fibrosis (F1-F2 staged according to the METAVIR score). Eligible patients (pioglidazone, 30 mg/die, os undergoing treatment for at least 1yr) added 1.5 mg subcutaneous dulaglutide weekly for 36 weeks. Fifty-seven MAFLD/T2D patients were studied (baseline, 3, 6 and 9 months). Plasma markers of hepatic dysfunction (ALT, AST, γ GT), cardiometabolic risk (triglycerides, total, non-HDL cholesterol, Apo-B100, Apo-B48, HbA1c, 1.5-anhydroglucitol [1,5-AG]), inflammation (hs C-reaction protein, TNF-α, IL-10/IL-6 ratio) were studied.
Results
Significant reduction in HVF ($P<0.05$) and LFC percentage ($P<0.02$), IL10/IL-6 ratio ($P<0.002$) and ALT ($P<0.05$), Apo-B100 ($P<0.001$), non-HDL cholesterol ($P<0.05$) and HbA1c ($P<0.02$) at 9 months were observed. HbA1c was inversely correlated with 1,5-AG and the factors significantly associated with advanced fibrosis were IL-10/IL-6 and 1.5-AG ($P=0.008$) (by multivariate logistic regression analysis). Only 5 patients experienced a worsening of METAVIR score/US-FLI and metabolic/inflammation biomarkers. Dual therapy were well tolerated and most events were gastrointestinal (nausea, diarrhea, vomiting, abdominal pain, decreased appetite, and fatigue) in nature.
Conclusion
Our study has several limitations. First, the sample size is relatively small. Second, the duration of drug treatment itself is longer due to the addition of drug (dulaglutide) to monotherapy (pioglitazone). Hence, it is difficult to distinguish the effect of the combination of drugs from that of long-term treatment. Notwithstanding the limitations described, it may be argued that MAFLD/T2D dual therapy (pioglidazone plus dulaglutide) showed metabolic and LFC improvement vs monotherapy (pioglidazone) group and reduction in liver stiffness, and ALT levels. Body weight gain (subcutaneous fat increase) mediated by pioglitazone monotherapy decreased following concomitant use of dulaglutide. Dual therapy might be effective for the treatment of MAFLD/T2D patients, as well as improving glycemic control and visceral obesity.

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Acquired partial lipodystrophy: leptin and glucose blood levels in a pregnant patient

Martina Romanisio[1], Leonardo Bighetti[1], Tommaso Daffara[1], Carola Ciamparini[1], Davide Vimercati[1], Rosa Pitino[1], Caterina Pelosini[2], Gianluca Aimaretti[1], Marina Caputo[1,3] & Flavia Prodam[1,3]
[1]Endocrinology, Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy; [2]Chemistry and Endocrinology Laboratory, University Hospital of Pisa, Pisa, Italy; [3]Department of Health Sciences, Università del Piemonte Orientale, Novara, Italy

Lipodystrophy syndromes are a rare and heterogeneous disease characterized by loss of subcutaneous adipose tissue, deposition of fat in ectopic areas, and

consequently metabolic impairment, and its recognition is based on physical examination and clinical history. Because of the complexity of the disease, pregnancy represents a dainty and challenging event, still understudied. Here we report a case of a 28 year-old Caucasian female followed for type 2 diabetes and hypertriglyceridemia since she was 21 in the context of acquired partial lipodystrophy. Past medical history included childhood lymphocytic leukemia treated by chemo- and radiotherapy and allogeneic bone marrow transplant and subsequently she developed heart disease with left ventricular dysfunction (ejection fraction EF 45% in 2007) that was treated with beta-blocker and ACEi, and it normalized during follow-up. Diabetes mellitus wasn't adequately controlled (time in range TIR 5%, time above range TAR 95%, time below range TBR 0%, glucose management indicator GMI 11.3%) with insulin, metformin, and semaglutide; hypertriglyceridemia was discreetly controlled with PUFA and fenofibrate. In December 2021 she became unexpectedly pregnant and semaglutide, metformin, fenofibrate, and ACEi were stopped, PUFA was reduced and, after gynecological consultation, acetylsalicylic acid was added. During pregnancy Ambulatory Glucose Profile (AGP) reports improved with a TIR in the third trimester of 77%. Leptin values were periodically evaluated during pregnancy and in the early post-partum period: a progressive increase of levels was shown, with a peak in the third trimester (41.53 ng/ml), then after the delivery, there was a decline. Despite achieving good glycemic control, at 33 weeks of gestation, the patient developed acute pulmonary edema with the need for urgent cesarean delivery. The echocardiographic evaluation showed severe left ventricular diastolic dysfunction (FE 30%) that was treated with invasive ventilation (NIV), diuretic, nitroglycerin, inotropic drug, and ivabradine. No adipose tissue depots were observed at cardiac MRI. Furthermore, on suspicion of Sheehan syndrome, the patient started cortone acetate and then discontinued due to evidence of normal HPA axis function. The newborn was in good general condition except for the development of transient hypoglycemia and the finding of triple X syndrome. The management of lipodystrophies in pregnancy appears to be challenging and still poorly studied. Increased leptin values may suggest placental or fetal involvement in the metabolic improvement of the patient.

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GLP-1RAs boost erectile function in men with type 2 diabetes and erectile dysfunction: results from a 1-year retrospective cohort study

Giuseppe Lisco[1], Vincenzo Triggiani[1], Emilio Jirillo[1], Edoardo Guastamacchia[1] & Vito Angelo Giagulli[1]
[1]University of Bari "Aldo Moro", Interdisciplinary Department of Medicine - Section of Internal Medicine, Geriatrics, Endocrinology and Rare Diseases, School of Medicine, Bari

Background
Glucagon-like peptide 1 receptor agonists (GLP-1RAs) are proven to boost serum testosterone levels in men with type 2 diabetes (T2D) and functional hypogonadism. Nevertheless, the therapeutic potential of this class of drugs on erectile dysfunction (ED) has yet to be entirely studied in men with T2D and functional hypogonadism.
Methods
A retrospective cohort study was conducted on 108 outpatients (60 [56, 65] years) with T2D and complaining of ED. Data were extracted from the database referring to patients with a 1-year follow-up on stable treatment with metformin alone (M, $n=45$) and GLP-1RAs as an add-on to metformin (GLP-1RA + M, $n=63$). Erectile function was assessed by the 5-item International Index of Erectile Function (IIEF5) at baseline and after 1 year of treatment. Values were compared between baseline (T0) and after 12 months of treatment (T12).
Results
ED was confirmed at baseline in all (IIEF5 score 13 to 19 points). After 12 months of treatment, glucose management was better in patients on GLP-1RAs + M (HbA1c T0: 8.3 ± 0.2 vs HbA1c T12: 7% ± 0.3%, $P<0.0001$) than in those on M (HbA1c T0: 7 ± 0.5 vs HbA1c T12: 7.3 ± 0.4, $P= 0.0007$). GLP-1RAs + M over M resulted in a significant weight loss (-5.82 ± 0.69 kg, $P<0.0001$), reduction in waist circumference (-4.99 ± 0.6 cm, $P<0.0001$), improvement in HbA1c (-0.56% ± 0.13%, $P<0.0001$), and fasting plasma glucose (-25.54 ± 3.09 mg/dl, $P<0.0001$), increase in total (+41.41 ± 6.11 ng/dl, $P<0.0001$) and free (0.44 ± 0.09 ng/dl, $P<0.0001$) testosterone levels, and gain in self-reported erectile function (IIEF5 score: +2.26 ± 0.26, $P<0.0001$). The gain in IIEF5 scores was more relevant in patients with higher baseline IIEF5 (estimated coefficient: 0.16 ± 0.08, $P= 0.045$), those having carotid stenosis (0.50 ± 0.24, $P= 0.045$), and showing weight loss from baseline (-0.08 ± 0.03, $P= 0.013$), regardless of serum testosterone. The leading determinant of the final IIEF5 score was a 1-year treatment with GLP-1RAs + M over M (2.74 ± 0.53, $P<0.0001$).
Conclusions
GLP-1RAs + M over M improved ED regardless of different background characteristics and testicular function of T2D patients and partially irrespective of therapeutic targets achieved after 12 months of treatment. Controlled trials are needed to confirm if GLP-1RAs have direct and helpful vasculature effects boosting erectile function in T2D.

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Study of genetic predisposition and other pathogenetic mechanisms underlying hypogonadotropic hypogonadism in type 2 diabetes mellitus

Biagio Cangiano[1,2], Alessandro Amodeo[1], Elena Lunati[3], Valeria Vezzoli[2], Elena Galazzi[2], Luca Persani[1], Paolo Fiorina[1] & Marco Bonomi[1,2]
[1]University of Milan, Milano, Italy; [2]Italian Auxological Institute San Luca Hospital, Milano, Italy; [3]Ospedale Fatebenefratelli e Oftalmico, Milano, Italy

Background
In patients affected by type 2 diabetes mellitus (T2DM) a high prevalence of hypogonadotropic hypogonadism (HH) has been reported, even if there is no consensus on its pathogenic mechanisms. In addition to acquired causes, an individual predisposition has also been suggested. The understanding of
Purpose
The aim of this observational study is to assess: (1) the prevalence of hypogonadism in T2DM using the validated criteria from the EMAS study; (2) the correlations of hypogonadotropic hypogonadism (HH) with specific clinical features and predisposing factors; (3) the enrichment in rare pathogenic or likely pathogenic variants in HH diabetic subjects compared to the general population.
Materials and Methods
We consecutively enrolled 167 male patients affected with T2DM from (aged 18 to 85); patients with other known causes of hypogonadism were excluded. In each patient we studied the gonadal function, classifying them according to the EMAS validated criteria according to calculated free testosterone and LH levels. The age, BMI, smoking habit, the severity of diabetic disease, its treatments, complications, as well as leptin levels and HOMA-IR values were recorded, and used in a multivariate logistic analysis. 33 HH patients with T2DM were analyzed using a Target-Next Generation Sequencing (NGS), to search for rare allelic HH variants (RV). To verify the prediction of pathogenicity, we classyfied the RV according to The American College of Medical Genetics and Genomics (ACMG) guidelines. We conducted the same NGS analysis in 79 controls selected from the general population and compared the prevalences using Fisher Exact Test.
Results
The 51% of patients with T2DM showed some degree of hypogonadism: 30% had HH, and 21% showed primary hypogonadism (PH). To logistic multivariate analysis corrected for confounders, HH was correlated with leptin levels ($P=0.039$) and smoking (pack-years, $P=0.027$). No significant enrichment in rare CHH variants was found in T2DM patients with HH, as compared to the general population. However, we found 1 likely pathogenic *TBX3* variant according to ACMG criteria among the cases.
Discussion
We confirmed a high prevalence of hypogonadism in diabetes in a large cohort of patients. Genetic predisposition does not appear to be a significant cause of HH in T2DM, although some sporadic cases may occur. The presence of a rare, probably pathogenic genetic variant, and the significant and independent association of HH with leptin levels and smoking habits, seem to suggest that different mechanisms could underlie HH in T2DM

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Comparison between most recent guidelines about NAFLD medical treatment

Irene Samperi[1], Marco Grasso[2], Maria Chantal Ponziani[3], Alberto Carpenito[4], Francesco Tassone[5], Carla Micaela Cuttica[6], Filippo Egalini[7], Roberta Guido[8], Morena Pisarro[9], Isabella Buffardi[9] & Anna Nelva[10]
[1]SSD of Diabetology and Metabolic Diseases- - Azienda Sanitaria Locale Novara, Novara, Italy; [2]Diabetology, Ospedale di Cittadella, Padova, Italy; [3]SSD of Diabetology and Metabolic Diseases - Azienda Sanitaria Locale Novara, Novara, Italy; [4]CAD Montoro-asl Avellino, Avellino, Italy; [5]SC Endocrinologia, Diabetologia & Metabolismo, ASO Santa Croce & Carle di Cuneo, Cuneo, Italy; [6]Unit of Endocrinology, Galliera Hospital, Genoa, Italy; [7]Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [8]Diabetology, ASL3 genovese, genoa, Italy; [9]Endocrinology, Rome, Italy; [10]Endocrinology, Biella, Italy

Background
Given the high prevalence of Nonalcoholic Fatty Liver Disease (NAFLD) in clinical endocrinology, diabetology, and primary care practice, international societies have addressed guidelines to drive clinicians in screening, diagnosis, and treatment for this condition.
Aim
compare the most recent guidelines to address similarities and differences and help clinicians choosing the most updated evidence. We considered Italian guidelines (2021), AACE-AASLD guideline (2022) and AASLD Practice Guidance (2023). Herein we present findings about pharmacotherapy.
Results
Italian guidelines used Methodological Manual for clinical practice guidelines developed by the Italian Istituto Superiore di Sanità, using the PICO approach. AACE guideline was conducted by a clinical practice committee that selected and graded articles. Recommendations were made on the grade for the quality of the literature and on expert opinion. AASLD didn't use a grading system therefore they present statements from experts, based on available literature, rather than recommendations. Guidelines address medication with different strengths and in a personalized approach as shown in the table.

Medication	Italian	AACE	AASLD
Vitamin E	Suggested	Consider in patients without DM	Consider
GLP1ra	Limited data	Recommended in patients with Dm^2 and biopsy NASH+ Recommended for the use of obesity and NAFLD Consider in patients with DM and a high probability of NASH	Consider Semaglutide in patients with DM and obesity
Pioglitazone	Suggested	Recommended in patients with Dm^2 and biopsy NASH+ Consider in patients with DM and a high probability of NASH	Consider in patients with DM
SGLT2i	Not suggested	No evidence	Limited data
DPP4i	Not suggested	Non recommended	Not indicated
Metformin	Not suggested	Non recommended	NA
Acarbose	NA	Non recommended	NA
Insulin	NA	Non recommended	NA
Orlistat	NA	Potential effect	NA
Naltrexone/bupropion	NA	Potential effect	NA
Ursodeoxycholic acid	Not suggested	NA	Not indicated
Obeticholic acid	Suggested (not yet approved)	NA	Limited data
Statins	NA	NA	Not indicated
Silymarin	NA	NA	Limited data, not indicated

NA: Not available

Conclusion
The prevalence of NAFLD is increasing worldwide and more efforts are being made to diagnose and treat this condition. Recently nomenclature has changed to MASLD (metabolic dysfunction-associated steatotic liver disease) to include patients with fatty liver regardless of the amount and pattern of alcohol intake with metabolic comorbidities (hypertension, dyslipidemia, overweight or high weight circumference, pre-diabetes or diabetes). Despite having no specific treatment approved for this condition several medications have been used. Guidelines underline the need to tailor the treatment based on patient comorbidities

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Obesity in transition towards diabesity: anthropometric determinants and markers of tissue damage

Chiara Mele[1], Stefania Mai[2], Martina Borrini[1], Beatrice Cavigiolo[1], Marina Caputo[3], Massimo Scacchi[4], Gianluca Aimaretti[1] & Paolo Marzullo[1]
[1]University of Piemonte Orientale, Department of Translational Medicine, Novara, Italy; [2]Istituto Auxologico Italiano, IRCCS, Laboratory of Metabolic Research, Piancavallo, Verbania, Italy; [3]University of Piemonte Orientale, Department of Health Sciences, Novara, Italy; [4]Istituto Auxologico Italiano, IRCCS, Division of General Medicine, Piancavallo, Verbania, Italy

Background
The term 'Diabesity' defines the complex relationship between obesity and type 2 diabetes mellitus (T2DM), that involves the convergent role of insulin resistance and chronic inflammation in amplifying the risk of systemic complications. To date, this link has not been fully characterized in terms of markers of tissue damage. The aim of this study was to investigate the association between the newly diagnosed glycemic alterations and the biomarkers of tissue damage through the interaction with the metabolic mileau.
Methods
This observational cohort study consecutively enrolled 656 adult subjects (M/F = 277/379, age 50.6 ± 14.9 years; BMI 47.5 ± 7.5 kg/m^2) with moderate-to-severe obesity and without a previous diagnosis of T2DM. For each patient, fasting glucose, glycated haemoglobin, and OGTT glucose and insulin levels were assessed. T2DM, impaired fasting glucose (IFG), and impaired glucose tolerance (IGT) were defined according to the ADA criteria, and analyzed in relation to metabolic, body composition and cardiorenal function parameters, intimal media thickness (IMT) and adipokines levels.
Results
The prevalence of screen-detected T2DM was 16.2% and the intermediate conditions of prediabetes, in particular IFG and IGT, were observed in 9.5% and 35.7% of cases, respectively. The waist-to-hip ratio (WHR) was found to be the most accurate anthropometric parameter in predicting the severity of glycaemic alterations ($P < 0.0001$). Among the markers of tissue damage, the most significant variations within the glycemic alteration categories concerned the estimated Glomerular Filtration Rate (eGFR) and microalbuminuria ($P < 0.01$ for both). The 2h post-OGTT glucose level was the glycaemic homeostasis index more strongly correlated with the IMT ($r = 0.21$, $P < 0.01$) and the markers of renal function and damage (eGFR: r = 0.09, $P < 0.05$; microalbuminuria: r = 0,20, $P < 0.01$), independently from sex and age. At the multivariable logistic regression analysis, age (OR = 1.03, 95%CI 1.01-1.05, $P = 0.001$), male sex (OR = 1.90, 95%CI 1.12-3.21, $P < 0.05$), C-reactive protein (OR = 1.35, 95%CI 1-05-1.74, $P < 0.05$) and adiponectin levels (OR = 0.94, 95%CI 0.88-0.99, $P < 0.05$) emerged as the main risk factor of T2DM in our cohort.
Conclusion
Our study identified the 2h post-OGTT glucose level as the most effective tool for the screening of glycemic alterations in the obese population. Moreover, we identified IMT, eGFR and microalbuminuria as the marker of tissue damage more closely associated with glycemic homeostasis in our cohort. Finally, the systemic inflammation index and adiponectin levels represent independent risk factors of screen-detected T2DM together with age and male sex.

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P272

TYG Index: a practical tool for evaluating metabolic parameters in obese individuals

Özge Başaksu[1,1], Feride Özkara[1], Rıfat Emral[1], Volkan Genç[2], Demet Çorapçıoğlu[2] & Mustafa Şahin[1]
[1]Ankara University, Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara University, General Surgery, Ankara, Turkey

Background and Aim
The triglyceride glucose (TyG) index has been proposed as a marker of insulin resistance. This study aims to evaluate the utility of the TyG index in routine practice for predicting diabetes, prediabetes, and metabolic dysfunction-associated fatty liver disease (MAFLD) in obese individuals.
Methods
The study retrospectively analyzed data from obese individuals at our outpatient clinic. The study recorded patient characteristics such as age, gender, fasting plasma glucose (FPG), fasting insulin, lipid profile, HbA1c, ALT, AST, vitamin D levels, and platelet counts. Additionally, the body mass index (BMI), Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), AST/Platelet Ratio Index (APRI), Fibrosis-4 Index (FIB-4), TyG Index, and TyG-BMI Index scores were calculated to establish the database.
Results
A total of 299 patients were examined in this study. The mean age of the patients was 37.53 ± 11.46 years, with 49.5% (148) female, and the mean BMI was found to be 44.16 ± 6.81 kg/m^2. The mean HbA1c values were 5.98 ± 1.02 and the mean TyG index values were 4.75 ± 0.29. Patients were divided into three groups based on their HbA1c values, namely normal, pre-diabetic, and diabetic, and were compared in terms of TyG index values. In post-hoc analysis, patients with diabetes had statistically significantly higher TyG index scores compared to both the pre-diabetic and normal groups ($P < 0.001$, $P < 0.001$, respectively). Additionally, patients with pre-diabetes had statistically significantly higher TyG index scores compared to the normal group ($P < 0.001$). According to the results of Pearson correlation analysis, the TyG index score showed a positive correlation with metabolic parameters such as APRI ($r = 0.245$, $P < 0.001$), HOMA-IR ($r = 0.306$, $P < 0.001$), LDL

($r=0.243$, $P<0.001$), and HbA1c ($r=0.475$, $P<0.001$), while it exhibited a negative correlation with HDL ($r=-0.313$, $P<0.001$). No statistically significant relationship was observed between FIB-4 index and TyG index score ($r=0.086$, $P=0.146$). In the stepwise regression analysis, with HbA1c as the dependent variable and age and TyG index as independent variables, the model revealed that TyG index score ($\beta=0.449$, $P<0.001$) and age ($\beta=0.223$, $P<0.001$) significantly predicted HbA1c levels.

Conclusion

The TyG index appears to be a practical parameter that can be used in daily practice, offering ease of use and lower cost. It seems to be a convenient method for the early assessment of the risk of diabetes development and the potential presence of MAFLD in obese individuals.

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P273

Diagnostic accuracy of FIB-4 score compared to Fibroscan assessment of liver fibrosis in overweight and obesity patients

Meliha Melin Uygur[1], Çağlayan Keklikkiran[2], Süreyya Uygur[3], Burak Gemici[4] & Oğuz Suveren[4,5]

[1]Department of Endocrinology and Metabolism Disease, School of Medicine, Recep Tayyip Erdoğan University, Rize, Turkey; [2]Recep Tayyip Erdoğan University, Department of Gastroenterology, Turkey; [3]yıldız Technical University, Department of Geomatic Engineering, Faculty of Civil Engineering, Turkey; [4]Recep Tayyip Erdoğan University, School of Medicine, Turkey; [5]Recep Tayyip Erdoğan University, Turkey

Objective

Increasing obesity rates are causing a surge in non-alcoholic fatty liver disease (NAFLD) prevalence which may progress further to non-alcoholic steatohepatitis (NASH) to cirrhosis. The utility of Fibroscan was shown in stratifying risk for significant liver disease in patients with obesity but it has a limited availability. The aim of the study was to compare the accuracy of Fibrosis-4 (FIB-4)) score to diagnose advanced fibrosis in overweight and obesity patients.

Methods

We conducted the study in 369 (145 men, 224 women) patients aged between 18-75 years old and body mass index over 25 kg/m^2 from department of endocrinology and metabolism disease and gastroenterology, School of Medicine, Recep Tayyip Erdoğan University. We performed a fibroscan assessment and collected biochemical, demographic, and clinical data. Patients were categorized as group I with mild/moderate fibrosis (F0- F2) and group II with advanced fibrosis (AF) (F3-F4) based on fibroscan liver stiffness measurement (LSM).

Results

FIB-4 score was significantly higher in group 2 than group 1 ($P<0.001$). There was no significant difference in alanine transaminase level (P:0.15) and platelet count (P:0.32) between the groups whereas gamma glutamyl transferase and aspartate transaminase levels were significantly higher in group 2 (P:0.003 andp:0.003, respectively). There was a positive correlation between FIB-4 score and LSM (r:0.416, $P<0.001$). The cutoff point of 1.04 for FIB-4 score provided 70% sensitivity and 62% specificity with an area under the curve equal to 72% ($P<0.001$).

Conclusion

FIB-4 score could predict advanced fibrosis in overweight and obesity patients particularly in settings where fibroscan assessment is limited. Based on this score, patients can be followed for progression of NAFLD, and prompt treatment modification could be implemented.

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P274

Impact of diabetes mellitus type 2 on the prognosis of metabolic steatopathy

Ahmed Mohamed Nefzi[1], Bouchabou Bochra[1], El Mouldi yosr[1], Nakhli Abdelwahab[1], Hemdani Nesrine[1], Benzarti Zeineb[1], Ben Nejma Houda[1] & Ennaifer Rym[1]

[1]Hôpital Mongi Slim, Hepato-gastroenterology, Marsa, Tunisia

Introduction

The coexistence of type 2 diabetes in patients with metabolic steatopathy is quite common due to a shared pathophysiology of the two conditions, primarily centered around insulin resistance. The objective of our study was to investigate the impact of type 2 diabetes on the prognosis of metabolic steatopathy.

Patients and Methods

This was a cross-sectional, single-center descriptive study that collected all cases of metabolic steatopathy presenting to outpatient clinics between March 2021 and December 2022. The age and various medical histories were specified. Anthropometric measurements were taken. A biological assessment, including a metabolic and hepatic profile, was conducted. Liver fibrosis was assessed using simple serum tests (APRI and FIB-4) and Transient elastography-Fibroscan. The quantification of the degree of steatosis was performed using the Controlled Attenuation Parameter (CAP) integrated into the Fibroscan device. We divided the study population into two groups: Group 1: diabetic patients and Group 2: non-diabetic patients. We compared the clinical, biological profiles, and the degree of liver fibrosis and steatosis in each of the two groups.

Results

We collected 139 patients with a mean age of 54.21 ± 10.7 years and a gender ratio of 0.52. The prevalence of type 2 diabetes was 43.2%. In terms of basic demographic data, a history of hypertension and associated dyslipidemia was significantly more common in Group 1, with p-values of 0.016 and 0.009, respectively. The average waist circumference of diabetic patients was significantly higher (105.2 cm versus 100.8 cm) ($P=0.05$). In terms of biological data, hypertransaminasemia was more frequently observed among diabetic patients ($P=0.037$), with a predominance of ASAT (42.1 versus 28.8 IU/l) ($P=0.025$). The average FIB-4 score was significantly higher in diabetic patients (0.149 versus 0.105) ($P=0.05$). Liver elasticity was higher in Group 1 (9.93 versus 5.77 kPa) ($P=0.001$). We did not observe a significant difference in terms of degree of hepatic steatosis between the two groups.

Conclusion

Type 2 diabetes accelerates the progression of hepatic fibrosis in patients with metabolic steatopathy and, therefore, worsens the prognosis for these patients.

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P275

Trajectories and associations of symptoms of mental health and well-being with insulin resistance and metabolic health in women with gestational diabetes

Ludmila Nicolazzi[1]

[1]CHUV, Department Woman-Mother-Child, Lausanne

Background

Gestational diabetes mellitus (GDM) is characterized by increased insulin resistance. There is a link between perinatal depression or anxiety and GDM. Mental health problems are associated with higher insulin resistance and could explain the underlying association between GDM and depression or anxiety symptoms. We investigated the trajectories and associations between symptoms of mental health and well-being with insulin resistance and metabolic health in women with GDM.

Methods

This study included the control group ($n=106$) of a randomized controlled trial in women with GDM that were followed-up during pregnancy and up to 1-year postpartum. We measured symptoms of mental health (Edinburgh Postnatal Depression Scale (EPDS), Anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A), well-being (The World Health Organization Well-Being Index (WHO-5)) and metabolic health, including insulin resistance variables (HOMA-insulin resistance (IR) and Matsuda Index of insulin sensitivity) as well as weight during pregnancy and in the postpartum.

Results

HOMA-IR was higher during pregnancy compared to 6-8 weeks postpartum and increased between 6-8 weeks and 1-year postpartum (all $P<0.05$). Matsuda index decreased between 6-8 weeks and 1-year postpartum ($P<0.001$). EPDS scores decreased between pregnancy and both 6-8 weeks and 1-year postpartum (all $P<0.05$). HADS-A scores did not change between pregnancy and the postpartum. WHO-5 scores improved significantly from pregnancy and both 6-8 weeks and 1-year postpartum ($P<0.001$). Correlation coefficients within outcome at the three different time points were high for metabolic measures and ranged between 0.94 to 0.96 for weight, from 0.77 to 0.89 for HOMA-IR and 0.64 for the Matsuda index (all $P<0.001$). Mental health and well-being variables were moderately correlated in all three time points. After adjustment for cofounders, Matsuda index was negatively associated with EPDS scores and positively associated to WHO-5 scores at 6-8 weeks postpartum. No other association between insulin resistance and mental health or well-being outcomes were found.

Conclusion

While insulin resistance fluctuated with values being lowest in the early postpartum and increasing thereafter, both depression and well-being scores decreased between

pregnancy and the postpartum and did not change in the postpartum period. Intraindividual variability was larger for mental health and well-being than for metabolic health outcomes at different time points, indicating a higher plasticity for mental health and well-being outcomes that could be acted upon. We found only few associations between mental health and well-being and metabolic health outcomes.

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Cell cycle synchronization enhances insulin secretion in MIN6 cells

Tapabrata Pramanik[1], Prachi Verma[1] & Aditya Mittal[1]
[1]Indian Institute of Technology Delhi, Kusuma School of Biological Sciences, New Delhi, India

Type I diabetes mellitus (DM) is characterized by an autoimmune destruction of the pancreatic β-cells that leads to absolute insulin deficiency. However, T1DM individuals undergoing exogenous insulin therapy may show partial remission of endogenous insulin secretion and better insulin sensitivity, and this remission may range between few months to many years. This partial remission is known as the 'honeymoon phase,' and extending the duration of this remission has been a centre stage for medical intervention towards T1DM. Since proliferation renders pancreatic β-cells immature, we aimed to investigate whether arresting cells can possibly enhance GSIS. In other words, we wanted to check whether cell cycle synchronization can possibly be an underlying reason behind the honeymoon phase. Among various cell culture model systems used for studying glucose stimulated insulin secretion (GSIS), Mouse Insulinoma 6 (Min6) cells is a widely used mouse pancreatic β-cell line which mimics pancreatic β-cell physiology. We treated Min6 cells with nocodazole (60 ng/ml) for 16 hours to arrest them at mitotic phase. An enhanced GSIS was observed at incremental EGC's, ranging from basal (2.8 mM) to hyperglycemic (25 mM) level. The amount of secreted insulin was measured by sandwich ELISA method. The synchronization of cells was confirmed by flow cytometry. The fold change in GSIS observed for the synchronized cells was significantly higher (statistically) as compared to the non-synchronized cells. Cellular protein content as well as secreted protein content in the supernatant medium remained constant, irrespective of EGC and synchronization, as measured by Bradford method. Thus, we show that synchronization of cells or proliferative arrest can enhance GSIS and might be one of the underlying reasons behind the remission of endogenous insulin secretion in T1DM individuals, commonly known as the honeymoon phase. We propose a model at the cellular level, in which initial destruction of some β-cells results in production of new β-cells that are synchronized, thereby providing higher levels of insulin secretion from lower number of cells. Subsequently, the higher metabolic load (resulting from higher insulin secretion as shown by us earlier) experienced by lesser number of β-cells results in further cell death eventually leading to complete destruction of β-cells. To our knowledge, this is the first cellular level model that correlates well with the clinical observation of honeymoon phase in T1DM.

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Evaluation of a new prototype ELISA for the detection of autoantibodies against IA2 in patients with type 1 diabetes mellitus

Skander Elleuche[1], Gia-Gia Hò[1], Alexander Kühnl[1], Malgorzata Baranowska-Dell[2], Kai Masur[3,4], Petra Augstein[5,6], Sandra Saschenbrecker[1], Christian Probst[1], Lars Komorowski[1], Kersten Dieckmann[1] & Cornelia Dähnrich[1]
[1]Institute for Experimental Immunology, affiliated to Euroimmun Medizinische Labordiagnostika AG, Lübeck, Germany; [2]Department of General, Visceral, Thoracic, and Vascular Surgery, Research Group of Predictive Diagnostics, University Medical Center Greifswald, Greifswald, Germany; [3]Leibniz Institute for Plasma Science and Technology (INP Greifswald), Greifswald, Germany; [4]Diabetes Competence Centre Karlsburg (KDK), Karlsburg, Germany; [5]Institute of Diabetes "Gerhardt Katsch", Karlsburg, Germany; [6]Department for Diabetology, Klinikum Karlsburg, Heart and Diabetes Center Karlsburg, Karlsburg, Germany

Introduction
Autoantibodies against insulinoma-associated antigen-2 (anti-IA2) are an important marker for diagnosis and prediction of new-onset type 1 diabetes mellitus (T1DM). Here we report on a new prototype Anti-IA2 ELISA with shorter total incubation time (3h15min) compared to the established EUROIMMUN Anti-IA2 ELISA (minimum 17h40min). The study evaluates the performance of the prototype assay.
Methods
The clinical performance of the prototype ELISA was evaluated using a sensitivity panel comprising sera from 32 patients with suspected T1DM and 111 patients with confirmed T1DM, and a specificity panel consisting of sera from 50 suspected cases each of connective tissue disease and celiac disease, and from 210 healthy donors. For method comparison, 32 samples from suspected T1DM cases and a subset of 100 samples from confirmed T1DM patients were additionally analyzed using the established EUROIMMUN Anti-IA2 ELISA and the Medipan CentAK anti-IA_2 M radioimmunoassay (RIA), respectively.
Results
The clinical sensitivity of the prototype ELISA amounted to 73.4% (105/143) at a specificity of 99.4% (308/310). Method comparison revealed a sensitivity of the prototype of 93.3% (28/30) referring to the established ELISA and 93.8% (61/65) referring to the RIA, while the overall agreement was 90.6% (29/32, ELISA) and 90.0% (90/100, RIA).
Conclusions
The results suggest that the new Anti-IA2 ELISA will be a valuable tool in supporting the serodiagnosis of T1DM. Reducing the processing time to a few hours minimizes the time required for laboratory testing, reinforcing the prototype's suitability to replace the established ELISA. Additionally, the new assay enables easier automation in conjunction with other ELISA with similar timelines on EUROIMMUN Analyzer I or EUROLabWorkstation ELISA.

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P278

Use of glycated albumin in transfusion-dependent β-thalassemic (TDT) patients with diabetes mellitus: preliminary results

Martina Verrienti[1], Alberto Gobbo[1], Camilla Alice Cattaneo[1], Elisa Mari[2], Olga Sofritti[2], Marcello Monesi[3], Stefano Pizzicotti[4], Filomena Longo[2], Maria Rosaria Ambrosio[1] & Maria Chiara Zatelli[1]
[1]Section of Endocrinology and Internal Medicine, Department of Medical Sciences, University of Ferrara, Ferrara, Italy; [2]Regional HUB Centre for Thalassaemia and Haemoglobinopathies, Department of Medicine, AOU S. Anna, Ferrara, Italy; [3]Primary Care Department, Diabetes Unit, Ferrara "Sant' Anna" Hospital, Ferrara, Italy; [4]Department of Translational Medicine and for Romagna, University of Ferrara, Ferrara, Italy

Background
Patients with transfusion-dependent β -thalassemia (TDT) often experience several endocrine complications, including diabetes mellitus (DM). In TDT, the reliability of glycated haemoglobin (HbA1c) assessment is compromised due to elevated erythrocytes turnover and frequent transfusions. Glycated Albumin (GA), a product of non-enzymatic albumin glycation, has been investigated as a medium-term glycaemic marker (21 days) in the general diabetic population. Since GA is not affected by erythropoiesis nor by iron imbalance, it could potentially serve as a reliable marker for diagnosing and monitoring DM in TDT.
Objective
To evaluate the use of GA assessment in a population of TDT patients with DM.
Methods
We conducted a single-centre observational study, enrolling 28 TDT adults (15F, 13M, mean age 53.7 ± 7.4 years, mean BMI 23.7 ± 3.4 Kg/m^2) with DM. Patients were tested for fasting glucose (FG), HbA1c, fructosamine, GA and iron deposit indexes (ferritin, T2* pancreas). GA measurement was performed using a standardized enzymatic quantitative method. Two hours after a standardized meal (50 g carbohydrates), post-prandial glycaemia (PPG) was assessed. Based on glycaemic control, patients were divided into groups according to FG (A $\geq$ 130 mg/dl; B $<$ 130 mg/dl) or PPG (C $\geq$ 180 mg/dl; D $<$ 180 mg/dl).
Results
GA was associated with FG (Pearson's $r=0.613$, $P<.01$), HbA1c (Pearson's $r=0.748$, $P<.001$), fructosamine (Pearson's $r=0.620$, $P<.001$), and with PPG (Pearson's $r=0.432$, $P<.05$), but not with sex, age, BMI and iron deposits. By using ROC curves we identified a GA cut-off value of 15.7% as displaying 100% sensitivity and 58% specificity to differentiate A from B patients (AUC=0.845, $P=.005$). Similarly, a GA threshold of 15.2% had 100% sensitivity and 50% specificity in discriminating C from D patients (AUC=0.769, $P=.025$).
Conclusion
To the best of our knowledge, these are the first data regarding the use of GA in diabetic TDT patients. The identified GA thresholds may help the identification of non-compensated TDT diabetic patients, taking into account the risk of false positives. Further studies, using continuous glucose monitoring to assess glycaemic control, are warranted in order to understand more about the role of GA in monitoring diabetic TDT patients.

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P279

Extracts of Vernonia amygdalina stimulated non-toxic insulin secretion from clonal pancreatic cells and improved glucose tolerance in mice with diet-induced obesity-diabetes

Ayokunle Falana[1], Simren Heer[1], Ayodele Falobi[1], Moji Adie[1], Joy Edeani[1], O Ogundepo[2] & Opeolu Ojo[1]
[1]University of Wolverhampton, Science and Engineering, Wolverhampton, United Kingdom; [2]Obafemi Awolowo University, Nigeria

[1]= School of Sciences, Faculty of Science and Engineering, University of Wolverhampton, Wolverhampton, UK
[2]= Department of Biochemistry, Obafemi Awolowo University, Ile-Ife, Nigeria
[3]= IRiD Biosciences, Wilding Road, Ball Green, Stoke-on-Trent, ST6 8BQ

Aim

Vernonia amygdalina extract is used traditionally for type 2 diabetes treatment in developing countries. Studies have reported antidiabetic properties of aqueous and methanolic extracts of *V. amygdalina* but mechanisms underlying these actions are poorly understood. This study investigates effects of *V. amygdalina* extracts on insulin secretion, cytotoxicity, cells viability, mechanism of action and intracellular calcium.

Methods

Insulin-releasing effect of *V. amygdalina* extract (0 –1000µ g/ml) were investigated using BRIN-BD11 cells. Effects of the extract (100µ g/ml) on insulin secretion at various glucose concentration, presence of established modulators of insulin secretion and in the absence of extracellular calcium were also investigated. Insulin concentrations were measured by ELISA. Effect of the plant extract on cytotoxicity and intracellular calcium concentration were also assessed. Acute *in vivo* effects of the extract were investigated using mice with diet-induced obesity-diabetes.

Results

The extract had total flavonoid and total phenolic contents of **** QE/g and **** GE/g respectively. *V. amygdalina* extract stimulated insulin secretion at concentration $\geq$0.1ug/ml in a dose-dependent manner (1.4 to 2.5-fold, $P<0.001$). The insulinotropic effects of the plant extract was not associated with cytotoxicity or impaired cell viability. Insulin-release increase with increasing glucose concentration (1.1mM to 5.6mM, 10%, $P<0.05$, and 5.6mM to 16.7mM, 13%, $P<0.05$). Actions of the extract was reduced in the presence of diazoxide (300µ M, 46%, $P<0.01$), verapamil (50nM, 34%, $P<0.01$) and in the absence of extracellular calcium (20%, $P<0.05$). Enhanced insulin secretion was observed in incubations containing KCl (30mM, 3.0-fold, $P<0.001$) and IBMX (200µ M, 1.9-fold, $P<0.01$). *V. amygdalina* extracts enhanced intracellular calcium concentration by 24% ($P<0.01$). Glucose tolerance and insulin secretion also improved by 23% ($P<0.01$) and 34% ($P<0.01$) respectively in diet-induced mice treated with the extract.

Conclusion

These results suggest that the anti-diabetic properties of *V. amygdalina* extract may involve the activation of the ATP-dependent pathway of insulin secretion. These results encourage further investigations of the anti-diabetic actions of *V. amygdalina* extracts.

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P280

New onset diabetes after transplantation (NODAT) in kidney transplant recipient in Montenegro

Danilo Radunovic[1], Snezana Vujosevic[2], Filip Tomovic[1], Vladimir Prelevic[1] & Sanja Borozan[2]
[1]Clinic for Nephrology, Clinical Centre of Montenegro, Podgorica; [2]Department of Endocrinology, Clinical Centre of Montenegro

Background and aim

Renal transplantation is considered to be the best renal replacement therapy for patients with end-stage renal disease. Posttransplant complications include NODAT, which is now considered to be determinant of loss of renal allograft, development of infections, and increased risk of morbidity and mortality. Prevalence of NODAT vary, from 2% - 53%.

Materials and methods

We examined the characteristics and risk factors for NODAT in patients with kidney transplants monitored at the Clinical Centre of Montenegro.

Results

Currently 147 patients with kidney transplants are being monitored. Of that number, 13 (8. 84%) have confirmed NODAT. The distribution by gender is 8 men (61. 5%) and 5 women (38. 5%), 8 (61. 5%) patients had obesity. The average age of patients with NODAT at the time of transplantation was 40.6 years. The average time from transplantation to the development of NODAT was 5 years. There were 7 (53. 8%) patients on calcineurin inhibitor (CIN) therapy (tacrolimus) and 6 patients (46. 2%) on ciclosporin therapy. All patients had additional corticosteroid (methylprednisolone), the dose of which was successively reduced after transplantation, while the maintenance dose was 5 mg every second day. There were 13 patients on mycophenolate mofetil (MMF) therapy. Two (15. 4%) patients are being treated with mTOR inhibitor (everolimus) developed breast cancer and were switched from CIN inhibitor to everolimus, both had steroid before transplantation due to the underlying diagnosis (SLE, sarcoidosis). One of the patients had proven BK nephropathy in the follow-up, for which therapy was corrected by reducing the dose of tacrolimus and corticosteroid, but he still developed NODAT. One patient had chronic hepatitis C infection, and developed NODAT after retransplantation with standard doses of immunosuppressants. One patient with primary diagnosis of ADPKD and biopsy-proven FSGS, developed NODAT after a second kidney transplant, another day after rituximab administration due to proven recurrence of FSGS in the transplanted kidney. One patient developed NODAT in the context of proven CMV reactivation after kidney transplantation and it is interesting that he developed an acute myocardial infarction within the same episode of CMV reactivation. NODAT was the earliest to develop after transplantation in patients who had previously received steroid therapy, elderly patients, and patients who had received ciclosporin therapy. All patients were treated with insulin.

Conclusion

The main risk factors for the development of NODAT were obesity, therapy with CIN inhibitors, and long-term use of corticosteroids before and after kidney transplantation.

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P281

Degenerative complications of diabetes type 2

Zakariaa Ilham[1,2], Saloua Elamari[2], Soukaina Laidi[2] & Marouan Fatima[2]
[1]Cheikh Khalifa Ibn Zayed Al Nahyan, Endocrinology, Casablanca, Morocco; [2]

Introduction

Diabetes is a major public health problem with a growing prevalence and heavy socio-economic impact. Its severity is closely linked to the complications it can cause, which can be prevented when detected early. The aim of this study was to assess the epidemiological and clinico-biological profile of patients with degenerative complications of type 2 diabetes in our department.

Methods

This was a prospective study that included all type 2 diabetic patients with at least one degenerative complication and who have come to our department for the first time between the months of September and November 2023. Epidemiological, clinical, and paraclinical data were collected from medical records and supplemented by patient bedside interviews.

Results

We included 101 patients; the average age was 68 years old. Two-thirds of the patients were men; hypertension and dyslipidemia were observed in 77.2%, obesity was present in 29.7%. The median duration of diabetes progression was 20 years. The average glycated hemoglobin (Hba1c) level was 9% and the mean fasting blood glucose level was 1.84 g/l. The majority of patients were on insulin therapy accounting for 52 %. Microangiopathies were found in 81.88% of patients while macroangiopathies were present in 80.2%, with a predominance of ischemic heart diseases at 56.43%. Eighty-seven percent of patients had unstructured follow-up with at least one consultation per year. There is a correlation between the age of diabetes, glycemic control and the onset of degenerative complications in type 2 diabetes.

Conclusion

Monitoring and screening for complications would help prevent degenerative effects of diabetes. The elements predisposing individuals to complications are likely still unknown and constitute a research avenue.

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P282

Rare case of hypoglycemia attributed to sildenafil in a patient with primary pulmonary hypertension

Elena Gross[1] & Romy Block[1]
[1]Northshore University, Division of Endocrinology and Metabolism, Skokie, United States

Introduction

Primary Pulmonary Hypertension (PPH) is a condition defined by atypically high blood pressure in the vessels in the lungs and heart. Due to the high blood pressure in the pulmonary system, the arteries in the lungs shrink and reduce oxygen flow

throughout the body. It is characterized by shortness of breath and chest pain, and can often be linked with heart disease, lung disease, or connective tissue disease. Patients with PPH are typically treated with Sildenafil or Tadalafil which is a phosphodiesterase inhibitor which relaxes the vessels to improve blood flow.
Case Presentation
A 55-year-old African American female with PPH presents with slurred speech, dizziness, and hypoglycemia. The patient was talking with someone on the phone and was unintelligible and EMS was called. The patient does not smoke or drink, works out with a trainer, and describes herself as a healthy eater. The patient was diagnosed with PPH in December 2022 and started treatment immediately after. She was then treated with a variety of medications including Sildenafil, Macitentan, Spironolactone, and Digoxin. The patient admits that she frequently forgets to take her mid day doses of medications Monday through Friday for the past 3 months which likely contributes to her worsening symptoms. The patient with PPH and HF was taken to the ER to rule out a stroke and was found to have hypoglycemia on arrival with a sugar of 38 mg/dl. She was treated with a dextrose solution of 25 g to improve her sugars and symptoms resolved. Her sugar dropped again in the ER and she was admitted for evaluation of an insulinoma. The workup was negative and the care team concluded that the hypoglycemia was not due to an issue with the patient's pancreas. Nutrition counseling was given including the addition of bedtime snacks of protein, fat, and carbohydrates and the avoidance of simple sugars. Her hypoglycemia improved but did not resolve. Then, Sildenafil was suspected of causing the low sugar. The medication was changed to 20 mg Tadalafil and the hypoglycemia resolved.
Discussion
There are case reports of hypoglycemia with Sildenafil in 2% of patients post trials. After being taken off the Sildenafil, the patient had improved sugars and no further hypoglycemia.
Conclusion
This case illustrates the possibility for patients to develop extreme hypoglycemia when on Sildenafil. Physicians should have a high index of suspicion for patients who have incidents of hypoglycemia on treatment.

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P283

Hepatic steatosis index as a non-invasive marker for liver steatosis in patients with endogenous cushing syndrome, Ercusyn krakow database

Mari Minasyan[1], Aleksandra Gamrat[1,2], Alicja Hubalewska-Dydejczyk[1,3], Elena Valassi[4,4] & Aleksandra Gilis-Januszewska[1,3]
[1]Kraków, Endocrinology, Oncological Endocrinology, and Nuclear Medicine Department, University Hospital, Krakow, Poland, Kraków, Poland; [2]Jagiellonian University Medical College, Doctoral School of Medical and Health Science; [3]Kraków, Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland, Kraków, Poland; [4]Barcelona, Endocrinology and Nutrition Department, Germans Trias i Pujol Hospital and Research Institute, Badalona, Spain, Barcelona, Spain

Introduction
Liver Steatosis(LS) can be one of the metabolic complications of Cushing Syndrome(CS). The data on the impact of cortisol on liver function are very limited, and there is only one study reporting a prevalence of LS of roughly 20%. Hepatic Steatosis Index (HSI) predicts LS based on ALT, AST, BMI, sex and co-existence of diabetes mellitus/impaired glucose intolerance.
Objectives
To evaluate the prevalence of LS in patients with CS at the time of diagnosis by using HSI.
Methods
We analyzed retrospectively adult patients from the ERCUSyN, Krakow database with complete HSI data available. 82 of 135 patients, aged 27-87 years, predominantly women ($n=64$), were eligible for the study. The HSI score was calculated using the following formula: $8\times$ (ALT/AST)+BMI+2(if type 2 diabetes)+2(if female). Collected data were from the baseline CS diagnosis. Patients with score 36 or above were classified as having a high probability of LS. We compared HSI results with the liver steatosis diagnosed based on abdominal ultrasonography (USG) findings, clinical and demographic factors.
Results
High HSI was observed in 81.7% patients (82.8% of females, 77.8% of males). HSI was elevated in 85%, 80% and 73% of patients with pituitary, adrenal and ectopic CS respectively. 41% of patients with elevated HSI were obese. HSI was elevated in among: 100% patients with confirmed liver steatosis on USG, 72% patients with normal USG and 78% patients who did not undergo USG. Conclusions: The prevalence of liver steatosis in active CS may be higher than previously reported. Further investigation should be undertaken to show if patients with high risk of LS based on HSI and normal liver image on USG, may benefit from liver MRI in order to confirm the diagnosis.

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Analysis of the use of integrated continuous subcutaneous insulin infusion systems in pregnant women with type 1 diabetes

Sara Hami Gil[1], Celia Gallego Díaz[1], Pavle Puzigaca[1], Manuel Romero Muñoz[1] & María Victoria Cózar León[1]
[1]Hospital Universitario Nuestra Señora de Valme, Endocrinología y Nutrición, Sevilla, Spain

Introduction and objective
Treatment with integrated continuous subcutaneous insulin infusion (CSII) and continuous glucose monitoring systems (CGM) helps to improve glycaemic control in people with type 1 diabetes mellitus (DM1). There is increasing use in pregnant women, but there are no protocols for its continuation during delivery. The aim of this work is to analyse glycaemic control during pregnancy, in addition to studying obstetric and neonatal outcomes.
Methods
Descriptive study of 10 patients with DM1 treated with the Minimed 670G or 780G system during pregnancy and delivery at the AGS Sur in Seville.
Results
The mean maternal age was 37.2 ± 3 years, 25.3 ± 10 years since diagnosis, 70% of patients had diabetic retinopathy with no other associated diabetic complications. Weight gain during pregnancy was 12.2 ± 4.7 kg. We present the glucometry parameters by trimester: 9 deliveries were term (8 without complications) and 1 preterm due to pre-eclampsia. 70% of the patients (3 caesarean sections) used intrapartum therapy with ISCI + MCG in automatic mode, with blood glucose levels in range without extra insulin, no postpartum hypoglycaemia was observed; 30% discontinued treatment (2 caesarean sections and 1 complicated delivery) with high blood glucose levels during and after delivery; one of them developed ketoacidosis in the immediate postpartum period. The weight of the NBs was 3377 +/- 599 g (2 macrosomic). Apgar >7 in 90% of them, neonatal hypoglycaemia 30%, shoulder dystocia 20%, severe respiratory distress with admission to neonatal ICU 10%
Conclusion
Therapy with integrated CSII + CGM systems achieves good glycaemic control in pregnant women with type 1 DM. Maintaining this therapy during labour allowed good glycaemic control during delivery and prevented hypoglycaemia in the immediate postpartum period. Studies and protocols for the use of these treatments during labour and immediate postpartum are needed.

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A cost-effectiveness analysis of inpatient continuous glucose monitoring vs capillary blood glucose

David Verissimo[1], Beatriz R Pereira[1], Joana Vinhais[1], Catarina Ivo[1], Ana Cláudia Martins[1], Joao Silva[1], Dolores Passos[1], Luis Lopes[1], J Jácome Castro[1] & Mafalda Marcelino[1]
[1]Armed Forces Hospital, Department of Endocrinology, Lisboa, Portugal

Introduction
We conducted a prospective study to compare the efficacy of continuous glucose monitoring (CGM) devices versus capillary blood glucose (CBG) in the glycemic control of inpatient type 2 diabetes on intensive insulin therapy. The use of CGM was associated with improved glycemic control, including an increased time in range (TIR) and reduced hyperglycemic events, being safe concerning hypoglycemias. The present study is the cost-effectiveness analysis associated with these results.
Aim
The primary objective was to compare the cost-effectiveness of achieving glycemic control (defined as the number of patients within TIR goals) between

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	Mean blood glucose (mg/dl)	GMI (%)	CV (%)	TIR (%)	TBR (%)	TAR (%)
1ª T (10-14 weeks)	131 ± 7	6.4 ± 0.2	30.5 ± 3	62.6 ± 6	1.9 ± 1	35 ± 7
2ª T (20-24 weeks)	126 ± 13	6.4 ± 0.2	29.4 ± 2	64.7 ± 5	1.5 ± 0.8	33.8 ± 5
3ª T (32-36 weeks)	124 ± 5	6.2 ± 0.1	28.8 ± 3	70.5 ± 5	1.7 ± 1	27.8 ± 5

both groups. Secondary endpoints included cost-effectiveness analyses of each of the TIR goals, for each percentual increment in TIR, for increasing the number of daily readings and for reducing inpatient glucose management costs.
Methods
Cost-effectiveness was evaluated by comparing the average cost-effectiveness ratio (ACER) between both groups and by calculating the incremental cost-effectiveness ratio (ICER). The interpretation of the ICER was based on willingness to pay threshold of 24,697.561 €/patient within TIR goal, according to Portugal's 2023 gross domestic product per capita.
Results
CGM group had a significantly higher number of patients with glycemic control (10 vs 2, $P = 0.021$), despite no difference between groups regarding most of TIR goals, with exception for 'Time above 250 < 5%' (16 vs 4, $P = 0.002$). In the ACER comparison, CGM showed lower median cost per effect for the primary outcome (11.1 vs 34.9 € /patient). As for secondary outcomes, CGM achieved lower ACER for 'Time in Range >70%' (7.8 vs 11.6 € /patient), for 'Time above 180 < 25%": 7.4 vs 9.9 € /patient, and 'Time above 250 < 5%": 6.9 vs 17.4 € /patient). Regarding ICER, CGM costed more 156 € /patient in glycemic control than CBG, considered as acceptable within the cost-effectiveness analysis plane. As for secondary outcomes, only 'hypoglycemia <4%' ICER showed a negative cost-effectiveness impact (-304 € /patient in glycemic control). The remaining were all positive and considered below the WTP threshold line.
Conclusions
There are no published data regarding the cost-effectiveness of CGM in inpatient settings. Our study suggests that the use of CGM may be more cost-effective inpatient diabetes glycemic control than CBG monitoring. CGM devices were associated with an improved glycemic control, mainly in reducing hyperglycemia, at a lower cost. Our results endorse the feasibility of incorporating these devices into the context of Portugal's national healthcare, presenting a favorable cost-effective option compared to CBG monitoring.

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The clock regulator bmal1 mediates the circadian control of gc-dependent skeletal muscle catabolism by driving PI3K (P100α)-GR interaction

Mariarosaria Negri[1], Claudia Pivonello[2], Feliciana Amatrudo[1], Roberta Patalano[3], Donatella Paola Provvisiero[3], Cristina de Angelis[3], Angelica Larocca[3], Chiara Simeoli[3], Annamaria Colao[3,4] & Rosario Pivonello[3,4]
[1]Università Telematica Pegaso, Dipartimento di Scienze Umanistiche, Naples, Italy; [2]Università Federico II di Napoli, Dipartimento di Sanità Pubblica, Naples, Italy; [3]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia, Andrologia e Nutrizione, Naples, Italy; [4]Federico II University, Unesco Chair for Health Education and Sustainable Developmen, Naples, Italy

The transcriptional activator Bmal1, reaching acrophase in the morning and bathyphase in the evening, is the main regulator of circadian clock. A mutual interaction between circadian clock and glucocorticoids (GCs) has been described as well as their implication in muscle metabolism. The current *in vitro* study aims at investigating Bmal1 involvement in muscle catabolism induced by GCs circadian exposure. To this aim, mouse myocytes C2C12 were serum-shocked to synchronize clock genes oscillation. Using acrophase and bathyphase of Bmal1, hydrocortisone (HC) administrations were aligned to daytime of human cortisol peaks and nadir. During Bmal1 acrophase, myocytes were exposed to physiological concentration of 450nM and to non-physiological concentrations of 650nM and 750nM HC. During Bmal1 bathyphase, myocytes were exposed to physiological concentration of 150nM and to non-physiological concentrations of 177nM and 300nM HC. Atrogenes circadian expression was measured by RT-qPCR, while mTOR and KLF15 expression by WB. To address Bmal1 involvement in GC-induced muscle catabolism, myocytes Bmal1-knockdown (Bmal1-KD) were performed using siRNA technology and mTOR and KLF15 expression after HC exposures were compared to negative control (NC). PI3K ($P100\alpha$)-GR/IRS-1 interactions in Bmal1 bathyphase and acrophase as well as in Bmal1-KD and NC myocytes exposed to 300nM HC were monitored by co-immunoprecipitation (Co-IP). Localization of structural protein myosin and of glucocorticoid receptor (GR) were detected by immunofluorescence (IF). At Bmal1 acrophase and bathyphase, no significant change in atrogenes levels was revealed. Conversely, only at Bmal1 bathyphase, 300nM HC significantly inhibited mTORC1 (61.03%; $P=0.005$ vs 150nM) and pp70S6K (49.80%; $P=0.002$ vs 150nM) and significantly stimulated KLF15 expression (53.34%; $P=0.02$ vs 150nM). In Bmal1-KD myocytes, displaying lower Bmal1 expression than NC (65%; $P=0.02$), 300nM HC significantly decreased mTORC1 (32.62%; $P=0.02$ vs NC) and significantly increased KLF15 expression (54.20%; $P=0.02$ vs NC). Co-IP demonstrated that 300nM HC, both in bathyphase and Bmal1-KD myocytes, facilitated PI3K ($P110\alpha$)-GR interaction (93.88% and 97.36% vs acrophase and NC respectively), simultaneously reducing PI3K ($P110\alpha$)-IRS-1 (31.01% and 27.58% vs acrophase and NC respectively) interaction. IF for heavy chain myosin revealed that compared to NC, myocytes Bmal1-KD plus 150nM HC showed reduced myotubes formation and nuclear GR expression, whereas Bmal1-KD plus 300nM HC showed reduced myotubes formation, increased nuclear GR expression and myosin co-localization. These data demonstrated that Bmal1 down-regulation contributes to muscle catabolism induced by GCs triggering PI3K ($P110\alpha$)-GR interaction and inhibiting myotube formation.

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Performance of a machine learning-based early warning system in hospitalized patients with diabetes mellitus

Pedro Caraballo[1], Karen Fischer[2], Parvez Rahman[2], Gyorgy Simon[3], Genevieve Melton[3], Hojjat Salehinejad[2], Bijan Borah[2] & M. Regina Castro[1]
[1]Mayo Clinic, Internal Medicine, Rochester, United States; [2]Mayo Clinic, Rochester, United States; [3]University of Minnesota, Minneapolis, United States

Introduction
Diabetes mellitus is a risk factor for micro-macrovascular complications and increases the risk of hospitalization, and adverse events. Early detection of impending deterioration can prompt interventions and prevent adverse events. Early warning systems (EWS) combined with rapid response teams can mitigate adverse events in the hospital setting. Machine learning-based EWS can use electronic health record data and automatically alert the care team with enough time for an early intervention. However, implementation of these systems can be impacted by their reliability, biases, and poor clinical adoption. Here we present our findings evaluating the performance of an EWS integrated into the EHR in patients with diabetes mellitus compared with those without diabetes.
Methods
We collected machine learning-based EWS scores for adult patients ($\geq$ 18 y-o) hospitalized on general wards. The EWS estimated the probability of an adverse event (mortality, cardiac arrest, intensive care transfer, or evaluation by rapid response team) on a scale of 0 to 100. We used three metrics to characterize and compare the distributions of the scores among patients with diabetes and without diabetes: the First Score 3 hours after admission; the Highest Score at any time during the hospitalization; and the Last Score just before an adverse event or before dismissal for those without an adverse event. Additional data was collected including age, sex, and length of stay.
Results
Among 61,151 admissions (female 51%, mean age 62(SD 18.5) years, length of stay 4.7(6.1) days) there were 15,727 (26%) patients with diabetes. Patients with diabetes had similar rate of adverse events compared to non-diabetics (11.92% vs 11.63%, $P=0.323$). However, the distributions of the First, Highest and Last Scores were higher in patients with diabetes and significantly different ($P<0.005$) when compared with non-diabetics (mean 32.5 vs 27.4, 46.3 vs 40.1 and 31.5 vs 27.2 respectively).
Conclusion
When using a machine learning-based EWS, patients with diabetes seem to have higher risk of deterioration when compared with nondiabetic. However, they seem to have the same proportion of adverse events compared to nondiabetics. These findings are reassuring of the hospital care received by patients with diabetes; despite their higher risk they are not suffering additional complications. Our study was performed in a single institution and did not investigate the specific causes or clinical interventions responsible for the findings. Additional assessment of these factors could prove to be important when planning best hospital practices for diabetic patients admitted in general wards.

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Asprosin- novel player in metabolic disorders

Iveta Nedeva[1,2], Vera Karamfilova[2] & Yavor Assyov[2]
[1]Medical University of Sofia, Epidemiology and Hygiene, Sofia, Bulgaria; [2]Medical University of Sofia, Internal Medicine, Sofia, Bulgaria

Background
Asprosin, a novel glucogenic adipokine, is encoded by two exons (exon 65 and exon66) of the gene Fibrillin 1 (FBN1) and mainly synthesized and released by

white adipose tissue during fasting. Asprosin plays a complex role in the central nervous system (CNS), peripheral tissues, and organs. It is involved in appetite, glucose metabolism, insulin resistance (IR) and cell apoptosis.
Objective
The aim of the current study was to determine the levels of asprosin in subjects from the entire spectrum of the carbohydrate metabolism.
Methods
A total of 153 causcasian subjects participated in this study: group 1, healthy volunteers; group 2, obese subjects without glycemic disturbances; group 3- subjects with prediabetes and group 4, patients with newly identified type 2 diabetes
Results
Subject with body mass index ≥ 30 kg/m^2 and dysglycemia (prediabetes and diabetes) showed significantly high levels of asprosin (1.40 ng/ml [IQR = 0.98-1.94]; 1.27 ng/ml [IQR = 0.86-2.12]; 1.09 ng/ml [IQR = 0.89-1.58]) compared to the control group (0.71 ng/ml [IQR = 0.54-0.92]; $P < 0.001$). Correlation analysis showed that serum asprosin also had significant positive associations with some anthropometric parameters, liver enzymes, fasting and post load glucose and insulin, LDL and triglycerides. Furthermore, we estimated a markedly relationship between asprosin concentrations and intima media thickness of the common carotid artery as well as neuropathy disability and vibration sensitivity. The circulating asprosin levels for differentiating subjects with carbohydrate disturbances and those with obesity were determined by ROC analysis. The AUC for disturbances of the glucose metabolism was 0.672 ($P < 0.001$; 95% CI = 0.581-0.751) and for obesity AUC was 0.849 ($P < 0.001$; 95% CI = 0.785-0.919).
Conclusion
Circulatin asprosin could be used as a predictive factor for early carbohydrate disorders and might be a potential new therapeutic target for the treatment of dysglycemia and obesity. Further prospective studies are needed to confirm this observation.

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Exploring the nexus of sex hormones and obesity in adult males: insights from a comprehensive clinical analysis

Yaoxia Liu[1], Tao Wang[2], Yerong Yu[3] & Min Zhang[1]
[1]Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China., Geriatric Endocrinology, Chengdu, China; [2]West China Second University Hospital, Sichuan University., Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, China; [3]West China School of Medicine/ West China Hospital of Sichuan University., Endocrinology and Metabolism., Chengdu, China

Background and purpose
Obese men often exhibit hypoandrogenemia. Although previous research has established obesity and metabolic-related disorders as key factors contributing to decreased androgens in males, there are rare studies to comprehensively understand the correlation between sex hormones and obesity, as well as metabolic indicators, particularly in non Caucasian populations. This study aims to comprehensively investigate the relationship between sex hormones and obesity in adult males using a large-scale clinical sample in non Caucasian populations.
Materials and Methods
Participants were screened based on inclusion and exclusion criteria, and the sex hormone indicators including sex hormone binding globulin (SHBG), total testosterone (TT), estradiol (E2), luteinizing hormone (LH), follicle stimulating hormone (FSH), free testosterone (FT), bioactive testosterone (BioT), as well as metabolic indicators including BMI, blood lipids, fasting glucose, blood uric acid were collected and analyzed.
Results
A total of 360 adult males were included. The findings showed that TT (ng/ml) exhibited a sequential decrease from the obese group, the overweight group and the normal group ($P < 0.05$). When BMI (kg/m^2) $\geq$ 28.326, a significant decrease in FT was observed (0.080 vs 0.090, $P < 0.05$), and when BMI (kg/m^2) $\geq$ 28.360, a significant decline in BioT was observed (1.85 vs 2.10, $P < 0.05$). Multivariate linear regression analysis revealed that SHBG was negatively correlated with BMI and triglycerides, and positively with age; TT was negatively correlated with BMI, blood glucose and TG; FT was negatively correlated with BMI, age, and blood glucose; BioT was negatively correlated with BMI, age, and blood glucose; E2 was positively correlated with BMI and negatively with TG. However, LH and FSH were positively correlated with age only.
Conclusion
Increased BMI and glucose levels correlated with lower androgen hormone levels including serum TT, FT and BioT, which reminds us to pay particular attention to the possibility of hypogonadism in obese men.

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The discourse of medical treatment for obesity: sentiment analysis of the literature

Georgios Gavriiloglou[1], Christos Savvidis[1], Efthymia Kallistrou[1], Vasiliki Tsiama[1] & Ioannis Ilias[1]
[1]Hippokration General Hospital, Department of Endocrinology, Athens, Greece

Aim
Obesity can be addressed through lifestyle interventions like modifying diet and engaging in physical activity. In cases where these measures prove ineffective, there is the option of administering medication (RxOb) or of surgical intervention. Sentiment analysis (SA) is an automated procedure employed to extract emotional information prevalent in a given body of text. Specifically, SA enables the determination of the "sentiment polarity" –whether the overall tone is positive or negative. Given the feasibility of implementing SA in medical texts (Artif Intell Med 2015; 64: 17-27), our objective was to employ SA to assess the medical literature's stance, distinct from that of the lay press, concerning RxOb.
Methods
We collected (using MeSH terms) the English language abstracts of randomized clinical trials (RCTs) on RxOb in PubMed, from 2013 to 2023. For SA, we used two, state-of-the-art artificial intelligence SA tools, to generate averaged sentiment scores for each publication. SA scores were categorized into positive (maximum +1.00), neutral (0), or negative (maximum -1.00). Statistical analysis for differences between each year's publications' SA was done with analysis of variance (ANOVA); Pearson's correlation was used to assess time trends.
Results
Seventy abstracts of RCTs were retained from an initial collection of 217 papers. The average $\pm$ SD SA was positive at 0.59 $\pm$ 0.35. The lowest SAs were noted in 2017 and the highest in 2022 ($P < 0.05$, ANOVA). A positive correlation between SA and time, specifically within the period 2017-2022, was found (r: = + 0.38, p: 0.008).
Discussion
RxOb is a dynamic and evolving field, with an expanding body of literature. SA of this literature offers a unique perspective by helping to uncover prevailing sentiments, trends, and perceptions. The application of SA to medical literature allows for the swift assessment of extensive published data collections, offering a rapid synthesis of overall findings that align with the outcomes of a conventional meta-analysis (Reg Anesth Pain Med 2022; 47: 151-154). Nevertheless, our findings are based on SA of existing literature and may not capture all relevant factors influencing sentiments. Future research could delve deeper into the underlying causes of this positive trend, such as specific breakthroughs or changing perceptions among healthcare professionals.

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Endoscopic argon plasma coagulation (APC) treatment for dumping syndrome and post-bariatric hypoglucemia in patients with ROUX-EN-Y gastric bypass

Sara Mera Carreiro[1], Blanca Bernaldo Madrid[1], Clara Rodríguez Carrillo[2], Patricia Espinosa De Los Monteros[1], Laura Avila Anton[1], Noelia Sánchez-Maroto García[1], Laura Martínez Suero[2], Teresa Rueda Ortín[1], Jose Miguel Esteban López-Jamar[2] & Miguel Angel Rubio Herrera[1]
[1]Hospital Clinico Universitario San Carlos, Endocrinology, Diabetes and Nutrition, Madrid, Spain; [2]Hospital Clinico Universitario San Carlos, Digestive System and Gastroenterology, Madrid, Spain

Background
Dumping syndrome (DS) and post-bariatric hypoglycemia (PBH) are some of the most challenging problems encountered during the follow-up of bariatric surgery (BS), especially after Roux-en-y gastric bypass (yRGB). When pharmacological and dietary treatment fail to control DS and PBH, surgical revision is often the next therapeutic step. Endoscopic treatment with argon plasma coagulation (APC) may be an alternative treatment by reducing the diameter of the gastro-jejunal anastomosis and thus slowing gastric emptying.
Objectives
To evaluate the efficacy and safety of endoscopic APC treatment in patients who have undergone yRGB and developed DS and PBH.
Material and methods
Retrospective study of patients who underwent endoscopic gastro-jejunal anastomotic reduction using APC at 1.9 liters/min flow and 90 watts in our center between 2018-2022 to treat refractory DS and PBH following yRGB. Improvement of DS symptoms according to Sigstad score, reduction of PBH with disappearance of Whipple's triad and anthropometric data were evaluated.

Statistics: Descriptive analysis and comparison of means (t-Sudent or U-Mann-Whitney) was carried out, cording to the normality distribution of variables.
Results
25 consecutive patients aged 52.3±9.2 years were recruited. Pre-surgery BMI was 42.7±5.5 kg/m^2; nadir BMI was 26.6±3.8 and BMI before APC was 30.8±6.3. Dumping symptoms appeared 26 (20-84) months after BS. Most patients received dietary (fractionated food, low-GI carbohydrates) and pharmacological treatment (acarbose, iSGLT1/2, octreotide). All patients had an average of 2 APC endoscopic procedures (range 1-4), initial gastro-jejunal anastomosis diameter of 26.8±7.2 mm and final diameter after APC of 16.4±4.4 mm. Adverse events were mild and did not require hospitalization: pain ($n=3$ (12%), vomiting ($n=2$ (8%), ulcer ($n=3$ (12%), bleeding ($n=1$ (4%), stenosis ($n=3$ (12%). Symptoms improved in 100% of patients with a decrease in Sigstad score from 6.8±2.6 to 0.9±2 points and the resolution of all PBH ($P<0.0001$). 84% of patients were able to discontinue pharmacological treatment. In addition, 80% of patients had a significant weight loss (%BW) ($P<0.01$) after APC during the 2-year follow-up: 7.6±5.2% (6 months), 8.9±4.8% (12 months), 6.6±5.6% (18 months) and 5.3±5.01% (24 months).
Conclusions
Endoscopic APC is an effective, safe and reproducible procedure for the management of DS and PBH in patients with prior yRGB who are refractory to dietary and pharmacological treatment, or even as a single first-line therapy. It also contributes to weight loss after weight regain in BS.

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The effect of ketogenic diet versus mediterranean diet on clinical and biochemical markers of inflammation in patients with obesity and psoriatic arthritis

Aikaterini Kountouri[1], Pelagia Katsimbri[2], Emmanouil Korakas[1], Loukia Pliouta[1], Vasileia Agapitou[1], Eirini Maratou[3], George Pavlidis[4], Ignatios Ikonomidis[4], Argyro Papathanasi[5], Sofia Malisova[6], Dionysios Vlachos[6], Evangelia Papadavid[5] & Vaia Lambadiari[1]
[1]Attikon University Hospital, Second Department of Internal Medicine, Chaidari, Greece; [2]Attikon University Hospital, Rheumatology and Clinical Immunology Unit, Fourth Department of Internal Medicine, Chaidari, Greece; [3]Attikon University Hospital, Department of Clinical Biochemistry, Chaidari, Greece; [4]Attikon University Hospital, Second Cardiology Department, Chaidari, Greece; [5]Attikon University Hospital, Second department of Dermatology and Venereology, Chaidari, Greece; [6]Independent Researcher, Athens, Greece

Background
Obesity is over-represented in patients with psoriasis (PSO) and psoriatic arthritis (PsA) and associated with higher disease activity and poorer treatment response. A substantial number of studies have highlighted the beneficial effect of weight loss in PSO and PsA disease activity. However, the data regarding the most efficacious diet pattern are scarce. The aim of our study to evaluate the effectiveness of Mediterranean diet (MD) and Ketogenic diet (KD), in patients with PSA
Methods
Sixteen patients were randomly assigned to start either with MD or KD for a period of 8 weeks. After a 6-week washout interval, the two groups were crossed over to the other type of diet for 8-week period. Disease activity was assessed using the Psoriasis Area and Severity Index (PASI) and the Disease Activity Index for Psoriatic Arthritis (DAPSA) score. Metabolic and disease parameters were evaluated at the beginning and at the end of each diet-intervention.
Results
At baseline, patients presented mean weight of 108.44 kg, mean PASI of 5.09 and a mean DAPSA of 54.02. At the end of the study, MD and KD resulted in significant reduction in weight($P=0.002$, $P<0.001$, respectively), in BMI ($P=0.006$, $P<0.001$, respectively), in waist circumference($P=0.001$, $P<0.001$, respectively), in total fat mass ($P=0.007$, $P<0.001$, respectively) and in visceral fat ($P=0.01$, $P<0.001$, respectively). After KD, patients displayed a significant reduction in PASI ($P=0.04$), DAPSA ($P=0.004$), IL-6 ($P=0.047$), IL-17 ($P=0.042$) and in IL-23 ($P=0.037$), whereas no significant differences were observed in these markers after MD ($P>0.05$), compared to baseline (table 1).
Conclusion
The 22-week MD-KD diet program in patients with PSA led to beneficial results in markers of inflammation and disease activity. KD had a more significant impact on weight loss and in parameters of disease activity. A larger number of patients and a longer follow-up period may be necessary to fully elucidate the effect of different diets on disease activity in patients with PSO and PsA.

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	Baseline	MD	KD	p-value†	p-value*
Weight (Kg)	108.44±19.01	101.21±17.95	98.17±17.46	0.002	< 0.001
BMI(kg/m^2)	39.90±7.60	37.40±7.75	36.30±7.33	0.006	< 0.001
WC (cm)	122.96±17.87	118.53±15.71	115.56±15.52	0.001	< 0.001
FatMass (kg)	46.83±12.76	42.30±12.84	40.51±12.80	0.007	< 0.001
Visceral Fat (%)	15.43±4.38	14.18±4.38	13.50±3.81	0.01	< 0.001
PASI	5.09±5.73	3.82±3.93	3.15±4.88	0.278	0.040
DAPSA	46.28±34.89	34.89±30.17	23.30±16.75	0.060	0.004
IL-6	9.85±17.94	8.17±12.85	6.33±12.47	0.666	0.047
IL-17	11.44±20.10	5.29±6.74	4.66±8.72	0.243	0.042
IL-23	23.59±11.04	19.15±9.70	17.86±9.97	0.151	0.037

† comparisons baseline and after MD, * comparisons between baseline and after KD

P293

Effectiveness of treatment with Vitamins B12 and D in patients with diabetic peripheral neuropathy by sudoscan

Tamar Maghradze[1], Eelena Shelestova[2] & Ramaz Kurashvili[2]
[1]National Centre for Diabetes Research, Endocrinology, T'bilisi, Georgia; [2]National Centre for Diabetes Research, T'bilisi, Georgia

Diabetic peripheral neuropathy (DPN) is the most common cause of neuropathy worldwide, its prevalence increases with diabetes duration (DD). About 60%-70% diabetic patients will eventually develop DPN. Vitamin B12/D (VitB12/D) deficiency is a global public health problem. Around 29.66% of diabetic patients have confirmed B12 insufficiency. Patients on Metformin have statistically lower values of B12 ($P=0.01$). Vitamin D deficiency is considered to be a contributing factor to the development of type 2 diabetes (T2DM).
Our aim was to study the effect of VitB12/D therapy in patient with T2DM and DPN.
Methods
Totally 52 patients were studied (27 males/33 females, mean age 51±5yrs, DD - 5-10 years, HbA1c at entry - 8,3±1,5%). Before initiating treatment with VitB12/D below tests were performed and following results were obtained: Vitamin B12 (150±20pg/mL [n - 200-835 pg/mL]), Vitamin D (15±25 ng/m [n - 30-100 ng/ml]); all neurological tests (10-g monofilament test, tip-term/temperature test, vibration test with the 128-Hz tuning fork, prick tests) were positive, and neurological examination with Sudoscan (a non–invasive method for the assessment of the small fiber function, Impeto Medical, France) revealed presence of mild small fiber neuropathy. Treatment with oral VitB12/D was initiated in all the patients.
Results
At month 3 post treatment initiation all tests were repeated. In 88% of patients VitB12/D levels were within the normal range; results of monofilament, tip-term/temperature test and Sudoscan examination improved in 41 patients (78,5%).
Conclusion
This study shows that 3-month treatment with VitB12/D improves condition of peripheral nerve fibers. Observations will continue.

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P294

The relationship between emotion regulation strategies, illness uncertainty and health-promoting self-care in individuals with type-2 diabetes mellitus

Merve Murat[1], Selda Celik[1], Seda Er[2] & Gulden Anataca[3]
[1]Health Sciences University, Turkey; [2]I stanbul Üniversitesi-Cerrahpaş a, Turkey; [3]Kanuni Sultan Süleyman Training and Research Hospital, Turkey

Introduction
Diabetes Mellitus is a significant metabolic condition characterized by its widespread occurrence and associated complications. Reports indicate that DM impacts 25% of the global population. The way individuals handle their existing

illnesses throughout their lifetimes is crucial in terms of uncertainty and self-care behaviors within chronic diseases such as DM. The connection between individuals' physiological parameters (HbA1c etc.) and uncertainty, as well as emotion regulation strategies, is highlighted. Examining the correlation between psychological and physiological variables in individuals with type 2 diabetes is emphasized as a pivotal aspect of disease management.
Aim
This study aims to assess how emotion regulation strategies impact physiological symptoms, illness uncertainty, and the practice of health-promoting self-care among individuals diagnosed with Type 2 DM.
Method
This is a descriptive cross-sectional study. The sample consisted of 433 patients who followed in a public hospital in Istanbul, Turkey. Data were collected using a Personal Information Form, the Cognitive Emotion Regulation Scale, the Mishel Uncertainty in Illness Scale, and the Diabetes Health Promotion Self-Care Scale.
Results
The participants, with a mean age of 52.84 ± 7.11 years, were mostly male (56.4%), married (80.8%), and university graduates (49.4%). In terms of diabetes and health characteristics, the participants had an average diabetes diagnosis duration of 4.33 ± 1.33 years, and the average HbA1c value was 8.61 ± 0.73%. Notably, 56.1% of participants received Oral Anti-Diabetic and Insulin treatment, and 37% took diabetes training for self-care. Daily living activities were successfully performed by 94.7% of participants, with only 2.5% requiring assistance. About 50.3% were uncertain about whether DM would impact their lives, and their overall health status was reported as good. Participants scored high on the Mishel Uncertainty in Illness Scale, Diabetes Health Promotion Self-Care Scale, and Cognitive Emotion Regulation Scale Subscales.
Conclusion
In conclusion, according to the study results, the interventions to strengthen people diagnosed with type-2 DM mental and physical health should be developed.
Keywords: diabetes mellitus, illness uncertainty, health promotion, emotional regulation strategies
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P295

Eating disorders in obese patients with type 2 diabetes

Meriem Adel[1], Marwa Chiboub[2], Asma Zelaiti[2], Hajer Kandara[3] & Ines Kammoun[2]
[1]Tunisia, Endocrinology, Tunis, Tunisia; [2]National institute of nutrition and food technology, Endocrinology, Tunis; [3]Tunisia, Endocrinology, Tunis

Introduction
Eating disorders (ED) are more prevalent among obese individuals with type 2 diabetes than in the general population. The co-occurrence of diabetes and ED can impair metabolic control, resulting in earlier and more severe degenerative complications, as well as increased morbidity and mortality. This study aims to assess the prevalence of eating disorders in obese patients with type 2 diabetes.
Method
A cross-sectional descriptive study was conducted at the endocrinology department of the National Institute of Nutrition and Food Technology. Forty-five obese type 2 diabetic patients were recruited. Each patient was asked to complete two questionnaires, the *Bulimic Investigatory Test Edinburgh* (BITE) and *Sick, Control, One stone, Fat, Food* (SCOFF). Anthropometric measurements and dietary survey data were collected for each patient.
Results
The mean age of the population was 58.2 ± 12.5 years, with a female predominance (91.1%). The mean Body Mass Index (BMI) was 34.8 ± 5.2 kg/m^2. All participants had android obesity. Eating disorders were present in 95.6% of the population, with unspecified type in all cases and specified type (according to the SCOFF questionnaire) in 35.6% of patients. According to the BITE questionnaire, bulimia/binge eating was found in 11% of patients. The most common unspecified eating disorder was cognitive restriction (71.1%). Night eating syndrome, external eating, and snacking were observed in 56%, 62.2%, and 49% respectively. A statistically significant positive correlation was found between eating disorders and anthropometric parameters: weight ($P = 0.016$), BMI ($P = 0.004$), waist circumference ($P = 0.018$), and obesity class ($P = 0.012$). No significant association was found between eating disorders and glycemic control, except for purging disorders ($P = 0.009$). There were no significant association found between glycaemic control and ED. Among the degenerative complications of diabetes, only neuropathy was significantly associated with snacking ($P = 0.013$).
Conclusions
The prevalence of eating disorders is significant among obese type 2 diabetics, highlighting the importance of early detection and appropriate management of these disorders.
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P296

Unveiling connections: type 2 diabetes, male hypogonadism, and inflammation –insights from a clinical study

Anis Grassa[1], Manel Jemel[1], Salma Salhi[1], Asma Krir[2], Ahlem Benhmid[2], Marwa Chiboub[1], Radhouane Gharbi[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technologies, Zouheir Kallel, Endocrinology, Tunis, Tunisia; [2]Pasteur Institute of Tunis, Tunisia

Introduction
The interplay between type 2 diabetes (T2D), male hypogonadism (HG), and inflammation has emerged as a fascinating area of medical research. Understanding the complex relationship among these factors is crucial for advancing our knowledge.
Methods
The study focused on 250 adult male patients with T2D recruited from outpatient clinics at the National Institute of Nutrition and Food Technology. A thorough assessment of gonadal hormones, including Sex Hormone-Binding Globulin and albumin, was conducted to calculate Free Testosterone (FT) and Bioavailable Testosterone (BT) using the Vermeulen formula [1]. Diagnostic criteria for HG included specific thresholds: Total Testosterone (TT) below 231 ng/dl, FT below 6.5 ng/dl, or BT below 150 ng/dl. Additionally, various inflammatory markers, such as CRP, IL6, and TNF-alpha, were assessed for all patients.
Results
Mean levels of TT, FT, and BT were 438.8 ± 172.1 ng/dl, 8.8 ± 2.8 ng/dl, and 194.7 ± 60.4 ng/dl, respectively. Median values (IQR) for inflammatory markers CRP, IL6, and TNF-alpha were 1.7 (0.9-3.3) mg/l, 2.5 (1.7-6.9) and 1.8 (1.0-2.5), respectively. A significant inverse correlation was found between TT and CRP ($r = -0.192$; $P = 0.010$), as well as FT ($r = -0.165$; $P = 0.031$). However, no such association was observed with BT ($P = 0.056$). The prevalence of HG was 27.2% ($n = 68$), and variations in inflammatory marker levels based on gonadal status were not statistically significant. Comparison between HG vs non-HG groups revealed median (IQR) CRP values of (2.00 mg/l vs 1.46; $P = 0.238$); IL6 values of (2.73 pg/mL vs 2.38; $P = 0.491$) and TNF-alpha values of (1.78 pg/mL vs 1.78; $P = 0.665$).
Conclusion
In conclusion, this study sheds light on the intricate relationship between DT2, male HG, and inflammation. While significant correlations were observed between testosterone levels and CRP, further research is needed to unravel the complexities of this association. Understanding these dynamics is essential for developing targeted therapeutic strategies and improving the overall care of individuals with both DT2 and male HG.
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An hepatomegaly in a child with type 1 diabetes and celiac disease: what could it be?

Yasmine Fakhfekh[1], Chaima Jemai[1], Yosra Ben Hmida[1], Yosra Htira[1], Dorsaf Ben Salem[1], Takwa Moussa[1], Zohra Hadj Ali[1], Imen Hedfi[1], Olfa Lajili[1] & Faika Ben Mami[1]
[1]National institute of nutrition of Tunis, C

Introduction
Type 1 diabetes mellitus (T1DM) and celiac disease are two frequently associated autoimmune pathologies. The association with hepatomegaly raises discussion of many diagnosis.
Case presentation
We report the case of a 12-years-old T1DM girl admitted at department C of the national institute of nutrition of Tunis for diabetic ketosis. She has T1DM since 5 years, with poor glycemic control (HbA1C = 10%) and poor therapeutic adherence. On examination, she had abdominal bloating with homogeneous hepatomegaly. Height was 146 cm (less than 2nd percentile), weight 38 kg (less than 2nd percentile) and body mass index of 17.8 Kg/m^2. Tanner stage was S1P1A1. Biological investigations showed, mixed dyslipidemia, normal liver and renal functions and normal TSH. AST/ALT ratio was 1.35. FSH and LH levels were low. Ultrasound abdomen revealed hepatomegaly with a liver span of 19 cm. Based on the clinical history and investigations, Mauriac syndrome seems to be the most likely diagnosis of our patient. A holistic multidisciplinary approach, in collaboration with the child psychiatrist, was opted, in order to optimize diabetes management and to reduce hepatic metabolic overload. Further investigations was conducted to rule out differential diagnoses, especially viral and autoimmune hepatitis.

Conclusion
Poor acceptance of type 1 diabetes leads to non-compliance with insulin therapy. Then, energy metabolism becomes defective with growth retardation and pubertal delay. Glucose accumulates in the liver leading to metabolic liver disease. Liver damage could be irreversible. Therapeutic education, good doctor-patient relationship and family support constitute the main cornerstones of the management of T1DM diabetes complicated by Mauriac syndrome.

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Current prevalence and patterns of hypolipidemic medication based on real-life nation-wide data on 10, 816, 286 individuals

Konstantinos Mathioudakis[1], Maria Yavropoulou[2], Maria Evangelia Koloutsou[2], Polyzois Makras[3], Evangelos Liberopoulos[4] & Konstantinos Athanasakis[5]
[1]IDIKA SA - E-Government Center for Social Security Services, Athens, Greece; [2]First Department of Propaedeutic and Internal Medicine, National and Kapodistrian University of Athens, Athens, Greece; [3]Department of Medical Research, 251 Hellenic Air Force & VA General Hospital, 3 Kanellopoulou St, 11525, Athens, Greece; [4]First Department of Propaedeutic and Internal Medicine, National and Kapodistrian University of Athens, Athens, Greece; [5]Laboratory for Health Technology Assessment (LabHTA), Department of Public Health Policy, School of Public Health, University of West Attica, Athens, 11521, Greece

Background
Hypercholesterolemia has an established causal role in the progression of atherosclerosis and development of cardiovascular disease (CVD). In studies carried out after 2002, the estimated prevalence of self-reported dyslipidemia in the Greek population ranges from 11% to 23%, whereas approximately 35% of mortality in Greece is attributed to cardiovascular disease (CVD). Relevant real-life data, however, are scarce.
Methods
In the present study we used theelectronic prescription database of the National Organization for Health Care Services Provision (IDIKA), embracing almost 100% of all prescriptions issued in Greece, to capture individuals who received hypolipidemic treatment during the year 2021.
Results
The study population consisted of 10,482,487individuals, accounting for the totalGreek population in 2021. The overall prevalence of medication-prescribed dyslipidemia accounted for the 19% of the total Greek population ($n=1,998,393$), beingslightly higher in women than in men (19.7% vs 18%, respectively) across all age groups and was gradually increased with advancing age (7% in those <50 years, to 44.5% in those aged 70 and above). Notably, 1052 individuals with medication-prescribed dyslipidemia were underage (accounting for 0.05% of the total underage population in Greece). Most common concomitant diseases were arterial hypertension (45.7%) diabetes type mellitus 2 (28.4 %), and coronary artery disease (14.4%). General practitioners(33,72%), Internists(33,69%), and Cardiologists(21,64%) prescribed the vast majority of hypolipidemic treatment. The annual cost of treatment per-patient was on average 144€ (total cost € 203,375,511)with rosuvastatin and atorvastatin being more frequently prescribed accounting for more than 80% of all prescriptions.
Conclusion
Approximately 18% of the total Greek population has been prescribed with a hypolipidemic agent during 2021. Prevention and control of dyslipidemia, as one of the most important modifiable risk factors for CVDremains a yet unmet challenge.
Keywords: dyslipidemia; hypolipidemic treatment; statins; cardiovascular disease; prevalence of dyslipidemia; Greek population
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P299

Effectiveness of dapagliflozin and sitagliptin fixed dose combination in indian patients with type 2 diabetes mellitus in real world settings: age stratified-analysis from a retrospective study

Ritesh Agrawala[1], Supratik Bhattacharyya[2], Prakadeesh Bharathi B[3], Vinay Kudrigikar[3], Prachi Ahire[3], Shruti Dharmadhikari[3], Chintan Khandhedia[3], Neeraj Markandeywar[3], Amey Mane[3] & Suyog Mehta[3]
[1]AMRI Hospital, Bhubaneswar; [2]SKN Diabetes and Endocrine Centre, Kolkata; [3]Sun Pharma Laboratories Ltd, Medical Affairs

Introduction and Objective
Incidence of type 2 diabetes mellitus (T2D) is rapidly increasing resulting in significant metabolic disorders and complications. Dapagliflozin and sitagliptin have complimentary mechanism of action and have shown synergistic effects in controlling blood glucose levels with advantage of low risk of hypoglycemia. Use of fixed dose combinations (FDC) is associated with improved patient compliance. This is an Age Stratified analysis of electronic medical record (EMR) based study assessing effectiveness of dapagliflozin + sitagliptin FDC in patients with T2D.
Methods
In this real-world, retrospective, observational, EMR based study, data of adult patients (age $\geq$18 years) of either gender with T2D having HbA1c $\geq$7% at baseline were included. Patients who were prescribed dapagliflozin and sitagliptin FDC in any visit other than baseline visit on EMR platform were included. Patients on insulin or other injectable antidiabetic medications were excluded. Primary endpoint was mean change in HbA1c from baseline to 3 months in patients with HbA1c $\geq$8% at baseline. This is an age stratified-analysis of primary outcome.
Results
Total 3,112 patients fulfilled selection criteria, of which 838 patients were eligible for primary analysis. Patients were stratified in following age groups - Group 1: age $\leq$ 50 years ($n=299$); Group 2: 51-60 years ($n=281$); Group 3: 61-70 years ($n=198$) and Group 4: $>$70 years ($n=60$). Mean HbA1c reduced from 9.29% at baseline to 7.98% at 3 months (change -1.31%, $P<0.001$). Significant reduction in HbA1c from baseline to 3 months was observed in all age groups - Group 1: 9.31% vs 7.90% [change -1.41%]; Group 2: 9.29% to 7.97% [-1.32%]; Group 3: 9.22% vs 8.05% [-1.17%]; Group 4: 9.49% vs 8.13% [-1.35%]. Fasting and Postprandial blood glucose (FBG and PPBG) reduced significantly in all age strata from baseline to 3 months. FBG changes - Group 1: 175.67 to 137.27 (-38.4 mg/dl; ($n=251$), Group 2: 166.83 to 136.19 (-30.64 mg/dl; ($n=236$), Group 3: 161.77 to 128.26 (–33.51 mg/dl, ($n=170$), Group 4: 155.61 to 123.66 (–31.95 mg/dl; ($n=53$). PPBG changes - Group 1: 252.19 to 200.02 (-52.17 mg/dl; ($n=205$), Group 2: 254.08 to 201.32 (–52.76 mg/dl; ($n=205$), Group 3: 240.52 to 197.63 (–42.89 mg/dl; ($n=154$), Group 4: 246.10 to 202.52 (–43.58 mg/dl; ($n=58$). $P<0.001$ for all comparisons.
Conclusion
In patients with T2D and higher HbA1c value, Dapagliflozin + Sitagliptin FDC showed significant reduction in HbA1c, FBG and PPBG across all age groups. These findings highlight utility of Dapagliflozin + Sitagliptin FDC in managing T2D irrespective of age.

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P455

Effect of prior GLP-1 RA treatment on clinical outcomes in patients with type 2 diabetes initiating treatment with tirzepatide

Mohammed Suliman[1], Adam Buckley[1], Matthew Allum[1], Nader Lessan[1], Nagi Mohammed[1], Carel le Roux[2] & Sara Suliman[1]
[1]Imperial College London Diabetes Centre, Abu Dhabi, United Arab Emirates; [2]Imperial College London, London, United Kingdom

Background
Tirzepatide is a GLP-1/GIP co-agonist treatment for type 2 diabetes. Participants in the SURPASS trials were GLP-1RA naïve, but in clinical practice many patients are switched from other GLP-1RAs.
Aims
To explore effects of prior GLP-1RA treatment on tirzepatide therapy outcomes.
Methods
Review of clinical data from an outpatient Diabetes centre. Adults with 6 months follow-up post tirzepatide initiation were included, ($n=1375$. GLP-1RA exposure was classified as 'naïve' (no GLP-1RA ever dispensed, ($n=192$), 'prior exposure' (no GLP-1RA in preceding 12 months), 'injectable semaglutide' 'oral semaglutide' or 'other injectable GLP-1RA". Linear regression analyses were adjusted for prior bariatric surgery and tirzepatide discontinuation.
Results
Mean (95%CI) adjusted change in weight was -7.0(-7.6; -6.3)kg in the naïve group, -5.2(-6.2; -4.2)kg in the prior exposure group, -5.4(-6.6; -4.1)kg in the oral semaglutide group, -4.4(-5.0; -3.9)kg in the other injectable GLP-1RA group, and -3.7(-4.1; -3.3)kg in the injectable semaglutide group at 6 months. Mean adjusted change in HbA1c was -1.22(-1.36; -1.07)% in the naïve group, -0.76(-0.96; -0.55) % in the prior exposure group, -0.79(-1.06; -0.53) in the group switched from oral semaglutide, -0.70(-0.81; -0.58) in the other GLP-1RA group, and -0.55(-0.62; -0.48)% in the injectable semaglutide group. Weight outcomes differed significantly between naïve and prior exposure ($P<0.05$), injectable semaglutide ($P<0.001$), and other injectable GLP-1RA ($P<0.001$) groups, and between the prior exposure and injectable semaglutide groups ($P<0.05$).

Conclusion
At 6 months, tirzepatide treatment resulted in significantly higher reductions in weight and HbA1c in GLP-1RA naïve patients than those switched from other GLP-1RAs. Individuals switched from injectable semaglutide had the least additional weight loss and HbA1c reduction.

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P456

Ghrelin system as a novel source of biomarkers and therapeutic tools in metabolic liver diseases

Antonio García-Estrada[1,2,3], Natalia Hermán-Sánchez[1,2,3], Betsaida Ojeda Pérez[1,2,3], Jose Cordoba-Chacon[4], Andre Sarmento-Cabral[1,2,3], Manuel Rodriguez-Peralvarez[1,5,6], Raul M. Luque[1,2,3,7], Juan Luis López-Cánovas[1,2,3] & Manuel D. Gahete[1,2,3,7]
[1]Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Cordoba, Spain; [2]University of Cordoba (UCO), Department of Cell Biology, Physiology and Immunology, Cordoba, Spain; [3]Reina Sofia University Hospital (HURS), Cordoba, Spain; [4]University of Illinois at Chicago (UIC), Department of Medicine, Division of Endocrinology, Diabetes and Metabolism, Chicago, United States; [5]Reina Sofia University Hospital (HURS), Department of Hepatology and Liver Transplantation, Cordoba, Spain; [6]CIBER Hepatic and Digestive Diseases (CIBERehd), CB06/04/0077, Cordoba, Spain; [7]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), CB06/03/0020, Cordoba, Spain

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the main hepatic manifestation of obesity. MASLD was recently defined as liver steatosis in the presence of at least one cardiometabolic risk factor and reduced or absent alcohol intake. MASLD prevalence is rapidly increasing, thus becoming the fastest growing aetiology of the most common primary liver cancer, hepatocellular carcinoma (HCC), and the leading cause of liver transplantation in HCC patients. Currently, there is no EMA/FDA approved drug specifically for MASLD treatment. In this scenario, neuroendocrine control regulatory systems, such as the ghrelin system, have been previously proven to be a reliable source of biomarkers and therapeutic opportunities in multiple endocrine-related cancer types (e.g., breast, prostate and pituitary tumours). Therefore, the purpose of this work was to assess the expression and possible clinical relevance of ghrelin system components (GSCs: ligands, receptors, etc.) in the MASLD-HCC progression. To achieve this, we analysed GSCs mRNA expression in 2 internal retrospective cohorts of chronic liver disease (CLD) and HCC [Retrospective-1: HCC vs non-tumoral adjacent tissue (NTAT) ($n=80$); Retrospective-2: HCC vs NTAT ($n=58$), cirrhotic ($n=33$) and healthy liver tissue ($n=5$)], 10 *in silico* cohorts [7 MASLD, 3 HCC; $n=(45\text{-}369)$], 4 diet-based mice models recapitulating MASLD-HCC progression (C57BL/6J, $n=119$) and 3 human cell lines modelling healthy liver (THLE-2) and HCC (Hep3B, SNU-387). Statistical associations with key clinical features of HCC were performed. In the HCC cell lines, the impact of GSCs administration on important tumour aggressiveness parameters was evaluated using different functional assays (proliferation, migration, colony and hepatosphere formation). Some GSCs showed a progressively increasing expression according to MASLD stage, followed by a drastic downregulation in HCC. This pattern was consistently observed through every cohort and *in vivo* and *in vitro* model, suggesting a biphasic GSCs expression regulation in CLD. Moreover, the inhibition of key GSCs in HCC was associated with several clinical features of tumoral aggressiveness such as histological differentiation, survival and recurrence rate, microvascular invasion and tumour nodule number and size. Remarkably, the *in vitro* administration of certain ligands of the GSC strongly hindered HCC cells proliferation and colony and hepatosphere formation. In contrast, healthy liver cells viability rate was not affected by these GSC ligands, suggesting a clinically safe approach. In conclusion, GSCs could be major players in the physiopathology of CLD as drivers of MASLD-derived hepatocarcinogenesis and the ghrelin system could represent a novel, yet unexplored origin of biomarkers and therapeutic options for CLD.

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Characteristics of presentation and management of people with hypoglycaemia while on continuous glucose monitoring devices - pilot data from DEKODE hypoglycaemia study

Charles Page[1], Aashritha Buchipudi[1], Ahmed Iqbal[2], Amanda Ling Jie yee[1], Haaziq Sheikh[1], Lakshmi Rengarajan[3], Ninoshka Merchant[1], Pranav Viswanath Iyer[1], Rajeev Raghavan[4] & Team Dekode[3]
[1]University of Birmingham Medical School, Birmingham, United Kingdom; [2]Department of Oncology & Metabolism, University of Sheffield & Sheffield Teaching Hospitals, Sheffield, United Kingdom; [3]Institute of Applied Health Research, University of Birmingham, Birmingham, United Kingdom; [4]Wolverhampton Diabetes Endocrine Centre, New Cross Hospital, Wolverhampton, United Kingdom

Background
Continuous glucose monitoring (CGM) is an increasingly important diabetes technology that has the potential to facilitate the avoidance of low glucose values. However, there is a paucity of information on admitted patients' characteristics, management, and outcomes of those admitted with hypoglycaemia despite being on CGM.
Objective
To explore the characteristics of the patient population, precipitating factors and outcomes of people admitted with hypoglycaemia while on CGM.
Methods
This retrospective study was conducted from October 2023 to January 2024 across five hospitals in the UK. All adults aged >18 years admitted to hospitals with hypoglycaemia while on CGM from November 2022 to October 2023 were included in the study. Data on sociodemographic, precipitating factors, management, outcomes and total time spent during hypoglycaemic episodes were collected. Data was analysed on SPSS 29.0.
Results
We identified 39 episodes of hypoglycaemia, with 37 occurrences in individuals with type 1 diabetes and 2 in those with type 2 diabetes. 34 episodes occurred while the person was an inpatient in the hospital. The median (interquartile) age was 49.0 (36.0-50.0) years. Their Charlson comorbidity index was 4 (4-6). 79.5% were men. The median (interquartile) HbA1c before admission was 98.0 (60.0-98.0) mmol/mol. 79.5% were level 1, 10.3% were level 2, and 10.3% were level 3 hypoglycaemia. 48.7% of episodes were due to missed meals. Patients spent 26 (16.0- 124.0) min in hypoglycaemia during these episodes. 7.7% of people received glucagon either at home, in an ambulance, or in a hospital for hypoglycaemia. However, only 5.1% were prescribed glucagon upon discharge.
Conclusion
The majority of hypoglycaemia was due to missed meals. Despite spending a median of 26 minutes in hypoglycaemia, only a small percentage received glucagon, and a mere 5.1% were prescribed glucagon upon discharge. These findings underscore the need for enhanced education and proactive management strategies for individuals on CGM to effectively prevent and address hypoglycaemic episodes, potentially improving patient outcomes and overall diabetes care.

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P458

Acute complications in diabetic patients during the month of ramadan: about 48 cases

Zaynab Hifdi[1], Soukaina Laidi[1], Saloua Elamari[1] & Marouan Fatima[1]
[1]Cheikh Khalifa Bin Zayed Al Nahyan Hospital, Casablanca, Morocco

Introduction
Diabetes, a disease on the rise worldwide, requires patients to make constant adjustments to their lifestyle. During the month of Ramadan, diabetic patients face additional challenges. The cultural practices associated with this month modify diet, sleep and physical activity, exposing patients to an increased risk of acute complications or decompensation of chronic complications. This study aims to analyze the prevalence and mechanisms of acute metabolic, cardiovascular and renal complications in diabetics during Ramadan. It also aims to propose approaches for preventing these complications.
Material and methods
We included all patients who had cardiovascular, metabolic and renal complications during Ramadan. we compared with patients who had the same complications but outside of Ramadan.
Results
We included 48 patients who had acute complications, 70% of whom during Ramadan. The study revealed that 89% of patients were at high risk of fasting during Ramadan. During this period, 51% of patients fasted, with only 3% having medical approval. Complications were more frequent during Ramadan, with 49% cardiovascular complications, 43% metabolic complications, and 8% renal complications, compared with 78%, 22%, and 0% respectively outside Ramadan.
Conclusion
Our study highlights a significantly higher prevalence of complications in diabetics during Ramadan compared with the period outside Ramadan. The results underline the importance of fasting risk stratification, therapeutic education, pre-Ramadan medical evaluation and therapeutic adjustment to prevent these complications in diabetic patients.

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Preoperative vitamin b1 levels are associated with reaching normal body mass index 1 year after bariatric surgery

Bruna Silva[1], Catarina Pereira[1], Catarina Chaves[1], Tatiana Basto[2], Catarina Gil[2], César Alvarez[2] & Filipe Cunha[1]
[1]Unidade Local de Saúde do Tâmega e Sousa, E.P.E., Endocrinology, Guilhufe, Portugal; [2]Unidade Local de Saúde do Tâmega e Sousa, E.P.E., General Surgery, Guilhufe, Portugal

Introduction
Vitamin B1 (VB1) deficiency can occur in patients with obesity and after bariatric surgery (BS). Nevertheless, pre-operative measurements of VB1 are still controversial. The relationship between serum VB1 and weight loss after BS has not been reported previously.
Objectives
To study the association between pre-operative VB1 levels and weight loss after BS.
Methods
Retrospective study of patients submitted to bariatric surgery - laparoscopic Roux-en-y gastric bypass (RyGB) or vertical gastrectomy (VG) with 1 year follow-up and a pre-operative serum VB1 measurement. The primary endpoint was reaching a body mass index (BMI) $\leq$ 25 Kg/m^2. Patients with VB1 $<$ 147 nmol/l and with VB1 $\geq$ 147 nmol/l (mean VB1 value) were compared. Multivariable logistic regression analysis models were built with variables associated with weight loss (age, sex, and type of surgery) along with additional variables added to the model one-at-a-time. The latter were those variables with different distribution between groups and with possible interference with VB1 levels and function.
Results
We analysed 98 patients. Mean VB1 levels were 147 (33) nmol/l. No patients were supplemented for VB1. Patients with VB1 levels $\geq$ 147 nmol/l had higher haemoglobin ($P=0.02$), leukocyte counts ($P=0.005$) and TSH ($P=0.05$). There were no differences observed between groups regarding age, sex, type of surgery, diabetes status, initial BMI, gamma-glutamyl transpeptidase (GGT), insulin, calcium, magnesium, zinc, folic acid, vitamin B12, albumin, or vitamin D levels. Patients with VB1 levels $\geq$ 147 nmol/l reached a BMI $\leq$25 Kg/m^2 more often 58.3% vs 36.0%, $P=0.03$, and had lower BMI at 1-year [24.2 (23.0-27.2) vs 25.8 (23.6-27.9) Kg/m^2, $P=0.06$] and higher excess BMI loss [100.9% (18.5) vs 94.5% (14.8), $P=0.06$] although not statistically significant. In the multivariate logistic regression analysis, for each 10 nmol/l increase in VB1 the OR (95% CI) for the association with the primary endpoint was 1.25 (1.07-1.46), $P=0.004$ adjusted for age, sex, and surgery type. This association was similar after additional one-at-a-time adjustments for: haemoglobin, leukocytes, calcium, magnesium, GGT, insulin, diabetes status, TSH, folic acid, vitamin B12, zinc and hepatic steatosis.
Conclusions
VB1 is associated with weight loss after BS. Per each 10 nmol/l increased the risk of reaching normal BMI 1-year after BS increased by 25%.

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P460

Polycystic ovary syndrome in type 1 diabetes mellitus: a cross-sectional study of 785 women with diabetes and 1152 controls

Sofia Toft[1], Neda Rajamand Ekberg[1], Hidaya Abdulrahim[1], Angelica Lindén Hirschberg[2] & Michael Alvarsson[1]
[1]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [2]Karolinska Institutet, Department of Women's and Children's Health, Stockholm, Sweden

Background
The prevalence of reproductive disturbances in women with Type 1 Diabetes Mellitus (T1DM) is high compared to the general population. One reason might be higher prevalence of Polycystic ovary syndrome (PCOS) in T1DM. In Sweden, with a high incidence of T1DM, the prevalence of PCOS in women with T1DM is not known. Neither is the T1DM-PCOS pathophysiology.
Aim
The aim of this cross-sectional study was to investigate the prevalence of PCOS in a Swedish T1DM population compared to population-based controls, as well as characterizing patients and controls with respect to hormonal and metabolic profile.
Method
A screening questionnaire covering medical background, gynaecological history and PCOS related symptoms was sent out to female T1DM patients of age 18-55 years in Stockholm. The questionnaire was also sent to women that were matched to the patient population by age and postal address and thus served as controls. Subjects who reported one or more symptoms related to PCOS or reported close female relatives with symptoms, were offered to participate in a clinical examination by a physician (including gynaecological examination with vaginal ultrasound, assessment of body hair by the modified Ferriman-Gallwey scale and fasting blood samples).
Results
785 women with T1DM and 1152 controls were included in the questionnaire part of the study. 40.3 % vs 29.5 % ($P<0.001$) of women with T1DM and controls, respectively, reported having at least one screening symptom. Women with T1DM reported to a greater extent oligomenorrhea (25.1 % vs 17.1 %, $P<0.001$) as well as excessive hair growth (14.9 % vs 8.7 %, $P<0.001$) compared to controls. More women with T1DM than controls reported the combination of oligomenorrhea and excessive hair growth (5.1 % vs 2.6 %, $P<0.01$). 102 women with T1DM and 97 controls were subsequently included in the clinical examination. 34.3% of women with T1DM and 22.7% of controls fulfilled the Rotterdam criteria of PCOS, OR = 1.8, ($P=0.07$). There was a higher rate of polycystic ovarian morphology in women with T1DM (45.5% vs 31.0 %, $P<0.05$) compared to controls. The rate of hyperandrogenism and oligomenorrhea was the same. When analysing PCOS positive subjects only, women with T1DM had significantly higher testosteron, SHBG, androstenedione and DHEAS compared to controls.
Conclusion
These results confirm the connection between symptoms of PCOS and T1DM, also in a Swedish population. Furthermore, in women with PCOS, hormonal deviances seem to be more pronounced in those with T1DM compared to controls.

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P461

Prognostics factors for regression from prediabetes to normoglycaemia: individual participant data meta-analysis

Najmeh Davoodian[1], Mojtaba Lotfaliany[1], Rachel Huxley[2], Crystal Lee[3], Julie Pasco[4] & Mohammadreza Mohebbi[5]
[1]IMPACT, the Institute for Mental and Physical Health and Clinical Translation, School of Medicine, Deakin University, Geelong, Australia; [2]Faculty of Health, Deakin University, Melbourne, Australia; [3]School of Population Health, Curtin University, Perth, Australia; [4]IMPACT, the Institute for Mental and Physical Health and Clinical Translation, Geelong, Australia; [5]Biostatistics Unit, Faculty of Health, Deakin University, Melbourne, Australia

Background
Prediabetes, a subclinical precursor to type 2 diabetes mellitus (T2DM) that currently affects approximately 374 million adults worldwide, is a risk factor for the development of cardiovascular disease and stroke, in addition to T2DM. Prediabetes can be reversed to normoglycemia; hence, we aimed to quantify the role of metabolic risk factors in prediabetes regression to normoglycemia.
Methods
We utilized the Obesity, Diabetes, and Cardiovascular Disease Collaboration database for our individual participant data meta-analysis. This database includes 19 prospective cohort studies involving 113,296 adults across various ethnicities and age groups. We included individuals with prediabetes with at least one follow-up in the analysis. Discrete-Time Hidden Markov Models were used to estimate hazard ratios for prognostic factors of prediabetes regression in each cohort study. These estimations were then pooled in the random-effects meta-analysis model.
Results
We included 19,255 participants with prediabetes at baseline, with a median follow-up of 9.8 years (IQR 5.8–12.3); 53% were women, with a mean age of 51 years for both sexes. Former smoking (hazard ratio 0.98, 95% CI 0.89-1.06), higher waist-to-hip ratio (0.86, 0.79-0.93), higher waist-to-height ratio (0.83, 0.75-0.92), higher value of waist circumferences (0.87, 0.71-1.06), overweight (0.88, 0.81-0.96), and obesity (0.86, 0.71-1.04), high diastolic (0.93, 0.87-0.99) and systolic (0.96, 0.91-1.01) blood pressure, low serum HDL-cholesterol (0.87, 0.81-0.92), and high serum triglycerides (0.88, 0.81-0.96) were associated with a lower likelihood of individuals with prediabetes achieving normoglycemia.
Conclusion
The role of metabolic risk factors in prediabetes regression underscores the importance of lifestyle modification in the prediabetes state, not only to reduce T2DM development but also to attain normoglycemia.

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P462

Glycemic control in patients with prediabetes acutely improves serum nlrp3 inflammasome and associated interleukins post-lifestyle modification

Hend Alfadul[1], Nasser Al-Daghri[1], Shaun Sabico[1], Malak Khattak[1] & Mario Clerici[2]
[1]Chair for Biomarkers of Chronic Diseases, King Saud University, Biochemistry, Riyadh, Saudi Arabia; [2]University of Milan, Medical-Surgery Physiopathology and Transplantation, Milano, Italy

Background
Prediabetes (PD) is a significant risk factor diabetes mellitus (DM) and as such, behavioral interventions are the primary management for PD. High blood glucose levels alter circulating NLRP3 inflammasome complex activity and correlated interleukins (ILs). There is limited data available on the activity of NLRP3 inflammasome and ILs in sera of patients with PD that may or may have not developed DM. This interventional study assessed the effects of NLRP3 inflammasome activation on DM development in PD individuals who followed a six-month behavioral intervention program.
Methods
This interventional study included 67 Saudi adults, 20 males and 47 females, (mean age = 41.9 ± 8.0 years, mean BMI = 33.15 ± 5.5 kg/m^2). Overnight-fasting serum samples were collected at baseline and at 6-month follow-up. Serum levels of NLRP3, capsase-1 and correlated ILs (IL-1α, IL-1β, IL-18, IL-33 and IL-37) were assessed using commercially available immunoassay kits at both visits.
Results
IL-1α levels significantly increased in the PD group that developed T2DM after 6 months of intervention (baseline: 0.6 (0.5–0.8), follow-up: 1.0 (0.9–1.4); $P=$ 0.046), IL-33 levels significantly decreased in the PD group that reverted to normal after 6 months of intervention (baseline: 3.2 (0.7–4.0), follow-up: 0.8 (0.6–2.1); $P<0.001$), IL-37 levels significantly decreased in the PD group that remained PD after 6 months of intervention (baseline: 4.2 (2.1–10.7), follow-up: 2.9 (2.1–2.9); $P<0.001$) and NLRP3 levels significantly decreased in the PD group that remained PD after 6 months of intervention (baseline: 0.13 (0.1–0.22), follow-up: 0.11 (0.07–0.18); $P=$ 0.01). In all participants with PD, after 6 months of intervention IL-33 levels significantly decreased (baseline: 3.2 (2.9–3.9), follow-up: 0.9 (0.6–3.0); $P=$ 0.001), IL-37 levels significantly decreased (baseline: 3.0 (2.1–8.5), follow-up: 2.9 (2.1–3.0); $P=$ 0.008) and NLRP3 levels significantly decreased (baseline: 0.1 (0.1–0.2), follow-up: 0.1 (0.1–0.2); $P=$ 0.05). Results also showed a positive overtime correlation between NLRP3 and both IL-1α ($r=$ 0.3, $P=$ 0.001) and IL-33 ($r=$ 0.03, $P=$ 0.028).
Conclusion
Glycemic control positively changed NLRP3 inflammasome complex activation post-behavioral intervention program in PD individuals and this maybe pivotal in reversing the detrimental metabolic and pro-inflammatory states.
Keywords: prediabetes, type 2 diabetes mellitus, lifestyle interventions, NLRP3, inflammasome, interleukins, inflammatory disease, chronic inflammation

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P463

Relationship between the levels of asprosin, interleukin-6 and adiponectin in patients with type 2 diabetes mellitus with or without chronic pancreatitis

Larysa Zhuravlyova[1], Mykyta Markevych[1] & Vladyslav Kaliuzhka[2]
[1]Kharkiv National Medical University, Department of Internal Medicine No.3 and Endocrinology, Kharkiv, Ukraine; [2]Kharkiv National Medical University, Department of Neurosurgery, Kharkiv, Ukraine

Background
Asprosin is a recently discovered hormone that plays a role in regulating glucose homeostasis and energy metabolism. It is produced in white adipose tissue and released into the bloodstream in response to fasting, stimulating the liver to produce glucose. Interleukin-6 (IL-6), a pro-inflammatory cytokine, is known to contribute to the chronic low-grade inflammation seen in obesity and type 2 diabetes mellitus (T2DM). It also plays a role in insulin resistance and impaired glucose metabolism. Adiponectin, on the other hand, is an adipokine with anti-inflammatory and insulin-sensitizing properties. Investigating the complex interactions and correlations among asprosin, IL-6, and adiponectin can deepen our understanding of the mechanisms contributing to insulin resistance and hyperglycemia in T2DM. This in turn may lead to the development of more targeted and effective therapeutic strategies for managing the condition.
Methods
A total of 75 patients (28 males and 47 females with a mean age of 54.4 ± 7.5 years) with T2DM were recruited at the Department of Endocrinology of Kharkiv Regional Hospital. Chronic pancreatitis (CP) was diagnosed in 42 T2DM patients. IL-6, adiponectin and asprosin levels in blood serum were measured in all the study subjects by enzyme-linked immunosorbent assay.
Results
Our findings revealed a significant positive correlation between asprosin and IL-6 levels in patients with T2DM, both with and without CP. Additionally, we observed a negative correlation between adiponectin levels and both asprosin and IL-6 levels in patients with T2DM, with and without CP. Patients with CP showed significantly higher asprosin levels than those without CP ($P<$0,001).
Conclusions
These results suggest that there may be a potential interplay between asprosin, IL-6, and adiponectin in the context of T2DM and CP. Further studies are needed to elucidate the exact mechanisms underlying this correlation and to explore the potential therapeutic implications of targeting these molecules in the management of T2DM with and without CP.

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P464

Combined dulaglutide-dapagliflozin treatment improves vascular dysfunction and albuminuria vs DPP4 inhibitors independently of glycaemic control

Emmanouil Korakas[1], Ignatios Ikonomidis[2], John Thymis[2], Aikaterini Kountouri[1], Loukia Pliouta[1], Konstantinos Katogiannis[2], Dimitris Benas[2], Konstantinos Balampanis[1], Vasiliki Prentza[1], Foteini Kousathana[1], Gavriela Kostelli[2], George Dimitriadis[3], Athanasios Raptis[1] & Vaia Lambadiari[1]
[1]Attikon University Hospital, Second Department of Internal Medicine, Chaidari, Greece; [2]Attikon University Hospital, Second Cardiology Department, Chaidari, Greece; [3]Sector of Medicine, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Background
The association between diabetes mellitus and diabetic nephropathy with vascular and endothelial properties is well-established. In this study, we compared the effect of combined treatment with dulaglutide and dapagliflozin versus DPP-4 inhibitors on endothelial glycocalyx, arterial stiffness, myocardial function and albuminuria in patients with type 2 diabetes mellitus and albuminuria.
Methods
A total of 60 patients with type 2 diabetes mellitus and albuminuria were randomized to combined dulaglutide and dapagliflozin treatment ($n=30$) or DPP-4 inhibitors (DPP-4is, ($n=30$). We measured at baseline and 4 and 12 months posttreatment: (a) perfused boundary region of the sublingual arterial microvessels (marker of endothelial glycocalyx thickness), (b) pulse wave velocity (PWV) and central systolic blood pressure (cSBP), (c) global left ventricular longitudinal strain (GLS) (d) urine albumin-to-creatinine ratio (UACR).
Results
Twelve months posttreatment, the combination of dulaglutide and dapagliflozin showed a greater improvement in all indices compared to DPP-4is, despite a similar reduction in glycosylated hemoglobin. Specifically, dual therapy showed greater improvements vs DPP-4is in PBR (2.10 ± 0.31 to 1.93 ± 0,23 μm vs 2.11 ± 0.31 to 2.08 ± 0.28 μm, $P<0.001$), in UACR (326 ± 61 to 142 ± 47 mg/g vs 345 ± 48 to 306 ± 60 mg/g, $P<0.01$), and in PWV (11.77 ± 2.37 to 10.7 ± 2.29 m/s vs 10.64 ± 2.44 to 10.54 ± 2.84 m/s, $P<0.001$), while only dual therapy showed improvement in cSBP (130.21 ± 17.23 to 123.36 ± 18.42 mmHg). Regarding GLS, both treatments were effective, but dual therapy showed a significantly higher percentage improvement compared to DPP-4is (18.19% vs 6.01%, respectively).
Conclusions
Twelve-month treatment with dulaglutide and dapagliflozin showed a greater improvement in vascular markers an albuminuria than DPP-4is in patients with type 2 diabetes mellitus and albuminuria. Early initiation of combined therapy as add-on to metformin should be considered in these patients.

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P465

PDE4 inhibition attenuates non-alcoholic fatty liver disease by increasing vldl secretion in obese animals

Hellen da Silva[1], Maria Amélia Montenegro[1], Juliana Gebenlian[2], José Antunes Rodrigues[2,2], Francisco de Paula[1,1] & Lucila Elias[2]
[1]University of Sao Paulo, Internal Medicine, Ribeirao Preto, Brazil; [2]University of Sao Paulo, Physiology, Ribeirao Preto, Brazil

Non-alcoholic fatty liver disease (NAFLD) is characterized by the pathological increase of lipid droplets, altered fat metabolism in hepatocytes and increased inflammation. Phosphodiesterase 4 (PDE4) modulates the inflammatory responses and its inhibitor can strongly reduce TNF-α release and inflammation. Additionally, PDE4 knockout mice were shown to be resistant to diet-induced obesity (DIO). The aim of this study was to investigate the role of pharmacological PDE4 inhibition in the NAFLD phenotype in DIO. To attain this purpose, obese mice were treated with rolipram, a PDE4 inhibitor. All experimental protocols were approved by the Ethics Committee for Animal Use of the Ribeirao Preto Medical School. Male C57Bl6 mice were fed with either chow or high-fat diet (HFD; 60% fat) for 12 weeks and in the 10th week they received daily subcutaneous injections of vehicle (VEH) or rolipram (2 mg/kg). Food intake and body weight were monitored and at the end of the study inguinal, retroperitoneal and brown fat pads were collected for analysis. Rolipram decreased the absolute value and change in body weight and energy intake in the HFD group, which was associated with a decrease in epididymal and retroperitoneal fat pad weight, with no effect in the chow group. Remarkably, PDE4 inhibition decreased liver triglycerides in obese animals and this effect was associated with increased noradrenaline content. Consistent with these results, histological analysis showed that rolipram decreased lipid accumulation in hepatocytes. No changes were found in plasma cholesterol, free fatty acids or triglycerides in the rolipram group compared to vehicle. In contrast, PDE4 inhibition increased PGC1-a and PPARa expression while it decreased Elov3 and MCP-1. To verify whether this effect persists regardless of change in the body weight, we fed animals with a HFD for 3 days and assessed the *in vivo* VLDL secretion by inhibiting the lipoprotein lipase enzyme in animals that received acute rolipram injection. PDE4 inhibition increased VLDL secretion in HFD-treated animals, but not in chow animals. In addition, this was associated with increased CD36 and EPAC content in the liver. These results indicate that PDE4 appears to play a role in the pathogenesis of NAFLD and reinforce PDE4 as a potential target for the treatment of obesity-associated liver disease.

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P466

Impact of simulation via instant messaging –birmingham advance (SIMBA) on clinician's confidence to manage type 1 diabetes mellitus using technological advances in endocrinology

Pavithra Sakthivel[1], Anisah Ali[1], Sangamithra Ravi[1], Rachel Shepherd[1], Abby Radcliffe[1], Rahul Sagu[1], Harshin Pallathoor Balakrishnan[2], Sumaya Najeem[2], Neelamabraprasad Goznee[2], Vyshnavi ND[2], Tamzin Ogiliev[3], Punith Kempegowda[4,5] & Simba & Comics Team[4]
[1]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom; [2]Far Eastern Federal University, School of Medicine, Vladivostok, Russian Federation; [3]Lancaster University Medical School, Lancatser, United Kingdom; [4]University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, United Kingdom; [5]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

Introduction
Various technological advances have infiltrated modern clinical practice. This is especially true for the management of type 1 diabetes mellitus (T1DM). User-friendly and convenient smartphone applications like Dexcom and Freestyle Libre have positively contributed towards the control and monitoring of diabetes for patients across the globe. Simulation via Instant Messaging –Birmingham Advance (SIMBA) conducted a virtual training session for clinicians in managing T1DM using these systems.
Aim
To improve healthcare professionals' (HCPs) knowledge and confidence in managing patients with T1DM using technological advances.
Methods
Anonymised case transcripts were created based on real-life clinical scenarios involving the management of T1DM using Freestyle Libre and Dexcom G6. They were used to train moderators, who then virtually simulated these cases with participants via WhatsApp. Clinicians' approach to each case was scored by moderators using a modified global rating scale to consider aspects including interpretation of relevant investigations and proposing an appropriate management plan. The simulation was followed by a discussion session led by a topic expert, delving into the key learning points from each case. Participants completed pre- and post-simulation surveys. Quantitative and thematic analysis of HCPs' perspectives and experience of the session was conducted.
Results
A total of 21 HCPs participated in the session, 95.2% of whom were based in the United Kingdom. Participants' self-reported confidence in using Freestyle Libre and Dexcom G6 improved from 66.7% and 33.3% to 90.5% ($P=0.0143$) and 76.2% ($P=0.0009$), respectively, following the simulation. 95.2% of participants agreed that the simulated topics applied to their clinical practice and reported that the simulation training had a positive influence on their knowledge of patient management and care provision. HCPs also believed the session improved their professionalism (52.4%), practice-based learning (76.1%) and communication skills (23.8%). Additionally, the simulation was considered impactful on a personal and professional level by 81% and 76.2%. Thematic analysis revealed that participants were more confident in offering continuous glucose monitoring (CGM) to their patients and interpreting data produced by CGM applications. Participants also gained awareness of non-medical aspects, such as the availability of educational programmes surrounding the use of technology to empower patients with T1DM.
Conclusion
SIMBA is an evidence-based educational programme that has improved HCPs' knowledge of utilising technological advancements in the management of patients with T1DM, thereby encouraging them to offer these tools to more patients and lead to better outcomes.

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P467

Transcriptome of periadrenal and subcutaneous fat in patients with hyperaldosteronism in comparison to patients with non-functional adenomas

Ulrich Dischinger[1], Christian G Ziegler[1], Lisa Kagan[1], Simon J Kloock[1], Mugdha Srivastava[2], Nada Rayes[3], Matthias Blüher[4] & Martin Fassnacht[1]
[1]University Hospital Würzburg, Division of Endocrinology and Diabetes, Würzburg, Germany; [2]University of Würzburg, Core Unit Systems Medicine, Würzburg, Germany; [3]University Hospital Leipzig, Department of Surgery, Leipzig, Germany; [4]University Hospital Leipzig, Department of Internal Medicine, Leipzig, Germany

Background
The crosstalk between the adrenal gland and different fat depots is largely unknown. As primary hyperaldosteronism leads to an increased risk of cardiovascular disease and associated pathologies (glucose intolerance, diabetes, hyperlipidemia), elucidating the interaction between aldosterone producing adenomas (APAs) and different fat depots might help to understand causality and open new diagnostic and treatment strategies.
Methods
Subcutaneous (s.c.) and periadrenal fat was collected from patients with APA (s.c. $n=13$, periadrenal, $n=20$) and, as controls, from non-functional adenomas (NFA, s.c. $n=7$, periadrenal $n=5$). mRNA was extracted from the samples and RNA sequencing was performed. Patients' characteristics were collected.
Results
RNA sequencing revealed a high number of differentially regulated genes in s.c. fat samples of patients with APA vs NFA ($n=$ 68 up, $n=259$ down), in periadrenal samples of patients with APA vs NFA ($n=$ 16 up, $n=117$ down), and in periadrenal vs s.c. samples of patients with APA ($n=$ 1632 up, $n=826$ down). Pathway analysis revealed (amongst others):
- an upregulation of the pathways 'Cushing syndrome' (enrichment score (ES) 0.6), 'aldosterone synthesis and secretion' (ES 0.6) and 'cortisol synthesis and secretion' (ES 0.7) in APA periadrenal vs APA s.c..
- an upregulation of the pathways 'steroid hormone biosynthesis' (ES 0.5), 'Cushing syndrome' (ES 0.4) and 'cortisol synthesis and secretion' (ES 0.6) in APA periadrenal vs NFA periadrenal.
- an upregulation of the pathways 'steroid hormone biosynthesis' (ES 0.5), and a downregulation of 'cortisol synthesis and secretion' (ES -0.6) and 'aldosterone synthesis and secretion' (ES -0.5) in APA s.c. vs NFA s.c.
Conclusion
RNA sequencing revealed a high number of differentially regulated pathways and genes in s.c. and periadrenal fat depots of patients with APA in comparison to patients with NFA. The findings point towards strong paracrine effects of APAs. Detected differences in subcutaneous fat might open new diagnostic strategies for hyperaldosteronism.

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P468

Weaning timing impact on adipose tissue remodelling in mice

Damien Dufour[1], Sandra Bryne[2], Philippe Collas[1], Boccara Charlotte[2] & Nolwenn Briand[1]
[1]Institute of Basic Medical Sciences, University of Oslo, Department of Molecular Medicine, Oslo, Norway; [2]Centre for Molecular Medicine Norway, Oslo, Norway

The adipose tissue is an endocrine organ distributed over multiple depots and broadly categorised into two main subtypes: white adipose tissue which stores energy as lipids and brown adipose tissue which dissipates energy in the form of heat. Adipocytes from the white depots are able to switch from a white to a brown-like phenotype, a process called beiging. This phenomenon is stimulated by cold exposure or sympathetic nervous system activation and is associated with improved metabolic health. Weaning, defined as the switch from milk to solid diet is a crucial developmental period. In mice, pups start feeding on pellets as soon as 15 days of age and stop breastfeeding around 28 days of age. Dietary alterations or overfeeding of lactating mother have long-term effects on the metabolism of offspring in both rodents and humans. To understand how weaning affects the adipose tissue in mice, we have analysed the kinetics of adipose tissue remodelling between 21 days of age (P21) and 35 days of age (P35). We have harvested the visceral perigonadal white adipose tissue (gWAT), the subcutaneous inguinal white adipose tissue (iWAT) and the interscapular brown adipose tissue (BAT) at P21, P28 and P35. Between P21 and P35, mice are accumulating WAT while BAT mass remains constant. This process is accompanied by a decrease in the proportion of beige adipocytes, and a reduced innervation and vascularisation density. We next used a model a weaning retardation whereby after 21 days of lactation (P21), four pups from the litter are kept with the dam until P28 (delayed weaning, DW) while the rest of the pups are separated (standard weaning, SW). At P28, DW mice show a decreased body mass but with a higher proportion of fat mass compared to SW controls. Indeed, iWAT mass is increased in the DW condition. Interestingly, at P56, SW mice have higher body mass and adiposity. Finally, delayed weaning induces an increase in the cutaneous temperature of male offspring only, reaching a temperature close to that of females. These results highlight the importance of the weaning period for the development of adipose tissue. Sexually dimorphic phenotypes and the uncorrelated increase in body and fat masses upon delayed weaning suggest an involvement of sexual hormones that will be further investigated.

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P469

Implication of metabolically healthy obesity on the risk of incident pancreatic cancer: a nationwide population-based cohort study

Hye Soo Chung[1]
[1]Hallym University, Internal Medicine, Korea, Rep. of South

Background
Lately, a few studies have showed different results regarding the relationship between metabolically healthy obesity and various cancers. We investigated the impact of metabolically healthy obesity on pancreatic cancer using a nationwide population-based cohort database.
Methods
Using the Korean National Health Insurance Service–Health Screening Cohort, we enrolled 347,434 Korean adults who underwent a health examination between 2009 and 2010 and were followed until 2015. This population was divided into four groups based on metabolically healthy status and body mass index: metabolically healthy normal weight, metabolically unhealthy normal weight, metabolically healthy obese, and metabolically unhealthy obese.
Results
During a median follow-up of 6.1 years, pancreatic cancer occurred in 886 individuals. The adjusted HRs for incident pancreatic cancer were 1.52 [95% confidence interval (CI) 1.27–1.81] and 1.34 (95% CI, 1.12–1.61) for the metabolically unhealthy normal weight and metabolically unhealthy obese phenotypes compared with the metabolically healthy normal weight phenotype after adjusting for several confounding factors. However, the metabolically healthy obese phenotype did not show an elevated risk of pancreatic cancer compared with the metabolically healthy normal weight phenotype. Moreover, the HR for pancreatic cancer gradually increased with an increase in number of metabolically unhealthy components, even after adjusting for body mass index (P trend <0.001).
Conclusions
Regardless of body mass index, metabolically unhealthy phenotype demonstrated significantly increased risk of pancreatic cancer, whereas obese individuals with metabolically healthy phenotype did not.

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P470

Visceral fat lipolysis using high-dose multichannel non-ablative energy-based device: anthropometric, biochemical and imaging mri study

Jesús Rodríguez Lastra[1]
[1]UAX, Physioterapy, Madrid, Spain

Objectives
Energy-based devices (EBD) have been used as a treatment for abdominal obesity, although its effects on visceral fat are not well known.
Methods
Twenty patients with abdominal obesity were treated with EBD (10 sessions of 60 minutes, and 20 minutes with capacitive and resistive electrodes temperature 45 ° C). We analysed anthropometric changes; visceral and subcutaneous fat was quantified by magnetic resonance imaging and blood samples were taken at the beginning and end of treatment.
Results
at the end of the treatment period, patients significantly reduced waist circumference, systolic blood pressure levels and visceral and subcutaneous fat mass ($P<0.05$). In addition, leptin levels, basal insulinemia and HOMA-IR index ($P<0.05$) were also reduced. No adverse effects were reported.
Discussion
The results present a window into the possibility of reducing visceral fat with improved metabolism. The follow-up of a patient who has attended re-evaluation shows that the effects are maintained over time.
Conclusions
EBD is a safe and effective method to reduce subcutaneous and visceral fat in abdominal obesity, with the consequent improvement of the metabolic profile. This can be a novel and non-harmful tool to reduce abdominal fat. Opening a new perspective for the treatment of obesity

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P471

Subgroup analysis of phase 3 study of fixed-dose combination of dapagliflozin, glimepiride and metformin IR in type 2 diabetes mellitus patients with HbA1c 9%-11%

Prakash Kurmi[1], Manish Singh[2], Vishal Gupta[3], Chikkalingaiah Siddegowda[4], Jitendra Shukla[5], Sandip Gofne[6], Nilesh Lomte[7], Kaustubh Shendkar[8], Dinesh Gangwani[9], Surendra Kumar[10], Sandeep Gupta[11], Aravind G Nagarajaiah[12], Amit Bhaskar[13], Prabhat Sharma[14], Arjun Baidya[15], Animesh Maiti[16], Ambana Gowda[17], Jayesh Ambaliya[18], Balachandra Giriappa K[19], Sunil Mahavar[20], Hemant Gupta[21], Dr Mandodari Rajurkar[22], Supriya Sonowal[22], Piyush Patel[23], Dipak Patil[22], Lalit Lakhwani[23], Pravin Ghadge[22], Suyog Mehta[24] & Sadhna Joglekar[25]
[1]Shivam Hospital, Mumbai, India; [2]Maya Hospital & Maternity Centre, Department of General Medicine, Kanpur, India; [3]GSVM Medical College, Department of Medicine, Kanpur, India; [4]Medstar Speciality Hospital, Bangalore, India; [5]Moti lal Nehru Medical College, Department of Medicine, Prayagraj, India; [6]District Civil Hospital, Aurangabad, India; [7]Hormone Care, Aurangabad, India; [8]Global Hospital and Research Institute, Department of Diabetology, Pune, India; [9]Priyadarshini Nursing Home, Mumbai, India; [10]S. P. Medical College & A.G of Hospitals, Department of medicine, Bikaner, India; [11]M.V. Hospitals and Research Center, Department of Medicine, Lucknow, India; [12]Victoria Hospital, Department of General Medicine, Bangalore, India; [13]Janta Hospital, Varanasi, India; [14]Maharaja Agrasen superspeciality Hospital, Department of General Medicine, Jaipur, India; [15]Nilratan Sircar Medical College and Hospital, Kolkata, India; [16]Medical College and Hospital, Kolkata, India; [17]Citizen hospital, Bangalore, India; [18]Pagarav Hospital & ICU, Department of Medicine, Gandhinagar, India; [19]BGS Global Institute of Medical Sciences, Department of General Medicine, Bangalore, India; [20]SMS hospital, Department of Medicine, Jaipur, India; [21]Grant Govt. Medical College and Sir J. J. Group of Hospital, Department of Internal Medicine, Mumbai, India; [22]Sun Pharma Laboratories Limited, India Clinical Research, Mumbai, India; [23]Ex Sun Pharma Laboratories Limited, India Clinical Research, Mumbai, India; [24]Sun Pharma Laboratories Limited, Medical Affairs & Clinical Research, Mumbai, India; [25]Ex Sun Pharmaceutical Industries Limited, Ex Senior Vice President- Medical Affairs and India Clinical Research, Mumbai, India

Background and Objective
Fixed-dose combination (FDC) of dapagliflozin + metformin + sulfonylurea with complementary mechanisms can provide effective glycaemic control, preserve beta-cell function, improved compliance without risk of weight gain, and reno-protective action in type 2 diabetes mellitus (T2DM) patients. This subgroup analysis aimed to assess efficacy and safety of triple-drug FDC versus (vs) two-drug combination in T2DM Indian patients with HbA1c 9%-11%.
Method
This subgroup analysis of phase 3, open-label, four-arm, active-controlled study (CTRI/2022/06/043249) included T2DM patients (glycated haemoglobin [HbA1c] 9%-11%) taking metformin 1000 mg 2000 mg/day and glimepiride 2 mg/day at screening). Patients received FDC of dapagliflozin + glimepiride + metformin IR tablet twice-daily (BID) (5 mg + 1 mg + 500 mg [test arm 1]/5

mg + 1 mg + 1000 mg [test arm 2]) OR co administration of glimepiride tablet + metformin IR BID (1 mg + 1 tablet of 500 mg [comparator arm 1]/1 mg + 2 tablets of 500 mg [comparator arm 2]) for 16 weeks. Post Week 16, up-titrated dose of glimepiride (2 mg) in respective treatments was provided to patients with HbA1c $\geq$ 7% in each arm. In this subgroup analysis, change from Baseline in HbA1c, fasting blood glucose (FBG) and post prandial blood glucose (PPBG) till Week 28 and safety parameters were assessed.
Results
This subgroup analysis included 251 patients (58 patients [test arm 1], 67 patients [comparator arm 1], 63 patients each in test arm 2 and comparator arm 2, respectively). Demographic and baseline characteristics were comparable across all arms. Adjusted mean (SE) reduction in HbA1c was statistically significant from Baseline to Week 16 in test arm 1 [-2.15% (0.09%)] vs comparator arm 1 [-1.42% (0.09%)] with difference of 0.73% ($P<0.0001$) and adjusted mean (SE) reduction in HbA1c was statistically significant from Baseline to Week 16 in test arm 2 [-2.06% (0.09%)] vs comparator arm 2 [1.44% (0.09%)], with difference of 0.62% ($P<0.0001$). Similarly, statistically significant reduction in HbA1c was observed at Weeks 8 and 12. Proportion of patients achieving HbA1c $<$ 7% was significantly higher in test arm 1 vs comparator arm 1 (52.7% vs 29.7%, $P=0.0106$) and in test arm 2 vs comparator arm 2 (61.9% vs 43.5%, $P=0.0398$), respectively at Week 16. Significant reduction in HbA1c, FBG and PPBG was observed from Baseline to Weeks 12, 16, and 28 in each arm. None of the patients reported serious adverse events/hypoglycaemia or required rescue medication.
Conclusion
In this subgroup analysis of patients with HbA1c 9%-11%, triple FDCs of dapagliflozin + glimepiride + metformin IR tablets showed statistically significant reduction in HbA1c from Baseline to Weeks 8, 12, 16 as compared to two-drug combination. Both treatments were well tolerated.

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How does neuropathic pain affect sleep quality in adults with type 2 diabetes ?

Sana Khamassi[1], Emna Bornaz[1], Haifa Abdesselem[1], Dorra Ben salem[1], Kamilia Ounaissa[1] & Chiraz Amrouche[1]
[1]National Institute of Nutrition, Outpatient Department and Functional Explorations, Tunis, Tunisia

Introduction
Diabetic peripheral neuropathy (DPN) is one of the most common and early manifested complication in adults with type 2 diabetes leading to severe repercussions including foot ulcers, amputations and chronic pain. Furthermore painful diabetic neuropathy can also negatively impact a wide range of key human physiological processes including sleep disturbance [1]. The aim of our study was to determine the effect of neuropathic pain on sleep component.
Materials
This is a cross-sectional study conducted in 100 patients with diabetes. The DN4 questionnaire was used to identify neuropathic pain. Sleep quality was evaluated using the Pittsburgh sleep quality index (PSQI) in its arabic-validated version [2]. It consists of 19 items grouped into seven subscales: self-reported sleep quality (C1), sleep latency (C2), sleep duration (C3), habitual sleep efficiency (4), sleep disturbance (C5), use of sleep medications (C6), and daytime dysfunction (C7). Higher scores in each dimension indicate poorer quality and the sum of components provides a global PSQI score. Scores $>$5 defined poor quality sleepers.
Results
Mean age was 54.45 $\pm$ 7.13 years with a sex ratio (F/M) of 2.57. Mean diabetes duration was 12.67 $\pm$ 7.35 years. Mean BMI was 29.49 $\pm$ 4.97 Kg/m^2, 32% of our patients were overweight and 49% were obese. Mean glycated hemoglobin and mean fast blood glucose were respectively 9.69 $\pm$ 2.02 % and 11.63 $\pm$ 4.80 mmol/l. More than half of our population was insulin-dependent (79%) and only 20% reported hypoglycemia. Peripheral neuropathy was found in 27 % of our sample. Eighteen percent among these patients were treated with pregabalin. Mean DN4 score was 1.82 $\pm$ 1.65 with extremes ranging from 0 to 6. The mean PSQI score was 7.89 $\pm$ 3.69 and 69% of our patients had poor sleep quality. Poor quality sleepers had higher DN4 scores (2.06 $\pm$ 1.74 vs 1.17 $\pm$ 1.21; $P=0.017$). When analyzing sleep components, DN4 score showed correlations with sleep efficiency ($P=0.031$; r = 0.227) and sleep disturbance ($P=0.027$; r = 0.232).
Conclusion
The findings from our study validate earlier research in the literature, highlighting the impact of neuropathy on sleep quality in individuals with diabetes, further exacerbating the impact of this complication.
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The association between serum cholecalciferol level and lipid profile in patients with latent autoimmune diabetes in adults

Iryna Tsaryk[1] & Nataliia Pashkovska[2]
[1]Ukraine, Department of Clinical Immunology, Allergology and Endocrinology, Chernivtsi, Ukraine; [2]Ukraine, Clinical Immunology, Allergology and Endocrinology, Chernivtsi, Ukraine

Introduction
The effect of cholecalciferol on regulation of the lipid profile is one of the proposed mechanisms for the relationship between cholecalciferol deficiency and cardiovascular diseases in patients with diabetes mellitus.
The aim of the study
To evaluate the dependence between cholecalciferol status and dyslipidemia in patients with different phenotypes of latent autoimmune diabetes in adults (LADA).
Material and methods
42 patients with LADA (19 –LADA1, 23 –LADA2) and 25 practically healthy individuals were examined. Lipidogram data (total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG) and cholecalciferol status were evaluated.
Results
Cholecalciferol level was registered 2.7 times lower in LADA1 group compared to control (14.63 [13.14; 15.98] ng/ml vs 40.00 [32.17; 53.00] ng/ml) and by 38.7% in LADA2 (24.51 [17.86; 32.93] ng/ml vs 40.00 [32.17; 53.00] ng/ml) ($P<0.001$). In LADA1 patients the level of cholecalciferol was lower by 40.3% ($p < 0.01$) compared to LADA2. The level of TC was 5.32 [4.83; 6.09] mmol/l in LADA1 and 5.23 [4.60; 6.10] mmol/l in LADA2 and probably differed between LADA1/control and LADA2/control (increase by 20.9% ($P<0.001$) and 18.9%, respectively ($P<0.001$)) without intergroup difference. The level of LDL-C was the highest in LADA2: by 74.2% compared with control and twice compared with LADA1 ($P<0.001$) and was 4.46 [3.99; 4.90] mmol/l; the level of HDL-C was 1.50 [1.15; 1.92] mmol/l and 1.05 [0.92; 1.13] mmol/l in LADA1 and LADA2, respectively, and was probably 19.8% lower in LADA1 ($P<0.05$) and by 43.9% in LADA2 ($P<0.001$) compared with control group, while in LADA1 the rate was 42.9% higher compared with LADA2 ($P<0.01$). The level of TG was significantly higher in patients with LADA1 and LADA2 by 84% and 48.1%, respectively, compared with the control group ($P<0.05$ and $P<0.01$, respectively) and did not differ significantly between LADA phenotypes, in the control group it was 0.81 [0.60; 1.10] mmol/l. In patients with the LADA1 phenotype, negative correlations of medium strength were recorded between TC and C-peptide level ($r=-0.562$; $p < 0.05$); LDL-C and cholecalciferol ($r=-0.533$; $P<0.05$); TG and IA-2 ab titers ($r=-0.618$; $P<0.05$). In LADA2, direct correlations of medium strength were registered between the HDL-C and cholecalciferol level ($r=0.682$; $P<0.05$); inverse correlations of medium strength –between LDL-C indicators and IA-2 ab titers ($r=-0.500$; $p < 0.05$).
Conclusions
Level of HDL-C is lower in patients with LADA2 phenotype as well as LDL-C is two times higher compare to LADA1 group. Lipid profile depends on cholecalciferol status, which indicates the importance of its adequate supplementation in patients with LADA.

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Relation of diabetic peripheral neuropathy and vitamin d deficiency

Ergita Nelaj[1], Irida Kecaj[1], Kei Xhixhabesi[1], Blerta Nikolla[1] & Margarita Gjata[1]
[1]University Hospital Center, Internal Medicine, Tirana, Albania

Introduction
Diabetic Peripheral Neuropathy (DPN) is a common complication of diabetes mellitus, which seriously affect patients' lives. Vitamin D deficiency is linked to the presence of inflammation and hyperglycemia, so it could be considered as a high risk factor for DPN. In this study we evaluated vitamin D level in diabetic patients and the association between vitamin D level and occurrence of diabetic neuropathy.

Materials and methods
Our study compressed 64 patients with type 2 diabetes mellitus, not supplemented with vitamin D, divided into 3 groups: 20 diabetic patients (10 males and 10 females) with painful DPN, 20 patients (10 males and 9 females) with painless DPN and 24 patients (10 males and 14 females) without DNP (with normal nerve conduction study).
Results
The average age of our patients was 57.04 years ± 11.05. 43.4% of patients were hypertensive; 27.8% had dyslipidemia; the mean BMI was 27.29 ± 6.24 Kg/m^2. The average duration of diabetes was 08.78 years. The mean level of 25 OH vitamin D in first group was lower than in second and third group; respectively 13.24 ± 5.19 vs 16.37 ± 6.75 ng/ml vs 19.23 ± 4.52 ng/ml. There was highly statistically significant difference between the three groups regarding vitamin D level. There is a significant negative correlation between vitamin D level and score of neuropathy where the lower vitamin D level, the higher neuropathy score ($P = 0.003$). No significance for age or duration of diabetes progression.
Conclusion
Vitamin D deficiency is common in diabetic subjects with peripheral neuropathy, mainly in the painful subtype. So, we recommended assessment of vitamin D levels in all diabetic patients as correction of vitamin D deficiency may delay the development of all subtypes DPN.

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Ultrasound diagnosis of diabetic nephropathy

Rostyslav Bubnov[1,2]
[1]Zabolotny Institute of Microbiology and Virology, NAS of Ukraine, Kyiv, Ukraine; [2]Clinical hospital ' Pheophania' , Ultrasound, Kyiv, Ukraine

Background
Diabetic nephropathy (DN) is a common complication of diabetes mellitus (DM), impacting the kidneys. Ultrasound serves as a valuable tool for evaluating manifestations of metabolic syndrome and nephropathy [1-3]. This study aims to investigate the efficacy of ultrasound (US) as a predictive diagnostic tool for identifying specific variants of nephropathy in patients with DM.
Methods
Thirty individuals with diabetes (age 38-76, 18 females) requiring medication for glucose control were compared with 30 age-matched controls (equal gender distribution). All participants underwent general clinical and laboratory tests. Abdominal US with convex 2-10 MHz probes was performed, including multiparameter US of the kidneys, utilizing Doppler, shear wave elastography (SWE), and measurement of fat accumulations, including visceral fat (VF) and subcutaneous fat (SF) thickness and areas [1].
Results
The resistive index (RI) in segmental renal arteries exhibited a significant increase ($P < 0.05$) in individuals with DM (0.77 vs 0.66) and correlated with higher glucose levels, insulin usage, and a history of multiorgan complications in DM. Diabetic nephropathy manifested as thinner parenchyma, smooth contours, and mild size reduction. Multiparameter US revealed increased visceral fat and various abnormalities, with distinct patterns linked to metabolic syndrome constituents. SWE showed a moderate increase in parenchyma stiffness (6.7 kPa vs 4.6 kPa, $P < 0.05$).
Conclusion
Multiparameter ultrasound is effective in detecting and distinguishing kidney disease patterns in DM. It provides valuable information for differentiation, modifying treatment approaches, and targeted prevention. The study underscores the significance of US in assessing diabetic nephropathy, offering additional insights into its manifestations.
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Risk factors and surgical outcomes of diabetic foot in patients with diabetes at larribere clinic in oran university hospital

Mohamed Samir Merad[1] & Fatiha Mohammedi[1]
[1]Oran 1 Ahmed Ben Bella Medical University, Endocrinology and Diabetology department -Larribere Clinic-University Hospital Dr Benzerdjeb, Oran, Algeria

Introduction
Lower limb amputation is associated with high morbidity and mortality. As a middle-income country, we are particularly vulnerable to diabetes-related problems. The aim of this study is to identify significant risk factors for amputations.
Materials and methods
This is a prospective descriptive study conducted from June 2020 to June 2022 on 102 patients hospitalized for diabetic foot at the Endocrinology-Diabetology Department of Oran University Hospital. The patients were divided into two categories according to the outcome: amputation or non-amputation. To identify the risk factors, we performed a bivariate analysis using SPSS 20 to compare the two groups.
Results
The study included 102 diabetes patients (50 men and 52 women) with a mean age of 63 ± 1 year. Of the 102 patients, 58 (56.9%) had undergone an amputation. Univariate analysis identified insulin therapy prior to admission (OR = 8.2, CI [1.7–40]; $P = 0.003$), dry gangrene lesion (OR = 8.6, CI [3.4–21.7]; $P = 0.000001$), and osteitis (OR = 4; CI [1.5–10.5]; $P = 0.004$) as risk variables. The study found significant associations between HbA1c levels and several complications, including retinopathy (OR = 3.5; CI [1.5-8.1]; $P = 0.004$), macroangiopathic complications (OR = 2.7 CI [1.1-6.7]; $P = 0.032$), peripheral neuropathy (OR = 3.3 CI [1.4-7.8]; $P = 0.007$), and arterial stenosis (OR = 6.6 CI [2-21]; $P = 0.001$). Independent predictive markers were male gender, prevalence of neuropathy, and hospital stay longer than 33.5 days.
Conclusion
Identifying risk factors for amputation is crucial to offering effective preventative strategies based on patient and caregiver education and early diagnosis of lesions.

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Mitochondrial diabetes and m.3243A > G mutation in MTL1 gene: MIDD/MELAS syndrome

Panagiota Christou[1], Maria Christou[1], Christos Zisidis[1], Athanasios Siolos[1], Ioanna Bouba[2], Eleni Bagli[3], Andreas Katsanos[3], Ioannis Georgiou[2] & Stelios Tigas[1]
[1]University Hospital of Ioannina, Department of Endocrinology, Ioannina, Greece; [2]University of Ioannina, Laboratory of Medical Genetics, Ioannina, Greece; [3]University Hospital of Ioannina, Department of Ophthalmology, Ioannina, Greece

Introduction/Aim
MIDD (maternally inherited diabetes and deafness) and MELAS (mitochondrial encephalomyopathy, lactic acidosis, stroke-like episodes) are rare, maternally inherited, multisystem disorders caused by mitochondrial DNA mutations. We present the case of a patient with mitochondrial diabetes and discuss the diagnostic challenges.
Case presentation
A 25-year-old female patient with a 7-year history of diabetes mellitus (DM) and suboptimal glycemic control (HbA1c 7.8%) on intensive insulin therapy was evaluated in our department. She reported no history of diabetic ketoacidosis, the total insulin dose was 1.21 IU/kg/day, serum C-peptide was 1.6 ng/ml and the antibodies associated with type 1 DM were negative. Family history: one sister diagnosed with MELAS syndrome (encephalopathy, epilepsy) and mother with insulin-treated DM since the age of 24 years and deafness. Clinical examination: Height 1.55m, BMI 28 kg/m^2, bilateral sensorineural deafness, retinal lesions. Cardiac ultrasound: mild left ventricular heart hypertrophy. On the basis of the medical history and clinical features a diagnosis of probable mitochondrial diabetes was made. Genetic analysis in both the patient and her mother revealed heteroplasmy for the pathogenic variant m.3243A > G in tRNA$^{Leu\ (UUR)}$, *MT-TL1* gene.
Conclusions/Discussion
Various syndromes including MIDD, MELAS and CPEO (chronic progressive external ophthalmoplegia) are caused by the mutation m.3243A > G. Although there is a significant phenotypic overlap, DM is a common feature of all three syndromes. In these rare, maternally inherited, mitochondrial disorders, multiple systems are affected (neuromuscular, eyes, heart, pancreas), and diabetes is due to a combination of insulin secretory defect as well as insulin resistance. It is estimated that mitochondrial DM is the cause of ~1% of the total DM population and m.3234A > G is the responsible pathogenic variant in over 85% of these cases. The therapeutic

choices include insulin, incretin analogs and/or oral antidiabetic medications. Metformin is however avoided because of the risk of lactic acidosis. Although there is no curative treatment, correct diagnosis of mitochondrial diabetes is necessary for the optimal management and genetic counselling of these patients.

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Advanced glycation endproducts (AGE) and severity of diabetic retinopathy association analysis in latvia

Zane Svikle[1], Dace Petersone[2], Beate Peterfelde[1,3], Julija Janceva[1,3], Renate Nagobade[1,3], Kristine Baumane[1,3], Janis Valeinis[2] & Jelizaveta Sokolovska[1]
[1]University of Latvia, Faculty of Medicine, Riga, Latvia; [2]University of Latvia, Faculty of Physics, Mathematics and Optometry, Riga, Latvia; [3]Riga East University hospital, Ophthalmology department, Riga, Latvia

Background
Diabetic retinopathy (DR) is one of the most common complication of diabetes and it has a significant impact on national and global health. Accumulation of advanced glycation endproducts (AGE) is recognized as a contributing factor in the development of diabetic complications. The evaluation of AGE has the potential to be an important biomarker in DR, reflecting the impact of prolonged high glucose levels on long-term metabolic memory.
Aim
The objective of this pilot study was to assess and compare the risk levels of AGE among patients at various stages of DR in Latvia.
Methods
In the study 72 participants with type 1 or type 2 diabetes were included. They were grouped based on the severity of their DR: "no retinopathy", "non-proliferative retinopathy", and the "proliferative retinopathy" group, which included also those who had undergone laser-photocoagulation treatment. The evaluation of AGE scores was performed noninvasively using an AGE reader from Diagnoptics, which measures tissue fluorescence. Subsequently, a formula was applied to derive continuous results without categorizing individuals into distinct AGE risk groups (AGE z-score = AGE mean–(0.024*age, years + 0.83)). Statistical analysis was conducted using Fisher's exact test, the Kruskal-Wallis test, and logistic regression models implemented in the R statistical software.
Results
Subjects in the group of 'no retinopathy' ($n = 37$) compared to 'non-proliferative retinopathy' ($n = 22$) and 'proliferative retinopathy' ($n = 13$) were statistically significantly ($P < 0.05$) with more prevalent type 2 diabetes, had shorter duration of diabetes, less diabetic neuropathy cases, higher BMI, lower HbA1c and lower AGE z-score. AGE z-score was statistically significantly ($P = 0.0019$) related to the presence and severity of DR. In 4 of these patients, it was observed that a year ago they had a higher AGE z-score. The multivariable-adjusted odds ratios of any DR across AGE quartiles were 1.00, 9.93 (95% confidence interval [CI] 2.12-64.06), 0.88 (95%CI 0.20–3.92) and 3.42 (95%CI 0.76–20.29). The employed variables included age, HbA1c, gender, type of diabetes and the duration of diabetes.
Conclusion
In this pilot study we illustrated the association between the second quartile of AGE z-score and the odds of any stage of DR. Analysis with larger sample size is planned in our study soon.
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"Glycemic control and hypogonadism in men with type 2 diabetes: cross-sectional study"

Anis Grassa[1], Manel Jemel[1], Salma Salhi[1], Bel Hadj Sliman Chayma[1], Meriem Adel[1], Marwa Chiboub[1], Hager Kandara[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technologies, Zouheir Kallel

Introduction
Hypogonadism (HG), a condition characterized by low levels of testosterone, is a common issue in men, particularly those with type 2 diabetes (T2D). The relationship between glycemic control and HG has been a topic of interest in recent years. In this study, we aimed to investigate the influence of glycemic control on HG.
Methods
This is a descriptive cross-sectional study involving 250 men with T2D aged 40 to 65 years, followed in outpatient consultations. All patients underwent both metabolic and hormonal assessments. Glycemic control was defined based on the criteria outlined by the American Diabetes Association (ADA) in 2022, while the diagnosis of HG was determined according to the criteria established by Vermeulen [1].
Results
The median age (IQR) of men with HG was 59 years [56-64], with a prevalence of 27.2% ($n = 68$). The mean duration of diabetes was 12.5 ± 7.4 years [Range: 1-31], more than half of the patients (62.2%) had over 10 years history of type 2 diabetes. The mean fasting glucose level was 10.9 ± 4.3 mmol/l [Range: 3.2-25.8]. The mean HbA1c was 9 ± 1.7% [Range: 5.6-14.5], and glycemic control was achieved in only 21.6% of patients. Comparatively, the mean duration of diabetes between the HG and non-HG groups was nearly identical (13.0 ± 7.3 vs 12.4 ± 7.5 years; $P = 0.594$). Additionally, the mean fasting glucose levels were comparable between the two groups, HG and non-HG (10.9 ± 4.2 vs 11.0 ± 4.4 mmol/l; $P = 0.827$). However, a significant association was found between HbA1c and the prevalence of HG ($P = 0.044$). The mean HbA1c values were 9.4 ± 1.8% and 8.9 ± 1.6% for the HG and non-HG groups, respectively. In terms of glycemic imbalance, it was more frequent in patients with HG, with percentages of 85.1% compared to 75.8% in the non-HG group, although this difference did not reach statistical significance ($P = 0.083$).
Conclusion
In conclusion, our study highlights the importance of monitoring and optimizing glycemic control, especially inT2D men, as it may play a role in the development or exacerbation of HG. Future research should thoroughly investigate the causal relationship between glycemic control and HG, considering additional factors that may contribute to this association.
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Tolvaptan fortnightly can reduce hyponatraemia related inpatient admissions

Aparna Chaudhary[1], Heather Sullivan[1], Tala Balafshan[1] & Ram Prakash Narayanan[1]
[1]St Helens Hospital, Diabetes centre, St Helens, United Kingdom

Hyponatremia generally defined as a serum sodium of less than 135 mmol/l is the most common type of electrolyte imbalance found in older adults. Its mild to moderate forms can predispose patients to falls, fatigue and a general decline. Severe hyponatremia can contribute to seizures, confusion and death. We present a case of a 70-year-old lady with severe symptomatic chronic hyponatremia secondary to SIADH. She also had progressive Alzheimer's dementia, anxiety, T1DM, hypertension, a stable meningioma, rheumatoid arthritis and hypercholesterolaemia. Her medication profile did not indicate any offending drugs and she was extensively investigated with no clear cause found for her SIADH. She was being managed with modified release slow sodium chloride tablets 1200 mg QDS in community and in the past been given short courses of demeclocycline and tolvaptan. Over the year previous to the endocrine clinic consultation, it was identified that she had multiple prolonged hospital presentations and inpatient admissions with increased confusion, absence seizures and agitation which then also destabilised her type 1 diabetes management. Sodium levels ranged between 114 -120 mmol/l. Due to her low sodium levels the memory clinic was hesitant to increase her memantine dose or prescribe anxiolytics for her Alzheimer's dementia and anxiety and her mental health team suspected the hyponatraemia was contributing to her general decline. She had also begun to not tolerate the sodium chloride tablets. This resulted in a significant deterioration in her quality of life. She experienced heightened anxiety, confusion and agitation exacerbated by repeated hospital admissions. Aiming to reduce the frequency of hospital admissions the patient was trialled on Tolvaptan 7.5 mg twice a month commenced in January 2023. Tolvaptan functions as a selective vasopressin receptor antagonist at the renal collecting ducts which increases free water clearance and in turn raises serum sodium concentrations. Safety netting advise was given to the family to not administer at times of obvious dehydration. The trial proved to be a success whereby the patients' sodium levels have largely been 125 mmol/l and above, thus also allowing her memantine doses to be increased. The patient has had no further hospital admissions in over a year and her grateful family reports that the patient is much happier, and her wider health has seen an improvement.

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Effect of L-arginine and agmatine on GLP-1 and PYY secretion in human NCI-H716 cells: the role of calcium sensing receptors

Sevim I Pek Acar Cömert[1], Adnan Berk Dinçsoy[2], Mehmet Özcan[3], Merve Ayan[4], Pergin Atilla[4] & Esin I leri Gürel[5]
[1]Giresun University, Faculty of Medicine, Physiology Department, Giresun, Turkey; [2]Muğla University, Faculty of Medicine, Physiology Department, Muğla, Turkey; [3]Zonguldak Bulent Ecevit University, Faculty of Medicine, Department of Medical Biochemistry, Zonguldak, Turkey; [4]Hacettepe University, Faculty of Medicine, Department of Histology and Embryology, Ankara, Turkey; [5]Hacettepe University, Faculty of Medicine, Physiology Department, Ankara, Turkey

Glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) are hormones secreted from enteroendocrine L cells following a meal that play a key role in regulating insulin secretion and glucose metabolism. Enteroendocrine L cells express calcium-sensing receptors (CaSRs), which serve as a physiological nutrient sensor for the release of hormones from the gastrointestinal tract. While calcium is the primary ligand for CaSR, its activity can also be controlled by amino acids and polyamines. Therefore, in human enteroendocrine L (NCI-H716) cells, we investigated the effects of L-arginine and agmatine, a naturally occurring polyamine generated from L-arginine, on GLP-1 and Pyy secretion, along with the involvement of CaSR in this effect. To investigate the effect of agmatine and L-arginine on GLP-1 and Pyy secretion, NCI-H716 cells were exposed to different concentrations of agmatine and L-arginine (20 mM and 40 mM), and GLP-1 and Pyy levels were measured. NPS 2143 and R568, which are negative and positive allosteric modulators of calcium-sensing receptors (CaSR), respectively, were also used to study the role of CaSR in hormone release. CaSR immunoreactivity and the second messengers (Ca^{+2} and cAMP) that may mediate GLP-1 and Pyy release were also examined. Agmatine and L-arginine alone at 20 mM and 40 mM did not lead to significant GLP-1 and Pyy secretion. However, when combined with NPS 2143, there was a decrease in GLP-1 and Pyy levels. The cAMP level was decreased in the 40 mM agmatine + NPS 2143 group, while it was increased in the group treated with 40 mM agmatine + R568. Additionally, 40 mM L-arginine led to an increase in intracellular calcium concentration, while NPS 2143 reduced it. CaSR immunoreactivity was not different between groups. As a result, it was observed that GLP-1 and Pyy secretion was not induced by L-arginine or agmatine in NCI-H716 cells. Interestingly, NPS 2143 administration caused changes in hormone and cAMP/calcium levels, supporting the idea that CaSRs may be involved in GLP-1 and Pyy secretion in response to L-arginine and agmatine.

Key Words: L-arginine, Agmatine, GLP-1, Pyy, CaSR, NCI-H716 cell line, NPS 2143, R568, Ca^{+2}, cAMP.

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The conjugation of tigerinin-1r with modified gastric inhibitory polypeptide enhanced its cellular uptake and metabolic actions

Opeolu Ojo[1], Ayodele Abiodun Falobi[1], Joy Nneka Edeani[1], Wendy Amy Ofosu[2], Lesley Smyth[3], Olivia Corcoran[4] & Simon Dunmore[1]
[1]Diabetes Research Group, Research Institute in Healthcare Sciences, School of Life Sciences, Wolverhampton, United Kingdom; [2]University of East London Stratford Campus, School of Health, Sport and Bioscience, London, United Kingdom; [3]University of West London, School of Biomedical Sciences, London, United Kingdom; [4]University of Wolverhampton, School of Life Sciences, Wolverhampton, United Kingdom

Aim
Previous reports indicate therapeutic potentials of tigerinin-1R, isolated from the skin secretions of *Hoplobatrachus rugulosus*, as an antidiabetic agent. Despite the report of its insulin-releasing effects, the peptide's mechanism of actions is poorly understood. This study investigates the impact of conjugation of tigerinin-1R with (dAla2)-GIP on the cellular uptake and anti-diabetic actions of the peptide.
Method
Amphipathicity, net charge and theoretical isoelectric point of the hybrid peptide were evaluated. Insulin-releasing effects of the hybrid (0 –3μ M) were investigated using BRIN-BD11. Cellular uptake, cytotoxicity and cell viability were assessed Effects of the peptide on erythrocyte haemolysis, glucose stimulated insulin-secretion, intracellular calcium concentration, membrane depolarisation, and glucose tolerance in high-fat fed mice were assessed.
Result
The conjugation of tigerinin-1R with (dAla2) GIP reduced the net charge from +1 to -1.9 and the theoretical pI reduced from 8.3 to 4.4. No significant change in amphipathicity was observed. The hybrid peptide stimulated non-toxic concentration-dependent insulin secretion at concentrations ≥10nM ($P<0.05$ to $P<0.001$). At 3μ M, the stimulatory effect of G-TGN was higher than that of tigerinin-1R (1.5-fold, $P<0.01$) and GIP (1.3-fold, $P<0.05$). The hybridization of GIP and tigerinin-1R did not affect cell viability nor cause erythrocyte haemolysis. Effects of G-TGN increased with increasing glucose concentration (1.1mM to 5.6mM, 1.3-fold, $P<0.05$ and 5.6mM to 16.7mM, 1.7-fold, $P<0.01$) and in the presence of KCl (30mM, 3.6-fold, $P<0.001$) and tolbutamide (200μ M, 2.4-fold, $P<0.01$). Verapamil (50nM, 23%, $P<0.05$), diazoxide (300μ M, 27%, $P<0.05$) and removal of extracellular calcium (19%, $P<0.05$) inhibited but not abolish the effects of G-TGN. The peptide enhanced intracellular calcium (23%, $P<0.01$) and increased membrane depolarisation (19%, $P<0.05$). Improvement in glucose tolerance in mice receiving G-TGN was higher compared with tigerinin-1R (19%, $P<0.05$) and GIP (13%, $P<0.05$). Cellular uptake of G-TGN increased by 3.6-fold compared to tigerinin-1R.
Conclusion
The conjugation of (dAla2) GIP with tigerinin-1R significantly enhanced its potential and encourages its development as a novel anti-diabetic drug.

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Etiological profile and evolution of secondary diabetes due to endocrinopathies

Deus Niyongabo[1], Nassim Essabah Haraj[1], Siham El aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital of Casablanca, Casablanca

Introduction
Endocrinopathies, characterized by dysfunctions in the endocrine system and its hormonal glands, emerge as a significant cause of secondary diabetes. These conditions induce complex disturbances in glucose metabolism, leading to insulin resistance or alterations in insulin production, pivotal factors in the development of secondary diabetes. This study aims to describe the etiological profiles of secondary diabetes and evaluate its evolution after treating the underlying endocrinopathies.
Patients and Methods
A retrospective study over a five-year period (2018-2023), involving 88 patients with secondary diabetes due to endocrinopathies, collected at the endocrinology department of Ibn Rochd University Hospital in Casablanca. Statistical analysis was conducted using the SPSS software.
Results
The mean age of the patients was 42.5 years ± 10.9, with a female predominance. The prevalence of diabetes was 47.7% in hypercortisolism, 36.3% in acromegaly, 11.3% in hyperthyroidism, and 4.5% in pheochromocytoma. The average duration of diabetes evolution was 5.6 years ± 3.5. Regarding glycemic control, 58% were unbalanced before treating the causal endocrinopathy, with an average HbA1C of 9.7% ± 2.4. After controlling the causal disease, glycemic control was achieved in 98.6% of patients with a transition to oral antidiabetic drugs. Degenerative assessment revealed diabetic retinopathy (12.8%), diabetic nephropathy (8.6%), and diabetic neuropathy (7.5%).
Conclusion
This study highlights the crucial importance of early recognition and treatment of endocrine disorders to prevent or effectively manage secondary diabetes. Targeted management of underlying endocrinopathies significantly improves glycemic control and reduces degenerative complications associated with secondary diabetes.

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P484

Beta-type estradiol receptor modulates hepatocyte responses to metabolic challenges

Debora Rocha[1], Eloisa Vilas-Boas[2], Camille Caldeira[1] & Alicia Kowaltowski[1]
[1]Instituto de Química, Departamento de Bioquímica, São Paulo, Brazil; [2], Faculdade de Ciências Farmacêuticas, São Paulo, Brazil

Non-selective hormonal therapy with estradiol attenuates metabolic dysfunction associated to post menopause. However, its effectiveness decreases over-time, and is associated hormone-dependent cancers development. Conversely, beta-type estradiol receptor (ERβ) activation has been showing promising outcomes in basic research, improving hepatic response to energy overload insult, in addition to presenting antitumor action. Therefore, we evaluated the ability of ERβ to promote metabolic effects on hepatocytes, focusing on mitochondrial function. AML12 cells were submitted to high glucose (20 mM) plus palmitate (200 μ M), and the effect of ERβ activation with diarilpropionitrile (0.1 or 1 nM, 24h) was evaluated through Extracellular Flux Analysis. We modulated different electron

transport chain complexes to assess basal, ATP-linked, maximal, reserve capacity, and non-mitochondrial respiration. Mitochondrial network volumes and shape were evaluated through fluorescence microscopy. The substrate commitment assay evaluated the ability of cells to shift the use of carbohydrates, lipids, or aminoacids when target points of entrance into mitochondria are inhibited sequentially. The substrate capacity assay assesses the maximal ability of cells to oxidize one type of substrate. We also checked for acute responses to adrenaline, as a physiological signal, compared outcomes, including the production of ketone bodies and lipid oxidation. Overload with palmitate plus high glucose affected basal, ATP-linked and maximal respiration, as well as reserve capacity (maximal respiration difference from basal) of mitochondria. ERβ activation treatment did not change these parameters. Mitochondrial morphology also didn't present expressive changes after treatment. These results indicate that ERβ activation doesn't overtly alter metabolic fluxes nor morphology under basal conditions. However, challenging these cells with physiological or pharmacological stimuli, the responses significatively changed. The hepatocytes present higher commitment to individual substrate oxidation, decreasing the ability to shift the source of ATP. This result was verified modulating pyruvate, glutamine, or palmitate entrance into mitochondria. The capacity to oxidize these substrates didn't change after treatment, except for pyruvate, meaning that these cells presented a decreased ability to exclusively oxidize carbohydrates. Finally, physiological responses were also different. In this assay, hepatocytes submitted to overload decreased the adrenergic response, and the treatment recovered to control levels. Basal production of ketone bodies followed the same pattern, increasing in energy overload conditions, and returning to control levels after treatment. In conclusion, ERβ activation made hepatocytes respond differently when challenged with pharmacological and physiological stimuli. Our results uncover the potential of selective ERβ modulation as an alternative to estradiol or ERA activation-based therapies for metabolic diseases.

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Diabetes mellitus in patients undergoing pancreatectomy (T3cDM): preliminary data analysis

Martina Borrini[1], Chiara Mele[1], Fabio Maroso[2], Rosa Pitino[1], Davide Vimercati[1], Raffaele Romito[2], Gianluca Aimaretti[1] & Paolo Marzullo[1]
[1]University of Piemonte Orientale, Department of Translational Medicine, Novara, Italy; [2]Maggiore della Carità Hospital, Department of General Surgery, Novara, Italy

Rationale and purpose
Glucose tolerance often changes in patients with pancreatic lesions and usually worsens after distal pancreatectomy; however, factors affecting interindividual variation in progression are unclear. Our study aimed to investigate the glyco-metabolic status in a series of patients undergoing pancreatic resection for treatment of benign or malignant lesions and risk factors involved in the developing T3cDM.
Methods
We conducted an observational retrospective study on 29 patients (F = 15; age, 67.4 ± 2.2y, Charlson's Comorbidity Index, 3.7 ± 0.3) subjected to distal spleno-pancreatectomy (DP, ($n = 18$), total duodeno-pancreatectomy (PD, ($n = 10$) or radical proximal-distal modular pancreato-splenectomy (RAMPS, ($n = 1$) in our university hospital. Pre- and post-surgical variables, glyco-metabolic status and the degree of glycemic control at diagnosis and during follow-up were assessed, together with pancreas autoimmunity and C-peptide levels. In a subgroup of T3cDM patients, glucose profiles obtained by continuous monitoring devices (CGM) were compared with those of an age- and sex-matched control group with T1DM.
Results
The overall prevalence of diabetes in our series was 62% (18/29), 50% of whom (9/18) developed it before surgery. In patients subjected to DP, T3cDM prevalence was 61% (11/18). Autoimmunity was negative in all cases. In the series as a whole, patients with diabetes were younger than patients without (63.3 ± 2.6y vs 74.0 ± 3.0y, $P < 0.05$), but no other anthropometric, biochemical, surgical or clinical-pathological features were identified as risk factors for T3cDM. Among T3cDM patients, 60% were treated with basal-bolus insulin regimen while the remainders were treated with combination therapies. Analysis of glucose control over time showed mean HbA1c values of 8.59 ± 0.42%. In a subgroup of insulin-treated T3cDM patients, CGM showed a higher glucose management indicator, an estimate of HbA1c, when compared to DMT1 patients (7.71 ± 0.37% vs 6.74 ± 0.20%, $P < 0.05$). Moreover, the former displayed longer TAR (20.00 ± 6.93% vs 5.00 ± 1.96%, $P = 0.06$) and shorter TBR (4.71 ± 1.06% vs 1.00 ± 0.44%, $P < 0.01$). There were no differences in insulin dosing between the two subgroups.
Conclusions
In our series, the prevalence of T3cDM in patients who underwent DP was 50%, which coexisted with a high prevalence of pre-surgical diabetes. Lower age at pancreatic surgery emerged as the only predictor of diabetes onset. Appropriate peri-operative diabetic assessment is mandatory for all patients undergoing distal pancreatic resections, and CGM could aid physicians, patients and their care-givers in building a better insight on glycemic outcomes and complications in patients developing T3cDM.

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The waist-to-height ratio represents better than body mass index the prognostic impact of obesity on metabolic steatopathy

Ahmed Mohamed Nefzi[1], Bouchabou Bochra[1], El Mouldi yosr[1], Nakhli Abdelwahab[1], Hemdani Nesrine[1], Benzarti Zeineb[1], Ben Nejma Houda[1] & Ennaifer Rym[1]
[1]Hôpital Mongi Slim, Hepato-gastroenterology, Marsa, Tunisia

Introduction
Overweight is a major prognostic factor in metabolic steatopathy. The Waist-to-Height Ratio (WHtR) has recently been introduced as a clinical marker predictive of cardiovascular complications related to obesity. The objective of our study was to evaluate the performance of this ratio in detecting complications related to metabolic steatopathy (Liver fibrosis and cardiovascular risk).
Patients and Methods
This was a prospective, cross-sectional, descriptive study including all patients with metabolic steatopathy who consulted between March 2021 and December 2022. Age, medical history, and various lifestyle habits were collected. Anthropometric measurements and blood pressure were taken. Body mass index (BMI) and the WHtR were calculated. Liver fibrosis was assessed using transient elastography (Fibroscan), with advanced liver fibrosis defined in this study as elasticity ≥ 9.7 kPa. Cardiovascular risk assessment was done using the GLOBORISK score, a validated tool for evaluating 10-year cardiovascular mortality. High cardiovascular risk was defined by a GLOBORISK score ≥ 20%.
Results
The study population included 107 patients with a mean age of 54.5 ± 10.1 years and a gender-ratio of 0.53. History of hypertension, type 2 diabetes, and dyslipidemia were noted in 44.9%, 43%, and 31.8% of patients, respectively. Smoking and alcohol use were noted in 11.2% and 8.4%, respectively. The mean BMI was 30.56 ± 5.7 kg/m^2, and the mean WHtR was 0.61 ± 0.08. Advanced liver fibrosis was found in 14% of patients. We observed a high cardiovascular risk in 35.5% of patients. The WHtR showed better performance than BMI in identifying patients at risk of advanced fibrosis, with respective areas under the ROC curve of 0.729 (95% CI 0.615 –0.843) and 0.7 (95% CI 0.577 –0.839). The cutoff for the WHtR in identifying patients at risk of advanced fibrosis was 0.6, with a sensitivity of 93% and specificity of 50%. In terms of high cardiovascular risk, the WHtR showed slightly better performance than BMI, with areas under the ROC curve of 0.65 (95% CI 0.53 –0.752) and 0.61 (95% CI 0.505 - 0.731), respectively. The cutoff for this ratio in predicting high cardiovascular risk was also 0.6, with a sensitivity of 65% and specificity of 42%.
Conclusion
The WHtR is a simple tool that better represents the impact of obesity on the prognosis of metabolic steatopathy, both in terms of liver fibrosis and cardiovascular risk.

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Blood glucose and insulin level during oral glucose tolerance test as predictors for treatment efficacy in obese patients

Tzvetelina Totomirova[1] & Mila Arnaudova[2]
[1]Military Medical Academy, Clinic of Endocrinology and Metabolism, Sofia, Bulgaria; [2]VITA MBAL, Endocrinology, Sofia, Bulgaria

Background
Oral glucose tolerance test (OGTT) is usually used to determine carbohydrate metabolism abnormalities in overweight patients. Measurement of glucose and insulin level on demanded 0 and 120 minute and some additional minutes could give information for obesity treatment choice and for patients' follow-up. The aim of our study is to assess whether glucose and insulin level measurement during oral glucose tolerance test could be used as predictors for treatment efficacy in obese patients.
Materials and methods
107 patients (55 women, 52 men, mean age 44.01 ± 12.87years) with mean weight 99.07 ± 18.73 kg, mean BMI 34.86 ± 6.0 kg/sq.m and mean HbA1c

5.75 ± 0.58% underwent OGTT at the end of treatment period. Additional measurements of glucose were performed on minute 60 and 180 as well as measurement of insulin level on 0, 60th, 120th, 180th minute. HOMA-IR was calculated. Patients had received different treatment for weight management including diet and exercise instruction, metformin and GLP1 analogues for the previous six months. A correlation between glucose, insulin level on different minutes and treatment efficacy results was assessed.
Results
Basal minute glucose level shows moderate significant correlation with weight decrease (phi = 0.61, $P < 0.05$). Glucose level on first hour is presenting with more strong correlation (phi = 0.72, $P < 0.05$) and the second hour blood glucose shows not significant correlation (phi = 0.47, $P = 0.24$). Insulin on 0, 60 and 120 min is presenting with strong correlation of weight loss ($P < 0.05$). HOMA-IR index is also correlating with therapeutic answer especially in metformin receiving group but not in GLP1 analogues treated group ($P < 0.05$). No difference was found depending on age, gender, and weight of patients and with weight at the start of the study.
Conclusion
Glucose and insulin level during OGTT could be used as predictors for future therapeutic efficacy and for treatment choice in obese patient. Defining such predicting factors is useful for clinical practice and should be objective of research.
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P488

Metabolic dysfunction-associated steatotic liver disease (MASLD) in obesity: a major role for transient elastography in the screening of significant liver fibrosis

Ana Carreira[1], Tânia Carvalho[1], Bernardo Canhão[2], Miguel Melo[1], João Madaleno[2], Armando Carvalho[2], Dírcea Rodrigues[1], Adélia Simão[2] & Isabel Paiva[1]
[1]Hospitais da Universidade de Coimbra, Unidade Local de Saúde de Coimbra, Endocrinology, Diabetes and Metabolism, Coimbra, Portugal; [2]Hospitais da Universidade de Coimbra, Unidade Local de Saúde de Coimbra, Internal Medicine, Coimbra, Portugal

Introduction
Metabolic dysfunction-associated steatotic liver disease (MASLD) is a leading cause of chronic liver disease (CLD). Screening of liver fibrosis by clinical scores is recommended in people with obesity, but their accuracy is still under discussion. Vibration-controlled transient elastography (VCTE) is among the best validated imaging tools to assess liver fibrosis, and is suggested in patients with indeterminate or high-risk clinical scores.
Aims
To assess the prevalence of MASLD and significant liver fibrosis in people with obesity, to identify clinical factors associated with fibrosis and to compare the accuracy of the FIB-4 and NFS scores against VCTE.
Methods
Interim analysis from a prospective cohort study conducted on people with a history of class II-III obesity, followed in a tertiary centre. All patients without history of bariatric surgery or significant alcohol intake were invited to undergo VCTE. Patients with other causes of steatosis/CLD were excluded. VCTE fibrosis scores of ≥ F2 (≥ 7kPa) were considered as significant, ≥ F3 as advanced and F4 as cirrhosis.
Results
33 cases were analyzed, with mean age of 44.1 ± 11.3 years and BMI of 38.9 ± 6.1 kg/m^2, 69.7% female. MASLD was diagnosed in 81.8%, with significant liver fibrosis in 30.3%, advanced fibrosis in 18.2% and cirrhosis in 6.1%. Aminotransferases were elevated in 27.3%; and aminotransferase elevation was associated with significant liver fibrosis (66.7% vs 16.7%, $P = 0.010$). People with diabetes showed more advanced fibrosis (42.9% vs 11.5%, $P = 0.093$). Fibrosis in VCTE correlated with BMI ($r = 0.371$, $P = 0.033$), steatosis ($r = 0.589$, $P < 0.001$), triglyceride ($r = 0.378$, $P = 0.030$) and aminotransferase levels (alanine: r = 0.442, $P = 0.010$; aspartate: r = 0.383, $P = 0.028$). Patients with recent weight loss of ≥10% had less significant liver fibrosis (0.0% vs 38.5%, $P = 0.073$). FIB-4 and NFS showed a specificity of 91.7% and 88.2% for excluding significant fibrosis, but failed to identify any of the cases of significant fibrosis. According to FIB-4, none of the cases with significant fibrosis would have undergone VCTE, whilst according to NFS, 85.7% (53.8% of the cases with an indeterminate score) would have undergone VCTE.
Conclusion
MASLD and liver fibrosis are highly prevalent in people with obesity. Higher BMI, diabetes, elevated aminotransferase and triglyceride levels were associated with increased liver fibrosis, while weight loss of ≥ 10% showed an opposite association. NFS was superior to FIB-4 as an initial screening tool, but both had a low accuracy for identifying significant fibrosis. This suggests that VCTE may have a major role in screening people with obesity and MASLD.
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Diabetes remission after bariatric surgery: a 10-years follow-up study

Inês Meira[1,2], João Menino[1,2], Juliana Gonçalves[1,2], Helena Ferreira[1,2], Ana Rita Leite[1,2], Patricia Ferreira[1], Sara Ribeiro[1,2], Telma Moreno[1,2], Diana Silva[1,2], Paula Freitas[2,3], Eduardo Lima da Costa[3], Joana Queirós[1] & CRIO .[3]
[1]São João Universitary Hospital Center, Porto, Portugal; [2]Faculdade de Medicina da Universidade do Porto - FMUP, Porto, Portugal; [3]CRIO – Centro Responsabilidade Integrada Obesidade., Porto, Portugal

Introduction
Although lifestyle measures and medical therapy are the cornerstone of type 2 diabetes (T2DM) management, achieving optimal glycemic control in T2DM patients with obesity remains challenging. There is strong and consistent evidence that bariatric surgery (BS) is an effective strategy to improve glycemia in diabetic patients and often leads to remission of T2DM in patients with obesity. The majority of the published literature supporting T2DM remission after BS has short- and medium-term follow-up. However, the durability of glycemic improvements and the potential for long-term "cure" in T2DM patients following BS remain insufficiently studied.
Aim
Determine the incidence of durable remission and relapse of T2DM rates 10 years after BS, characterize the glycemic profile of these patients after surgery, and identify factors predicting persistent remission of T2DM.
Methods
Retrospective observational study of patients with T2DM undergoing BS between 2010 and 2013. Exclusion criteria included patients undergoing gastric band surgery, those without initial and 10-year post-surgery HbA1c or fasting plasma glucose (FPG) determination, and those undergoing revisional surgery or deceased during the follow-up period. Paired t-tests, Wilcoxon signed rank and McNemar tests were used to assess the differences in the metabolic status during the follow-up, as appropriate. Logistic regression models were used to assess predictors of T2DM remission.
Results
Ninety-five patients were included, 84% of whom were women, with a mean age of 48.8 ± 9.1 years and a mean HbA1c of 7.0 ± 1.5%. Ten years after surgery, the rate of complete T2DM remission was 31%, partial remission was 15%, and late recurrence after initial remission was 24%. Patients with lower HbA1c (OR = 0.50; $P = 0.05$) and taking fewer antidiabetic drugs (OR = 0.31; $P = 0.01$) preoperatively were more likely to maintain long-term remission. The surgical technique used and the duration of T2DM did not reach statistical significance as predictors of remission in multivariate analysis. Patients with T2DM maintained reductions in FPG ($P < 0.001$), HbA1c ($P < 0.001$), number of antidiabetic drugs ($P < 0.001$), and insulin use ($P < 0.001$) ten years post-BS.
Conclusion
In conclusion, BS can induce a significant and sustainable remission and improvement of T2DM. Consistent with previous studies, our data suggests that when the main goal of surgical treatment is durable diabetes remission, earlier surgical intervention is likely to be more effective. Longer follow-up reports and prospective, randomized controlled studies are important to confirm these findings.
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P490

Body mass index is a better predictor than waist circumference to assess the risk of advanced hepatofibrosis

Szymon Suwała[1] & Roman Junik[1]
[1]Nicolaus Copernicus University, Collegium Medicum, Department of Endocrinology and Diabetology, Bydgoszcz, Poland

Introduction
Obesity is the primary element of the metabolic syndrome, wherein one of the key reasons that heightens the risk of cardiovascular problems is the presence of liver fibrosis. Invasive core needle biopsy of the liver is considered the definitive method for diagnosing hepatofibrosis, however, non-invasive fibrosis indicators like FIB-4 are becoming more commonly utilized in routine clinical settings. Obesity can be defined in various ways, with the most prevalent methods relying on the measurement of body mass index (BMI) or waist circumference (WC). The aim of the study was to assess which definition of obesity (based on BMI or WC) more effectively indicates an increased risk of liver fibrosis.
Material and methods
The authors analyzed retrospective medical data from 2100 patients who were hospitalized in endocrinology department between 2013 and 2020 in whom all

necessary factors were evaluated: weight, height (to calculate BMI), waist circumference, alanine and aspartate aminotransferases and platelet count (to calculate FIB-4 for hepatofibrosis prediction). Obesity was defined in three ways, appropriate to the Caucasian population: WC $\geq$80 cm (females) or $\geq$94 cm (males) –criterion A; WC $\geq$88 cm (females) or $\geq$ 102 cm (males) –criterion B; BMI $\geq$30 kg/m^2 –criterion C. In order to determine suitable thresholds for identifying a higher risk of advanced liver fibrosis authors used cut-offs for age-dependent FIB-4: $\geq$1.21 for patients up to 49 years of age, $\geq$1.96 for patients aged 50–59 years and $\geq$2.67 for patients aged 60–69 years. Evaluation of relative risks (RR) was employed using the Chi-squared test with comparison to patients not meeting a given criterion, each time also providing the 95% confidence interval (95%CI).
Results
Criterion A was met by 82.29% of patients, criterion B was met by 63.52% of patients, and criterion C was met by 42.90% of patients. For criteria A and B, the analysis based on WC revealed statistically insignificant values for the relative risk (P=0.283 for criterion A, P=0.588 for criterion B). Only criterion C, based on BMI, showed a statistically significant increase in relative risk, which was 63% (RR 1.63%; 95%CI: 1.26-2.10; P<0.001).
Conclusion
Body mass index seems to be a better predictor of the risk of advanced liver fibrosis depending on age - patients with obesity defined by this index should be treated as potentially exposed to this complication of the metabolic syndrome and active diagnostics should be undertaken in this direction.

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P491

Diabetes and severe obstructive sleep apnea syndrome: effect on right ventricle systolic function

Syrine Dardour[1,2], Sahar Abidi[2], Fattah Kadardar[1], Habib Bessrour[2] & Hedi Ben slima[1]
[1]Menzel Bourguiba hospital, Menzel Bourguiba, Tunisia; [2]The Military Hospital of Tunis, Tunis, Tunisia

Introduction
The interaction between diabetes and obstructive sleep apnea syndrome (OSAS) is little recognized. We hypothesized that diabetes and OSAS act synergistically to increase the risk of right ventricular systolic dysfunction and that treatment of OSAS would improve right ventricular (RV) systolic function in patients with diabetes plus OSAS.
Methods
Cross-sectional study including 100 patients with severe OSAS, 49 of whom have associated diabetes. Echocardiography was performed to study right systolic function and the effect of nocturnal continuous positive airway pressure(CPAP) ventilation in the diabetes and OSAS subgroup.
Results
We did not note any significant difference for the following ultrasound parameters: Tricuspid annular plane systolic excursion (TAPSE), Systolic Shortening Fraction, Global Longitudinal Strain of the RV. We noted a significant difference for the Systolic Wave Velocity at the lateral wall of the tricuspid annulus using Tissue Doppler Imaging (S'wave) parameter which was lower in the diabetes group (12.35 cm/s Vs 13.95 cm/s P=0.005). When OSAS is associated with diabetes, Systolic RV dysfunction was observed in 25% of the sample (64% in diabetics versus 36% in non-diabetics P=0.083). We found a marked improvement in the systolic function of the RV in patients with diabetes using CPAP (A systolic dysfunction rate of the RV at 12. 5% vs 87.5% in non-fitted P<0.001).
Conclusion
In patients with severe obstructive sleep apnea syndrome and diabetes, right ventricular dysfunction primarily involves the S'Wave parameter and CPAP improves right systolic function in diabetic patients with severe OSAS.

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P492

The dependence of anxiety and depression indicators on serum cholecalciferol level in patients with latent autoimmune diabetes in adults

Nataliia Pashkovska[1] & Iryna Tsaryk[1]
[1]Ukraine, Clinical Immunology, Allergology and Endocrinology, Chernivtsi, Ukraine

Introduction
Literature data showed the association between serum cholecalciferol concentration and level of anxiety and depression in patients with classical types of diabetes mellitus. However, a clear relationship between these indicators in patients with latent autoimmune diabetes in adults (LADA) has not yet been established.
The aim of the study
To evaluate the dependence between level of anxiety, depression and cholecalciferol status in patients with LADA.
Material and methods
42 patients with LADA (19 –LADA1, 23 –LADA2) and 25 practically healthy individuals were examined. In addition to general clinical research methods cholecalciferol status was evaluated. The levels of anxiety and depression were determined using the Spielberg's and Beck's questionnaires, respectively. The levels of anxiety were registered as level of situational anxiety and personal anxiety.
Results
Cholecalciferol level was registered 2.7 times lower in LADA1 group compared to control (14.63 [13.14; 15.98] ng/ml vs 40.00 [32.17; 53.00] ng/ml) and by 38.7% in LADA2 (24.51 [17.86; 32.93] ng/ml vs 40.00 [32.17; 53.00] ng/ml) (P<0.001). In LADA1 patients the level of cholecalciferol was lower by 40.3% (p< 0.01) compared to LADA2. The level of situational anxiety was 34.00 [27.75; 45.50] in LADA1 and 42.50 [23.00; 55.00] in LADA2 (higher by 25% than in patients with LADA1, P<0.05) and probably differed between LADA1/control and LADA2/control –control level 23.00 [16.00; 34.00] (decrease by 32.4% (P<0.01) and 45.9%, respectively (P<0.001)). The level of personal anxiety was higher in LADA1 group by 20.7% compared to control (29.00 [22.5; 40.25] vs 23.00 [20.00; 34.00]) (P<0.05) and did not significantly differ between LADA phenotypes. The level of depression was significantly higher in patients with LADA1 (17.00 [12.00; 22.50]) and LADA2 (12.00 [7.75; 15.00]) by 3.4 times and 2.4 times, respectively, compared with the control group (5.00 [3.00; 7.00]) (P<0.05); the difference between LADA phenotypes showed that depression level was higher by 41.7% in patients with LADA1 compared to LADA2 group (P<0.05). In patients with the LADA1 phenotype, negative correlations of medium strength were recorded between level of depression and C-peptide level (r=-0.348; p<0.05); level of depression and serum cholecalciferol indicator (r=-0.443; P<0.05). In LADA2, inverse correlations of medium strength were registered between high-density lipoprotein cholesterol indicator and level of depression (r=-0.328; p<0.05).
Conclusions
Level of anxiety and depression depends on serum cholecalciferol level (especially in LADA1 phenotype) which indicates the importance of its adequate supplementation in patients with LADA.

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Sleep apnoea and degenerative complications in type 2 diabetes

Meriem Adel[1,1], Rayene Ben mohamed[1], Marwa Chiboub[1], Lina Ghram[1], Hajer Kandara[1], Manel Jemel[1] & Ines Kammoun[1]
[1]National institute of nutrition and food technology, Endocrinology, Tunis

Introduction
Obstructive sleep apnoea (OSA) is notably prevalent in individuals with type 2 diabetes (T2D). This syndrome not only elevates cardiovascular risk but is also implicated in the advancement and exacerbation of microangiopathy. The objective of our study was to evaluate the prevalence of diabetic complications in patients with type 2 diabetes who have OSA.
Method
A cross-sectional study was conducted on 130 patients with DT2 who were hospitalized in the Endocrinology Department of the National Institute of Nutrition and Food Technology in Tunis. The inclusion criteria were patients aged 30 years or older with type 2 diabetes diagnosed for at least 2 years. The study excluded patients with known OSA, any endocrinopathy that could be the cause of OSA, acute respiratory failure, acute or chronic bronchopneumonia, or bronchopulmonary tumour pathology. Screening for OSA was conducted using the Berlin questionnaire and the ApneaLink sleep screening device.
Results
The mean age of the patients was 59.37$\pm$7.80 years, with a sex ratio of 0.58. Hypertension, hypercholesterolaemia and hypertriglyceridaemia were present in 68%, 69.2% and 33.8% of the cases respectively. The mean Body Mass Index was 30.53$\pm$5.16 kg/m^2. The mean duration of diabetes was 12.54$\pm$7.81 years. The mean HbA1c was 11.15$\pm$1.82%. Among our patients, 18.5% were smokers with a mean of 35.79 pack-years, and 8.5% were occasional alcohol drinkers. A total of 76.9% had at least one diabetic microangiopathy. Diabetic retinopathy was present in 54.47% of patients: mild in 26.78%, moderate in 5.35% and

proliferative in 36.6%. Nephropathy was present in 30.8% of patients. Diabetic neuropathy occurred in 58.8% of cases. Macroangiopathic complications was found in 36,9% of patients: Coronary insufficiency, Stroke and arteritis of the lower limbs occurred in 15.3%, 5.3% and 26.9% respectively. Sixty-two-point three percent of patients were at high risk of OSA according to the Berlin score. The OSA was mild in 41%, moderate in 15% and severe in 5% of cases. A statistically positive association was found between diabetic nephropathy and high risk of OSA, which persisted after multivariate analysis. However, no association was found between macroangiopathies and high OSA risk.
Conclusion
OSA is associated with complications related to T2D. There is moderate evidence suggesting a connection between OSA and Chronic Kidney Disease (CKD) in patients with Type 2 T2D. Robust prospective studies with extended follow-up periods are crucial to investigate the potential correlation between OSA and T2D complications.

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P494

Diabetic ketoacidosis - severe case, in a type 1 diabetes patient, with chronic diarrhea and mental disorders -case report

Ema Lumi[1], Tomi Punmira[2], Qirjako Gjino[3], Vlefta Bejko[4] & Agron Ylli[5]
[4]Regional Hospital, Korce, Albania, Endocrinologist, Head of Internal Unit, Korce, Albania; [2]Regional Hospital, Korce, Albania, Anesthesiology & Reanimation, Korce, Albania; [3]Regional Hospital, Korce, Albania, Gastroenterologist, Internal Unit., Korce, Albania; [4]Regional Hospital, Korce, Albania, Head of Emergency Department, Korce, Albania; [5]University Hospital Center "Mother Teresa", Prof. Dr. Endocrinologist, Head of Endocrinology Department., Tirana, Albania

Introduction
Diabetic ketoacidosis(DKA) is a serious acute complication of Diabetes mellitus that can be life - threatening. DKA is most common among people with type 1 diabetes. It is usually presented with hyperglicemia, ketoacidosis and presence of ketone bodies in the urine. Chronic diarrhea(CD) is defined as three or more loose stools daily for at least four weeks. There are many possible causes of chronic diarrhea. The most common causes are: Crohn disease & Ulcerative colitis (inflamatory diseases of gastrointestinal tract), malabsorption, endocrine diseases as hyperthyroidism, diabetic autonomic neuropathy, etc.
Case report
A 40-years old male was presented in emergency in serious condition, with tachycardia, shortness of breath, nausea and vomiting, diarrhea, fever, polyuria and polydipsia, etc. Medical history: Type 1 diabetes from 10 years, medical disorders treated with clonazepam and chronic diarrhea in the last year. He hadn't take insulin for 3 days consequently. Labs: glycemia = 1757 mg/dl, urea = 117, kreatinine = 1.92, Ph = 6.74, BE= -33, Na^+=106, K^+= 8.5, CL^-=73, Troponin = neg, leukocytes = 21200 with left deviation of formula, ketone bodies in urine=50 mg/dl, INR = 1.45, hypoalbuminemia, etc. Treatment: intensive tratment with iv insuline, intensive rehydration with normal saline, sodium bicarbonate, sc enoxaparinë, iv Ampicillin, omeprazol, human albumin, elektrolites, vitamines, etc. 24-hours later all clinic and biochemical markers were normalized. Check up for the etiology of CD: TSH, FT3, FT4 in normal range, HbA1c=11%, normal thyroid and abdominal ultrasound, calprotectin fecal test = 245 mg/kg (>100 highly positive), fecal fats-positive, fecal ascarids-positive, elastic fibres-negative. Normal in Colonoscopy. Probably diabetic autonomic neuropathy diarrhea or Irritable bowl syndrome. After 9days he was discharged from the hospital in good condition with medications: insuline basal-bolus, probiotics, rifaximin 200 mg, and clonazepam. Follow up in 6 months: colonoscopy.
Conclusion
Regular treatment of Diabetes mellitus, especially type 1 diabetes, is very important. Missed doses of insuline can lead to complications like DKA. Comorbidity of diabetes and chronic diarrhea is fairly common. Diabetic patient have 2-4 fold probability to have CD than normal people. Patient with mental disorders are more prone to gastrointestinal problems.
Key words: Diabetic Ketoacidosis (DKA), Chronic Diarrhea (CD), Mental disorders.
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P495

Comparative analysis of economic burden between cardiovascular and renal complications in hospitalized tunisian patients with type 2 diabetes: a retrospective study

Souhir Maalej[1], Fatma Mnif[1], Siddiqa Soomauroo[1], Abdel Mouhaymen Missaoui[1], Nadia Charfi[1], Faten Hadjkacem[1], Mouna Elleuch[1], Mohamed Abid[1] & Nabila Rekik[1]
[1]Hedi Chaker University Hospital, Endocrinology, Sfax

Background
Diabetes mellitus poses a global chronic health challenge, with Tunisia experiencing a concerning surge in type 2 diabetes (T2D) prevalence. Cardiovascular and renal complications are prominent and severe consequences associated with T2D. Evaluating the costs related to managing these complications is crucial to enhance care quality, optimize resource utilization, and ultimately reduce the growing economic and social burden of this chronic disease.
Materials and Methods
A retrospective descriptive study was conducted to collect data on diabetic patients with chronic cardiovascular and renal complications. The study included patients hospitalized in the Endocrinology Department of Hedi Chaker University Hospital in Sfax from January 1 to December 31, 2022. We assessed the cost of managing cardiovascular and renal complications in our hospitalized patients.
Results
The study involved 114 patients, with a sex ratio of 1.28. The average age at hospitalization was 65.38 ± 10.17 years. The average hospitalization duration in our population was 7.2 ± 4.5 days, with a minimum stay of 2 days and a maximum stay of 26 days. The hospitalization of 37 patients with cardiovascular complications alone was the most expensive, reaching 144,955.60 TND, equivalent to 46,017.65 USD, representing 56.6% of all expenses. The average cost per patient was 3,917.72 TND, or 1,243.72 USD. The 53 patients with both cardiovascular and renal complications ranked second in terms of costs, with expenditures totaling 97,548.38 TND, equivalent to 30,967.74 USD, accounting for 38.1% of the overall cost. The average cost per patient in this group was 1,840.54 TND, or 584.30 USD. Finally, the management of 24 patients with only renal complications was less costly, representing only 5.3% of total expenses, or 13,592.19 TND, equivalent to 4,314.98 USD. The average cost per patient in this group was 566.34 TND, or 179.80 USD. The table details the expenses of various analyzed elements based on the categories of complications.
Conclusion
The comprehensive cost analysis of managing cardiovascular and renal complications in diabetic patients reveals significant economic implications. Optimizing healthcare strategies is imperative to alleviate the financial burden and enhance patient outcomes.

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P496

Assessment of overactive bladder syndrome symptoms (OABSS) score following the start of sodium-glucose co-transporter-2 inhibitors in individuals with type-2 diabetes mellitus

Derya sema yaman kalender[1], Ümit Çavdar[1], Mehmet Sercan Ertürk[1] & Barış Önder Pamuk[1]
[1]Katip Çelebi University School Of Medicine, Atatürk Training And Research Hospital, Department of Endocrinology and Metabolism, Izmir, Turkey

Background
In addition to glucose-lowering effects, Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2i) are the preferred treatment of choice in patients with heart failure due to their diuretic effects through glucosuria and natriuresis. However, there is limited data about urinary symptoms associated with SGLT2i use.
Objectives
Low urinary tract symptoms such as increased urinary frequency, urgency, or incontinence due to SGLT2i use are not described in many studies. We aimed to show whether SGLT2i use is associated with low urinary symptoms.

Abstract P495

Cost (TND)	Accommodation	Glycemic monitoring	Cardiovascular investigations	Radiological investigations	Biological investigations	Medical treatment	Total (%)
Cardiovascular complications	8260,00	491,83	119160,00	6853,60	8202,40	1987,77	144955,60 (56,6%)
Renal complications	5600,00	301,85	482,40	1620,40	4888,00	699,55	13592,19 (5,3%)
Cardiovascular and renal complications	14840,00	829,10	58712,80	6609,20	14446,40	2110,88	97548,38 (38,1%)
Total (%)	28700,00 (11,21%)	1622,78 (0,63%)	178355,20 (69,65%)	15083,20 (5,89%)	27536,80 (10,75%)	4798,20 (1,87%)	256096,18 (100%)

Methods
Fifty-four patients (22 male, 32 female) with type-2 diabetes mellitus (DM), over 18 years of age, without urinary infection, chronic kidney disease, or organic lower urinary tract disease were included in the study. Initially, all patients were screened for low urinary tract symptoms with the OABS-8 questionnaire before SGLT2i treatment. Whether an overactive bladder was detected or not, all patients were asked to fill out the questionnaire again at the first and third months of the treatment. Changes in symptom scores were investigated in terms of association with SGLT2i use. HbA1C, fasting blood glucose, body mass index, and blood pressure values were also evaluated.
Results
All patients' mean OABS-8 total score was 10.10 ± 5.03, significantly decreasing after SGLT2i administration. 17 out of 54 patients were with OABSS before the SGLT2i treatment. Mean total scores at baseline were 15.41 ± 4.0 and 7.1 ± 2.35 in patients with OABSS ($n = 17$) and patients without OABSS ($n = 37$), respectively. The total score of patients without OABSS was significantly decreased in the first and third months of the treatment. On the other hand, 17 patients who had OABSS showed a significant reduction in their total score in the first month but not in the third month (Table-1).

Table 1: Mean values and changes of OABSS scores in all groups

	Baseline	1st Month	3rd Month	P value
Total (n:54)	10.10 ± 5.03	8.89 ± 6.55	10.00 ± 8.26	0.002
Without OABSS (n:37)	7.1 ± 2.35	6.9 ± 6.18	6.6 ± 5.46	0.012
With OABSS (n:17)	15.41 ± 4.0	12.41 ± 5.78	16 ± 9.06	0.047

Conclusion
Although there are concerns about increased low urinary tract symptoms associated with the diüretic effects of SGLT-2 inhibitors, our study did not show an increase in OABSS scores.

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P497

Western-style diet in the presence of elevated circulating testosterone induces adipocyte hypertrophy and t-cell dysfunction in rhesus macaques

Benjamin Burwitz[1], Sofiya yusova[1], Jacob Robino[1], Diana Takahashi[1], Addie Luo[1], Ov Slayden[1], Cecily Bishop[1], Jon Hennebold[1], Charles Roberts[1] & Oleg Varlamov[1]
[1]The Oregon National Primate Research Center, Beaverton, United States

Hyperandrogenemia (elevated testosterone, T) and metabolic dysfunction are hallmarks of polycystic ovary syndrome (PCOS), which can have varying degrees of ovulatory dysfunction. Adipocyte hypertrophy, induced by obesity and hyperandrogenemia, has been suggested to contribute to the systemic low-grade inflammation thought to be one of the drivers leading to reproductive dysfunction in women with PCOS. However, whether hyperandrogenemia and adipocyte hypertrophy per se induce a proinflammatory response is unknown. Therefore, the primary objective of this study was to focus on the metabolic and immunological effects of WSD and mild hyperandrogenemia on the systemic and tissue-resident proinflammatory milieu using a nonhuman primate (NHP) model. To test whether T + WSD disrupts the immune milieu that may affect normal egg implantation and other relevant reproductive processes, we conducted immune cell profiling during the mid-luteal phase, the interval during the menstrual cycle when the uterine endometrium is permissive for embryo implantation. Individual treatments (i.e., T or WSD alone) were not included in this study because we previously determined that combined treatment led to earlier and more severe metabolic and reproductive impairments, including increased numbers of arrested antral follicles and reduced fertility. Immune cells residing in visceral omental white adipose tissue (OM-WAT), corpus luteum and the contralateral ovary, endometrium, lymph nodes, bone marrow, and peripheral blood mononuclear cells were characterized by flow cytometry during the luteal phase of the reproductive cycle. Following one year of treatment, T + WSD animals became more insulin-resistant and exhibited increased body fat and adipocyte hypertrophy compared to controls. T + WSD treatment did not induce macrophage polarization towards a proinflammatory phenotype in the tissues examined. While the major T-lymphoid cell subsets were not significantly affected by T + WSD treatment, we observed a significant reduction in the frequency of effector memory CD8 + T-cells (Tem) in OM-WAT, but not in other tissues. Notably, OM-WAT Tem frequencies were negatively correlated with insulin resistance as assessed by Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). Collectively, our data show that short-term T + WSD treatment induces weight gain, insulin resistance, and adipocyte hypertrophy, but does not have a significant effect on systemic and tissue-resident proinflammatory markers, suggesting that adipocyte hypertrophy and mild hyperandrogenemia alone are not sufficient to induce a proinflammatory response. Additionally, hyperandrogenemia may induce immune tolerance in T-cells. Dysregulation of T-cell function can lead to immune-related complications that may affect implantation and early pregnancy outcomes.

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Endocrine-Related Cancer

P88

The BRAF K601E mutation in thyroid tumors: One alteration with a dual clinical significance

Elisabetta Macerola, Paola Vignali, Rebecca Sparavelli, Marcello Poma, Agnese Proietti, Liborio Torregrossa, Ferruccio Santini, Rossella Elisei, Gabriele Materazzi, Fulvio Basolo & Clara Ugolini
University of Pisa, Pisa, Italy

Background
BRAF^{K601E} mutation is a class 2 oncogenic *BRAF* mutation which causes constitutive activation of MAPK pathway functioning as RAS-independent activated dimers. In thyroid cancer, the *BRAF*^{K601E} is more rare than the *BRAF*^{V600E}, and it has been mostly associated to clinically indolent follicular architecture neoplasms. This is a mono-institutional study aimed at evaluating the frequency and clinical role of *BRAF*^{K601E} mutation, either when it is identified in indeterminate thyroid nodules or in thyroid cancer.
Methods
The institutional database was searched for thyroid nodules and tumors positive for the *BRAF*^{K601E} between 2019 and 2023. Mutational screening was performed by real-time PCR in nodules with indeterminate cytology (fine-needle aspiration material) and by NGS in thyroid cancer (tumor tissue).
Results
In 5-year time interval of molecular diagnostics activity, the K601E mutation was detected in 20 out of 1173 cases (1.7%). Specifically, it was identified in 17 out of 824 indeterminate nodules (2.1%) and in 3 out of 349 carcinomas (0.9%). In thyroid cytology, nodules with K601E mutation were TIR 3A ($n = 11$) or TIR 3B ($n = 6$), according to the Italian system. Patients with K601E-positive nodules were younger (mean age 37 years ± 10.8) compared to those with non-K601E nodules in the same time period (mean age 49.9 years ± 15.2), while nodule size appeared similar in mutated (mean 2.5 cm ± 0.8) and non-mutated (mean 2.4 ± 13.4) cases. On histology, K601E positive nodules were benign tumors (follicular adenoma, $n = 1$), low-risk neoplasms (NIFTP, $n = 3$) or malignant neoplasms (minimally invasive encapsulated follicular variant PTC, $n = 10$; solid subtype PTC, $n = 2$; classic PTC, $n = 1$). None of the malignant neoplasms showed extrathyroidal extension, nor lymphovascular invasion; two tumors had central neck lymph node metastases (N1a). The three advanced thyroid *BRAF*^{K601E}-positive carcinomas showed aggressive histology (two widely invasive follicular thyroid carcinoma; one anaplastic thyroid carcinoma). Patients age was 65, 65 and 74 years, respectively. Two patients with follicular carcinoma experienced disease recurrence, and in one of them histological transformation to poorly differentiated thyroid carcinoma was identified on biopsy.
Conclusions
The *BRAF*^{K601E} mutation is rare in thyroid nodules and cancer, where it can have a dual clinical significance. In indeterminate cytology, it is mostly found in young adults, and it is predictive of malignant neoplasms with no aggressive phenotypic features. However, it can be found also in aggressive thyroid tumor types, including anaplastic thyroid cancer. Therefore, the *BRAF*^{K601E} mutation role in thyroid pathology should not be underestimated.

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Effectiveness of temozolomide treatment in SDHx mutant and wildtype metastatic pheochromocytoma and paraganglioma – results of a European restrospective multicentre study

Hanna Remde[1], Julien Hadoux[2], Joakim Crona[3], Rossella Libe[4], Eugénie Lim[5], Guido Di Dalmazi[6], Emanuela Arvat[7], Magalie Haissaguerre[8], Letizia Canu[9], Gregory Kaltsas[10], Peter Igaz[11], Henri Timmers[12], Svenja Noelting[13], Marcus Quinkler[14], Timo Deutschbein[15], Martin Fassnacht[1] & Kroiss Matthias[16]
[1]University Hospital Würzburg, Würzburg, Germany; [2]Institut Gustave Roussy, Villejuif, France; [3]University of Uppsala, Uppsala, Sweden; [4]Hôpital Cochin-Port Royal, Paris, France; [5]St. Bartholomew's Hospital, London, UK; [6]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [7]University of Turin, Torino, Italy; [8]Bordeaux University, Bordeaux, France; [9]University of Florence, Firenze, Italy; [10]National and Kapodistrian University of Athens, Athens, Greece; [11]Semmelweis University, Budapest, Hungary; [12]Radboud University Medical Centre, Nijmegen, Netherlands; [13]University Hospital Zürich, Zürich, Switzerland; [14]Endokrinologie in Charlottenburg, Berlin, Germany; [15]Medicover MVZ Oldenburg, Oldenburg, Germany; [16]LMU University Hospital, München, Germany

Background
Pheochromocytomas and paragangliomas (mPPGL) are rare neuroendocrine tumors. Therapeutic options in advanced and irresectable mPPGL are limited. Two small retrospective studies demonstrated the effectiveness of temozolomide

in patients with mPPGL and suggested that patients with mutation in the succinate dehydrogenase B (SDHB) gene might benefit more than SDHB wildtype cases.
Aim
To re-evaluate safety and effectiveness of temozolomide in a larger cohort of patients with mPPGL and identify predictors of clinical response.
Methods
Data from patients with mPPGL who had received treatment with temozolomide were collected in an international retrospective setting at 15 reference centres in Europe. The objective response rate (ORR) and non-progression rate (NPR) were the primary outcome measures. The association of SDHB mutation status in and treatment response was assessed using Fisher's exact test.
Results
Radiological outcome assessment was available for 67 (94.3%) of 71 patients included into the study at data cut-off. Best response was partial response (PR) in 18 patients and stable disease (SD) in 29. The ORR was 27% and the NPR 70%. Germline SDHB mutation was available for 56 patients including 24 (43%) patients with an SDHB mutation and 32 (57%) patients with SDHB wildtype. Objective treatment response was observed in both groups but was significantly more frequent in patients with SDHB mutation (41.6% vs 12.5%, $P=0.027$). Accordingly, non-progression rate was higher in patients with SDHB mutation compared to those with SDHB wildtype (83% vs 56%, $P=0.044$).
Conclusion
Treatment with temozolomide in mPPGL can be effective in both patients with SDHB mutation and those with SDHB wildtype. However, objective response rates and non-progression rates are higher in patients carrying an SDHB mutation.
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P90

Does mitotane offer lasting cure or transitory benefits following adrenocortical carcinoma surgery?

Cristina Álvarez Escolá[1], Jorge Hernando Cubero[2,3], Miguel Angel Mangas Cruz[4], Jesus García Donas[5], María José Picón César[6], Miguel Paja Fano[7], Laura Gonzalez Fernandez[8], Lorena González Batanero[9], Lourdes García-García-Doncel[10], Javier Molina-Cerrillo[11], Javier Martinez Trufero[12], Brenda Veiguela Blanco[13], Beatriz Febrero Sánchez[14], Felicia A Hanzu[15], Carlos Lopez[16], Concepción Blanco[17], Teresa Ramón y Cajal[18], Jersy Jair Cardenas Salas[19], Nuria Valdés[20], Paula Jimenez Fonseca[21] & Alberto Carmona bayonas[22]
[1]Hospital Universitario La Paz, Endocrinology and Nutrition, Madrid, Spain; [2]VHIO Institut d'Oncologia, Medical Oncology, Barcelona, Spain; [3]Hospital Universitario Vall d'Hebron, Medical Oncology, Barcelona, Spain; [4]Hospital Universitario Virgen del Rocío, Endocrinology and Nutrition, Sevilla, Spain; [5]Comprehensive Cancer Center CLARA CAMPAL, Medical Oncology, Madrid, Spain; [6]Hospital Universitario Virgen de la Victoria, Endocrinology and Nutrition, Málaga, Spain; [7]Hospital Universitario Basurto, Bilbao, Spain; [8]Hospital Universitario Gregorio Marañón, Endocrinology and Nutrition, Madrid, Spain; [9]Hospital Universitario de Canarias, Endocrinology and Nutrition, La Laguna, Spain; [10]Hospital Jerez de la Frontera, Endocrinology and Nutrition, Jerez de la Frontera, Spain; [11]Hospital Universitario Ramón y Cajal, Medical Oncology, Madrid, Spain; [12]Hospital Universitario Miguel Servet, Medical Oncology, Zaragoza, Spain; [13]Hospital Universitario de Cabueñes, Endocrinology and Nutrition, Gijón, Spain; [14]Hospital Universitario Virgen de la Arrixaca, Surgery, Murcia, Spain; [15]Hospital Clínic de Barcelona, Endocrinology and Nutrition, Barcelona, Spain; [16]Hospital Universitario Marqués de Valdecilla, Medical Oncology, Santander, Spain; [17]Hospital Universitario Príncipe de Asturias, Endocrinology and Nutrition, Alcalá de Henares, Spain; [18]Hospital de la Santa Creu i Sant Pau, Medical Oncology, Barcelona, Spain; [19]Hospital Universitario Fundación Jiménez Díaz, Endocrinology and Nutrition, Madrid, Spain; [20]Hospital Universitario de Cruces, Endocrinology and Nutrition, Baracaldo, Spain; [21]Hospital Universitario Central de Asturias, Medical Oncology, Oviedo, Spain; [22]Hospital Universitario Morales Meseguer, Medical Oncology, Murcia, Spain

Introduction
The role of mitotane as an adjuvant therapy for adrenocortical carcinoma (ACC) remains a contentious topic due to the scarcity of robust randomized clinical trials, attributed to the low incidence of this neoplasm. Despite this, the prognosis following surgery for localized tumors is generally poor, leading to varied clinical practices.
Methods
This study utilized patient data from the ICARO registry of the GETHY group and SEEN, with disease-free survival (DFS) and overall survival (OS) as endpoints. A Cox multivariable model was employed, considering factors such as tumor size, Ki67 index, age, T stage, nodal involvement, venous invasion, radiotherapy, and adjuvant mitotane usage.
Results
The ICARO database included 357 patients treated between 1983 and 2023 across 34 centers. Among these, 223 patients had localized, non-metastatic tumors at diagnosis and underwent surgery after a median of 41 days from diagnosis. Open surgery was performed in 142 (64%) cases, with laparoscopic procedures in the remainder. R0 resection was achieved in 162 (73%) cases. Of the 223 patients with follow-up data, 138 (62%) were female, aged between 20 and 88 years, with a median age of 50 years. Functional symptoms were present in 85 (38%) patients, with Cushing's syndrome in 51 of these. Radiotherapy was administered in 27 (12%) cases, and 111 (49.7%) patients received adjuvant mitotane therapy for a median of 23 months. Mitotane levels were monitored in 93/111 patients, starting at 2 g/day. At the time of analysis, the median DFS was 28 months (95% CI, 20.8–61.3), and the median OS was 86.1 months (95% CI, 54.6–152). After adjusting for confounding factors, there is insufficient evidence to reject the null hypothesis of no effect of mitotane on DFS (Hazard Ratio [HR] 0.67, 95% CI, 0.42–1.05), or on OS (HR 0.58, 95% CI, 0.32–1.02). However, factors such as tumor size (T), nodal involvement (N), age, Ki67 index, and venous invasion were associated with recurrence and death. The effect was clearly time-variant (Schoenfeld test = 0.008), with a crossing of the Kaplan-Meier curves at 24 months.
Conclusion
In post-operative ACC cases, current evidence on adjuvant mitotane's efficacy is not definitive. However, if effective, its impact seems time-limited, likely reaching its peak within two years under conventional usage patterns. This suggests a potential requirement for prolonged maintenance therapy, emphasizing the need for in-depth research into its long-term outcomes.
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Clinical impact and genetic alterations in the DAXX gene in patients with neuroendocrine tumors of the gastroenteropancreatic system and the lung

Darko Katalinic[1], Lars Toetome[2], Ivan Aleric[1], Ivana Skrlec[3], Jasminka Talapko[3] & Aleksandar Vcev[1]
[1]Faculty of Dental Medicine and Health and Faculty of Medicine, University of Osijek; [2]Center for Cancer Medicine, Oslo, Norway; [3]Faculty of Dental Medicine and Health, University of Osijek

Introduction
Neuroendocrine tumors (NETs) comprise a unique heterogeneous group of malignant growths that range from benign and multi-focal to highly malignant and metastatic. They are characterized by well-differentiated morphologic features and the ability to secrete neuropeptides, resulting in characteristic clinical syndromes. However, they are often diagnosed from the metastases of an unknown primary tumor. Therefore, high-quality genetic and immunohistochemical markers are needed to confirm the diagnosis. Here we conduct integrated genome and immunohistochemistry analysis (IHC) of the *DAXX* (death domain-associated protein) gene as well as analysis of disease-free survival (DFS) and overall survival (OS) in patients diagnosed with NETs.
Material and methods
The study consisted of 65 patients with NETs. During the study period, 36 patients were diagnosed with neuroendocrine tumors of the lung (L-NETs) and 29 patients with neuroendocrine tumors of the gastroenteropancreatic system (GEP-NETs). Tumor-DNA was isolated from fresh-frozen tumor tissue. The IHC analysis was conducted according to the standard histopathological protocol. The real-time PCR was performed for the *DAXX* gene.
Results
A total of 24 patients (36.9%) were found with mutations in the *DAXX* gene. The cumulative number of mutations detected in NETs >3 cm was significantly higher ($P<0.001$) in comparison to NETs <3 cm. We also found that mutations of the *DAXX* gene were strongly associated with increased features of malignancy including lymphovascular invasion and higher tumor grade. All patients with the mutated *DAXX* gene had a shorter DFS ($P<0.002$) and OS ($P<0.003$).
Conclusion
Our study identified a significant relation between the genomic profile of the *DAXX* gene and DFS as well as the OS in patients diagnosed with L-NETs and GEP-NETs. The *DAXX* molecular alterations influence the malignant potential of L-NETs and GEP-NETs and can predict the malignant progression. Therefore, they could be considered as a possible prognostic stratification tool.
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P92

How well does 'real world' management of Immune check point inhibitor induced hypophysits (ICI-Hp) reflect the European Society of Endocrinology (ESE) 2023 clinical practice guidelines (CPG)?: Experience from a single tertiary care centre

Shani Apsara Dilrukshi Mathara Diddhenipothage[1], Jacqui Warden[2], Katie Herbert[2], Riccardo Poli[1], Nicholas Coupe[2], Miranda Payne[2], Jeremy W Tomlinson[1] & Helen Turner[1]
[1]Oxford Centre for Diabetes, Endocrinology, and Metabolism, Endocrinology, Oxford, UK; [2]Department of Oncology, Churchill Hospital, Oxford, UK

Introduction
Hypophysitis (Hp) is a serious adverse effect (AE) of Immune check-point inhibitor (ICI) therapy in malignancy. We evaluated 6 yeas of clinical expereince with ICI against the recent ESE CPG 2023 which provides practical guidance on the management of this condition based on up-to-date evidence.
Methods
A quality improvement project (QIP) included all patients with ICI-Hp ($n=17$) referred to a dedicated Endocrine-ICI clinic (January 2017-November 2023), to determine presentation, management, and outcomes.
Results
There were 50% males, median age 63 y (IQR 51,73)] and symptom onset occurred 12 w (IQR 9,15) of ICI therapy, after the 3rd (IQR 3,4) cycle; underlying malignancy: metastatic melanoma (76%), renal cell carcinoma (12%) and mesothelioma (12%). All received Ipilimumab (Ipi), alone (5.8%) or in combination with Nivolumab (82%). Fatigue (76%), headache (71%) and nausea (65%) were common symptoms; 12% were asymptomatic. Hyponatremia 41%. All had acute secondary hypocortisolism (SHC) (random morning cortisol <100 nmol/l in 82%, <50 nmol/l in 53%). Acute secondary hypothyroidism (SHT) and hypogonadism (SHG) were reported in 35%. Low prolactin (PRL) (<110 mIU/l) 30%; elevated PRL (446-1119) 18%. Enlarged pituitary was the commonest (75%) pituitary imaging abnormality ($n=16$, performed ≤ 12 w), followed by thickened stalk (31%), supra-sellar extension (12%), mild optic-chiasm compression ($n=1$, biopsy: lymphocytic Hp). Specific management of Hp varied; IV methylprednisolone (MPP) 1 mg/kg per day ($n=4$) (indication severe headache), oral prednisolone 30–40 mg/d ($n=6$), oral dexamethasone 10 mg/d ($n=1$), and hydrocortisone (HC) 40 mg/d for 48 h ($n=4$). Symptomatic Hp recovery occurred in all; (33% within 48 h) and scan abnormalities [at 15 w (IQR 13, 22), $n=14$). One patient developed acute psychosis with high-dose MPP. Long term, all received standard HC (20 mg/d) replacement and age/weight-based levothyroxine in persistent SHT. None required sex hormone replacement. In those evaluated for pituitary recovery; There was no recovery in SHC ($n=10$), whilst recovery of SHT and SHG was reported in 43% [at 5 w (IQR 4,10)] and 67% [at 10 w (IQR 8,13)] respectively. Lack of cancer progression was noted in 65% [2.5 y (IQR 2, 6)]. Treatment with high dose GCs was not associated with cancer progression ($P=1.00$), or all-cause mortality ($P=0.515$).
Conclusions
Despite antedating ESE CPG, our practice is aligned with current guidance. GC dose (not strictly aligned with CPG) chosen for symptom severity had no effect on disease course. SHC following ICI-HP was irreversible, however recovery of SHT and SHG should be actively sought on long term follow up.

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P93

Risk of differentiated thyroid cancer among Danish women with polycystic ovary syndrome

Sarah Sørensen[1], Clarissa Frandsen[1], Thomas Maltesen[1], Christian Munk[1], Ulla Feldt-Rasmussen[2,3], Allan Jensen[1] & Susanne Kjær[1,4]
[4]Danish Cancer Society, Copenhagen, Denmark; [2]Rigshospitalet, Department of Endocrinology and Metabolism, København, Denmark; [3]Institute of Clinical Medicine, Faculty of Health and Clinical Sciences, Copenhagen University, Copenhagen, Denmark; [4]Department of Gynecology, Rigshospitalet, Denmark

Background
Gender disparity and age pattern in the incidence of thyroid cancer indicate a link between hormonal- and reproductive factors and risk of thyroid cancer. Thus, polycystic ovary syndrome (PCOS) may be a plausible risk factor for this malignancy.
Aim
In this nationwide cohort study, we investigated the association between PCOS and the risk of differentiated and papillary thyroid cancer.
Methods
We included all Danish women born during 1962–1996 ($n=990\,990$). PCOS- and cancer diagnoses, covariates, migration, and vital status were obtained from following Danish, nationwide health- and population registers: The Danish Civil Registration System, the Danish Cancer Register, the Danish National Patient Register, The Danish National Prescription Register, the Danish Medical Birth register, and educational registers at Statistics Denmark. We used the unique, personal identification number assigned to all Danish citizens at birth or immigration, which is used as key identifier all over in the Danish society to link individual level data from the above-mentioned registers. Cox-proportional hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CI) for differentiated thyroid cancer overall and separately for papillary thyroid cancer according to diagnosis of and time since diagnosis of PCOS.
Results
The study cohort comprised 990 850 women. At baseline, 5584 women were diagnosed with PCOS (0.6%). At baseline, Obesity, diabetes type II, use of hormonal contraception, and previous diagnosis of benign thyroid disease were more frequent in women with PCOS, than in women without PCOS. Highest obtained level of education and parity status were similar between the two groups. During follow-up (16 975 570.8 years), we identified 980 women with differentiated thyroid cancer, fifteen of whom were previously diagnosed with PCOS. We found a tendency towards an increased rate of differentiated thyroid cancer in women with PCOS (HR = 1.52, 95% CI: 0.91–2.53). The association was strongest in the first 10 years after the PCOS diagnosis (HR = 3.81, 95% CI: 1.90–7.65). None of the women were diagnosed with differentiated thyroid cancer within the first three years following PCOS. Results were similar for papillary thyroid cancer.
Conclusions
We found a tendency towards an increased rate of differentiated and papillary thyroid cancer in women with PCOS, which was strongest the first 10 years after PCOS and potentially related to prior benign thyroid disease. Even this large study was limited by few exposed cases and therefore a relatively low statistical power.

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P94

Cervico-mediastinal hematoma: Atypical presentation of parathyroid carcinoma associated to hashimoto thyroiditis

Martina Cicia[1], Giampaolo Papi[2], Alfredo Scillitani[3], Stefania Corrado[4], Pietro Locantore[1] & Alfredo Pontecorvi[1]
[1]Fondazione Policlinico Universitario A. Gemelli, Endocrinology and Diabetology, Rome, Italy; [2]Azienda USL Modena, Endocrinology Unit, Modena, Italy; [3]Casa del Sollievo della Sofferenza in San Giovanni Rotondo, Endocrinology Unit, Foggia, Italy; [4]University of Modena and Reggio Emilia, Pathology Unit, Modena, Italy

Introduction
Parathyroid carcinoma (PC) accounts for $<1\%$ of all forms of primary hyperparathyroidism. PC is characterized by very high serum PTH and calcium levels and presents with osteopenia/osteoporosis, nephrolithiasis, asthenia, neuropsychiatric symptoms. Here, we report the unusual presentation of a PC.
Case presentation
A 48-year-old woman was referred to our Center for the sudden appearance of a large painful hematoma in the cervico-mediastinal area. Neck US showed a solid, markedly hypoechoic lesion ($40\times80\times55$ mm), extending from the right thyroid lobe to the mediastinum, associated to blood leakage in the right perithyroid area. The thyroid displayed a diffusely hypoechoic structure, without nodules. Lab tests showed: TSH 2.1 mIU/ml, Calcitonin <1 pg/ml, PTH 460 pg/ml, Calcium 14 mg/dl, Calcium ion 2.1 mmol/l, Calciuria 535 mg/24 h, Phosphorus 2.5 mg/dl, Creatinine 0.65 mg/dl, 25-OH vitamin D 10 ng/ml, CEA 2 ng/ml. Femoral-lumbar DXA detected osteopenia and renal US showed a stone within the left kidney. Neck CT demonstrated a huge mass extending from the right thyroid lobe up to the right upper bronchus and displacing the esophagus and the trachea controlaterally.
Treatment
The patient was rehydrated, treated with furosemide, cholecalciferol and bisphosphonate and submitted to right lower parathyroidectomy + right hemithyroidectomy + lymphadenectomy of the right VI cervical level. Histological examination was diagnostic for non-angio-nor neuro-invasive PC associated to lymphocytic thyroiditis; all removed lymph nodes were benign.
Outcome and follow-up
The post-operative course was regular. The patient was discharged with calcitriol and calcium carbonate therapy, then suspended. The search for mutation of the CDC73 gene was negative. The 30-day follow-up included blood tests showing normal PTH and calcium concentrations and subclinical hypothyroidism with

TSH elevated at 18 mcIU/ml Neck US did not detect residual neoplasm and 99mTc-MIBI parathyroid scan was negative. Levothyroxine therapy 50 µg/day was undertaken. Eight years after diagnosis, the patient is in good general condition, with no clinical, biochemical or imaging evidence of disease persistence/recurrence.
Conclusions
We have described the unique case of a PC presenting with pain and hematoma in either the anterior neck and the mediastinum, associated with autoimmune thyroiditis. Although parathyroid hemorrhage is a rare event, it should always be suspected when a painful swelling suddenly appears in the neck region in a hypercalcemic patient. Given the high prevalence of HT in the general population, we believe that the association between PC and autoimmune thyroiditis in our patient should be considered casual.

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P95

Do immune checkpoint inhibitor-related endocrinopathies affect survival rates in cancer patients? Presentation of two case reports

Daria Sazonova[1], Nikita Kutakov[2], Alexander Lutsenko[1], Elena Przhiyalkovskaya[1] & Ekaterina Troshina[1]
[1]Endocrinology Research Centre, Moscow, Russian Federation; [2]Clinical Hospital 'Lapino' of the 'Mother and Child' Group of companies, Moscow region, Russian Federation

Background
Immune checkpoint Inhibitors (ICIs) have revolutionized the treatment of vast array of cancers. Despite their efficacy, ICIs can cause various side effects related to the mechanism of action. Immune-related endocrine events (irEEs) are one of the most common immune-related adverse events (irAEs), accounting for 8.1% of all cases. We report two patients with durable responses to ICIs and concurrent serious irEEs.
Case 1
A 58-year-old woman with metastatic non-small cell lung cancer has been receiving nivolumab for 13 months after 4 previous lines of systemic therapy were ineffective. The patient developed primary hypothyroidism after 14 weeks of ICIs (TSH 82 mIU/l, FT4 0.67 pmol/l) and levothyroxine 100 µg/d was prescribed. After 4 weeks, she noted an episode of hypotension (90/60 mmHg), general weakness, nausea and vomiting. Lab tests showed low morning cortisol 2.8 nmol/l, Na 135 mmol/l with high ACTH 827 pg/ml, renin 184 µIU/ml, K 5.1 mmol/l. Primary adrenal insufficiency was diagnosed and all symptoms resolved after hydrocortisone 25 mg/d and fludrocortisone 0.1 mg/d treatment. To date, the patient has received 26 nivolumab infusions 240 mg/2weeks, with complete metabolic response according to 18F-FDG PET/CT.
Case 2
A 55-year-old woman with localized cutaneous melanoma, which was surgically resected and 6 months later recurred with jugular lymph nodes and liver metastases. Combination ICIs therapy was initiated (nivolumab + ipilimumab), then switching to nivolumab, which she has been receiving for 13 months. Within 4 weeks after ICIs were initiated, she noticed frequent episodes of hypoglycemia (up to 3.0 mmol/l), severe weakness, hypotension (80/60 mmHg), nausea and vomiting. Lab tests showed low morning cortisol 6.4 nmol/l, ACTH 2.1 pg/ml, renin 2.78 µIU/ml, Na 124 mmol/l, C-peptide 0.83 ng/ml, insulin 1 µU/ml, TSH 0.12 µIU/ml, FT4 8.98 pmol/l with normal-range K4.27 mmol/l. Central hypothyroidism and adrenal insufficiency were diagnosed. MRI scan identified empty sella. Symptoms of ICI-induced hypophysitis resolved after initiation of hydrocortisone 20 mg/d and levothyroxine 75 µg/d. The patient has received 26 nivolumab infusions 240 mg/2 weeks. Last 18F-FDG PET/CT confirmed complete metabolic response.
Conclusion
Increased overall survival and progression-free survival have been reported in cancer patients with ieEEs. However, causes of this correlation remain unknown, which warrants further research. Our cases demonstrate the importance of vigilant monitoring of endocrinopathies among cancer patients receiving ICIs in order to diagnose life-threatening complications in time.

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Increased calcitonin level in cases with multinodular goitre and ectopic Cushing syndrome – diagnostic challenges

Mihaela Vlad[1,2], Balas Melania[1], Iuliana Gavanescu[3], Golu Ioana[1], daniela-georgiana amzar[1], Memu Eustatiu[4] & Baderca Flavia[5]
[1]'Victor Babeş' University of Medicine and Pharmacy, 2nd Internal Medicine, Timişoara, Romania; [2]"Victor Babeş" University of Medicine and Pharmacy, Center for Molecular Research in Nephrology and Vascular Disease, Timişoara, Romania; [3]Timiş County Emergency Clinical Hospital, Timişoara, Romania; [4]Emergency City Hospital, Thoracic Surgery, Timişoara, Romania; [5]Victor Babeş University of Medicine and Pharmacy, Microscopic Morphology – Histology, Timişoara, Romania

Introduction
Calcitonin is produced by parafollicular C cells of the thyroid, increased values being considered the hallmark for the medullary thyroid carcinoma (MTC). We discussed two challenging cases with high calcitonin, multinodular goitre and ACTH-dependent paraneoplastic Cushing syndrome.
Case 1
A 45-year-old female patient was admitted into our clinic due to severe fatigue, central obesity, proximal muscle atrophy, round face, buffalo hump, dorsal kyphosis due to osteoporotic vertebral fractures, high blood pressure. Laboratory evaluation revealed high morning and midnight serum cortisol, with no suppression on low-dose dexamethasone suppression test and high plasma ACTH (65.7 pg/ml), indicating an ACTH-dependent Cushing' syndrome. Pituitary magnetic resonance imaging (MRI) didn't reveal any pituitary adenoma. On thyroid ultrasound a mixed hypoechoic nodule of 6/6/8 mm in the right lobe was detected and increased calcitonin level (79.6 pg/ml). A MTC with ectopic paraneoplastic secretion of ACTH was suspected. The Calcitonin-stimulation test with Omeprazole was done, with no stimulation for Calcitonin. More extensive imaging exploration revealed a well-defined lung nodule of 10 mm. The tumor was removed and the pathology report confirmed a carcinoid tumor, stage pT1bN0M0, with Ki-67 index of 2%, and positive immunostaining for ACTH, calcitonin, chromogranin and synaptophysin. After surgery, ACTH, cortisol and calcitonin levels decreased significantly (5.4 pg/ml, 2.42 ng/dl and <2 pg/ml).
Case 2
A 44-year-old hypertensive women was admitted with typical Cushing's syndrome features and amenorrhea for 5 years. Hypercortisolism was confirmed (increased basal and nocturnal serum cortisol, unsuppressed after 1 mg dexamethasone, high ACTH levels-253 pg/ml), increased chromogranin A (2980 ng/l, NR 27–94), hyperglycemia, severe hypokalemia. The imagistic investigations showed no pathological pituitary, pulmonary and abdominal lesions. Pelvic CT and MRI confirmed an ovarian tumoral mass of 15 cm. As the patient presented 2 highly suspicious left thyroid nodules and increased calcitonin (291 pg/ml), MTC with ectopic ACTH-secretion was considered, but the pathology revealed papillary thyroid cancer. After the removal of ovarian tumor, the values of ACTH, cortisol, calcitonin, and chromogranin A decreased significantly.
Discussions
In both cases, the absence of a clear ACTH source imposed the extensive hormonal and imagistic exploration. Calcitonin determination was included in the work-up flow due to the presence of thyroid nodules. The outcome of both cases underline that the high values for calcitonin don't indicate a MTC, always.
Conclusion
When calcitonin level is elevated, but thyroid evaluation is not clear suggestive for a medullary thyroid carcinoma, an extrathyroidal neuroendocrine tumor should be taking into account for differential diagnosis.

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Spontaneous and treatment-related changes in calcitonin doubling rate of medullary thyroid cancer. Long-term experience in a patient with multiple endocrine neoplasia type 2B

Judit Tőke[1], Zsuzsánna Réti[2], Miklós Garami[3], Ildiko Kalina[4], Gergely Kiss[1], Zoltán Sápi[5], Ádám Gy. Tabák[1,6,7] & Miklos Toth[1]
[1]Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary; [2]George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Targu Mures, Romania; [3]Semmelweis University, Pediatric Center, Budapest, Hungary; [4]Semmelweis University, Medical Imaging Centre, Budapest, Hungary; [5]Semmelweis University, Department of Pathology and Experimental Cancer Research, Budapest, Hungary; [6]Semmelweis University, Department of Public Health, Budapest, Hungary; [7]University College London, UCL Brain Sciences, London, UK

Introduction
Medullary thyroid carcinoma (MTC) in multiple endocrine neoplasia type 2B (MEN2B) syndrome is associated with RET mutation. Patients harbouring de

novo mutations are usually diagnosed in more advanced stages of the disease. We present the case of a young female patient with MEN2B diagnosed with stage IV medullary thyroid carcinoma at the age of 10 years.
Aim
Characterizing the efficacy of the different sequences of therapies and disease progression by calculating calcitonin doubling rates based on serial calcitonin measurements.
Methods
Different phases of spontaneous tumor development, the efficacy of surgical interventions and individual drug treatment intervals were analyzed with calcitonin doubling rates (Ct-DR).
Results
De novo mutation involving the Met918Thr in exon 16 of the RET proto-oncogene confirmed the genetic background of the disease in our patient. In 2006-2015, she underwent four operations. We found a less steep increase in log-transformed calcitonin levels after the first compared to subsequent operations. A significant drop in serum calcitonin after a pheochromocytoma removal was suggestive of calcitonin secretion, confirmed by subsequent immunohistochemical analysis. After suffering multiple surgical interventions for local and regional recurrence, the disease still progressed, leading to metastatic disease in the fifth year after diagnosis. The patient underwent five different types of TKI treatment (sunitinib, vandetanib, cabozantinib, lenvatinib, and selpercatinib), with different responses and multiple adverse effects. Three of the five TKIs resulted in an immediate drop of serum calcitonin followed by significantly less steep increases than untreated periods for vandetanib and selpercatinib. Even after the initial drop in calcitonin, we found a continuously decreasing calcitonin trajectory for selpercatinib. Sunitinib and cabozantinib had to be discontinued due to severe side effects. Vandetanib was used for the longest time, slowing the progression of the disease, and causing tolarable adverse events. The best treatment response, as reflected by negative Ct-DR and lack of side effects, was observed with selpercatinib, granting a stable disease and improving quality of life after 17 years from diagnosis.
Conclusion
Our case illustrates the long-term survival of a young MEN-2B patient diagnosed with advanced medullary thyroid carcinoma. The case presents how the effectiveness of different treatment modalities can be approached using log-transformed calcitonin levels.

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P98

Targeting focal adhesion kinase (FAK) and spleen tyrosine kinase (SYK) in gastrointestinal neuroendocrine tumors: Unveiling mechanisms and anti-proliferative effects

Lara Toffoli, Francesca D'Este, Marilyn Dainotto, Angeliki Ditsiou & Teresa Gagliano
University of Udine, Department of Medicine (DMED), Udine, Italy

Gastrointestinal neuroendocrine tumors (GI-NETs) present a challenging and diverse landscape, necessitating effective treatment strategies. Despite advancements, the demand for targeted therapies, particularly for advanced or metastatic cases, persists. Enhancing outcomes in GI-NETs management is crucial, emphasizing the need for ongoing research and development. In our laboratory, we conducted a multitarget compound screening, identifying FAK (BI-0319) and SYK (BI1002494) kinase inhibitors for their anti-proliferative effects on GI-NETs cell lines. SYK and FAK are pivotal in focal adhesions, influencing cell adhesion and migration. SYK, classically associated with immune responses, also impacts focal adhesions, influencing cell movement. FAK, a central adhesion complex component, activates during cell-ECM interactions, governing cell behaviour. Their interplay highlights the intricate relationship between immune signalling (SYK) and adhesion dynamics (FAK), contributing to a comprehensive understanding of cellular processes. Our objective was to characterize the mechanisms of action of FAK and SYK inhibitors in GI-NETs cell lines.
Methods
Using the Small intestine NET cell line GOT1 and colorectal cancer NET cell line COLO320DM as models, cells were cultivated in both 2D and 3D. Cell viability was assessed using crystal violet and cell-titer glo assays. Apoptosis was measured using the 3/7 caspase assay. Protein expression was detected by western blot and immunofluorescence. Gene expression was determined using QPCR.
Results
Both cell lines exhibited high levels of SYK and FAK. The IC50 of FAK (BI-0319) and SYK (BI1002494) was determined in both 2D and 3D. Apoptosis activation using the caspase 3/7 assay revealed limited engagement. Growth curve and real-time time-lapse analyses showed both compounds had significant anti-proliferative effects, delaying cell proliferation, and eventually leading to cell death.
Conclusion
FAK (BI-0319) and SYK (BI1002494) serve as valuable tools to understand the roles of SYK and FAK in GI-NETs biology. Further studies are warranted to investigate their roles in controlling the cell cycle and microtubule formation.

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Metastatic paragangliomas – real world data in a single tertiary center

Foteini Thanasoula[1], Sofia Vlachou[2], Evanthia Kassi[3], Anna Angelousi[1] & Gregory Kaltsas[2]
[1]1st Dpt of Internal Medicine, Unit of Endocrinology, National and Kapodistrian University of Athens, Laikon Hospital, Greece; [2]1st Dpt Department of Propaedeutic and Internal Medicine, Unit of Endocrinology, National and Kapodistrian University of Athens, Laikon Hospital, Greece; [3]Department of Biochemistry,1st Dpt Department of Propaedeutic and Internal Medicine, Unit of Endocrinology, National and Kapodistrian University of Athens, Greece

Background
Paragangliomas(PGLs) and pheochromocytomas (PHEOs) are rare extra-adrenal neuroendocrine tumors of the sympathetic and parasympathetic nervous system. Metastatic status is defined by the abnormal presence of non-chromaffin tissue in extra adrenal organs. The incidence of metastases rises up to 10–17% and may appear even 10 years after the initial diagnosis.
Methods
We retrospectively analysed medical files of patients followed in a tertiary hospital (Center of excellence of rare adrenal diseases). Therapeutic modalities as well as mortality and progression status were recorded.
Results
Twenty seven patients diagnosed with metastatic PHEOs/PGL were included (mean $\pm$ s.d. age in years: 39 ± 15.6). Six patients presented with synchronous metastases and 21 patients developed metastases within a median time of 7 years of follow-up. The 60% of PHEOs and 40% of PGLs were functional. Genetic analysis was performed in 59% of the total included patients ($n = 2/12$ patients with PHEOs and $n = 7/15$ with PGLs) and was found positive in 9 patients (56%) (2 with SDHA, 1 with SDHB,5 with SDHD and 1 with EPAS1 mutation). Median PASS was 7 (min–max:1–9) for PHEOs and GAPP was 6 (min–max:4–7) for PGLs. Median Ki-67% index levels was 5 (min–max:-1–70). Median progression-free survival (PFS) for metastatic disease was 5.9 years (min:0.48-max:15.25) within a median follow-up time of 7 years. Local recurrence was treated either with radiotherapy in 6/27 patients or with second surgery in 10/27 patients, while 2 of them underwent also a third operation. In total, 12 patients were treated with chemotherapy (Cyclophospamide – vincristine -dacarbazine (CVD) or temozolomide) as first line treatment after surgery, $n = 6$ with molecular targeted treatment (MTT) including sunitinib/ cabozatinib /pazopanib as second line and $n = 6$ patients were treated with radiopeptides (PRRTS) or $n = 4$ treated with MIBG analogues. The estimated median PFS was 5,39 months (min:3,02-max:55) for chemotherapy, 6.96 (min:2.76-max:55.68) for MTT, 7.9 (min:6.6-max:180) for radiopeptides and 36.6 (min:16.2-max:124.2) for MIBG therapy. Four patients were lost during follow-up. The observed mortality rate was 21%.
Conclusions
Metastatic PHEOs/PGLs are rare adrenal entities and their management remains challenging requiring a multidisciplinary decision. In most cases metastases occur many years after the initial diagnosis and often they require multiples lines of treatment. In our study, radiopeptides showed the longer PFS comparing with the other systematic treatments.

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P100

Incidentaloma on Ga-68-DOTANOC PET; prevalence and clinical significance

Carlien De Herdt[1], Naert Laura[2], Stroobants Sigrid[2] & De Block Christophe[1]
[1]Antwerp University Hospital, Endocrinology, diabetology and metabolism, Edegem, Belgium; [2]Antwerp University Hospital, Nuclear Medicine, Edegem, Belgium

Introduction
Over the past years Ga-68-DOTANOC PET/CT is increasingly performed, which may lead to an increase in encountering incidentaloma. In 2022, a systematic review was published about incidentaloma on Ga-68-DOTANOC/DOTATE,

describing a prevalence of 4.5% and a relatively high rate of malignancy (13%). However, it was estimated that the overall prevalence was underestimated and the frequency of malignancy overestimated because of publication bias.
Methodology
The result of Ga-68-DOTANOC PET/CT's performed in adults between 2017 and 2022 in the Antwerp University Hospital were retrospectively screened for incidentaloma (= an increased, non-physiological uptake of the isotope, not related to the indication for imaging).
Results
1240 Ga-68-DOTANOC PET/CT's were performed in 804 subjects. In total, 127 incidentaloma were diagnosed in 115 subjects with a mean age of 64 ± 13 years and F/M ratio of 68/47. The most frequently reported locations of incidentaloma were the thyroid ($n=24$), brain ($n=23$) and prostate ($n=21$), followed by the spleen ($n=18$), breast ($n=12$), stomach ($n=8$), uterus ($n=4$), liver ($n=2$), pancreas ($n=2$), esophagus ($n=2$), kidney ($n=2$), ovarium ($n=1$) and mediastinum ($n=1$). In 33 (26%) incidentaloma no further investigations were performed. Rate of malignancy was 5% (3 breast cancers, 2 renal cell carcinomas and 1 prostate cancer). Increased isotope uptake in the brain, thyroid, prostate and spleen were most frequently caused by meningioma ($n=15$), benign nodules ($n=4$), benign prostate hypertrophy ($n=8$) and accessory spleen ($n=16$), respectively.
Conclusion
This is the largest single-center study describing the prevalence and etiology of Ga-68-DOTANOC incidentaloma to date. Evaluating the images of 804 subjects a prevalence of 16% was found which is higher than the prevalence of 4.5% earlier described in the systematic review of Bentestuen *et al*. The difference can be explained by the inclusion of accessory spleen in our study and the systematic review including studies focusing on incidentaloma in one specific organ. Incidentaloma were most frequently encountered in the thyroid (19%), followed by the brain (18%) and prostate (17%). The rate of malignancy in this study was 5%, which is lower than the rate of 13% described in the systematic review, possibly secondary to the inclusion of case reports with the tendency to publish the exceptional. No thyroid cancer was diagnosed in this study, however 67% of the thyroid incidentaloma did not underwent an ultrasound. With this abstract we want to stimulate other centers to publish their frequency of incidentaloma on Ga-68-DOTANOC PET/CT which may help in interpretation.

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Comparison of existing guidelines on the perceived endocrine symptoms of breast cancer patients – preliminary results

Trine Lund-Jacobsen[1], Valdemar Mendez[1], Rasmus Jansen[1], Djordje Marina[1], Simone Marstrand[1], Kristian Buch-Larsen[1], Gabriella Martino[2] & Peter Schwarz[1]
[1]Copenhagen University Hospital, Rigshospitalet, Department of Endocrinolgogy and Metabolism, Copenhagen; [2]University of Messina, Department of Clinical and Experimental Medicine, Messina, Italy

Background
Through the decades, aromatase inhibitor maintenance therapy for patients with postmenopausal non-metastatic estrogen receptor-positive breast cancer has improved significantly. This study focuses on the patient's further breast cancer course and clarifies the extensive symptom burden that the endocrinologist should be aware of.
Aim
The study aims to gain insight into a potential gap between the endocrine symptoms outlined in guidelines versus the symptoms that the clinicians register in the medical records after the patients have expressed the symptoms at the consultations and in semi-structured interviews.
Methods
A Mixed-Method study. Symptoms were classified according to the National Cancer Institute (NIH) and clustered according to the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life C30 (QLQ-C30) questionnaire (EORTC QLQ C30) and new domains (menopausal, body alteration, gastrointestinal, eye-, skin-, mouth- and sex-related). Patients with early breast cancer in follow-up treated with aromatase inhibitors (letrozole, exemestane or anastrozole) were included. Symptom registration was compared with the European Medicines Agency (EMA), the Food and Drug Administration (FDA), international and national guidelines for the standard evidence-based clinical practice: oncological (American Society of Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO), Danish Breast Cancer Group (DBCG) and Danish Multidisciplinary Cancer Group (DMCG)) and endocrine societies (Endocrine Society, European Society of Endocrinology (ESE) and Danish Endocrine Society (DES)).
Results
Patients for the medical record audit were included over a recruitment period of 3 months ($n=23$). Single symptoms were identified by the NIH definition ($n=235$). Patients included in the semi-structured interviews ($n=19$). Single symptoms were identified by the NIH definition ($n=321$). Several symptoms identified in the medical records and interviews were also registered in the guidelines but described with different frequencies e.g., dry mouth. The breast cancer population and their symptoms were, however, not mentioned at all in best-practice endocrine guidelines and very few in some of the best-practice oncology guidelines.
Conclusion
Our results indicate that symptoms either are not outlined in the best practice guidelines or do not embrace the total patient-experienced symptoms as outlined by the physicians and patients with breast cancer. There seems to be a discrepancy between the frequency of various symptoms. Four domains: role functioning, social functioning, Global Health status/QOL, and sex-related symptoms found in medical record audits and patient interviews were exclusively absent from the guidelines. There is a need to implement the most frequent symptoms in national as well as international guidelines.

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P210

The lived experience of people with adrenocortical carcinoma

Phillip Yeoh, Wladzia Czuber-Douchan & Jackie Sturt
King's College London, Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, London, UK

Background
Adrenocortical carcinoma (ACC) is a rare and aggressive cancer of adrenal glands with an incidence worldwide around 0.7–2 cases per million per year in adult populations. The median age at diagnosis is 56 years old, with women and white Caucasians being more frequently affected. Overall median survival rate can be as low as 17 months with 5-year survival rate around 31.2%. Our systematic review identified the lack of qualitative study on the experiences of ACC. Consequently, an explorative approach using interpretative phenomenology couple with Van Manen hermeneutic methodology was used to explore the meanings of living with ACC. I have 24 years of immersion in looking after people living with ACC. This methodology allows me to use my experience, knowledge, and skills to make sense of people's experiences.
Aims
The study aims to investigate the lived experience of people diagnosed with ACC. The study objectives are: i) to understanding meaning and impact of ACC on physical, emotional, mental and psychological on people's wellbeing; ii) to understand how they manage their condition; iii) to find out their sources of help and support of living with ACC.
Method
Twenty-one participants living with ACC were purposively recruited and individually interviewed online using semi-structured questions. They were recruited from ACC support groups from US, Canada, UK, EU, Africa and Australia. The interviews were transcribed and analysed using thematic analysis. Five key main themes that emerged are: existential conundrums, inadequate care & support, life is like a roller coaster, anchoring ways for survival, living, and moving on. Lived time, lived space, lived body, and lived relation (van Manen 1997, 2014) will be used to gain insight into participants' experiences and inform future supports and interventions needed. Theory on survivorship by Mullan (1985) and Bowen Family System Theory (Kerr & Brown, 1988) were used to guide interview process to find the impact and meaning of ACC on people's lives. What the work means to the research area: The aim to improve understanding on the people with this condition so that further studies can be undertaken to improve the experiences and care pathways for them.

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P213

Endocrine autoimmunity during immunotherapy for cancer – a snapshot from an Oncologic Institute in Romania

Elena Lazar[1], Ioana Andreescu[2], Ana Lazar[3], Simona Coniac[3] & Corin Badiu[2,3]
[1]Institute of Oncology, Bucharest, Endocrinology, Bucharest; [2]National Institute of Endocrinology, Endocrinology IV, Bucuresti; [3]Carol Davila University of Medicine and Pharmacy, Bucharest

Background
In the last decade, immunotherapy proved to be the frontline in the fight against cancer in a rocketing area of cancer types. Boosting the body's inherent immune system, a new set of toxicities raised, labeled as immune-related adverse events (irAEs). Endocrine disorders, particularly thyroid dysfunctions, are by far the most frequent irAEs during immune checkpoint inhibitors (ICIs) therapy. New research data explored their predictive impact in cancer patients' overall survival. An in-depth endocrinological specific study was performed to evaluate endocrine irAEs caused by ICIs.
Methods
This is a retrospective analysis of endocrine irAEs from a cohort of cancer patients (mainly lung cancer and malignant melanoma) treated with ICIs in the Oncology Institute 'Prof. Dr. Alexandru Trestioreanu', Bucharest, Romania, from 1 October 2022 to 31 December 2023. The Institute endocrinologist assessed, followed and subsequently treated all the occurring endocrinopathies during immunotherapy. Endocrine irAEs were evaluated according to current medical practice based on routine clinical, biological and imaging criteria.
Results
Of 22 cancer patients that developed endocrine irAEs, we identified 5 cases of hypophysitis, 18 cases of thyroid disorder, 1 case of primary adrenal insufficiency, with one or more endocrine glands being affected. The anterior pituitary disorder involving several hormonal axes such as, thyroid, adrenal and gonadotropic deficiencies were common, with no proof of growth hormone deficit or hypoprolactinemia.
Conclusions
The expected increasing number of both malignancies and ICIs-treated cancer patients in the future exposes the endocrinologist face to face to a new area of pathology. Diagnosing and managing endocrine irAEs requires a collaborative effort between the oncologist and the endocrinologist to promote a better quality of life and a higher survival rate for cancer patients.

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P300

An apparently non-functional retroperitoneal SDHB-related paraganglioma

Ximena Carolina Vivas Vaca, Manuel Miguel Delgado Gómez, Ana Herrero Ruiz, Álvaro Valverde Márquez, Adriana Sofía Sánchez Velasco & María Teresa Mories Álvarez
Salamanca Health Care Complex, Endocrinology and Nutrition, Salamanca, Spain

Introduction
Paragangliomas (PGLs) are rare neuroendocrine tumors that arise from sympathetic or parasympathetic extra-adrenal paraganglia. PGLs have an extremely variable clinical presentation, depending on the localization, tumor size, catecholamine production, compressive symptoms, etc. Germline mutations in PGLs are associated in 30-35% of patients. Mutation in genes encoding the subunits of succinate dehydrogenase (SDH) leads to an increased risk of metastasis, specially SDHB mutation (35-75%). SDHB-related PGLs may be asymptomatic due to low tumoral catecholamine secretion or dopaminergic phenotype.
Case presentation
We report a case of 43-year-old man with no medical history or family history of interest, referred to our department for preoperative study. The patient presented a 4.1×5.2 cm retroperitoneal mass detected on CT scan for pain in the right groin. PGL was the first diagnosis suspicion. Laboratory tests showed 24-hour urinary excretion of normetanephrine, metanephrine and serum chromogranin A concentration within reference range. The patient underwent ^{123}I-MIBG scintigraphy with SPECT/CT that did not detect any functional lesion. Genetic testing was positive for heterozygous mutation in c.565Y>C p.(Cys189Arg) of the SDHB gen (there are 3 familial cases described). Laparotomy resection of the retroperitoneal mass was performed. Postoperative histopathological examination confirmed an extra-adrenal PGL of 4.5 cm. Lymph nodes were negative for malignant cells. During the follow-up, the patient remained well for 4 years (laboratory analysis and control CT were normal). Due to persistent pain in the right groin, laboratory tests and full body scan were carried out before the scheduled date. Surprisingly, significant elevation in 24-h urinary fractionated metanephrines [634μg/24-h (reference range <76 μg/24-h)] and 24-h urinary fractionated normetanephrine [3064 μg/24-h (reference range <444 μg/24-h)] were observed; 3-metoxitiramine and chromogranin were within the normal range. Control CT scan revealed a recurrent retroperitoneal tumor of 3.2×4.7 cm and two new masses (3.3×3.5 cm aortocaval and 1.4×1.9 cm duodenal). SPECT/TC with somatostatin analogue showed pathological accumulation in the described lesions. After alpha blockage with doxazosin, resection of the masses was performed and histopathological examination confirmed to be metastatic PGL. ^{68}Ga-DO TATATE PET/CT was carried out in order to consider metabolic therapy, which revealed increased uptake on the residual tumor post operatively.
Conclusions
– The clinical evolution observed in our patient, from non-functional to functional PGL and from localized to metastatic disease, shows us the unpredictable evolution of Cys189Arg mutation of the SDHB gen-related PGL.
– Our case demonstrates the importance of a rigorous follow-up of patients with SDHB-related PGL due to high metastatic potential.

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P301

Dual targeting Boolean logic gate CAR-T cells for selective tumor antigen encounter exert potent antitumor efficacy in advanced adrenocortical carcinoma

Marc Philipp Schauer[1,2], Andrea Stabile[2], Laura-Sophie Landwehr[1], Barbara Altieri[1], Martin Fassnacht[1,3], Justus Weber[2] & Michael Hudecek[2]
[1]University Hospital Würzburg, Department of Internal Medicine I, Division of Endocrinology & Diabetes, Würzburg, Germany; [2]University Hospital Würzburg, Department of Internal Medicine II, Center for Cellular Immunotherapy, Würzburg, Germany; [3]Comprehensive Cancer Center Mainfranken, University of Würzburg, Würzburg, Germany

Adrenocortical carcinoma (ACC) is a rare and aggressive endocrine malignancy that produces glucocorticoids in 60% of cases causing clinically relevant hypercortisolism. Since, we observed in another study, that shaping these immunosuppressive and life-threatining properties with corticosteroid inhibitors not only led to a glucocorticoid receptor-related downregulation of ROR1 but also to the upregulation of another promising membrane bound oncogenic antigen* (AG), we sought to investigate the role of a dual targeting approach using bispecific CAR-T cells in ACC. We initially evaluated AG-expression in a representative cohort of ACC samples ($n=62$) using qRT-PCR and immunohistochemistry (IHC) and show that the AG is sufficiently and homogenously overexpressed in human ACC tissues ($P<0.001$). Moreover, it is strongly associated with a poor median overal survival ($Chi^2=6.207$, $P=0.013$) and disease progression ($Chi^2=5.485$, $P=0.019$). We further demonstrate high levels of AG-expression in four different ACC cell lines using qRT-PCR and qFACS-analysis. To evaluate the interplay between ROR1 and AG we used Duolink technology, RNA-Nanostring nCounter sequencing, qRT-PCR and IHC. While observing a strong downregulation of ROR1 after corticosteroid inhibitor treatment on the one hand, we demonstrate a strong increase of AG-expression after different doses of metyrapone (21-fold change, $P=0.003$) and ketoconazole (35-fold change, $P<0.001$) on the other (values are shown for NCI-H295R cell line, respectively). Next, we used non-viral sleeping beauty transposons and CRISPR/Cas9 to generate different mono- and bispecific CAR-T cells targeting ROR1 and AG and evaluated their antitumor functionality *in vitro*. We observed potent antitumor efficacy, cytokine release and proliferation upon antigen contact of all different CAR-T cell modifications. To maintain T cell functionality, to prevent CAR-T cell tonic signalling and to reduce on-target off-tumor toxicities (OTOT) by aiming two antigens, we also attempted to apply Boolean logic gating to our CAR-T cells to prevent toxicity in healthy tissues that express very low levels of one of our two antigens. We exploited the approach of a new way of CAR engineering using co-opted intracellular proximal T cell signalling molecules that can be repurposed into surface receptors demonstrating no OTOTs of CAR-T cell function in single antigen positive tissue *in vitro*. Our preliminary data demonstrate an interplay between two CAR-T cell targets which can be used for a combined treatment approach with steroid inhibitors. We also show Boolean logic gating as novel and potentially safer approach of CAR-T cell engineering in advanced ACC. *The investigated antigen will be kept confidential because of patent law reasons.

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P302

Alteration in the molecular components of machinery that regulate gene expression mechanisms and genomic stability in thyroid cancer and their association with tumour behaviour and/or clinical features

Andrea Martínez Vara[1,2], Francisco Porcel Pastrana[1,2,3,4], Isidoro Di-Caro[1,2,3], André Sarmento-Cabral[1,2,3,4], Rafael Sánchez Sánchez[2,3], Ana Romero Lluch[5], Pilar Santisteban[6], Elena Navarro González[5], María A Gávez Moreno[1,2,3], Raúl M Luque[1,2,3,4] & Antonio J Martínez Fuentes[1,2,3,4]
[1]Maimónides Institute for Biomedical Research of Córdoba (IMIBIC), Córdoba, Spain; [2]Universidad de Córdoba, Biología Celular, Fisiología e

Inmunología, Córdoba, Spain; [3]Reina Sofía University Hospital (HURS), Córdoba, Spain; [4]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Córdoba, Spain; [5]Servicio de Endocrinología y Nutrición, Hospital Virgen del Rocío, Sevilla, Spain; [6]Instituto de Investigaciones Biomédicas "Alberto Sols", Consejo Superior de Investigaciones Científicas; Universidad Autónoma de Madrid (CSIC-UAM) and Centro de Investigación Biomédica en Red de Cáncer (CIBERONC), Instituto de Salud Carlos III (ISCIII), Madrid, Spain

Emerging evidence indicates that the cellular machineries controlling gene expression mechanisms and genomic stability are altered in several endocrine-related cancers (ERCs), leading to some oncogenic events associated with tumour progression/aggressiveness. However, whether this phenomenon also occurs in thyroid cancer has not been yet explored. Therefore, this study was focused on: 1) investigating the potential alteration in the levels of components of the molecular machineries that control either RNA metabolism [Splicing machinerie, RNA-Exosome complex, Non-sense Mediated Decay (NMD)] or genomic stability (shelterin-telomerase) in clinically well-characterized human papillary and medullary thyroid cancer samples compared to its adjacent non-tumour tissue; and, 2) whether these alterations might be associated with relevant clinical parameters. Results revealed a clear dysregulation of several components of these machineries in papillary and medullary thyroid cancer samples, wherein the expression of specific components was associated with key clinical parameters. Based on these results, we explored different functional (e.g. proliferation, migration, and tumour-spheres and colonies formation) and mechanistic (gene expression/signalling pathways) assays in human thyroid cancer cell models (TCP1 and Cal62). In general, these *in vitro*studies revealed that different molecular components of splicing, RNA-exosome, NSMD and telomerase machineries significantly modulated cell aggressiveness features in thyroid cancer cells. Moreover, we targeted the key splicing-factor-3B-subunit-1 component (SF3B1; a core component of the splicing machinery) with the specific inhibitor pladienolide B as well as with a specific siRNA to carry out the silencing of SF3B1 expression. Results revealed that both pladienolide-B treatment and the silencing of SF3B1 significantly decreased different aggressiveness parameters (proliferation, migration, tumour-spheres and colonies formation) in thyroid cancer cells, thus confirming the critical role of SF3B1 and consequently, of the splicing machinery, in thyroid pathophysiology. Altogether, our data demonstrate a drastic dysregulation of the key components of the molecular machineries controlling gene expression mechanisms and genomic stability (particularly splicing) in papillary and medullary thyroid cancer samples that might be associated to the tumorigenesis of this ERC. In particular, the genetic and/or pharmacological inhibition of SF3B1 may represent a promising novel therapeutic strategy worth to be explored through randomized controlled trials that could improve the outcome of patients affected by clinically aggressive thyroid cancer.

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P303

Clinical characteristics and survival of patients with functional pancreatic neuroendocrine tumors

Bojana Popovic, Sanja Ognjanovic, Dusan Ilic, Valentina Elezovic Kovacevic, Milica Opalic Palibrk, Lena Radic, Katarina Krstic, Marijan Micev & Djuro P Macut
University Clinical Centre of Serbia, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Beograd, Serbia

Aim
Functional neuroendocrine tumors (NETs) represent a specific diagnostic and therapeutic challenge, since hormonal clinical syndrome can severely complicate clinical picture and affect treatment. Our aim was to analyze characteristics and survival of functional pancreatic NETs.
Materials and methods
We retrospectively analyzed data from 272 patients with pancreatic NETs treated at our department from the year 2005 till 2023. The patients underwent standard radiological, pathohistological and hormonal evaluation. All tumors were graded according to current ENETS guidelines. Disease stage was defined according to the ENETS/AJCC TNM staging system. Differences between continuous variables were analyzed by non-parametric tests and differences between frequencies by χ^2-test. Overall survival was analyzed by Kaplan–Meier method, and differences by Cox-regression analysis. Statistical analysis was performed by SPSS software.
Results
Functional tumors were diagnosed in 61 patients (22.4%): 24 insulinomas (8.7%), 11 serotoninomas (18%), 8 gastrinomas (13.1%), 6 patients with ectopic Cushing's syndrome (9.8%), 3 patients PTHrP secretion (4.9%), 2 glucagonomas (3.3%), and 1 VIP-oma (1.6%), while the remaining 6 patients had combinations of 2 or more aforementioned hormonal hypersecretions. Majority of functional NETs were well differentiated (NET G1 29.5%, NET G2 41.0%, NET G3 13.1%, NEC G3 1.6%, MiNEN 1.6%), and better differentiated compared to nonfunctional NETs ($P=0.018$). Functional tumors were significantly smaller ($P<0.05$), more related to MEN1 syndrome ($P=0.005$), and with lower disease stage than nonfunctional ($P=0.011$). Median overall survival of functional NETs was 104.0 months (95%CI 100.2–206.8). This was not different to nonfunctional tumors ($P=0.259$), except that NET G3 functional NETs had a tendency towards shorter survival. There was significant difference in survival within a group of functional NETs ($P<0.05$), with patients with insulinomas having the longest, and patients with ectopic Cushing's syndrome having the shortest survival. Patients with insulinomas had significantly longer survival when compared to nonfunctional NETs overall ($P=0.013$), but this was due to insulinomas being exclusively grade G1 and G2 (55.6% and 44.4% respectively), and of lower stage (SI and SII 73.7%). When G1 and G2 insulinomas were compared to respective nonfunctional tumors, there was no significant difference in survival ($P=0.326$ and $P=0.909$ respectively). On the other hand, patients with ectopic Cushing's syndrome had significantly shorter survival compared to nonfunctional NETs irrespectively of grade or stage ($P=0.008$ and $P=0.007$ respectively).
Conclusion
Almost one quarter of patients with pancreatic NETs have a recognizable hormonal syndrome. Despite some more favorable features compared to nonfunctional tumors, certain hormonal profiles independently affect survival.

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P304

Basal calcitonin and calcium gluconate test in suspect medullary thyroid carcinoma: Are we expecting too much from stimulated calcitonin?

Renato Diana[1], Erika Grossrubatscher[2], Renato Cesare Cozzi[2], Paolo Dalino Ciaramella[2] & Iacopo Chiodini[1,2]
[1]University of Milan, Department of Biotechnology and Translational Medicine, Milan, Italy; [2]Ospedale Niguarda Ca' Granda, Endocrinology Unit, Milan, Italy

Introduction
Basal calcitonin (bCT) and calcium-stimulated calcitonin (sCT) levels are useful in the management of Medullary Thyroid Cancer (MTC). Nowadays several bCT/sCT cut-offs have been proposed but univocally accepted values are still lacking. We identified gender-specific CT cut-offs in a series of patients who performed calcium gluconate test at our Centre.
Methods
Our study includes a total of 35 patients (12 males and 23 females) with thyroid nodules and biochemical suspect of MTC that performed calcium gluconate test from 2017 to 2023 and underwent total thyroidectomy according to available sCT cut-off reported in literature (until 2020 in males bCT 68 pg/ml, sCT 544; in females bCT 26, sCT 79; since 2021 in males bCT 34, sCT 466; in females, bCT 30, sCT 79). Patients with RET gene mutation were excluded. We compared bCT and sCT levels with histological results in order to define best internal cut-offs to predict diagnosis of MTC.
Results
The best cut-offs of bCT and sCT for the diagnosis of MTC were: >29.6 pg/ml (Sensitivity, Sn 85.7%, Specificity, Sp 100%, Diagnostic accuracy, DA 91.6%, $P<0.0001$) and >1242 pg/ml (Sn 57.1%, Sp 100%, DA 75%, $P=0.12$) in males; >14.6 pg/ml (Sn 100%, Sp 90%, DA 95.6%; $P<0.0001$) and >442 pg/ml (Sn 61.5%, Sp 90%, DA 73.9%, $P=0.08$) in female. According to these cut-off values, bCT was able to identify MTC in 100% of females and 85.7% of males (one male case of MTC with both negative bCT and sCT underwent total thyroidectomy for symptomatic goitre). With bCT we didn't have false positive cases in males and we had one false positive case in females. Conversely, sCT showed an inadequate diagnostic accuracy and a non-negligible risk of misdiagnosis. If we had applied only sCT cut-offs in order to decide for surgery, we would have had missed 7 patients with MTC (2 males, 5 females). Indeed, these patients had positive bCT and negative sCT and underwent thyroidectomy according to available sCT cut-off at the time of surgery.
Conclusions
In our series bCT had higher diagnostic accuracy than sCT for diagnosis of sporadic MTCs. Stimulated test seems to provide no diagnostic improvement as compared to bCT and, given its low sensitivity, it may lead to miss some MTCs cases that could be correctly identified by bCT.

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P305

Cell cycle regulation in parathyroid adenomas and multiglandular parathyroid disease: Similarities, differences and heterogeneity

Romans Uljanovs, Boriss Strumfs & Ilze Strumfa
Riga Stradins University, Department of Pathology, Riga, Latvia

Background
Primary hyperparathyroidism represents the third most common endocrine pathology. Recently, the morphological classification of underlying parathyroid lesions underwent significant alterations: the former primary parathyroid hyperplasia was reclassified as multiglandular parathyroid disease (MPD), a term that is in line with clonality studies and surgeons' needs; and the entity of atypical parathyroid tumour was separated from adenoma. Although the diagnostics of hyperparathyroidism is largely dependent on laboratory and radiological findings, pathological investigation of surgically removed glands can help to verify the diagnosis, to reach it in difficult cases and to assess the pathogenesis.
Aim
The **aim** of our study was to evaluate expression of cell cycle and apoptosis-related proteins in parathyroid adenoma and MPD in comparison to unequivocal parathyroid carcinoma and normal/atrophic glands.
Materials and methods
Expression of Ki-67, p21, p27, cyclin D1 and Bcl-2 were detected by immunohistochemistry and quantified (%) in adenomas (102) and MPD (27), compared to carcinoma (5) and normal glands (45). Descriptive statistics, Kruskal–Wallis test with Bonferroni correction and Mann–Whitney test were applied.
Results
The mean fraction of Ki-67 was 1.6% in adenomas and 1.0% in MPG, contrasting with 0.4% in normal glands and 5.8% in carcinoma; the highest values were in parallel: 3.4% vs 2.8% vs 1.0% vs 11.8%. p21 protein showed the highest expression in MPD (mean 15.7%; highest 29.8%), followed by adenoma (12.8%; 23.7%), carcinoma (7.6%; 15.6%) and normal glands (3.1%; 3.8%). Cyclin D1 levels in MPD (24.5%; 42.5%) exceeded the expression in adenoma (21.0%; 22.8%) although the levels were highest in carcinoma (31.5%; 41.8%) and low in normal tissues. Loss of p27 was significant only in carcinomas (59.0%), contrasting with 92.8% in adenomas, 94.3% in MPD and 97.9% in normal tissues. Similarly, loss of BCL2 was notable in carcinoma (28.2%), compared to adenoma (66.7%), MPD (61.3%) and normal glands (75.6%). Notably, nuclear markers showed remarkable heterogeneity by dense clusters of positive cells. Across all groups, significant differences were disclosed regarding the mean and highest fraction of Ki-67 (both $P<0.001$), p21 (both $P<0.001$), cyclin D1 ($P=0.02$) and p27-expressing cells ($P=0.010$). In contrast, adenomas, compared to MPD, featured higher proliferation but lower cyclin D1 levels; these groups did not differ by p27 and Bcl2.
Conclusion
The immunophenotype shows enhanced proliferation along with regulatory similarities between adenoma and multiglandular parathyroid disease, indicating pathogenetic links. Expression of cell cycle-related proteins in hyperfunctioning parathyroid tissues shows remarkable heterogeneity by dense clustering of positive cells, suggesting paracrine signalling mechanisms.

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P306

Long-acting starch (Glycosade(R)): An effective treatment for insulinoma-induced hypoglycemia – A case report

Karen Andrea Castillo Arias, Diego Duminy, Mireia Mora, Clara Viñals, Felicia A Hanzu, AIDA OROIS & Adriana Pane
Hospital Clínic Barcelona, Barcelona, Spain

Introduction
Insulinoma is a rare, generally benign neuroendocrine tumor, primarily manifesting as hypoglycemia in non-diabetic patients. Although surgery is the gold standard treatment for insulinoma, managing hypoglycemia becomes challenging in cases where surgery is not feasible. This challenge arises due to significant side effects that often limit the use of most drugs and therapeutic alternatives.
Case report
A 90-year-old non-diabetic man was admitted to our hospital for study due to unexplained recurrent symptomatic hypoglycemia. After excluding common causes of outpatient hypoglycemia, a post-fasting blood test revealed endogenous hyperinsulinism with blood glucose at 2.4 mmol/l, insulin at 9.6 µIU/ml (66.6 pmol/l, elevated), proinsulin at 14.6 pmol/l (elevated), and C-peptide at 2.31 ng/ml (0.76 nmol/l, elevated). Anti-insulin antibodies were negative, and urinary sulfonylurea determination was also negative. An abdominal CT scan identified a 15-mm solid nodular lesion in the tail of the pancreas. A gallium-68-tetraxetane Tyr3-octreotate PET-CT scan indicated that the mass had a maximum normalized uptake value of 19.22 and expressed somatostatin receptors 2 and 5, confirming the diagnosis of insulinoma. Due to the patient's high surgical risk, conservative medical management was chosen. Upon admission, intravenous dextrose treatment was initiated. After confirming the suspicion of insulinoma, low doses of diazoxide were attempted. However, due to the development of symptoms such as heart failure, lower limb edema, and hyponatremia upon increasing the diazoxide dose, a dietary approach took priority. The use of modified corn starch in fractionated doses, guided by continuous glucose monitoring, was introduced.
Discussion
There is limited evidence supporting the use of glycosade to treat hypoglycemia in insulinoma. Glycosade, a modified corn starch with slower absorption than normal corn starch, is employed in patients with glycogenosis to prolong the time between meals. Given its absorption profile, ease of administration, minimal short-term side effects, and relatively low cost, we consider it a valuable dietary alternative for controlling hypoglycemia. This is especially relevant today, as continuous glucose monitoring allows for a more accurate estimation of each patient's hypoglycemia pattern. This approach proves particularly applicable in patients who are inoperable, frail, and at high risk of adverse effects from traditional medical therapies.

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P307

The intrinsically disordered activation function 1 of Progesterone receptor is involved in the dynamics of the receptor complex

Pheck Khee Lau[1], Shi Hao Lee[1], Chew Leng Lim[1], Qian Yee Woo[1], Amanda Woo[1] & Valerie Lin[1,2]
[1]School of Biological Sciences, Nanyang Technological University, Singapore, Singapore; [2]Nanyang Technological University, School of Biological Sciences,, Singapore, Singapore

Progesterone receptor (PgR) is critically involved in the development of the mammary gland and the uterus in response to progesterone. It is also implicated in cancer development of these organs. An in depth understanding of how it works is pivotal for developing therapeutic interventions. PgR is a member of the nuclear receptor superfamily of transcription factors with conserved domain structures. Its transcription activity is mainly mediated by the activation function 1 (AF1) in the disordered N terminal domain (NTD) and the highly structured activation function 2 (AF2) in the ligand binding domain (LBD). It is established that AF2 forms coregulator binding interface upon ligand binding. But little is known about how AF1 works. We identified 3 critical AF1 residues K464, K481 and R492 that can be monomethylated. Mutations of these three residues to phenylalanine (KKR/FFF) largely abolished PR activity in reporter gene assay but increased AF1 interactions with coactivator SRC1 and AF2. We further determined the effect of AF1 mutations on PR regulation of cell growth, adhesion and global gene expression in MCF-7 cells stably expressing the Wt PRB or the AF1 mutant. It was found that KKR/FFF mutations significantly impaired the effect of PR on cell proliferation and cell spreading. RNA-Seq analysis revealed that the KKR/FFF mutation considerably impaired PR regulated gene expression in 40% of the genes, which included most of the well characterized PR target genes. Importantly, the impaired gene regulation by KKR/FFFF mutant is not associated with a reduced enhancer/promoter occupancy. Considering stronger interactions of AF1-KKR/FFF with AF2 and coactivator SRC1, our data lend support to the tripartite relationship among AF1, AF2 and coregulators, in which AF1 plays a key role in modulating dynamics of PgR transcription complex.

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P308

Possible prognostic role of BMI before chemotherapy in the outcomes of women with ovarian cancer

Stavroula Paschou[1], Aggeliki Andrikopoulou[2], Nikoletta Mili[3], Anna Svarna[2], Maria Kaparelou[2], Katerina Stefanaki[1], Nikolaos Dedes[2], Efstathia Liatsou[2], Nikolaos Thomakos[4], Dimitrios Haidopoulos[4], Theodora Psaltopoulou[2], Efstathios Kastritis[2], Flora Zagouri[2], Meletios-Athanasios Dimopoulos[2] & Michalis Liontos[2]

[1]Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, Endocrine Unit and Diabetes Center, Department of Clinical Therapeutics, Athens, Greece; [2]Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece., Hematology and Oncology Unit, Department of Clinical Therapeutics, Athens, Greece; [3]Aretaieio Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece., 2nd Department of Obstetrics and Gynaecology,, Athens, Greece; [4]Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece., 1st Department of Obstetrics and Gynaecology, Athens, Greece

Introduction
Survival rates for ovarian cancer remain distressingly low. Despite established prognostic factors, the need for identifying modifiable parameters to influence survival outcomes is imperative. Overweight and obesity, prevalent conditions, have been implicated in cancer development and potentially poor survival. However, conflicting data on the association of Body Mass Index (BMI) with Progression-Free Survival (PFS) and Overall Survival (OS) in ovarian cancer patients necessitate further exploration.
Aim
This study aims to investigate the prognostic role of BMI before chemotherapy in women with ovarian cancer, specifically focusing on PFS and OS.
Patients and methods
A retrospective analysis encompassed 1136 patients diagnosed with ovarian carcinomas between 1995 and 2018. Patients were categorized based on BMI at presentation, and a comprehensive examination of clinicopathological, treatment, and survival data was conducted.
Results
In the patient population, normal weight patients (BMI < 25 kg/m^2) demonstrated a median PFS of 12.8 months (95% CI 11.7–13.9 months), while overweight/-obese patients (BMI ≥ 25 kg/m^2) exhibited a significantly longer median PFS of 14.9 months (95% CI 13.6–16.4 months, $P=0.006$). No statistically significant difference was noted in median OS between the two BMI groups. Subgroup analysis for different histological subtypes revealed a statistically significant benefit for overweight and obese patients with serous and endometrioid histology (mPFS 12.9 months, 95% CI 11.7–14.0 vs 15.6 months, 95% CI 13.9–17.3, $P=0.012$ and 14.6 months 95% CI 13.7–15.5 vs 25.6 months, 95% CI 9.5–41.7, $P=0.031$, respectively). Additionally, BMI ≥ 25 kg/m^2 demonstrated a significant advantage in advanced-stage disease.
Conclusions
The study underscores the intricate association between BMI and ovarian cancer prognosis. While PFS demonstrated a significant difference between BMI groups, OS did not exhibit such disparity.

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P309

Cystic mediastinal lesions as presenting manifestation of papillary thyroid cancer

Eleana Zisimopoulou, Maria Boudina, george christantoniou, Chrysanthi Zouli, Mariana Stamati, aimilia fotiadou, chrysanthi balodimou & Alexandra Chrisoulidou
Theagenio Cancer Hospital, Endocrinology, Thessaloniki, Greece

Background
Distant metastasis, as the initial manifestation of papillary thyroid cancer (PTC), is uncommon. Here, we present two unusual cases of large cystic mediastinal lesions, with histology indicative of metastasis from PTC as first diagnosis.
Case presentation
We present two male patients, aged 46 and 50 years old, who were referred to our department. The first patient, complained of persistent cough and underwent a thorax CT which revealed a large 10 cm cystic mass. Due to compressive symptoms, he underwent surgical excision of the cystic mass. The histopathology revealed neoplastic cells in the lining of the cyst, with positive immunohistochemistry for TTF-1 and PAX-8. Additionally, two lymph nodes were found in the surrounding fat tissue, constituted of cells of epithelial origin, positive in thyroglobulin (Tg), TTF-1 and PAX-8. The second patient presented with similar symptoms (persistent cough, shortness of breath in minimal exercise) and underwent a thorax CT. A large cystic mass of 8.2 cm was revealed in the mediastinum, which was surgically removed. The histopathology identified a cyst with peripheral lymphocytes and the presence of two neoplastic lesions in the surrounding fat tissue, consisting of epithelial cells with papillary architecture and positive immunochemistry in Tg and TTF-1. The work-up that followed included imaging of the thyroid by ultrasound, identification of suspicious lesions and total thyroidectomy. In the first case, a 6.7 cm PTC of tall cell variant was revealed. In the second case, the histopathology indicated a multifocal PTC metastatic to cervical lymph nodes. They both received a therapeutic dose of radioidine ablation (100 mCi). Imaging, six months after the diagnosis, did not reveal any further metastases. At present, nearly a year after operation, both patients receive thyroxine suppression therapy and are on close monitoring including measurement of thyroglobulin levels, thyroid ultrasound and thorax CT imaging.
Conclusions
In the literature, mediastinal lesions related to thyroid cancer are uncommon. However, thyroid cancer may present with extracervical manifestations such as mediastinal lesions, which probably represent the cystic degeneration of mediastinal lymph nodes. Therefore, thyroid cancer may be a part of the differential diagnosis of cystic mediastinal lesions.

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P310

Immunohistochemical profiling of HIF-2α and SSTR2 with the tumor microenvironment in metastatic pheochromocytoma and paraganglioma

Masaki Uchihara[1,2], Akiyo Tanabe[1], Yuki Kojima[2], Tatsunori Shimoi[2], Akiko Maeshima[2], Kotaro Umamoto[1], Eijiro Nakamura[2], Akihiko Shimomura[1], Chikako Shimizu[1], Kan Yonemori[2] & Hiroshi Kajio[1]
[1]National Center for Global Health and Medicine; [2]National Cancer Center Hospital

Introduction
Metastatic pheochromocytomas and paragangliomas (PPGLs) are rare endocrine malignancies with limited effective treatment options. Immunotherapy, a breakthrough in oncology, is effective in some cases of PPGLs; however, the response rate remains limited. Therefore, one strategy to improve immunotherapy is combining drugs with different action mechanisms and target resistance. The association between the tumor microenvironment (TME), including tumor-associated macrophages (TAMs) with hypoxia-induced factor-2α (HIF-2α) and somatostatin receptor 2 (SSTR2) in PPGLs, is critical for optimizing combination therapeutic strategies with immunotherapy, remains largely unexplored.
Methods
We analyzed the expression of HIF-2α, SSTR2A, and TME components, including tumor-infiltrating lymphocytes (CD4 and CD8), TAMs (CD68 and CD163), and PD-L1, using immunohistochemistry in patients with PPGLs. We also evaluated the association between these biomarkers, the prognosis, and the response to systemic chemotherapy.
Results
Among 45 patients with PPGLs, HIF2α and SSTR2A were positively expressed in 14 (31.1%) and 21 (46.7%) patients, respectively. Positive correlations were observed between CD4, CD8, CD68, and CD163 levels. A negative correlation was found between the CD163/CD68 ratio (an indicator of M2 polarization TAMs) and SSTR2A expression ($r=-0.385$, $P=0.006$), with a stronger correlation in metastatic cases ($r=-0.535$, $P=0.009$). HIF-2α expression positively correlated with PD-L1 IHS ($r=-0.348$, $P=0.013$). The co-expression of PD-L1 (IHS > 10) and HIF-2α was found in seven patients (15.6%). In light of the negative correlation between SSTR2A and the CD163/CD68 ratio, our analysis assessed the time of tumor progression across the four groups based on these parameters. All 11 patients in the low CD163/CD68 ratio and the negative expression of the SSTR2A group showed no progression or detection of metastasis. No association was observed between HIF-2α positivity, CD163/CD68 ratio, and response to CVD chemotherapy.
Conclusion
We found a negative association between M2 polarization TAMs and SSTR2A expression in PPGLs. We also observed a relationship between high PD-L1 expression and increased HIF-2α expression. Our data provides the potential of combination therapy with immunotherapy and peptide receptor radionuclide therapy or HIF-2α inhibitors as a treatment option in selected PPGL populations.

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P311

The impact of primary tumor site on clinical manifestation and prognosis of ectopic Cushing's syndrome (ECS). Do pulmonary neuroendocrine tumors stand out?

Aleksandra Gamrat[1,2], Mari Minasyan[1], Maria Aleksandra Komisarz-Calik[1], Ewelina Rzepka[1], Joanna Paleń-Tytko[1], Marta Opalinska[1], Alicja Hubalewska-Dydejczyk[1] & Aleksandra Gilis-Januszewska[1]

[1]Jagiellonian University Medical College, Chair and Department of Endocrinology, Kraków, Poland; [2]Jagiellonian University Medical College, Doctoral School of Medical and Health Science

Introduction
Ectopic Cushing's syndrome (ECS) is a rare disease with limited and error-prone published data on the epidemiology, clinical presentation and diagnosis of ECS.
Objectives
This study aims to examine the clinical course of patients with ECS in relation to the primary tumor localization.
Methods
Thirty-five consecutive ECS patients at a tertiary clinical center were analyzed. The clinical, biochemical (including CRH/desmopressin tests/BIPSS in selected cases) and imaging (CT/MRI, somatostatin receptor imaging, and FDG PET/CT) assessment were performed. Three patients with SCLC were excluded from further analysis.
Results
The primary lesion was identified in 28/32 patients. Neuroendocrine tumor (NET) constituted 47% of all ECS (60% gastroenteropancreatic (GEP-NETs), 40% thoracic (1 thymic and 5 pulmonary carcinoids (PC)). The median follow-up was 12 months, in the PCs was significantly higher compared to the GEP-NETs (54 vs 11 months). There were 18 deaths (56.25%). In patients with PC, 1 patient died due to pulmonary embolism, while in the GEP-NETs 8(89%) patients died due to disease progression. In patients with disseminated disease 1 patient underwent chemotherapy, 4 were treated surgically, 4 with PPRT. 5/6 of PCs underwent radical surgical treatment, all were treated with steroidogenesis inhibitors. There was a significant difference in the mean age at diagnosis between women and men ($F=64.25$ vs $M=51.06$ years, $P=0.02$). The dominant clinical feature for the entire group were muscle weakness (78.13%) and edema (62.5%). Typical changes in appearance characteristic of Cushing's syndrome occurred in 6(16%) of patients, in 4/5 PC. PCs comparing to other ECSs showed more frequently striae (80% vs 14.81%, $P=0.003$), fat tissue redistribution (80% vs 51.85%, $P=0.10$). No PC experienced weight loss, observed in 11(47.4%) others ECSs ($P=0.05$). The median nocturnal serum cortisol was higher in patients with NETs compared to other ECSs (61 vs 25.5 μg/dl, $P=0,058$). In the GEP-NETs, the median concentration of both morning cortisol (71 vs 42 μg/dl, $P=0.02$) and midnight cortisol (64 vs 25.5 μg/dl. $P=0.008$) was higher than in other ECSs. In PCs, there was a strong correlation between the midnight serum cortisol and the severity of hypocalcemia (Spearman's coefficient -0.90, $P<0.05$), which was not present in GEP-NETs.
Conclusion
The clinical picture of ECS is highly variable. PCs tend to display more prevalent classic symptoms of CS and notably extended survival times compared to other ECSs. Further studies are needed to understand the natural history of ECS and to improve the diagnosis and treatment outcomes of this rare disease.

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P498

Once-daily oral paltusotine in the treatment of patients with carcinoid syndrome: interim results from a phase 2, randomized, parallel-group study

Aman Chauhan[1], Amr Mohamed[2], Keith Usiskin[3], Cosina Mui[3], Joseph Dillon[4], Xiaolin Fan[3], Shagufta Shaheen[5], Juan Manuel O'Connor[6], Simron Singh[7], Hjalmar Lagast[3] & Alan Krasner[3]
[1]University of Kentucky Healthcare, Lexington, USA; [2]University Hospital, Case Western Reserve University, Cleveland, USA; [3]Crinetics Pharmaceuticals, San Diego, USA; [4]University of Iowa, Carver College of Medicine, Iowa City, USA; [5]Stanford Medicine, Stanford, USA; [6]Instituto Alexander Fleming, Buenos Aires, Argentina; [7]Sunnybrook Health Sciences Center, Toronto, Canada

Background
Carcinoid syndrome (CS), the most common functional neuroendocrine tumor (NET) syndrome, is characterized by watery diarrhea or cutaneous flushing. While somatostatin receptor ligand (SRL) depot injections are mainstay treatments for CS, discomfort with injections and inadequate symptom relief at labeled doses are seen with many patients. Paltusotine is an investigational once-daily, oral, selective SST2 agonist in development for the treatment of acromegaly and CS. In patients with acromegaly, paltusotine has been shown to maintain IGF-I control at levels similar to those for injected depot SRLs.
Methods
This ongoing open-label, multicenter study examines the safety, tolerability, pharmacokinetics, and exploratory efficacy of paltusotine in the treatment of patients with CS. Eligible patients had documented, well-differentiated, grade I or II NETs with CS. Patients who were actively symptomatic (average of ≥ 4 BMs per day or >2 flushing episodes per day in ≥ 2 days over a 2-week period) and naïve to SRL therapy, or patients with symptom control on SRLs and demonstrated symptom worsening after SRL washout, were randomly assigned to receive 40 mg or 80 mg of once-daily oral paltusotine for 8 weeks. Safety assessments included adverse event (AE) monitoring, clinical laboratory tests, physical examinations, vital signs, and electrocardiograms. Exploratory efficacy was assessed using a daily electronic symptom diary.
Results
This interim analysis includes 16 patients who received paltusotine and had been in the study long enough to complete the randomized treatment period. Mean age was 61 years; 56% of patients were female. Six patients were naïve to SRL therapy and 10 were previously controlled on SRLs. Four patients met the entry criteria for flushing only, 6 for BM only, and 6 for both. One patient discontinued prior to the end of randomized treatment. At Week 8, mean reduction from baseline in daily BM frequency was -1.3 and in daily flushing frequency was -2.2. Mean decrease in daily frequency of urgent BM episodes was -0.6; mean decrease in flushing severity (worst flushing score, rated on a scale from 0 to 10) was -2.9. Four patients had their paltusotine dose increased during the randomized treatment period. There were no serious AEs considered related to study treatment and no AEs leading to discontinuation. No new safety signals were identified.
Conclusions
Interim data from this phase 2 study suggest that oral paltusotine controls the symptoms of CS and is well tolerated.

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P499

Early detection of recurrence and progress using serum steroid profiling by LC–MS/MS in patients with adrenocortical carcinoma

Otilia Kimpel[1], Barbara Altieri[1], Ulrich Dischinger[1], Carmina Fuss[1], Max Kurlbaum[1,2] & Martin Fassnacht[1,3]
[1]University Hospital, University of Würzburg, Germany, Division of Endocrinology and Diabetes, Dept. of Medicine,, Würzburg, Germany; [2]Core Unit Clinical Mass Spectrometry, Central Laboratory, University Hospital Würzburg, Germany; [3]Comprehensive Cancer Center Mainfranken, University of Würzburg, Germany

Background
Serum liquid chromatography–tandem mass spectrometry (LC–MS/MS) steroid profiling is used for the diagnosis of adrenocortical carcinoma (ACC). Guidelines recommend endocrine work-up in addition to radiological imaging for follow-up in ACC, but data on this topic are scarce.
Aim
To retrospectively investigate an earlier detection of a recurrent or progressive disease by using endocrine follow-up with LC–MS/MS measurements in comparison to radiological imaging.
Methods
Patients were included in this retrospective study if pre-therapeutic hormone values, regular tumour evaluation by imaging, steroid measurements by LC–MS/MS, and details on therapies were available. The utility of steroid profiles in detecting recurrence or disease progression was assessed, whereby 'endocrine progress' was defined by elevation of at least 3 of 13 analysed hormones.
Results
Patients were divided in two cohorts. Cohort A included 47 patients after R0 resection, of whom 15 experienced recurrence and 32 did not. In cohort B, 52 patients with advanced disease (including 7 patients of cohort A with recurrence) could be evaluated on 74 visits when progressive disease was documented. In 20 of 89 cases with documented recurrence and disease progression, 'endocrine progress' was detectable prior radiological progress. In these cases, recurrence/-progression was detected in median 32 days earlier by steroid measurement than by imaging, with 11-deoxycortisol and testosterone being the most sensitive markers. In 25/89 cases, no steroid hormones were elevated although a recurrence or a progressive disease was confirmed by radiologic imaging, whereas the remaining 44/89 cases did either have only 1–2 elevated steroids or the altered hormone pattern was only detected at the time, when the progress was also documented by imaging. In only 5/89 patients (5.6%) with recurrent or progressive disease an 'endocrine progress' (defined by at least 3 elevated steroids) was falsely diagnosed. Finally, patients with an early detection of a recurrence or a progression were compared to patients without reliable elevated steroid hormones. We saw a significant difference in the documented tumour mass in patients with or without an early detection (11.4 cm vs 7.4 cm; $P=0.039$). Mitotane could have an influence on steroid elevation since one third of patients without a clear steroid elevation had a mitotane plasma level above 14 mg/l, whereas this was only the case in 10% with an earlier 'endocrine progress' ($P=0.034$).

Conclusion
In conclusion, steroid profiling by LC–MS/MS is of value in detecting recurrent/progressive disease in ACC especially in patients with significant tumour volume.

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P500

Catching the silent culprits: Prospective TERT promoter mutation screening for minimally invasive follicular and oncocytic thyroid carcinoma in clinical practice

L Samuel Hellgren[1,2], Adam Stenman[3,4], Catharina Larsson[1,2], Jan Zedenius[3,4] & C Christofer Juhlin[1,2]
[1]Karolinska Institutet, Department of Oncology-Pathology, Stockholm, Sweden; [2]Karolinska University Hospital, Department of Pathology and Cancer Diagnostics, Stockholm, Sweden; [3]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [4]Karolinska University Hospital, Department of Breast, Endocrine Tumors, and Sarcoma, Stockholm, Sweden

De-escalation of thyroid cancer treatment is crucial to prevent over-treatment of indolent disease. However, it also underscores the importance of identifying potential clinically aggressive cases that require completion lobectomy and adjuvant radioiodine therapy. *TERT* promoter mutations are molecular events closely associated to high-risk thyroid tumors with poor outcome, and may serve as markers for cases at risk of dissemination. In various international guidelines, minimally invasive follicular thyroid carcinoma and oncocytic thyroid carcinoma (miFTC/miOTC) measuring less than 2 cm (pT1a/1b) are classified as low-risk lesions. The Swedish national guidelines recommend no additional treatment beyond diagnostic lobectomy for these patients. Our study aimed to explore the association between size-based risk assessment and *TERT* promoter mutations. Between 2019 and 2023, 77 miFTCs/miOTCs diagnosed at our department underwent digital droplet PCR analysis of tumor DNA targeting *TERT* promoter mutational hotspots C228T and C250T. Histopathological, immunohistochemical and clinical variables were collected at the end of the study (January 2024). In total, *TERT* promoter mutations were found in 8 out of 77 cases (10.4%), 6 miFTCs, and 2 miOTCs. Mutated cases were pT2 ($n=2$) and pT3a ($n=6$), but no mutations were found among the pT1a/b tumors ($n=11$). Mutated tumors displayed an average size of 55.6 mm (range 37–100 mm), significantly larger than wildtype tumors with an average size of 38.2 mm (range 9–130 mm) (*P*-value: 0.014). There were no significant differences between patients with mutated or wildtype tumors regarding patient sex, age at surgery or the Ki-67 proliferation index. In conclusion, *TERT* promoter mutations in miFTC/miOTC are associated with larger tumor size. Clinical routine sequencing of pT1a/b miFTCs and miOTCs may not be beneficial. The current strategy of releasing small, low-risk lesions as outpatients without additional treatment is supported by our molecular risk stratification, indicating that *TERT* promoter mutational sequencing in clinical routine could be reserved for larger tumors.

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P501

Clinical features and outcome in patients with functional head and neck paragangliomas: French national cohort and literature review

Iuliia Pinigina[1], Philippe Ceruse[1], Philippe Herman[2], Cardot Catherine[3], Magalie Haissaguerre[4], Erika Cornu[5], Laurence Amar[6], Marie Batisse-Lignier[7], Laurence Chardon[1], Sara Barraud[8], Loic Feuvret[1], Marc Janier[1], Lasolle Hélène[1], Francoise Borson-Chazot[1] & Abeillon Juliette[1]
[1]Hospices Civils de Lyon – HCL, Lyon, France; [2]Lariboisière Hospital AP-HP, Paris, France; [3]Hospital Center University De Lille, Lille, France; [4]Hospital Center University De Bordeaux, Bordeaux, France; [5]Médipôle Lyon-Villeurbanne, Villeurbanne, France; [6]European Hospital Georges Pompidou, Paris, France; [7]Jean Perrin Center, Clermont-Ferrand, France; [8]Hospital Robert Debré, Reims, France

Objectives
Management of functional head and neck paragangliomas (HNPGLf) presents a substantial challenge due to their rarity, the lack of standardized treatment protocols, their complex neurovascular anatomical location, and the cardiovascular risks associated with catecholamine (CA) hypersecretion. This study aimed to describe the clinical characteristics of HNPGLf and their treatment outcomes.
Methods
We retrospectively analyzed a cohort of HNPGLf patients treated at seven French EURACAN-COMETE centers from 2000 to 2023. The secretory nature was defined by CA-methylated metabolites (MM) exceeding 3 times the upper limit of normal. In addition, a comprehensive literature review was conducted.
Results
The French cohort included 20 patients (70% female, median age: 39.5 years). HNPGLf were vagal ($n=10$), jugulo-tympanic ($n=10$), and carotid ($n=3$), with a median largest dimension of 43 mm (range: 23–80), secreting noradrenaline and/or dopamine. Diagnoses were established based on tumor syndrome ($n=15$), signs of CA hypersecretion ($n=1$), germline SDHD mutation ($n=1$), and incidental findings ($n=1$). Eight out of 19 tested patients had SDHx mutations. Treatment modalities included surgery ($n=8$), external beam radiation therapy (EBRT) ($n=5$), radiosurgery ($n=1$), proton therapy (PT) ($n=1$), and ^{177}Lu-DOTATATE ($n=2$). The median post-therapeutic follow-up was 39.7 months (range: 4.1 – 176.9). There were 3 cases of morphological progression, but no metastasis. 70.6% of patients showed significant secretory improvement, with 7 patients normalizing MM levels (all had surgery), and 5 showing partial biochemical response (EBRT $n=2$, radiosurgery $n=1$, PT $n=1$, ^{177}Lu-DOTATATE $n=1$). Neurological complications occurred in 64.7% cases, primarily after surgery. The Literature cohort comprised 17 patients with demographic characteristics, clinical presentations, and tumor features similar to the French cohort. However, the proportion of females was lower (35.5%), and the secretory profile was unspecified in 41.2% of cases because total metanephrine levels were used for diagnosis. Three out of 4 tested patients had SDHx mutations. Outcomes and complications were comparable to that observed in the French cohort, except for a shorter median post-treatment follow-up (9.5 months).
Conclusion
This study presents, to the best of our knowledge, the largest reported HNPGLf cohort to date. Surgical, radiotherapeutic and radiometabolic interventions achieved tumor and secretory control in 70.6% of cases. Longer-term studies are warranted to identify the best therapeutic strategy.

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P502

Ovarian neuroendocrine tumor metastases can induce estrogen production in postmenopausal patients

Merijn Mulders, M F van Velthuysen, Eva Maria Roes, Leo Hofland, Wouter W de Herder & Hans Hofland
Erasmus MC, Rotterdam, Netherlands

Background
Neuroendocrine tumors (NET) are malignant neoplasms that can be associated with specific hormonal syndromes. We describe a novel syndrome of postmenopausal vaginal bleeding and ovarian estradiol overproduction due to ovarian NET localizations.
Methods
A clinical workup was performed for 2 index patients with ovarian metastases of small bowel neuroendocrine tumors and symptoms of postmenopausal vaginal bleeding. Ovarian tissue was collected after oophorectomy, cultured ex vivo and incubated with anti-hormonal and antitumoral drugs. Electronic medical records were screened for postmenopausal patients with ovarian NET localizations and similar symptoms that presented in our center between 1991 and 2023.
Results
In the index patients, clinically significant ovarian estrogen production was demonstrated by a combination of ovarian vein sampling and normalization of circulating estrogen levels after oophorectomy. *Ex vivo* and *in vivo* endocrine tests were unable to identify a paracrine mechanism of ovarian estradiol over-production by NET cells, although a link with gonadotrophins was observed in one case. A retrospective analysis revealed that 21% (14/66) of postmenopausal patients with an ovarian NET localization reported symptoms of vaginal blood loss. Estradiol and gonadotrophin levels were available in 7 of these patients and were compatible with aberrant estradiol production in postmenopausal women.
Conclusions
Together, these findings support the presence of a novel NET-associated hormonal syndrome, which is presumably caused by paracrine effects of infiltrating NET cells on ovarian steroidogenesis.

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P503

Presurgical lactate dehydrogenase (LDH) levels: A risk factor for disease progression in operated adrenocortical carcinomas

Ana Carreira, Joana Guiomar, Diana Festas, Diana Catarino, Dírcea Rodrigues, Carolina Moreno, Miguel Melo & Isabel Paiva
Hospitais da Universidade de Coimbra, Unidade Local de Saúde de Coimbra, Endocrinology, Diabetes and Metabolism, Coimbra, Portugal

Introduction
Adrenocortical carcinoma (ACC) is a rare malignancy with high recurrence and poor prognosis. Lactate dehydrogenase (LDH) is an enzyme of the glycolytic pathway that is associated with tumour progression in several cancers. To date, evidence on the prognostic value of LDH in ACC is limited.
Aims
To assess the impact of LDH in disease-free survival (DFS) in operated ACC.
Materials and methods
Retrospective cohort study of patients with ACC that were followed in a tertiary centre from 1991 to 2023. Cases where adrenalectomy was not performed were excluded. Elevation of baseline (presurgical) LDH was defined according to the laboratory cut-off ($\geq$ 247 U/L). The prognostic value of clinical, biochemical and histopathological variables was assessed by the analysis of Kaplan–Meier curves and Cox proportional hazard regression. A cut-off of LDH was obtained from the analysis of ROC curves.
Results
A total of 33 cases were analysed; 75.8% female, mean age at diagnosis of 49.9 $\pm$ 12.7 years, 62.1% functioning tumours, ENSAT stages II in 57.6%, III in 27.3% and IV in 15.2%. Resection was R0 in 69.7%, R1 in 18.2%, R2 in 6.1% and indeterminate in 6.1%. Baseline LDH ranged from 159 to 1848 U/L, with a median of 382.0 (IQR 271.0–621.0). Adjuvant mitotane was performed in 78.1%, chemotherapy in 25.0% and radiotherapy in 28.6%. Disease progression (RECIST 3) occurred in 66.7%; 43.3% with local recurrence and 64.5% with metastasis. Median DFS was 1.0 year, and overall survival 3.9 years (0.0-11.6). Functioning tumours (HR 3.77, CI 1.34–10.63, $P=0.012$), ENSAT stages III-IV (HR 3.49, CI 1.48–8.27, $P=0.004$), mitotic grade of >20/50HPF (HR 4.47, CI 1.50–13.30, $P=0.007$) and elevated baseline LDH (HR 7.84, CI 1.04–59.32, $P=0.046$) showed lower DFS. Each increase of 100 U/L in LDH predicted an increase of 10.2% on the risk of disease progression (CI 1.01–1.20, $P=0.028$). LDH was significantly higher in functioning tumours, with a median of 524.0 U/L (IQR 299.0–663.0) vs 242.5 U/L (IQR 173.8–493.8), $P=0.036$, and showed a correlation with urinary free cortisol (UFC) ($r=0.540$, $P=0.006$) and with tumour size ($r=0.473$, $P=0.013$). Elevated LDH, unlike functioning tumours or UFC, was associated with the development of metastases after diagnosis (80.0% vs 20%, $P=0.023$). Baseline LDH $\geq$ 266.5 U/L predicted disease progression with 95% sensitivity and 71.4% specificity (AUC 90.0%, $P=0.002$).
Conclusions
Baseline LDH levels were associated with disease progression and poor prognosis in operated ACC. LDH levels may help guiding therapeutic decisions in ACC, along with the other well-established prognostic factors.

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P504

Advanced ACC stage: Therapeutic approach and biological findings

Alessandra Cossa[1], Sara Pagotto[2], Silvia Perconti[2], Elisa Taschin[3], Elena Sofia Scialis[2], Simone De Fabritiis[2], Maria Elena Aloini[4], Diana Liberata Esposito[2], Iolanda Matarazzo[5], Fabio Verginelli[2], Lavinia Vittoria Lotti[6], Francesca Schiavi[3], Renato Mariani Costantini[2] & Antonio Stigliano[4]
[1]Surgery, Rome; [2]Center for Advanced Studies and Technology, Chieti; [3]Familial Cancer Clinical and Oncoendocrinology, Veneto Institute of Oncology, Padua; [4]Endocrinology, Clinical and Molecular Medicine, Rome; [5]Radiology, Surgical and Medical Sciences and Translational Medicine, Rome; [6]Sapienza University of Rome, Experimental Medicine, Rome

Adrenocortical carcinoma (ACC) is a rare and aggressive cancer most frequent in middle-aged females. Management is challenging and debulking surgery has been advocated to improve survival and quality of life in advanced disease. We report a remarkable case in a 60-year-old female without individual or familial risk factors who, despite good performance status, presented with a 10.3 $\times$ 5.5 $\times$ 9.0 cm right adrenal mass, liver metastases, inferior vena cava thrombosis, hypercortisolism, and hyperandrogenism. The patient underwent debulking surgery with adrenalectomy, intracaval thrombectomy and liver metastasectomies. Pathology and immunohistochemistry confirmed high-grade ACC with hepatic metastases and neoplastic inferior vena cava thrombosis, mENS@T stage pIVa (pT4, pN2, pM1). Transmission electron microscopy revealed that both the primary and the metastatic tumor were a mosaic of two cell morphotypes with differential affinity for osmium tetroxide. The most abundant corresponded to large electron-lucent cells, the other (<30%) to thinner electron-dense cells with cytoplasmic filopodia, the latter characteristics reportedly associated to oxidative stress. Both morphotypes showed mitochondrial hypertrophy and hyperplasia, accompanied, particularly in dark cells, by mitochondrial swelling and cristae degradation, known to be linked to respiratory dysfunction. Genetically, the primary and the metastatic samples demonstrated microsatellite-stable phenotype. No alterations in 81 cancer-related genes, including *TP53*, *MEN1* and *PRKAR1A*, three major ACC-related genes, were detected at germline level, while a pathogenic *TP53* c.843C>A p.(Asp281Glu) transversion was detected with strikingly conserved 27% variant allele frequency in both primary and metastatic DNA. Despite adjuvant mitotane, CT scans at one month showed multiple hepatic and bilateral pulmonary metastases with pleural and mediastinal involvement, consistent with rapid deterioration of the hormonal and clinical picture. Death ensued 40 days after surgery. This case challenges the utility of debulking surgery in advanced ACC. Furthermore, its ultrastructural and genetic features suggest that mitochondrial dysfunction and adaptive cooperation between tumor cells differing in *TP53* status and morphotype might contribute to biological aggressiveness.

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Growth differentiation factor 15 (GDF-15) is induced by mitotane in adrenocortical carcinoma and associated with poor prognosis and impaired responsiveness to immunotherapy

Isabel Weigand[1], Alexandra Triebig[1], Maier Tanja[1], Tanja Anderlik[2], Hanna Remde[2], Laura-Sophie Landwehr[2], Otilia Kimpel[2], Miriam Reuter[2], Jochen Schreiner[1], Florian Wedekink[3], Eva Hoster[4], Paul Schwarzlmueller[1], Martin Reincke[1], Jörg Wischhusen[3], Martin Fassnacht[5] & Kroiss Matthias[1]
[1]LMU University Hospital, Department of Internal Medicine IV, Germany; [2]University Hospital Würzburg, Department of Internal Medicine I, Germany; [3]University Hospital Würzburg, Department of Obstetrics and Gynecology, Germany; [4]Ludwig-Maximilians-University, Institute for Medical Informatics, Biometry and Epidemiology, Germany; [5]University Hospital Würzburg, Department of Internal Medicine I, Germany

Background
Treatment of adrenocortical carcinoma (ACC) is unsatisfactory in advanced stages. Oral mitotane remains a mainstay of treatment. Response rates of ACC to immune checkpoint inhibition (ICI) are disappointing and markers of response have not been identified. Tumoural infiltration with cells of the adaptive immune system is sparse in ACC tissue. Growth/differentiation factor 15 (GDF-15) is a cytokine that has been described to impair tumoral immune infiltration and is explored as a treatment target. We previously found GDF-15 to be induced in ACC cells upon mitotane treatment.
Aim
To assess the value of serum GDF-15 for the diagnosis of ACC, as a predictor of prognosis and serum marker of response to ICI.
Methods
Clinical data from patient records were retrieved. GDF-15 was measured in serum samples. 151 patients had ACC (99 prior, 52 during mitotane) and 42 patients benign adrenal tumors (ACA). Serum GDF-15 was analyzed in a second cohort of 27 ACC patients, including 11 responders, who received ICI. mRNA expression of GDF-15 and genes related to immune response was quantified in 58 ACC tumour samples.
Results
Serum GDF-15 did not differ significantly between patients with ACC and ACA. In 40 paired specimens from patients with active ACC, serum GDF-15 increased from 0.6 $\pm$ 2.2 ng/ml prior mitotane to 2.3 $\pm$ 3.9 ng/ml after mitotane initiation ($P<0.0001$). Plasma mitotane significantly correlated with serum GDF-15 (Spearman $r=0.58$). In ACC patients, serum GDF-15 below the median of 0.81 before and 2.17 ng/ml after mitotane was associated with significantly longer patient survival compared to GDF-15 above the median. After adjustment for ENSAT stage and Ki-67 index, this association remained statistically significant with hazard ratios of 2.3 (95% CI 1.14–4.81, $P=0.021$) and 2.9 (95% CI 1.28–6.82, $P=0.01$), respectively. GDF-15 levels in responders to ICI were significantly lower than in non-responders ($P=0.039$) and patients with serum GDF-15 below the median (4.4 ng/ml) showed a trend towards longer progression-free survival with ICI. Expression of pro-inflammatory immune-related genes was lower in ACC tissue with GDF-15 expression above the median.
Conclusion
Mitotane induces GDF-15 secretion and is associated with poor overall survival and impaired response to ICI. Hence, GDF-15 may serve as a serum marker of disease

and response to ICI in ACC. GDF-15 may contribute to sparse tumoural infiltration with immune cells in ACC.

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Primary hyperparathyroidism due to parathyroid cancer or atypical adenoma. a third-level spanish hospital experience

Carolina Sánchez Malo[1], Roberto Carlos Romo Remigio[1], María Dolores Martín Salvago[2], María ..[1], Rodolfo González Sendra[3] & Maria Carmen Rosa Garrido[4]

[1]Hospital of Jaen, Endocrinology and Nutrition, Jaén, Spain; [2]Hospital of Jaen, Anatomic Pathology, Jaén, Spain; [3]Hospital of Jaen, General Surgery, Jaén, Spain; [4]Hospital of Jaen, Unit of Investigation, Jaén, Spain

Parathyroid carcinoma (PC) is very rare and difficult to differentiate from atypical parathyroid adenoma (AA). *En-bloc* surgical resection is recommended, but most cases are diagnosed after non-radical surgery, and it is recommended to expand it. Given the rarity of the cases, the difficulty in the histological diagnosis (HD) and the unpredictability of the evolution, we analyzed our experience with PC and AA.

Material and methods

We conducted a retrospective analysis of 20 patients whom received surgery for primary hyperparathyroidism (PHP) from 2000 to 2022 with an HD of PC and AA. We collected data from age, sex, ultrasound data, parathyroid scintigraphy, clinical signs, pre- and post-surgery tests (PTH, calcium, phosphorus, and vitamin D), type of surgery, persistence of disease, and survival. Statistical analysis was done using SPSS®.

Results

Of our 20 patients, 11 were men and 9 women. HD of PC 12 and AA in 8. Age 61 years (28–77). We found no differences between PC or AA in pre-surgery, ultrasound, scintigraphy, clinical data, type of surgery (5 en bloc and 15 parathyroidectomies) laboratory parameters, tumor size, Ki67 or survival. We found differences in biochemical parameters before and after surgery with no differences according to AP or type of surgery. All patients are still alive. We have not expanded surgery in any case of PC diagnosed after parathyroidectomy.

Conclusions

We did not find clinical, biochemical or imaging characteristics that guide the diagnosis of PC or AA pre-surgery. The clinical and analytical evolution of PHP after surgery is independent of the HD in cases of AA and PC in our setting. Parathyroidectomy achieved the same survival as en bloc surgery.

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P507

SRSF6 modulates histone-chaperone HIRA splicing to orchestrate androgen and E2F signalling in prostate cancer

Antonio J Montero-Hidalgo[1,2,3,4], Juan Manuel Jiménez Vacas[1,2,3,4,5], Enrique Gómez-Gómez[1,3,6], Ricardo Blázquez-Encinas[1,2,3,4], Rafael Sánchez-Sánchez[1,3,7], Antonio Jesús Martínez-Fuentes[1,2,3,4], Eduardo Eyras[8,9], Justo P Castaño[1,2,3,4], Adam Sharp[5,10], David Olmos[11], Manuel D Gahete[1,2,3,4] & Raul M Luque[1,2,3,4]

[1]Maimonides Institute of Biomedical Research of Cordoba (IMIBIC); [2]University of Cordoba, Department of Cell Biology, Physiology and Immunology; [3]Reina Sofia University Hospital (HURS); [4]CIBER Physiopathology of Obesity and Nutrition (CIBERobn); [5]Institute of Cancer Research; [6]Reina Sofia University Hospital (HURS), Urology service; [7]Reina Sofia University Hospital (HURS), Anatomical Pathology service; [8]The John Curtin School of Medical Research; [9]EMBL Australia Partner Laboratory Network at the Australian National University; [10]Royal Marsden NHS Foundation Trust; [11]Hospital Universitario 12 de Octubre, Department of Medical Oncology

Prostate cancer (PCa) is one of the most common endocrine-related cancers (ERCs) among men worldwide. The aggressiveness of this tumor pathology is highly influenced by different endocrine-related factors, highlighting the crucial role of androgens. Therefore, the main therapeutic approach for PCa patients is based on the pharmacological blockade of androgen-signaling. However, some patients become unresponsive and develop a highly lethal castration-resistant disease, pointing out the urgent need for effective therapeutic strategies. In this regard, the splicing process dysregulation has been considered as a cancer hallmark, but the role of certain splicing-factors remains unknown in different ERCs. Therefore, we aimed to characterize the levels and functional role of SRSF6 in PCa. To that end, we analyzed the SRSF6 levels (copy-number/mRNA/protein) across eight well-characterized PCa cohorts and the Hi-Myc transgenic model. Furthermore, we evaluated the functional response of different normal-like (RWPE-1) and PCa-derived (LNCaP/22Rv1/DU145/PC-3) cell-lines and xenograft models in response to the genetic modulation (overexpression/silencing) of SRSF6. Finally, we performed RNA-Seq together with different bioinformatic analyses to explore the molecular mechanisms underlying the functional effects upon SRSF6 modulation in PCa cells. We found that SRSF6 was upregulated in human and mouse PCa tissues, and its levels were associated with relevant clinical parameters of PCa aggressiveness (e.g. Gleason-score, presence of metastasis at diagnosis, etc.). Additionally, the SRSF6 overexpression increased, while its silencing decreased different functional parameters of tumor aggressiveness *in vitro* (i.e., proliferation, migration, colonies and tumorsphere formation) and *in vivo* (i.e., tumor growth, mitosis). Mechanistically, we demonstrated that SRSF6 regulates the splicing pattern of the histone-chaperone *HIRA*, consequently affecting the activity of the H3.3 histone variant in PCa cells [being also corroborated in breast cancer (BCa) cells] and disrupting pivotal oncogenic pathways [androgen-signaling and E2 Promoter Binding Factor (E2F) activity] in PCa cells. Altogether, our results unveiled new conceptual and functional avenues in PCa, with potential therapeutic implications, by demonstrating that SRSF6 is overexpressed and associated with the aggressiveness of PCa by regulating, among other key oncogenic pathways, AR- and E2F-activity, through the modulation of HIRA splicing. This critical mechanism, also observed in BCa, suggests that SRSF6 is a key player not only in PCa, but also in other ERCs. Therefore, these findings present a unique opportunity for further therapeutic research and clinical exploration of targeting SRSF6 in PCa/advanced-stage PCa, BCa, and, potentially, further ERC types.

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P508

Adrenal tumors in children and adolescents in Sweden: A diagnosis related groups-based analysis from 2005–2019

Eleni Terezaki[1,2], Jan Calissendorff[1,3], Buster Mannheimer[4], Jonatan Lindh[5] & Henrik Falhammar[1,3]

[1]Karolinska University Hospital, Endocrinology, Stockholm, Sweden; [2]Karolinska University Hospital, Centre for Inherited Metabolic Diseases, Stockholm, Sweden; [3]Karolinska Institutet, Molecular Medicine and Surgery, Stockholm, Sweden; [4]Karolinska Institutet, Clinical Science and Education Södersjukhuset, Stockholm, Sweden; [5]Karolinska University Hospital, Laboratory Medicine, Division of Clinical Pharmacology, Stockholm, Sweden

Adrenal tumors (ATs) are uncommon in children and adolescents. The aim of this nation-wide retrospective registry-based cohort study was to characterise the various ATs in this population and demonstrate their differences from ATs in adults. All patients under the age of 21 in Sweden with verified adrenal lesions according to ICD-codes between 2005 and 2019 were identified in linked nation-wide registries. Out of the total 232 patients, 121 (52.2%) were boys, with boy predominance preserved even in benign ATs. Mean age was 8.7 ± 7.9 years. Malignant ATs were found in 57% of patients, while 34% of patients had benign ATs with mean age at diagnosis of 4.4 and 14.5 years respectively. The most prevalent diagnosis was neuroblastoma (37.0%), followed by benign adenoma (29.7%) – of which 10% hormonally active, pheochromocytoma (8.6%) and adrenocortical carcinoma (7.3%). Hormone related prodromal symptoms were detected in 16% of patients. Endocrine commorbidities were observed in 46.6% of cases with the most common being hypertension (28%) and adrenal insufficiency (17.7%). In contrast to adults, 13 out of 20 cohort patients with pheochromocytoma had a concurent genetic syndrome and 9 out of 20 had another concomitant tumor, 7 of which were endocrine tumors. Patients were primarily treated and operated at tertiary hospital in 72.4% and 98.9% of cases respectively. 47.8% of individuals received chemotherapy and 42.2% were operated. The most common post-operative complication was adrenal insufficiency (23.5%), and was more prevalent in adrenocortical carcinomas (56.3%) and hormone-producing benign adenomas (57.1%). Unexpectedly 40% of patients with pheochromocytoma and 11.1% of benign adenomas without overt hormonal production were in need of corticosteroid replacement post-operatively. Mortality rate was 19,4%, rising to 33.3% in patients with malignant ATs and 100% within 2 years for the 5 patients with adrenal metastasis. In conclusion, ATs

were found to be rare in children and adolescents in Sweden. Hormone producing or malignant ATs were the most common diagnoses with the latter having a poor prognosis.

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P509

Variants of genes that reduce the function of the progesterone receptor, vitamin D receptor, and 1α-hydroxylase enzyme are associated with an earlier onset of breast cancer

Alisa Dymova[1], Tatyana Shkeleva[2], Svetlana Kalinchenko[3], Marina Zhilenko[4] & Svetlana Samoylova[5]
[1]Moscow, Gynecology department, Moscow, Russian Federation; [2], Moscow; [3]Peoples' Friendship University of Russia - RUDN University, Clinic prof. Kalinchenko, Moscow, Russian Federation; [4], gynecology department, Moscow, Russian Federation; [5]First Moscow State Medical University, Department of Oncology, Radiotherapy and Plastic Surgery, Russian Federation

Background
Previous studies have investigated the association between genetic variability in the progesterone receptor gene and various hormonally-related conditions, such as breast cancer (BC), endometrial and ovarian cancers. Vitamin D deficiency can also lead to oncological conditions, including BC. Progesterone and Vitamin D induce their hormonal effects on target cells by binding the active form of the hormone to its receptors. Therefore, any genetic variations that may cause the dissociation of progesterone and vitamin D receptors, as well as a reduction in the synthesis of the active hormone form, may lead to increased susceptibility to BC. Notably, earlier studies did not take into account the morphological characteristics of tumors and the influence of molecular-genetic features on the age of disease manifestation.
Objective
This study aimed to assess the association between functional-reducing variants in the PGR, VDR, and CYP27B1 genes with the risk of hormone-dependent breast cancer (HBC) and the age of disease manifestation.
Methods
A retrospective case-control study was conducted, involving 87 women aged 40–72 years. Of these, 42 women had a diagnosis of HBC, and 45 women had no history of HBC in their personal or familial medical records. Genotyping was performed using SNP genotyping methods through direct sequencing. Functional-reducing variants in the progesterone receptor gene PGR c.1486G>T; p.Val660Leu, vitamin D receptor BsmI Polymorphism IVS10+283G>A, and 1α-hydroxylase enzyme g.57764205A>G; c.1137-29T>C were investigated.
Results
A significantly higher frequency of the minor allele of PGR (45% vs 16%), VDR (29% vs 17%), and the functional-reducing allele of the CYP27B1 enzyme (43% vs 12%) was observed among patients with HBC compared to the control group, confirming the association of these genetic variants with the risk of developing HBC. A significant association of PGR and VDR genotypes with HBC was observed in younger patients up to 55 years old. In older patients, the frequency of PGR and VDR variants decreased and approached the control group, indicating the contribution of other factors to the pathogenesis of the disease after the age of 55.
Conclusions
This report confirms the contribution of PGR, VDR, and CYP27B1 gene variants to the etiology of BC. The low sensitivity of PGR and VDR receptors is associated with earlier forms of HBC. Genotyping of vitamin D receptors (VDR), the activity of the 1-α-hydroxylase enzyme (CYP27B1), and progesterone receptors (PGR) in the future will enable the development of a screening strategy for identifying women at risk of developing HBC.

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Environmental Endocrinology

P201

Systematic review of thyroid hormone patterns observed after exposure to endocrine disruptors in humans

Isabel Forner[1], Asma Baig[1] & Andreas Kortenkamp[1]
[1]Brunel University London, Uxbridge, United Kingdom

The Hypothalamic Pituitary Thyroid (HPT) axis is well-known as a classic endocrine negative feedback loop: increased levels of thyroxine (T4) in the blood are associated with a reduction of thyroid stimulating hormone (TSH) production and vice versa. However, the HPT axis is sensitive to alterations by a number of endocrine-disrupting chemicals (EDCs). Exposure to specific EDCs can deregulate the negative feedback loop and alter the TH/TSH levels. The intrinsic mechanisms for such deregulations are still unclear. Our aim is to investigate the different TH/TSH patterns associated with EDC exposures in different population groups. Therefore, we conducted an extensive systematic literature search of peer-reviewed epidemiological studies. Based on our eligibility criteria, we selected studies where the authors included TH/TSH measurements in pregnant women, workers or the general population, and the levels of the target chemicals were characterised in the corresponding human sample. We retrieved more than 25,000 studies, of which 532 were further assessed. Cross-sectional, case-control and cohort studies were the predominant study designs. A large range of chemicals were included with the predominance of heavy metals, per- and polyfluoroalkyl substances, bisphenols, phthalates, pesticides, polybrominated and polychlorinated compounds. Our results showed that the idealized view of the HPT axis is not supported by the evidence when EDCs are involved. Some EDCs induced reductions or increments of T4 and/or T3 levels but the expected TSH increase or decrease did not materialise. Similarly, changes in TSH levels did not induce alterations in T4 and/or T3. The mechanisms by which various EDCs disrupt the HPT axis and induce such patterns have not yet been fully identified. For this reason, the complexity of the EDC mode of action needs to be considered in order to identify chemicals that are potentially damaging to human health. Acknowledgement: The ATHENA project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 825161.

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P202

Urinary iodine concentration and markers of thyroid activity in pregnant faroese women

Herborg Líggjasardóttir Johannesen[1], Stig Andersen[2], Stine Linding Andersen[3], Maria Skaalum Petersen[4] & Anna Sofía Veyhe[5]
[1]National Hospital of the Faroe Islands, Endocinology and internal medicine, Tórshavn, Faroe Islands; [2]Aalborg University Hospital South, Arctic Health Research Centre, Aalborg, Denmark; [3]Aalborg University Hospital South, Clinical Biochemistry, Aalborg, Denmark; [4]National Hospital of the Faroe Islands, Department of Research, Tórshavn, Faroe Islands; [5]University of the Faroe Islands, Health Science, Tórshavn, Faroe Islands

Introduction
Mild iodine deficiency in the Faroe Islands raises a concern for pregnant women. Iodine is essential for thyroid hormone synthesis, making it crucial for thyroid function during pregnancy and foetal growth. World Health Organization (WHO) classifies iodine intake in pregnant women as insufficient if the median urinary iodine concentration (UIC) is below 150 µg/l. We investigated how UIC relates to thyroglobulin (Tg) and thyroid-stimulating hormone (TSH) in serum as markers of thyroid activity.
Method
This was a cross-sectional study with longitudinal aspects in the Faroe Islands. We recruited 645 Faroese pregnant women early in the second trimester from June 2020 to April 2022 for blood and spot urine samples. UIC was measured in spot urine using the Sandell-Kolthoff reaction modified according to Wilson and van Zyl. TG measurements were conducted in 143 randomly selected participants. Serum Tg and TSH were measured using immunoassays (BRAHMS and Alinity I; Abbott).
Results
Overall, the median UIC was 110 µg/l and the median TSH was 1.23 mIU/l. There were 32 participants with UIC <50 µg/l, for whom we also had corresponding Tg values. For the entire group, 61 participants had UIC <50 µg/l regardless of Tg presence. Serum Tg levels were higher in the group with UIC <50 µg/l ($n=32$) compared to those with UIC from 50-100 µg/l or above. On the other hand, neither serum Tg nor TSH differed between groups of pregnant women with UIC of 50-99 vs 100-149 vs 150-299 µg/l, but TSH was slightly lower with UIC <50 µg/l (median 1.09 mIU/l ($n=61$)) and higher with UIC >300 µg/l (median 1.51 mIU/l ($n=42$)).
Conclusion
Among pregnant women in the Faroe Islands, TSH was similar between groups of pregnant women with UIC in the range from 50-300 µg/l. Similarly, serum Tg was raised only in the group with UIC below 50 µg/l. Results suggest that the lower limit of UIC recommended by WHO in pregnancy may be too strict when evaluated according to markers of thyroid activity.

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P203

Exploring a new avenue of disseminating peer-reviewed information on thyroid and PCOS conditions

Maiar Elhariry[1], Kashish Malhotra[2], Punith Kempegowda[3] & Kashish Goyal[4]
[1]University of Birmingham, College of Medical and Dental Sciences; [2]University of Birmingham Medical School, Institute of Applied Health Research; [3]University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital; [4]Delhi Heart Institute and Multispeciality Hospital

Background
In the current digital age, social media brought information to our fingertips but also facilitated the spread of misinformation. The exponential growth of short video platforms shows potential for formulating evidence-based techniques to ensure the dissemination of accurate information without bias.
Objectives
1. To create and disseminate peer-reviewed short videos about PCOS and Thyroid conditions. 2. To explore content creators' experience, video outreach and audience engagement on social media.
Methods
This project was run from December 2022 to May 2023 in collaboration with British Thyroid Foundation and PCOS Vitality. Scripts based on the most searched topics in PCOS and thyroid conditions were created and reviewed by experts and patients to ensure scientific accuracy and acceptability. Once finalised, we invited medical students to create videos using the scripts. The videos were reviewed, edited to fit the requirements, and posted on TikTok, Instagram, youTube, and Twitter. Video engagement across social media over two months was analysed. Content creators were invited to a semi-structured virtual interview to explore their experiences and motivation to participate. Two independent authors coded the interview transcripts using Nvivo 12.0 to identify themes using thematic inductive analysis.
Results
Over 2 months, the videos received 718 likes, 120 shares, and 54686 views for 20 videos -19458 on TikTok, 12944 on Instagram, 2606 on youTube, and 19678 on Twitter. There was an increase in followers across all platforms - from an 89% increase on TikTok to a 5% increase on Twitter. Analysis of participant experience yielded 4 main themes: Views on social media, advice when using social media, reasons for participating, and thoughts on this project. Regarding views on social media, content creators highlighted the advantages of social media, including 'large outreach' (12 references), 'convenience' (10 references), and 'accessibility to opportunities' in fields of interest (7 references). The most common themes about advice were awareness of 'audience's demographics' (9 references), 'sharing on more than one platform' (5 references), and 'collaborating with organisations' (3 references). Content creators mentioned that 'non-restricting participation criteria', 'convenience' (8 references) and 'ability to record from home with a pre-written script' (6 references) made it easier to participate.
Conclusions
Disseminating peer-reviewed information is a great way of harnessing the power of social media to increase awareness, tackle misinformation, and provide a channel for the public/patients to receive evidence-based information. Medical students have untapped potential to be content creators working with relevant authorities and patient support groups.

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P204

The short-term effect of apparent temperature on the hydration marker plasma sodium

Anna Franzén[1], Mats Pihlsgård[1], Ulf Ekelund[2,3], Simon Timpka[1,4] & Sofia Enhörning[1,5]
[1]Lund University, Department of Clinical Sciences, Malmö, Sweden; [2]Lund University, Department of Clinical Sciences, Lund, Sweden; [3]Skåne University Hospital, Emergency Medicine, Lund, Sweden; [4]Skåne University Hospital, Department of Obstetrics and Gynecology, Malmö, Sweden; [5]Skåne University Hospital, Department of Internal Medicine, Malmö, Sweden

Introduction
A recent study suggests that copeptin, a surrogate measure of the hormone vasopressin and a known risk marker of cardiometabolic disease and decreased hydration, is non-linearly related to outdoor temperature with increased levels in both hot and cold temperatures. The same u-shaped relationship has been suggested between outdoor temperature and other hydration markers. In this study, we investigated the effect of apparent outdoor temperature on plasma sodium, the main contributor to increased plasma osmolality and vasopressin secretion.
Method
Data on plasma sodium from all adult patients visiting one of eight emergency departments ($n = 331,311$) in 2017- 2018 in the southernmost region in Sweden (approximately 1.3 million inhabitants) were used. To investigate the association between apparent outdoor temperature (mean value the day of blood sampling) and plasma sodium, a cubic spline regression model with knots at the 25th, 50th, 75th and 90th temperature percentile was used. To investigate the relationship between apparent temperature and odds of hypo- and hypernatremia (P-Sodium <135 mmol/l and >145 mmol/l, respectively) among patients, a logistic regression model with the same knots was used. All of the analyses were adjusted for age, sex, day of the week, glucose, potassium and eGFR in a first model and ambulance arrival, hospital admission and current medication (diuretics, renin-angiotensin blocking agents, selective serotonin reuptake inhibitors and antidiabetics) on top of model one in a second model.
Results
Plasma sodium among patients was significantly and non-linearly associated with apparent temperature ($P < 0.001$ for both). The highest plasma sodium concentration was observed at -0.2 degrees C mean outdoor temperature. The associations between apparent temperature and hyper- and hyponatremia, respectively, were significant and non-linear ($P < 0.001$ for all). The odds of hyponatremia decreased with around 15% at mean temperatures between 0 to 10 degrees C, and increased at temperatures below -5 and above 19 degrees C. Hypernatremia increased with around 15% at temperatures around 0 degrees C and at temperatures above 20 degrees C.
Conclusion
Among patients seeking acute care, plasma sodium is related to outdoor temperature and reaches its highest concentration during cold temperatures. Our results indicate that hypohydration is more common during winter and could help explain the winter peak in copeptin concentration observed in previous studies. Given the pleiotropic hormonal effects of vasopressin, moderately increased water intake to lower vasopressin might mitigate adverse health effects of outdoor temperatures.

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P205

Real-life exposure to toxic metals: impact on thyroid gland function and male reproductive system in rats

Đurica Marić[1], Katarina Baralić[1], Dragana Vukelić[1], Ivan Milošević[2], Anja Nikolić[2], Danijela Đukić-Ćosić[1], Zorica Bulat[1] & Aleksandra Buha[1]
[1]University of Belgrade - Faculty of Pharmacy, Department of Toxicology 'Akademik Danilo Soldatović', Belgrade, Serbia; [2]University of Belgrade - Faculty of Veterinary Medicine, Department of Histology and Embryology, Belgrade, Serbia

Toxic metals can disrupt the endocrine system, harming the thyroid and male reproductive function, as indicated by epidemiological and experimental studies. A human biomonitoring study in Serbia determined the levels of toxic metals (Cd, Pb, As, Hg, Cr, and Ni) in the blood to identify real life scenario of exposure. On the basis of the metal measured levels, the doses for the oral 90 days treatment of male Wistar rats were calculated. The experiment included a control group and treatment groups that received doses reflecting the lower confidence limit of the Benchmark dose for effects on hormone levels (M1), median concentrations (M2) and 95th percentiles concentration of each metal (M3). Serum levels of the hormones TSH, fT4, fT3, T4, T3, testosterone, FSH and LH were determined. A histological analysis of the thyroid gland tissue was performed, while the redox status parameters (IMA, MDA, SH groups, GSH and SOD) were determined in the testicular tissue. Additionally, SPINA-GT and SPINA-GD were calculated with the SPINA Thyr software. In group M2 there was a statistically significant decrease in TSH levels and an increase in fT4 levels, while in group M3 a decrease in fT3 levels was observed. The levels of T4 and T3 remained relatively stable in all groups, although a decreasing trend of T3 in M3 and an increasing trend of T4 in M2 were observed. A significant decrease in SPINA-GD in all treated groups indicates a decreased activity of peripheral deiodinases, while the secretory activity of the gland was not significantly changed in any of the treated groups. Histological analysis of the thyroid tissue showed changes in all treated groups, despite the fact that in some of the treated groups no changes were observed in the levels of TSH and thyroid hormones, which can be explained by the activation of compensatory mechanisms. The analysis of reproductive hormones in the serum showed that only in the group that was exposed to the highest doses of the tested metals (M3), there was a significant decrease in the level of LH. In the M1 group, group treated with the lowest doses of metals, a decrease in the levels SH groups, GSH, and SOD was observed. This outcome may be a consequence of depletion of antioxidant protection reserves. It can be concluded that environmentally relevant doses of metals mixtures can affect the function and structure of the thyroid gland and the male reproductive system.

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P206

The influence of environmental and behavioral factors on male infertility associated hormones

Dinu Draganescu Daniela[1], Adrian Albulescu[2], Suzana Vladoiu[1], Fudulu Alina[2], Anca Botezatu[2], Ples Adriana[2], Iancu Iulia Virginia[2], Cristina Stancu[1], Andrei Muresan[1], Oana-Monica Popa[1], Luminita Udrea[1], Ioana Adina Rugescu[2], Dinu Draganescu Daria[1], Ruxandra Dumitrescu[2] & Corin Badiu[1,3]
[1]National Institute of Endocrinology; [2]Stefan S Nicolau Institute of Virology; [3]Carol Davila University of Medicine and Pharmacy, Endocrinology, Bucuresti

Male infertility arises as a global public health in the context of the dramatic decrease in birth rates. However, the underlying causes of male infertility remain unknown in many cases. An increasing number of studies suggest that environmental and behavioral factors (smoking, drinking, etc) may affect the hormone levels and other pathways involved in male fertility. The aim of this study was to investigate the influence of various environmental factors and hormonal profiles in a cohort of idiopathic infertile men. This study included 33 blood and seminal samples from patients with idiopathic infertility and 21 from the control group. Infertile group (age between 20-55 years old) inclusion criteria were: modified seminal parameters, failure to achieve pregnancy after at least one year of trying, while the exclusion criteria was: known causes for infertility. The patients filled out a standardized questionnaire designed to gather information regarding their age, smoking and drinking habits, radio frequency (RF) exposure/day, medical history, and place of residence. The percentage of smoking patients was 18.18% in infertile group, respectively 28.57% in control group, while regarding alcohol behavior, 18.18% of infertile patients reported consuming alcohol, and 19,04% in control group. The hormonal profile varies depending on a couple of behavioral/environmental factors. Estradiol levels were slightly decreased in the control group with less than 4 hours of RF exposure/day, while the infertile group displayed an opposite image, with higher levels in the case of more than 4 hours/day RF exposure. Estradiol also displayed a significant increase in the patients who consume alcoholic beverages, regardless of their fertility status ($P=0.0292$). Free testosterone also varies between drinkers and non-drinkers, regardless of their fertility status as well ($P=0.0233$). Testosterone levels also displayed variation between infertile RF exposure groups, with increased levels in the >4 hours/day group ($P=0.0276$). The same trend was observed in the case of free testosterone ($P=0.0029$). Other factors that impacts testosterone levels are smoking behavior, with a significant increase in the case of smokers ($P=0.0233$), and drinking behavior, with an increase in the case of alcohol consumption ($P=0.0398$) The landscape of male infertility should take into account environmental and behavioral factors. This preliminary study showed an important role of these factors in modifying hormone expression levels, especially testosterone, which ultimately may affect the quality of the reproductive function.

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Pituitary and Neuroendocrinology

P101

Assessment of 24h ambulatory blood pressure in women with sheehan syndrome: prevalence of hypertension and disruption of the circadian blood pressure rhythm

Salma Salhi[1], Ibtissem Oueslati[1], Elyes Kamoun[1], Anis Grassa[1], Meriem Mabrouk[1], Fatma Chaker[1], Meriem Yazidi[1] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
Patients with Sheehan's syndrome (SS) may experience alterations in blood pressure (BP) regulation, possibly due to hormones deficiencies and hormone replacement treatment. The aim of the present study was to assess the 24h ambulatory BP in women with Sheehan syndrome.
Methods
This was a monocentric cross-sectional study involving 50 women with complete anterior hypopituitarism secondary to SS and 50 age and body-mass index (BMI) matched control women. All participants underwent clinical examination, laboratory tests, and BP measurement using ambulatory 24h-monitoring.
Results
The mean age was 62.2 $\pm$ 9.4 years in patients vs 60.6 $\pm$ 8.4 years in controls ($P=0.385$). The prevalence of hypertension before the study was 30% in patients with SS and 6% in controls ($P=0.002$). Newly diagnosed hypertension was established in 48% of patients and 58% of controls. The overall prevalence of hypertension was 78% in patients and 64% in controls ($P=0.123$). Altered nycthemeral variations in BP was observed in patients, who had more frequent non-dipper or riser profile than controls ($P<0.001$). Additionally, they had significantly higher frequency of nocturnal hypertension (38% vs 3%; $P=0.002$). SS was positively associated with a non-dipper/riser BP profile (Odds Ratio (OR) $=4.09$; 95%-confidence interval (CI): 1.58-10.55, $P=0.003$). Factors associated with hypertension in patients included age >50 years (OR$=14.25$, 95%-CI: 1.30-155.22, $P=0.029$), duration of SS $>$ 20 years (OR$=6.8$, 95%-CI: 0.96-47.3; $P=0.034$), BMI $\geq$ 26 kg/m^2 (OR$=12.19$, 95%-CI: 2.56-57.93, $P<0.001$), waist circumference $\geq$ 100 cm (OR$=6.78$, 95%-CI: 1.51-30.39, $P=0.007$), waist circumference/height ratio $\geq$ 0.62 (OR$=14.66$, 95%-CI:3.00-71.67, $P<0.001$), and visceral fatty area $\geq$ 150 cm^2 (OR$=6$, 95%-CI: 1.20-30.01, $P=0.022$). Hypertensive patients had a significantly higher cumulative dose of hydrocortisone compared to non-hypertensive patients (439.1 ± 227 vs 315.9 ± 193, $P=0.006$). Thirteen percent of hypertensive patients were on a daily hydrocortisone dose >20 mg, while all non-hypertensive patients were on 15 to 20 mg/day.
Conclusion
Our results showed a high prevalence of hypertension in women with SS and a higher disruption of the circadian BP rhythm in patients than in controls. Age, disease duration, BMI, visceral adiposity, and cumulative hydrocortisone dose were associated with hypertension.

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P102

Establishing BMI-Related thresholds for the 1 mg dexamethasone suppression test: a retrospective analysis

Claudio Urbani[1], Davide Corleo[1], Caterina Venturi[1], Giulia Marconcini[1], Fausto Bogazzi[2], Isabella Lupi[1], Ferruccio Santini[2] & Luca Manetti[1]
[1]Azienda Ospedaliero Universitaria Pisana, Endocrinology I Unit, Pisa, Italy; [2]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy

Background
Cushing Syndrome (CS) is associated with metabolic disturbances, including obesity. The 1 mg Dexamethasone Suppression Test (1mgDST) is widely used to assess cortisol regulation in suspected CS patients. However, its interpretation may require adjustments based on individual factors, such as body mass index (BMI), due to obesity's influence on cortisol metabolism. The literature offers differing cutoff values for obese patients. This study aimed to establish BMI-related cutoffs for the 1 mgDST.
Methods
This is a historical-prospective study focused on 1,694 subjects who underwent the 1 mgDST between January 2014 and November 2021. Among them, 1,000 consecutive overweight or obese individuals were included, alongside 100 healthy-weight controls. Exclusion criteria included hypercortisolism, medications affecting dexamethasone metabolism, recent steroid or estrogen use, adrenal masses, and alcohol abuse. Data collection included anthropometric measurements, clinical features indicative of hypercortisolism, medication history, and 1 mgDST results. Waist circumference and waist-to-hip ratio were collected for obese. Body Surface Area (BSA) and BMI were calculated. BMI subgroups were established: healthy weight, overweight, and different obesity classes. Patients failing to suppress cortisol (cortisol $>$ 1.8 mg/dl) underwent a second-level assessment involving 0800 hours ACTH sampling, Low-Dose Dexamethasone Suppression Test, and urinary free cortisol tests. Statistical analysis involved group comparisons test, correlation analysis tests, and multivariate logistic regression, and Receiver Operating Characteristic (ROC) curve analysis.
Results
Among the study group, 71 patients did not achieve cortisol suppression after the 1 mgDST. Among them, 39 were excluded from a CS diagnosis based on the second-level evaluation, while 32 were lost to follow-up or declined further assessment. Overweight (n°$=96$) and obese (n°$=772$) individuals differed from healthy-weight controls, being older and having more males. Cortisol values after 1 mgDST were significantly lower in overweight/obese patients (median 0.6 vs 0.7 mg/dl; $P=0.002$). Correlation analyses showed positive associations between cortisol values and age, BMI, BSA, waist circumference, and waist-to-hip ratio, while gender negatively influenced cortisol levels. Multivariate logistic regression highlighted age's positive independent association with cortisol levels ($r=0.012$; $P<0.0001$). ROC curve analysis in overweight/obese patients revealed an optimal cortisol cutoff of 2.1 mg/dl. This threshold remained valid across obesity classes.
Conclusion
This study contributes to establishing BMI-related thresholds for the 1 mgDST, enhancing its diagnostic accuracy in overweight/obese patients. The optimal cortisol cutoff of 2.1 mg/dl proved reliable across various obesity classes, aiding in distinguishing CS from other conditions. Also, age-related variations in test results were observed. Further prospective studies with larger cohorts are required to validate and refine these thresholds.

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P103

Prevalence of hypopituitarism in adults treated with intensity-modulated radiotherapy for primary, non-pituitary, brain tumours

Darran Mc Donald[1,2], Niamh McDermott[1], Maria Tomkins[1,2], Liam O'Connell[3], Clare Faul[2,3], David Fitzpatrick[3], Chris Thompson[1,2], Michael O'Reilly[1,2] & Mark Sherlock[1,2]
[1]Beaumont Hospital, Department of Endocrinology, Dublin, Ireland; [2]Royal College of Surgeons in Ireland, Department of Medicine, Dublin, Ireland; [3]St Luke's Radiation Oncology Network, Dublin, Ireland

Background
Improved survival rates from brain tumours have resulted in patients living longer with the effects of radiotherapy. Advances in conventional fractionated radiotherapy, such as intensity-modulated radiotherapy (IMRT), enable radiation to be delivered more precisely while partially sparing surrounding structures including the hypothalamic-pituitary axis. Despite these advances, the precise risk of hypopituitarism associated with IMRT in survivors of adult-onset non-pituitary primary brain tumours remains poorly understood.
Methods
A retrospective cohort study was conducted among patients referred to the endocrinology service in Beaumont Hospital, Ireland's National Centre for the Management of Brain Tumours. Patients with adult-onset primary brain tumours treated with IMRT between 2011 and 2022 were included. Endocrine surveillance typically consisted of annual baseline pituitary assessments and either a synacthen (SST) or insulin tolerance/glucagon stimulation test based on whether patients were candidates for growth hormone (GH) replacement.
Results
The study included 69 patients (26 women) with a median age of 38.0 (IQR 30.0-46.2) years at radiotherapy completion. Gliomas were the most common neoplasm ($n=38$), followed by meningiomas ($n=17$), pinealomas ($n=6$), medulloblastomas ($n=5$) and 'other' brain tumours ($n=3$). Median total delivered radiotherapy dose was 54 (IQR 54-60) Gray. The prevalence of hypopituitarism was 26/69 (38%) after a median of 50 (IQR 29-76) months follow up. Thirty-nine patients had baseline pituitary function testing and an SST while 30 patients had baseline pituitary function testing and dynamic GH assessment. Nineteen of the thirty patients (63.3%) who underwent dynamic GH assessments had GH deficiency. All these patients had normal IGF-1 levels at the time of diagnosis. The risk of adrenocorticotrophic hormone (ACTH), gonadotropin, and thyroid stimulating hormone (TSH) deficiency was 17/69 (24.6%), 10/69 (14.5%) and 6/69 (8.7%), respectively. Five patients out of 69 (7.2%) developed panhypopituitarism. Fifty-two percent (36/69) of patients exhibited hyperprolactinaemia at their most recent assessment. Spearman's rank identified significant positive correlations between time interval following radiotherapy and the risk of developing any hormone deficiency ($r_s=0.27$, $P=0.03$), gonadotropin ($r_s=0.37$, $P=0.002$), TSH ($r_s=0.26$, $P=0.03$) but not GH or ACTH deficiency.
Conclusion
This study demonstrated a high prevalence of hypopituitarism in adult-onset non-pituitary brain tumour survivors treated with IMRT. Almost two-fifths developed hypopituitarism at a median of 50 months follow up. The evolution of hypopituitarism occurred in a time-dependent fashion. Long-term systematic endocrine surveillance is crucial to enable timely diagnosis and treatment of hormone deficits, with the aim of optimising quality of life and preventing hypopituitarism-related complications in this patient cohort.

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P104

Increment in KI-67 proliferation indices over time is associated with worse survival outcomes in small-intestinal neuroendocrine tumours

Kosmas Daskalakis[1,2], Marina Tsoli[3], Göran Wallin[2], Angelika Kogut[4], Rajaventhan Srirajaskanthan[5], Christopher Harlow[5], Georgios Giovos[6], Martin Weickert[6], Beata Kos Kudla[7] & Gregory Kaltsas[3]
[1]General Hospital of Athens Korgialeneio - Benakeio Hellenic Red Cross, Athina, Greece; [2]Örebro University, Department of Surgery, Faculty of Medicine and Health, Örebro, Sweden; [3]National and Kapodistrian University of Athens, Endocrine Oncology Unit, 1st Department of Propaedeutic Internal Medicine, Laiko Hospital, Athens, Greece; [4]Medical University of Silesia, Department of Endocrinology and Neuroendocrine Neoplasms, Department of Endocrinology and Pathophysiology, Katowice, Poland; [5]King's College Hospital, London; [6]University Hospital Coventry & Warwickshire, Coventry; [7]Medical University of Silesia, Department of Endocrinology and Neuroendocrine Neoplasms, Department of Endocrinology and Pathophysiology, Katowice

Introduction
A change in the biological behaviour of Small-Intestinal Neuroendocrine Tumours (SiNETs), as reflected by an increase in the Ki-67 proliferation index may occur over time. The purpose of this study was to evaluate longitudinal changes in Ki-67 indices of SiNETs and assess the impact of these in overall survival (OS).
Patients and methods
We screened 551 patients with SI-NETs diagnosed from 1993, through 2021, identified using the SI-NET databases from five European referral centres. Only patients with well-differentiated tumours and available baseline tumour samples, as well as follow-up re-biopsies were included. Pathology reports were reviewed with regard to tumour histopathology and Ki-67 indices. To avoid immortal time bias, baseline for survival estimates was defined as the date of re-biopsy.
Results
We included 47 patients. Median Ki-67 index at SI-NET diagnosis was 2% (range 0.5-15%). Twenty-seven patients had grade 1 (G1) tumours (57.4%), and 20 G2 (42.6%). Mean time to re-biopsy was 48.8 months (SD: +/-162.5). At re-biopsy, the median change in Ki-67 index (absolute value; follow-up minus time of diagnosis) was 1% (range -10 to +38%). An increase in Ki-67 occurred in 20 patients (42.6%); in 11 patients the change in Ki-67 resulted in progression to higher tumour grade. The patients with an increment in Ki-67 $\geq$ 1%, with or without grade progression had a median OS of 46 months compared to 53.7 months in patients with stable or decreasing Ki-67 (hazard ratio 3.26, 95% CI: 1.11-9.58, $P=0.031$).
Conclusion
Increment in Ki-67 indices over time was observed in approximately 40% of SiNETs included in this study and was linked with worse survival outcomes. Further studies on molecular pathways with sequential biopsies at disease progression are necessary to shed light on the mechanisms that render a neoplasm more aggressive during the disease course.

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P105

Infectious complications during cushing's disease: about 51 cases

Bassiratou Hamza Maliki[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]CHU Ibn Rochd - Casablanca, Morocco, Casablanca, Morocco

Introduction
Infections are very frequent in Cushing's disease with impact on quality of life.
Objective
The aim of our study is to describe infectious manifestations in Cushing's disease
Material and methods
Retrospective study of 51 patients diagnosed for Cushing's disease followed at the Ibn Rochd CHU Endocrinology from Casablanca from 2012 to 2023. Infectious complications were detected either at diagnosis or during monitoring. The statistical analysis was done by the SPSS version 25 software.
Results
We included 51 patients including 45 women and 6 men, the average age of patients was 36.20 years (17-69). The average seniority of the disease was 2.5 years. The average Clu was 657 mg/24 hours (116.8 - 2196). To pituitary MRI: macroadenoma in 27 patients, microadenoma in 21 patients and normal in 5 patients. The infectious complications found are: mycoses of large folds 66.67%($n=$ 34), intertrigo interdes macerated 72.55%($n=$ 37), cystitis 39.21%($n=$ 20), acute pyelonephritis 17.65%($n=$ 9), infection Pulmonary 27.45% ($n=$ 14), dental abscesses 11.76% ($n=$ 6), erysipelas of the leg 25.49% ($n=$ 13), candidosal vulvovaginitis 64.70% ($n=$ 33), esophageal candidiasis in 3 patients, 2 patients are complicated by post -operative meningitis of surgery by transphenoidal route. All our patients have healing with antibiotic and/or antifungal treatment and the management of Cushing's disease.
Conclusion
Infectious complications are frequent in Cushing's disease, hence the interest of early screening and adequate management in order to improve the quality of life in its patients.

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P106

Diagnostic value of a 3% hypertonic saline infusion test in differential diagnosis between adh deficiency and primary polydipsia

Nino Katamadze[1], Ekaterina Pigarova[1], Olga Rebrova[1] & Larisa Dzeranova[1]
[1]Endocrinology Research Centre

Aim
To assess the diagnostic value of a 3% hypertonic saline infusion test in comparison with a set of clinical and laboratory data (including a water deprivation test and MRI data) for the purpose of differential diagnosis between ADH deficiency and primary polydipsia (PP).
Materials and Methods
An interventional comparative study included 90 patients with confirmed polyuria-polydipsia syndrome. In order to assess the diagnostic characteristics, all subjects underwent sequential tests with osmotic stimulation: a 3% hypertonic saline infusion test and a water deprivation test.
Results
The study analyzed data from 90 patients who had underwent both osmotic stimulation tests. Based on the results of an analysis of the clinical, anamnestic, laboratory and instrumental data (MRI) and the results of a water deprivation test, a final diagnosis of ADH deficiency was made in 48 (53%) patients and 42 (47%) patients were diagnosed with PP. A diagnostic accuracy of the 3% hypertonic saline infusion test were calculated: sensitivity 98% (95% CI: 89%; 100%); specificity 98% (95% CI: 87%; 100%. Adverse events were studied: chills occurred significantly more often (31% vs 12%, $P<0.003$) during the 3% hypertonic saline infusion test, other signs of dehydration (dizziness, fog before the eyes, headache), and an increase in Na level >155 mmol/l were observed at equally frequency during both tests. The duration of the water deprivation test was 7 times higher than that of the 3% hypertonic saline infusion test (11 [11; 16] hours vs 1,5 [2; 2,5], p <0.001).
Conclusion
The 3% hypertonic saline infusion test has a high overall diagnostic accuracy (98%; 95% CI 92% to 100%) if compared to the set of clinical, laboratory and instrumental data of patients (including a water deprivation test). The advantage of the 3% hypertonic saline infusion test is its short duration and, as a consequence, better tolerability and compliance, while no significant differences in the occurrence of adverse events during the tests were noted.

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P107

Circulating levels of mir-375 in cushing's disease patients and evaluation of its role in the regulation of sstr2 expression in murine pituitary corticotroph tumor cell model

Claudia Pivonello[1], Roberta Patalano[2], Tatiana Montò[2], Mariarosaria Negri[3], Feliciana Amatrudo[3], Donatella Provvisiero[2], Chiara Simeoli[2], Nicola Di Paola[2], Angelica Larocca[2], Erminio Crescenzo[2], Annamaria Colao[2,4] & Rosario Pivonello[2,4]
[1]Università Federico II di Napoli, Dipartimento di Sanità Pubblica, Naples, Italy; [2]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia. Andrologia e Nutrizione, Naples, Italy; [3]Università Telematica Pegaso, Dipartimento di Scienze Umanistiche, Naples, Italy; [4]Università Federico II di Napoli, UNESCO Chair for Health Education and Sustainable Development, Naples, Italy

In vitro studies suggest that glucocorticoids (GC) long-term exposure down-regulates SSTR2 but not SSTR5 expression in human and mouse ACTH-secreting tumor cells (AtT20), limiting the efficacy of octreotide (OCT), a somatostatin-receptor ligand with high affinity for SSTR2, in the treatment of Cushing's disease (CD). In AtT20, dexamethasone treatment increased miR-375 expression, whose analysis revealed a seed-sequence for SSTR2, supporting the hypothesis that excessive GC exposure can lead to epigenetic SSTR2 downregulation. The current study aims to evaluate miR-375 levels in CD patients and miR-375 impact on SSTR2 expression in AtT20/D16 cell model. Circulating and tissue miR-375 expression was evaluated by RT-qPCR in 21 CD patients and 19 healthy subjects; and in 6 human corticotroph pituitary tumors and 2 normal pituitaries, and in AtT20/D16 and somatotroph GH3 cell lines, respectively. SSTR2 protein expression and cellular localization were evaluated by western blot (WB) and immunofluorescence (IF) following miR-375 inhibition in AtT20/D16 in presence or not of OCT. Proliferation assay and flow cytometry were assessed to investigate the impact of miR-375 regulation on 72h of OCT at 10^{-8}M and 10^{-7}M treatment in AtT20/D16. Circulating miR-375 expression was higher in CD patients ($P<0.0001$) compared to healthy subjects, as well as tissue levels in human corticotroph pituitary tumors than in normal pituitaries. AtT20/D16 and GH3 cells exhibited an inverse pattern of expression, with low levels of SSTR2 messengers and high levels of miR-375 in AtT20/D16 and an opposite expression pattern in GH3 cells. miR-375 inhibition significantly increased membranous SSTR2 protein expression, evaluated by WB and IF, in AtT20/D16 ($P=0.0310$ and $P=0.0154$, respectively) compared to untreated cells. Receptor internalization, induced by 20 min of OCT10^{-7}M treatment, appeared stronger when OCT10^{-7}M was combined with miR-375 inhibitor. OCT10^{-7}M but not 10^{-8}M decreased cell proliferation (6.8%, $P=0.011$) compared to control. This effect was potentiated by miR-375 inhibition (miR-375inh+OCT10^{-8}M 9,0%, $P=0.023$ and miR-375inh+OCT10^{-7}M 10.1%, $P=0.0001$, vs control; miR-375inh+OCT10^{-8}M 8.5% $P=0.0058$ vs OCT10^{-8}M). Interestingly, miR-375 inhibition alone and in combination with OCT tend to increase the percentage of cells in early (miR-375inh 32.5%; miR-375inh+OCT10^{-8}M 25.7%; miR-375inh+OCT10^{-7}M 31.8%) and late apoptosis (miR-375inh 4.2%; miR-375inh+OCT10^{-8}M 4.9%; miR-375inh+OCT10^{-7}M 4.0%) compared to control (22.6% and 4.0%) and OCT alone (OCT10^{-8}M 31.8% and 3.2%; OCT10^{-7}M 27.8% and 2.5%) respectively, by inducing PARP, Caspase3 and ERK1/2 phosphorylation. Concluding, these data suggested that SSTR2 protein expression can be epigenetically downregulated by GC-induced increase of miR-375 expression at least partially and negatively influencing OCT action in corticotroph pituitary tumors.

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P108

Soluble α-klotho protein, nesfatin-1 and IGFBP-3 concentrations in the biochemical diagnosis and monitoring treatment effects in patients with acromegaly

Magdalena Ostrowska[1], Wojciech Zgliczyński[1] & Piotr Glinicki[1,2]
[1]Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland; [2]EndoLab Laboratory, Centre of Postgraduate Medical Education, Warsaw, Poland

Introduction
Active acromegaly is diagnosed based on clinical symptoms and biochemical tests, such as elevated GH concentration, IGF-1 concentration above the reference range for sex and age. However, due to certain limitations associated with IGF-1 measurements, alternative biomarkers are being sought that may be useful at various stages of the diagnostic and therapeutic process.
Purpose
Evaluation of the usefulness of serum soluble α-klotho protein, nesfatin-1 and IGFBP-3 determination in the biochemical diagnosis and treatment monitoring in patients with acromegaly.
Materials and Methods
The concentrations of soluble α-klotho protein, nesfatin-1 and IGFBP-3 were determined in patients at the time of acromegaly diagnosis, as well as after 3 and 12 months following the removal of the pituitary adenoma. The examined biomarkers were measured in 35 patients at the time of diagnosis and in 25 patients after 3 and 12 months post-surgery. Measurements of soluble α-klotho protein and nesfatin-1 were conducted using the ELISA immunoassay, while IGFBP-3 was determined using the isotopic method (RIA immunoassay).
Results
The concentration of soluble α-klotho protein was higher ($P=0.0001$) at the time of disease diagnosis compared to the control group. However, no difference was observed in the soluble α-klotho protein concentration at 3 and 12 months after surgery in the study group ($P=0.214$) vs the control group ($P=0.407$). The concentration of soluble α-klotho protein was lower ($P=0.0001$) 3 months after surgery than at the time of disease diagnosis. No difference was observed in the concentration of soluble α-klotho protein at 3 and 12 months after surgery ($P=0.802$). The IGFBP-3 concentration was lower ($P=0.0001$) at 3 and 12 months after surgery than at the time of disease diagnosis ($P=0.0001$). No differences were observed in the IGFBP-3 concentration at 3 and 12 months after surgery ($P=0.122$).
Conclusion
Determination of concentrations of the biomarkers tested: soluble α-klotho protein and IGFBP-3, may be useful in the diagnosis of patients with acromegaly. The concentration of nesfatin-1 did not show discriminatory properties in patients with acromegaly.

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P109

Utilization of MRI in the work-up of mild hyperprolactinemia

Jared Galloway[1], Maria Flynn[2], Jennifer Mann[3], Sana Ghaznavi[1], John Lysack[4], David Campbell[1] & Kirstie Lithgow[1]
[1]University of Calgary, Cumming School of Medicine, Division of Endocrinology, Canada; [2]University of Calgary, Cumming School of Medicine, Division of Internal Medicine; [3]University of Calgary, Cumming School of Medicine, Division of Neurosurgery; [4]University of Calgary, Cumming School of Medicine, Division of Radiology

Background
Hyperprolactinemia is a biochemical finding with a broad differential diagnosis and is commonly measured during the work up for amenorrhea, galactorrhea, or hypogonadism. Diagnostic workup of hyperprolactinemia should be performed in a stepwise fashion to avoid incorrect diagnoses and/or unnecessary investigations. As mild hyperprolactinemia (i.e. <100 mg/l) can be physiologic or spurious, repeating the prolactin level is a crucial step in the initial workup. Unnecessary or premature imaging can lead to incidental findings which generate further investigations and surveillance, causing undue burden on patients and the healthcare system. Our primary objective was to quantify the frequency and proportion of MRI sella ordered for isolated mild hyperprolactinemia when not confirmed by repeat measurement. Our secondary objective was to assess the frequency and type of incidental findings resulting from inappropriate or premature neuroimaging.
Methods
A retrospective chart review was performed between 2012 and 2022 in the province of Alberta, Canada. Potentially eligible cases were identified by a data analyst from Alberta Health Services. Inclusion criteria were 1) patients >18 years of age; 2) elevated serum prolactin <100 mg/l; 3) MRI sella performed following the detection of hyperprolactinemia. Cases with neuroimaging performed for alternative indications were excluded. We classified ordering of MRIs as 'appropriate' or 'inappropriate' based on the clinical indication and the presence or absence of repeat prolactin measurement.
Results
Initial screening identified 3,768 cases. Of these, 1,967 (52%) had two or more prolactin measurements prior to the MRI while 1,801 (48%) had a single prolactin measurement. In 823/1801 cases (46%) the indication for imaging was categorized as appropriate on the basis of clinical suspicion of pituitary or hypothalamic disease (e.g.: amenorrhea, mass effect symptoms). For the remaining cases ($n=978$), the ordering of neuroimaging was categorized as inappropriate. Of the MRIs performed for these cases, 61% ($n=592$) reported normal findings and 39% ($n=386$) reported one or more abnormal findings. The abnormal findings were as follows: 21% ($n=201$) reported a microadenoma, 2% ($n=21$) reported a macroadenoma, and 17% ($n=164$) reported other incidental findings (e.g.: white matter changes, cysts).
Conclusion
In 26% ($n=978$) of mild hyperprolactinemia cases, neuroimaging was performed prematurely without repeating a prolactin measurement or without an appropriate indication. Furthermore, these scans generated a large number of incidental findings which require additional investigation and follow-up. We plan to apply our results to future systems level quality improvement initiatives.

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P110

Obesity in survivors of childhood-onset craniopharyngioma – impact of parental body mass index at craniopharyngioma diagnosis?

Julia Beckhaus[1,2], Maria Eveslage[3], Brigitte Bison[4], Carsten Friedrich[1] & Hermann Müller[1]
[1]Carl von Ossietzky Universität Oldenburg School VI - School of Medicine and Health Sciences, Department of Pediatrics and Pediatric Hematology/Oncology, Klinikum Oldenburg AöR, Oldenburg, Germany; [2]Carl von Ossietzky Universität Oldenburg School IV - School of Medicine and Health Sciences, Divison of Epidemiology and Biometry, Oldenburg, Germany; [3]Institute of Biostatistics and Clinical Research, University of Münster, Münster, Germany; [4]University of Augsburg, Faculty of Medicine, Diagnostic and Interventional Neuroradiology, Augsburg, Germany

Background
It is well known that both genetic backgroup and lifestyle influence the development of 'general' obesity. However, the role of parental body mass index (BMI) on the development of obesity in long-term survivors of childhood-onset craniopharyngioma (CP) is not well understood. This study aimed to analyze the correlation of patients' BMI at diagnosis, and last visit and parental BMI at CP diagnosis and further explored potential risk factors for obesity in CP patients.
Patients and methods
291 CP patients and their parents recruited in the German KRANIOPHARYNGEOM studies were included. Correlations between patient's BMI SDS at CP diagnosis and last visit and parental BMI at CP diagnosis were analyzed. The associations between hypothalamic damage, maternal/paternal BMI and CP patients' obesity at last visit were analyzed by multivariable logistic regression.
Results
After a median follow-up of 9.38 years, 52% of CP patients developed obesity (BMI >3SDS). Patient's BMI SDS at last visit was moderately correlated with BMI-SDS at CP diagnosis ($r=0.48$, 95%-CI 0.38-0.58, $P<0.001$), and also with maternal BMI at diagnosis ($r=0.28$, 95%-CI 0.17-0.38, $P<0.001$) and paternal BMI at diagnosis ($r=0.3$, 95% CI-0.19-0.41, $P<0.001$). Hypothalamic involvement (HI) and surgical hypothalamic lesions (HL) of posterior hypothalamic structures (grade II) were independent risk factors for obesity. With increasing maternal or paternal BMI, the probabilty of developing obesity as a patient with CP increased. However, the contributing role of parental BMI to the pathogenesis of obesity was small compared to the impact of HL.
Conclusion
We conclude that besides HL, parental disposition for obesity is associated with the development of obesity in patients after CP. Hypothalamus-sparing treatment strategies are most effective in prevention of hypothalamic obesity. Our results indicate that also the family situation could have an influence on the development of obesity after CP and might be a therapeutic target.

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P326

A randomised phase 3 trial to assess efficacy and safety of CAM2029, an octreotide subcutaneous depot, in patients with acromegaly

Diego Ferone[1], Julie Silverstein[2], Pamela Freda[3], Laurence Katznelson[4], Federico Gatto[1], Pinar Kadioglu[5], Pietro Maffei[6], Jochen Seufert[7], Joanna L. Spencer-Segal[8], Elena Isaeva[9], Alexander Dreval[10], Maria Harrie[11], Agneta Svedberg[11] & Fredrik Tiberg[11]
[1]Endocrinology Unit, Department of Internal Medicine, IRCCS Ospedale Policlinico San Martino, Genova, Italy; [2]Division of Endocrinology, Metabolism and Lipid Research, Department of Neurosurgery, Washington University School of Medicine, St. Louis, MO, United States; [3]Department of Medicine, Vagelos College of Physicians & Surgeons, Columbia University, New york, Ny, United States; [4]Departments of Neurosurgery and Medicine, Stanford University School of Medicine, Stanford, CA, United States; [5]Division of Endocrinology-Metabolism and Diabetes, Department of Internal Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey; [6]Department of Medicine, Padua University Hospital, Padua, Italy; [7]Division of Endocrinology and Diabetology, Department of Medicine II, Medical Faculty, University of Freiburg, Freiburg, Germany; [8]Department of Internal Medicine and Michigan Neuroscience Institute, University of Michigan, Ann Arbor, MI, United States; [9]Interregional Clinical Diagnostic Center, Kazan, Russian Federation; [10]Endocrinology Department of Moscow Regional Research Clinical Institute, Moscow, Russian Federation; [11]Camurus AB, Lund, Sweden

Background
Acromegaly is a rare endocrine disorder characterised by excess growth hormone (GH) and insulin-like growth factor 1 (IGF-1) that is associated with significant morbidity and impaired quality of life (QoL). Standard-of-care (SoC) treatments for acromegaly typically require healthcare provider administration, pose a substantial treatment burden, and leave scope for improved disease control. CAM2029, an octreotide subcutaneous depot with ~5x higher bioavailability than octreotide long-acting release (LAR), is designed for once-monthly self-administration as a ready-to-use syringe or injection pen. Here, we report findings from the pivotal trial of CAM2029 in patients with acromegaly.
Methods
In this Phase 3, multinational, randomised, double-blind, placebo-controlled trial (NCT04076462), patients on stable SoC treatment (octreotide LAR or lanreotide Autogel) who had IGF-1 $\leq$1x upper limit of normal (ULN) at screening were randomised 2:1 to once-monthly CAM2029 20 mg or placebo for 24 weeks. The primary endpoint was the proportion of patients with IGF-1 $\leq$ULN (mean of week 22/24 measurements). The key secondary endpoint was the proportion of patients with both IGF-1 $\leq$ULN (week 22/24 mean) and mean GH <2.5 µg/l (week 24). Patient-reported outcomes (PROs) were compared at baseline and week 24.
Results
Seventy-two patients were randomised to CAM2029 ($n=48$) or placebo ($n=24$). A significantly greater proportion of CAM2029 vs placebo recipients achieved the primary (IGF-1 response: 72.2% vs 37.5%; $P=0.0018$) and key secondary endpoints (IGF-1 and GH response: 70.0% vs 37.5%; $P=0.0035$). These results were supported by all sensitivity and supportive analyses. Median time to loss of response (IGF-1 $>$ULN) was 8.4 weeks in the placebo arm and was not reached in the CAM2029 arm. Mean IGF-1 remained below ULN throughout the study for patients receiving CAM2029 but not for patients receiving placebo. PROs showed improved QoL, treatment convenience, and patient satisfaction for CAM2029 vs baseline SoC, with numerically greater improvements vs placebo. CAM2029 was well tolerated with a comparable safety profile to SoC; no new or unexpected safety signals were observed. One treatment-related serious adverse event (cholecystitis) occurred in the placebo arm, and 5 patients discontinued treatment due to injection site erythema/induration (CAM2029: $n=3$; placebo: $n=1$) or migraine (CAM2029: $n=1$).

Conclusion
CAM2029 provided robust biochemical control of acromegaly superior to placebo, substantially improved PROs vs baseline SoC and placebo, and had a safety profile consistent with SoC. These findings support CAM2029 as a potential therapeutic alternative to SoC acromegaly treatments that addresses unmet patient needs.

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P112

Metabolic syndrome in women with sheehan syndrome: prevalence and associated factors

Salma Salhi[1], Ibtissem Oueslati[1], Emna Talbi[2], Anis Grassa[1], Arige Abid[1], Meriem Yazid[1], Moncef Feki[2] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia; [2]La Rabta University Hospital, Laboratory of Biochemistry, Tunis, Tunisia

Introduction
Sheehan's syndrome (SS) is characterized by a deficiency in pituitary hormone secretion. It is now being closely inspected for its implication in the onset of metabolic syndrome (MS). The aims of this study were to determine the prevalence of MS and assess its associated factors in women with SS.
Methods
We carried out a cross-sectional study involving 50 patients diagnosed with SS and 50 controls, matched for age and body-mass index (BMI). Waist circumference measurement, 24-hour ambulatory blood pressure monitoring, and laboratory tests were performed in all participants. MS was defined according to the IDF-2009 criteria.
Results
The average age was 62.2 $\pm$ 9.4 years in patients and 60.6 $\pm$ 8.4 years in controls ($P=0.385$). The mean BMI was 29.6 $\pm$ 6,0 kg/m^2 in patients vs 30.0 $\pm$ 5.0 kg/m^2 in controls ($P=0$, 741). Waist circumference was significantly higher in patients (101.3 $\pm$ 10.2 cm) than in controls (95.7 $\pm$ 10.5 cm) ($P=0.007$). It was $\geq$ 80 cm in 98% of patients and in 86% of controls ($P=0.027$). The prevalence of MS was 64% in patients and 40% in controls ($P=0.016$). Among these patients, 87% of women with SS and 100% of the CG had three to four MS criteria. The coexistence of all five MS criteria was observed only in patients (13%). SS was positively associated with MS (Odds Ratio=2.66,: 1.18-5.98, $P=0.016$). In women with SS, age, diagnostic delay, disease duration, GH levels, FT4 levels, daily dose of levothyroxine, daily and cumulative dose of hydrocortisone, and estroprogestative therapy were not associated with MS.
Conclusion
These results emphasize the need for monitoring and managing components of MS in individuals with SS. Clinicians should develop targeted interventions that can effectively mitigate the risk of MS and its associated complications in this specific population.

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P113

2-[18F]FDG PET imaging biomarkers for clinical and metabolic assessment in ectopic cushing syndrome. increased spleen FDG uptake as a helpful parameter to predict the presence of metastases - a pilot study

Ewelina Rzepka[1], Joanna Kokoszka[2], Marta Opalinska[1], Katarzyna Sitarz[3], Anna Grochowska[4], Anna Sowa-Staszczak[1], Alicja Hubalewska-Dydejczyk[1] & Aleksandra Gilis-Januszewska[1]
[1]Jagiellonian University Medical College, Chair and Department of Endocrinology, Krakow, Poland; [2]Endocrinology, Oncologic Endocrinology, Nuclear Medicine and Internal Diseases Department, University Hospital in Krakow, Poland; [3]University Hospital in Krakow, Poland; [4]Department of Radiology, University Hospital in Krakow, Poland

Introduction
2-[18F]FDG PET/CT, commonly used for neoplastic lesions detection, also allows assessment of the severity of the inflammatory processes. Moreover, glucose uptake in spleen and bone marrow may be a useful biomarker of systemic inflammation. Patients with Cushing syndrome demonstrate many metabolic changes involving muscles and fat tissue. Some mechanisms are known, but their relationship to glucose metabolism is not well investigated. Our study aimed to correlate glucose metabolism with the use of 2-[18F]FDG PET/CT in skeletal muscle, adipose tissue, bone marrow and spleen with clinical and metabolic parameters in patients with EAS.
Materials and Methods
Analysis of 2-[18F]FDG PET/CT scans in 13 consecutive patients with EAS in comparison to healthy age, BMI and sex-matched control group was performed. On unenhanced CT scans the body composition on cross-sectional computed tomography images at the L3 level - skeletal muscle area (SMA), skeletal muscle index (SMI), visceral fat area (VFA), visceral fat index (VFI), subcutaneous fat area (SFA), subcutaneous fat index (SFI), intermuscular adipose tissue (IMAT) were assessed. Additionally, cross-sectional area (CSA) and mean attenuation (MA) of each psoas muscle at the L4 level were measured. In 2-[18F]FDG-PET scans, glucose uptake of each psoas (at the L4 vertebra) and femoris muscle (SUV max, SUV peak and SUV mean, target to background ratio [TBR]), as well as glucose uptake of subcutaneous (SAT) and visceral fat (VAT) (SUV max, SUV peak and SUV mean) were analysed. Spleen and bone marrow glucose metabolism (SUV mean, SUV max, spleen to liver ratio [SLR], bone marrow to liver ratio [BLR]) were also evaluated. The results were correlated with clinical and hormonal markers of the disease.
Results
We observed significant positive correlation between presence of metastases and spleen SUV max and SUV mean ($P=0.03$, $P=0.03$). Significant negative correlations between morning cortisol level, midnight cortisol level, cortisol after 1 mg of dexamethasone and VAT SUV peak were seen ($P=0.049$, $P=0.029$, $P=0.017$, respectively). Midnight cortisol level was negatively correlated with SAT SUV peak and SUV max ($P=0.048$, $P=0.032$, respectively).
Conclusion
Increased spleen FDG uptake, considered to be a surrogate marker of cancer-related inflammation, could be helpful to predict the presence of metastases in EAS. Negative correlation between cortisol levels and glucose metabolism parameters in fat could reflect the dominant role of insulin resistance in adipocytes, abnormal perfusion and vascular function in adipose tissue of EAS patients.

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P114

Obesity-Related pseudo-cushing syndrome and pituitary incidentaloma: a case study

Vittoria Strinati[1], Gabriele Veroi[1], Davide Masi[1], Paola Nevi[1], Valentina Ventimiglia[1], Mikiko Watanabe[1], Stefania Mariani[1], Lucio Gnessi[1] & Carla Lubrano[1]
[1]Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza University of Rome, Rome, Italy

Introduction
The diagnosis of Cushing's syndrome (CS) can be challenging for endocrinologists due to its multifaceted presentation. Accurate differentiation between Pseudo-Cushing syndrome (PCS) and true CS is crucial as their treatment approaches and outcomes vary significantly.
Case Report
A 43-year-old male patient with grade III obesity (BMI: 49.9 kg/m^2) presented to our Endocrinology outpatient clinic with a complex medical history including hypertension, impaired fasting glycemia, Basedow disease and recent hypogonadism. The patient reported a rapid and substantial weight gain of approximately 60 kg within 5 months during the Covid-19 pandemic. Physical examination revealed a 'cushingoid' appearance with facial plethora, central obesity, *striae rubrae*, and retronucal adipose tissue deposition. The patient underwent initial investigations for endogenous hypercortisolism, including overnight 1 mg dexamethasone suppression test (DST), urinary-free cortisol test, ACTH test. However, the results did not fully meet the diagnostic criteria for endogenous hypercortisolism. Therefore, an oral 2-mg 48-h low-dose dexamethasone suppression test (LDDST) was performed, revealing a lack of suppression of serum cortisol level and thus confirming the diagnosis of endogenous hypercortisolism. To investigate the possibility of Cushing Disease (CD), a 3 Tesla dynamic contrast-enhanced magnetic resonance imaging (MRI) was performed, revealing an area of delayed enhancement in the left half of the gland, measuring approximately 4 mm, and suggestive of microadenoma. Despite this finding, the possibility of PCS could not be ruled out, as the patient reported emotional distress and depressed mood despite denying alcohol consumption. The patient underwent a combined LDDST-CRH test. The basal cortisol level before CRH infusion was 30.5 nmol/l, and the cortisol level 15 minutes after CRH infusion was 35.7 nmol/l ($<$39 nmol/l). Although the result was not definitive, it indicated the possible presence of PCS and, therefore a 'wait and see' approach was adopted. The patient was started on a low-calorie diet and received medical treatment to manage comorbidities. A follow-up biochemical assessment was conducted after 3 months, which confirmed the diagnosis of PCS with concomitant non-functioning pituitary microadenoma. The patient exhibited remarkable compliance with the recommended diet, leading to a substantial weight loss of 25 kg. Additionally, diabetes and hypertension appeared well-controlled.

Conclusion
Differential diagnosis between CD and PCS is complex and may require multiple tests over time. The possibility of pituitary incidentalomas on MRI should always be considered. In cases where there is uncertainty regarding the diagnosis, a follow-up evaluation of the patient at 3-6 months, both clinically and biochemically, can be useful.

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P115

The value of digital quantification of somatostatin receptor subtypes 2 and 5 immunostaining in GH-secreting pituitary tumors

Claudia Campana[1,2], Jessica Amarù[1], Angelo Milioto[1], Federica Nista[1], Peter M. van Koetsveld[2], Anand Iyer[2], Marica Arvigo[1], Diego Ferone[1,3], Leo J. Hofland[2] & Federico Gatto[3]
[1]University of Genova, Endocrinology Unit, Department of Internal Medicine and Medical Specialties, School of Medical and Pharmaceutical Sciences, Genoa, Italy; [2]Erasmus Medical Center, Department of Internal Medicine, Division of Endocrinology, Rotterdam, Netherlands; [3]IRCCS Ospedale Policlinico San Martino, Endocrinology Unit, Genoa, Italy

Introduction
Immunohistochemistry (IHC) of somatostatin receptor subtype 2 (SST_2) is a predictive factor for first-generation somatostatin receptor ligand (fg-SRL) response in acromegaly patients. A semi-quantitative immunoreactivity score, IRS, has been proposed as the gold-standard to evaluate SST_2 IHC expression. Recently, our group developed a quantitative method to determine SST_2 expression using an open-source digital image analysis (DIA). We aimed to validate the DIA on both SST_2 and SST_5 in a new cohort of GH-secreting pituitary tumors. We then correlated fg-SRL response with SST expression, evaluated with both IRS and DIA methods.
Material and Methods
SST_2 and SST_5 expression was assessed in paraffin-embedded tissues from 42 GH-secreting pituitary tumors, using both IRS and DIA. The DIA software calculates the staining intensity (intensity/area) and the percentage of positive cells (%PC-DIA) based on four representative images. The IRS was independently performed by two researchers. Correlations were performed evaluating the 'total' receptor expression (IRS vs intensity/area) and the %PC (%PC-IRS vs %PC-DIA). GH and IGF-1 data were collected at baseline after surgery and following 6-month fg-SRL treatment.
Results
Mean SST_2 IRS was 6.41 ± 3.35, mean DIA intensity/area was 0.17 ± 0.14, and mean %PC-DIA was 63.42 ± 29.67%. As concerns SST_5, mean IRS was 4.66 ± 3.26, mean DIA intensity/area was 0.07 ± 0.09, and mean %PC-DIA was 38.27 ± 38.84%. A good correlation was observed between DIA and IRS for 'total' receptor expression (rho = 0.924 and rho = 0.872, for SST_2 and SST_5, respectively), as well as for the %PC (rho = 0.649 and rho = 0.748, all $P < 0.0001$). Twenty-four out of 42 patients (57%) were treated with fg-SRLs after surgery. A significant positive correlation was observed between GH decrease and SST_2 expression, quantified with DIA (intensity/area: rho = 0.707, %PC: rho = 0.625, $P < 0.005$) and total IRS (rho = 0.655, $P = 0.017$), but not with the %PC-IRS (rho = 0.356, $P = 0.123$). Similarly, a significant positive correlation was observed between IGF-1 xULN decrease and SST_2 expression for both DIA parameters and total IRS (rho ranging from 0.517 to 0.617, $P < 0.05$), but not for %PC-IRS (rho = 0.235, $P = 0.334$). No correlation was observed between GH, IGF-1 xULN decrease and SST_5 expression.
Conclusion
The DIA is a reliable quantification method to assess both SST_2 and SST_5 expression. SST_2, but not SST_5, expression correlated with GH and IGF-1 decrease following fg-SRL treatment. This correlation was statistically significant using both IRS and DIA when 'total' SST_2 expression was assessed. The %PC correlated with treatment response only when evaluated using the DIA, thus showing the superiority of this quantitative method.

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P116

Cell lineage specific differences in clinical behavior of clinically non-functioning pituitary adenomas according to the 2017 WHO classification – a systematic review and meta-analysis

Loren van der Hoeven[1,2,3], Tessa Slagboom[2,4], Arjan Malekzadeh[5], Jantien Hoogmoed[3,6], Madeleine Drent[2,3,4], Eleonora Aronica[7], Dirk Jan Stenvers[1,2,3,4] & Alberto Pereira[1,2,3]
[1]Amsterdam UMC, Location University of Amsterdam, Department of Endocrinology and Metabolism, Amsterdam, Netherlands; [2]Amsterdam Gastroenterology Endocrinology and Metabolism, Amsterdam, Netherlands; [3]Endo-ERN European Reference Network on Rare Endocrine Conditions; [4]Amsterdam UMC, Location Vrije Universiteit, Department of Endocrinology and Metabolism, Amsterdam, Netherlands; [5]Amsterdam UMC, Location University of Amsterdam, Medical Library, Amsterdam, Netherlands; [6]Amsterdam UMC, Location University of Amsterdam, Department of Neurosurgery, Amsterdam, Netherlands; [7]Amsterdam UMC, Location University of Amsterdam, Department of Neuropathology, Amsterdam, Netherlands

Background
In 2017, the World Health Organization (WHO) adjusted the histopathological classification of pituitary adenomas (PAs) by including pituitary cell lineage specific transcription factors (TFs), elucidating a continuous spectrum between true null cell (NCA), silent, clinically silent, and functioning adenomas. The definitions of non-functioning (silent) gonadotroph, corticotroph, somatolactotroph and thyrotroph adenomas were previously reserved for immunohistochemically hormone positive (IHC hormone+) PAs, but have been expanded to also include PAs with positive immunohistochemistry of the corresponding cell lineage specific TF (SF-1+, TPIT+ or Pit-1+) despite negative IHC of the anterior pituitary hormones (TF+/hormone- PAs). On the other hand, the definition of NCA has been narrowed to adenomas that are IHC negative both for anterior pituitary hormones and TFs. It is, however, not clear, if, and to what extent, the novel histopathological classification translates into differences in clinical behavior in clinically non-functioning pituitary adenomas.
Objectives
To systematically review potential cell lineage specific differences in the prevalence of cavernous sinus invasion in clinically non-functioning PAs.
Methods
The conduct and reporting of this systematic review and meta-analysis were in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-statement). A comprehensive literature search in Medline, Embase and CENTRAL was performed on July 11th 2023. Cohort and cross-sectional studies were only included if the WHO 2017 histopathological classification of at least one transcription factor was applied using immunohistochemistry, and at least one clinical outcome related to invasion was reported.
Results
A total of 26 articles were included for the outcome of invasion, including a total of 2253 participants. Invasion of the cavernous sinus occurred more often in NCAs and TPIT+ non-functioning PAs compared to SF-1+ (prevalence ratio (PR) 1.60 [95% CI 1.29 – 1.97], and 1.43 [95% CI 1.22 – 1.69]). Invasion of the cavernous sinus also occurred more often in NCAs compared to PIT-1+ (PR 1.44 [95% CI 1.03 – 2.02]). There were no differences in cavernous sinus invasion between PIT-1+ compared to SF-1+, NCA compared to TPIT+ and TPIT+ compared to PIT-1+, although a trend was observed for TPIT+ being more often invasive compared to PIT-1+ (PR 1.51 [95% CI 0.88 – 2.59]).
Conclusion
The 2017 WHO classification enables to identify histopathological subgroups of clinically non-functioning PAs with distinct clinical behavior in terms of cavernous sinus invasion, with NCAs and TPIT+ PAs being more often invasive in the cavernous sinus compared to SF-1+ non-functioning PAs.

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P117

Proton beam radiotherapy for treatment of functional pituitary adenomas

Dana Erickson[1,1], Herndon Justine[2], Nadia Laack[1] & William Breen[1]
[1]Mayo Clinic, Rochester, United States; [2]Mayo Clinic, Endocrinology, Rochester, United States

Background
Proton beam therapy (PBT) provides high doses of radiation to the targeted tissues while minimizing exposure to surrounding structures. Although rarely used in patients with functional pituitary adenomas (FPA) it might be nessesary in certain clinical situations. There is paucity of data regarding short- and long-term endocrinologic outcomes.
Objectives
In patients undergoing PBT, determine rate of remission of FPA(normal hormonal values off medical suppressive therapy [MST]), control of FPA (reduction in MST and remission) and rate of hypopituitarism.

Methods
Review of prospectively set up database of adults from tertiary referral center with FPA 2015. Baseline data included demographics, tumor pathology, prior history of surgery/radiation, MST, hormonal data and incidence of pituitary insufficiencies (PI). Biochemical hormonal data, change in MST, remission of functional excess, and incidence of new PI was abstracted at 6 months, and 1, 2, 3, 4, 5 years, and up to two additional time points up to 2023. Statistical analysis includes descriptive statistics presented as number (%) and median [IQR].
Results
Twelve patients with FPA of total 40 pathologies of pituitary origin underwent PBT. Median age of patients was 43.9 years old [30.8, 56.4], median follow-up was 24 months [12, 60]. Median PBT Gy was 52.2 [50.4, 54], in median of 28 fractions. Tumors included GH-secreting in 6 (50.0%), followed by two (16.7%) ACTH-secreting, two (16.7%) PRL-secreting, one (8.3%) TSH-secreting, and one (8.3%) plurihormonal. All patients had prior surgeries (range 1-4), 3 (25%) had previous photon radiation. Eleven (91.7%) were uncontrolled despite 9 (75%) being treated with MST. The 3 (25%) patients who were not on MST had increase in size of their tumor prompting PBT. At least one PI was observed at baseline in 9 patients (75%), secondary hypogonadism most common (7, 58.3%). At 6 months remission occured in 2 (16.7%). At the end of follow-up, 3 (25%; 2 GH-secreting and 1 ACTH-secreting) had achieved remission, 2 (16.7%, 1 GH-secreting and the TSH-secreting) were controlled, with MST reduced, 4 (33.3%) were controlled but MST not reduced, and persistent hyperfunction was observed in 3 (25.0%). Only one patient (16.7%) without PI at baseline developed adrenal insufficiency at 3-years post-treatment.
Conclusion
PBT is a reasonable consideration for treatment of selected FPA for control or reduction of MST need with little newly developed PI, recognizing the already high initial prevalence of PI in this cohort a still limited follow-up.

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P118

Hyponatremia after COVID-19 is frequent in the first year and increases re-admissions

Betina Biagetti[1,2], Adrian Sanchez-Moltavá[1,3], Albert Puig-Perez[1,2], Isabel Campos-Varela[1,4], Florencia Pilia[1,5], Emilie Anderssen-Nordahl[1,6], Didac González-Sans[1,7], Marta Miarons[1,8] & Rafael Simo Canonge[1,2]
[1]Vall d'Hebron University Hospital, Barcelona, Spain; [2], Endocrinology; [3], Infectious Diseases Department; [4], Liver Unit; [5], Pneumology Department; [6], Clinical Pharmacology; [7], Systemic Autoimmune Diseases Unit; [8], Pharmacy Department

Background
Hyponatremia has been related to worse outcomes from COVID-19 infection during hospital admission. However, little is known about the incidence and prevalence of hyponatremia after discharge and the associated risk factors.
Methods
Prospective observational 24-month follow-up study of patients admitted at a tertiary hospital during the first COVID-19 wave. Kaplan-Meier curves and Cox proportional hazard models were used to assess the main variables in predicting hyponatremia on follow-up (HyPO-FU).
Results
A total of 161 out of 683 (24.4%) developed HyPO-FU. The group with HyPO-FU comprised of more men [(62.3%) vs (49.2%); $P<0.01$], older [65.6 $\pm$18.2 vs 60.3$\pm$17.0; $P<0.01$], had more comorbidities such as diabetes, hypertension, heart failure and renal failure ($P<0.01$), hyponatremia on admission [(46.1%) vs (28.5%) $P=0.01$], and were more frequently re-admitted [(16.2%) vs (3.8%); $P<0.01$) compared to patients without HyPO-FU. The mean rate of HyPO-FU was higher in the first year 23.6 per 100 individuals per year. After a stepwise Cox regression analysis, the independent risk factors of developing HyPO-FU were diabetes [OR: 2.12, IC: 95% (1.48-3.04)], hypertension [OR: 2.18, IC: 95% (1.53-3.12)], heart failure [OR: 3.34, IC: 95% (1.72-6.48)] and previous invasive ventilation support requirement [OR: 2.38, IC: 95% (1.63-3.50)].
Conclusion
HyPO-FU was frequent in the first year after COVID-19 infection, and the risk was higher in older men with comorbidities, increasing rehospitalisation. The independent associated risk factors were diabetes, hypertension, heart failure and the requirement of invasive ventilation support. Further studies aimed at evaluating the beneficial effects of correcting hyponatremia in these patients are warranted.

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P119

Management of carcinoid heart disease in neuroendocrine tumor patients: a retrospective study

Ignacio Jiménez Hernando[1], Laura González Fernández[1], Rogelio García Centeno[4], Marta Pérez Noguero[1], Mónica Gómez-Gordo Hernanz[1], Gloria Collado González[1], Isabel Losada Gata[1], Alberto García Piorno[1] & Olga González Albarrán[1]
[1]Gregorio Marañón General University Hospital, Endocrinology and Nutrition, Madrid, Spain

Introduction
Approximately 20% of neuroendocrine tumor (NET) patients experience carcinoid syndrome (CS), primarily associated with metastatic ileal NETs. CS manifests with symptoms such as diarrhea, flushes, and cardiac complications. Carcinoid heart disease (CHD) is a negative prognostic factor in NETs. However, the considerable variability in reported diagnoses and treatment approaches in the literature creates uncertainty about optimal management in this specific population.
Methods
A cross-sectional, single-center retrospective study was designed. Patients with CS followed during 2023 in our hospital were included, focusing on those with associated carcinoid heart disease. Epidemiological, clinical, biochemical, therapeutic, and evolutionary variables were recorded.
Results
Fifteen patients (9 females and 6 males) with a mean age of 65 years (45-77 years) were included. The primary tumor location was intestinal (jejuno-ileal) in 14 cases, with only 1 pancreatic case. Tumor grade was G2 in 60%, G1 in 33.3%, and G3 in 6.7%. Diarrhea was present in 80% of cases, and flushing in 60%. Biochemically, the mean chromogranin A (CgA) was 356 units (range 3.2 - 3515), and mean 5-hydroxyindoleacetic acid (5HIAA) was 77 mg/24h (range 12.4 - 437). Regarding CHD, this comorbidity was present in 20% of patients (3/15). The time from oncologic diagnosis to carcinoid heart disease diagnosis was less than 4 months (1-120 days). Two patients underwent cardiac surgery (one with a biological prosthesis and the other with a mechanical prosthesis). After surgery, their dyspnea improved according to NyHA from II-III to I-II, respectively. One patient underwent a second surgery and died due to complications. All three patients were being treated with somatostatin analogues. Only the patient with the mildest heart disease (NyHA I) received PRRT treatment. There were no statistically significant differences in CgA and 5HIAA values at diagnosis between patients with and without CHD.
Conclusions
Significant variability exists in the treatment approaches for patients with carcinoid heart disease, and mortality after valve replacement remains high. Chromogranin A and 5HIAA were not predictive markers for CHD presence in our CS population.

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P120

Approaching the reality of restoring GH secretion and growth with the investigative oral growth hormone secretagogue (GHS) LUM-201 in moderate pediatric growth hormone deficiency (PGHD)

Peter Clayton[1], Fernando Cassorla[2], OraGrowtH210 Trial Group[3], OraGrowtH212 Trial Group[3], Michael Johnson[4], Aleksandra Bruchey[3], Christopher Smith[3], Erik Brincks[3], Pisit ' Duke' Pitukcheewanot[3], John McKew[3] & Michael Thorner[3]
[1]University of Manchester, Division of Developmental Biology & Medicine; Paediatric Endocrinology, Manchester, United Kingdom; [2]University of Chile, Institute of Maternal and Child Research, Santiago, Chile; [3]Lumos Pharma, Inc., Austin, TX, United States; [4]University of VA Health System, Keswick, VA, United States

Over 40 years ago, the first enkephalin analogs that stimulated growth hormone (GH) release were synthesized in 1984, leading to the development of GHRP-6. In 1995, Merck developed a potent non-peptide orally active long-acting growth hormone GHS, ibutamoren, and cloned the GHS receptor in 1996, which led to ghrelin being identified as its natural ligand in 1999. These discoveries uncovered a new physiological pathway for GH regulation linking the GI tract and the hypothalamic-pituitary axis (HPA). In 1998, the first oral ibutamoren (now known as LUM-201) clinical trial in PGHD included pre-pubertal children with a broad spectrum of PGHD, resulting in positive growth responses coming from those with an intact HPA. Later, it was understood the best candidates for this investigative oral treatment were pre-pubertal children (those with standard stimulation testing peak GH between ≥ 3 <10 ng/ml) that respond positively to the LUM-201 Predictive Enrichment Marker (PEM) test. PEM+ responders have basal serum IGF-1 >30 ng/ml and a peak serum GH ≥ 5 ng/ml after administering a single dose of 0.8 mg/kg LUM-201. Oral once-daily LUM-201

has been studied in two phase 2 trials in PEM+ PGHD focusing on safety and effectiveness. The OraGrowthH212 trial has evaluated GH pulse profiles at baseline and after 6 months of LUM-201 at 1.6 and 3.2 mg/kg/day, while the OraGrowthH210 trial has investigated dose responses using 0.8, 1.6, and 3.2 mg/kg/d vs rhGH comparator arm. The OraGrowthH212 trial demonstrated a 62% increase in GH secretion and an 80% increase in IGF-1 concentration after 6 months of LUM-201, enhancing annualized height velocity (AHV) by 60%, which remained steady at 12 months. In the OraGrowthH210 trial, the 1.6 mg/kg/d dose achieved the highest AHV over 6 months (8.2 cm/yr), maintained at 12 months (8.0 cm/yr), comparable to historical responses in moderate PGHD and within the targeted 2 cm/yr margin of the rhGH comparator arm. Notably, LUM-201 achieved the reported growth rates with GH secretion at approximately one-fifth of the amount absorbed from daily rhGH injection. Both studies reported a favorable investigational safety profile. Oral LUM-201 allows the restoration of normal pulsatile endogenous GH secretion to support similar growth to that achieved with daily pharmacological rhGH while maintaining normal feedback mechanisms. This innovative approach to treating PGHD will remove the burden of frequent injections with an oral therapy that achieves physiological GH profiles and therefore meets the core objectives of all endocrine therapies, namely to restore normal hormonal homeostasis.

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P121

Adipsic diabetes insipidus - a rare complication of craniopharyngiomas

Alexandru Florescu[1,2], Irina Puscasu[1], Viviana Popa[1], Adina Nicolaica[1], Andra Berigoi[1], Mihaela Florea[1], Stefana Bilha[1,2] & Cristina Preda[1,2]
[1]Saint Spiridon County Hospital, Endocrinology, Iaşi, Romania; [2]Universitatea de Medicină şi Farmacie 'Grigore T. Popa' din Iaşi, Endocrinology, Iaşi, Romania

Introduction
Craniopharyngiomas are rare tumors which are typically located in the sellar and suprasellar region. They can be solid or mixed, cystic-epithelial. Treatment options include surgery, radiation or intracystic therapy. Adipsic diabetes insipidus is a rare, life-threatening disease which can sometimes be associated with craniopharyngioma, either because of tumor mass effect, or as a postprocedure complication. Ultimately, this can cause severe hypernatremia, so long term management requires a careful interplay between low dose vasopressin analog treatment and fluids.
Case report
We present the case of a 32-year-old patient, operated at 10 years for craniopharyngioma, relapsed and re-operated (a total of 5 interventions), complicated with hydrocephalus (for which a ventriculo-peritoneal shunt was inserted), panhypopituitarism (in substitution treatment with LT4, cortison acetate and testosterone), central diabetes insipidus (in treatment with vasopressin analogues) and hypothalamic syndrome (hyperphagia, somnolence, hyperhidrosis, adipsia, hyperthermia). The last cerebral MRI (2021) describes post-operative continuity defects and altered structure of the sellar region and floor of the anterior cerebral fossa, and possible remaining pituitary tissue of 9/3 mm. In october 2023, he presents for reevaluation, accusing: sleepiness, night vision disorders, hyperphagia, adipsia, pain in the lower limbs, generalized muscle weaknes and adipsia. Clinical exam revealead a BP of 109/65mmHg, a HR of 110bpm, and a BMI = 40.16 kg/m^2, and a 24 hour urine ouput of 500 mL/day of hyperchromic, cloudy urine. Biochemical evaluation revealead hypernatremia (160 mmol/l), and hormonal evaluation revelead euthyroid status under LT4 substitution, normal cortisol (under 25mg cortison acetate/daily) and low testosterone levels (limited treatment compliance). Considering the severe hypernatremia, caused by adipsia and aggravated by diabetes insipidus, oral and parenteral fluid repletion was initiated and the dose of vasopressin analogues was considerably reduced, with subsequent normalization of serum sodium to 145 mmol/l, and a urine output of 2500mL/day (urine density 1000). Upon discharge, lower dose vasopressing analogue therapy was continued, and a minimum of 2L fluid intake was recommended.
Conclusion
Adipsic diabetes insipidus is a rare, life-threatening condition, which causes severe hypernatremia through intracellular dehydration, but also extracellular hyperhydration. The mainstay of therapy is a delicate balance between vasopressin analogue treatment and fluid intake; and an individual approach must be selected in the management of these patients. Finally, even with appropriate medical treatment, adipsic diabetes insipidus remains a hard to manage condition, so patient and family education regarding fluid intake as well as frequent, careful assessment of clinical and biochimical status is of utmost importance.

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P122

Cushing's syndrome: normalization of cortisol is just the beginning

Gretchen Jordan[1] & Leslie Edwin[1]
[1]Cushing's Support and Research Foundation, Lilburn, United States

Introduction
Cushing's Syndrome is caused by elevated levels of cortisol and is characterized by dozens of non-specific physical, metabolic, and neuropsychological symptoms. The extent of damage a patient will face is directly related to time to diagnosis, experience of the doctors and surgeon, and the support and education they receive after surgery. The spectrum of long-term needs faced by patients who have been exposed to prolonged elevated cortisol are not well represented in the literature and not well understood by most doctors.
Method
In 2023, a committee of patient advocates built a quality of life survey with over 150 questions using examples from two previous patient-created studies. This survey was translated into Spanish and French, then shared amongst multiple global support communities. SurveyMonkey was used for layout and response collection.
Results
The survey received 438 responses from 38 countries. Though the majority of respondents were from the United States, the unprecedented collaborative efforts of international patient organizations was reflected in the volume of responses and added depth to the data. **Cushing's is overwhelming** – Over 90% of respondents said they were negatively impacted by the complexity of symptoms and that it is almost impossible to fully understand the diagnosis in the beginning. **Delay in diagnosis equates to worse long-term prognosis –** It took more than 10 years for a full quarter of respondents to get an accurate diagnosis. **Mental health support is vital** – It was nearly unanimous that mental health support should be part of a patient treatment package (99.3%) and that therapy can be helpful even when a patient has good coping skills (95.7%); a need to process trauma after Cushing's was expressed by 92% of participants. **Peer support can be priceless** – 98% agree that it is beneficial to share experiences with other patients, and 94% said that a 'peer sister' or 'peer brother' to guide a patient along the way would be helpful. **The devastating reality** – Almost three quarters of patients reported that grief has been constantly present throughout the journey and they were not prepared for what life was like after surgery, and concern is nearly unanimous about life-shortening cardiovascular damage and changes to the brain.
Conclusion
For a rare disease like Cushing's, it is imperative to partner with an advocacy group that can help provide crucial missing data that paints a bigger picture of the patient experience and ultimately leads to faster and better treatment.

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P123

Longterm-outcomes in patients with cushing's disease vs non-functioning pituitary adenoma after pituitary surgery: an active-comparator cohort study

Roxana Wimmer[1], Sara Germann[1], Rahel Laager[1], Beat Müller[1], Philipp Schütz[1], Nina Kaegi-Braun[1] & Alexander Kutz[1]
[1]Aarau, University Department of Medicine, Clinic for Endocrinology, Diabetology, and Metabolism, Kantonsspital Aarau, Aarau, Switzerland and Medical Faculty of the University of Basel, Basel, Switzerland, Aarau, Switzerland

Objective
There is increasing evidence that multisystem morbidity in patients with Cushing's disease (CD) is only partially reversible following treatment. We investigated complications from multiple organs in hospitalized patients with CD compared to patients with non-functioning pituitary adenoma (NFPA) after pituitary surgery.
Design
Population-based retrospective cohort study using data from the Swiss Federal Statistical Office between January 2012 and December 2020.
Methods
Through 1:5 propensity score matching, we compared hospitalized patients undergoing pituitary surgery for CD or NFPA, addressing demographic differences. The primary composite endpoint included all-cause mortality, major adverse cardiovascular events (i.e., myocardial infarction, unstable angina, heart failure, cardiac arrest, ischemic stroke), hospitalization for psychiatric disorders, sepsis, severe thromboembolic events, and fractures in need of hospitalization. Secondary endpoints comprised individual components of the primary endpoint and reintervention due to disease persistence or recurrence.
Results
After matching, 113 CD patients (mean age 45 years [SD, 15], 74.3% female) and 390 with NFPA (47 years [SD, 15], 69% female) were included and followed for a median of 54.2 months (IQR 1, 116) after surgery. CD presence was associated

with a higher incidence rate of the primary endpoint (43.2 vs 16.4 events per 1,000 person-years, HR 2.55; 95% CI 1.44 to 4.52). CD patients also showed significantly increased hospitalization rates for psychiatric disorders (HR 4.53; 95% CI 2.06 to 9.99) and sepsis (HR 4.41; 95% CI 1.18 to 16.44).
Conclusion
Even after pituitary surgery, CD patients faced a higher hazard of complications, especially psychiatric hospitalization and sepsis.

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P124

Neuropsychological profile in acromegaly: cross sectional analysis and preliminary prospective long-term study

Alessandra Mangone[1,2], Giorgia Abete Fornara[3], Elisa Sala[2], Giulia Carosi[2], Giulia Del Sindaco[1,2], Arianna Cremaschi[2], Roberta Mungari[2], Veronica Lotito[1,2], Giulio Bertani[3], Marco Locatelli[3], Emanuele Ferrante[2] & Giovanna Mantovani[1,2]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurosurgery Unit, Milan, Italy

Background
Psychopathological distress is a significant burden in acromegaly, mostly in terms of depression and anxiety. Patients are also reported to experience an impairment in cognitive performance, yet literature is highly heterogeneous.
M&M
We conducted a cross-sectional study recruiting 44 acromegalic patients (59% females, 29.5% with active disease, 70.5% controlled/in remission) referring to our tertiary center between 2011 and 2023 and 40 healthy controls matched for sex, age, and educational level. We explored the psychological status through Beck-Depression-Inventory-II (BDI) and State-Trait-Anxiety-Inventory X1 and X2 (STAI X1-X2) and 12 standardized tests exploring different neuropsychological areas (short- and long-term verbal and visuo-spatial memory, selective attention, attentional shifting, verbal fluencies, inhibitory functions, constructional praxis, deductive reasoning and perseverative behavior). Moreover, we performed a prospective analysis of a subgroup of 9 patients recruited at diagnosis and followed-up for 10 years. Both functions were assessed at four time-points: T1) before surgery; T2) 3 days post-operatively; T3) 12 months after and T4) 10 years after surgery.
Results
In cross-sectional study, 10 patients (22.7%) reported a pathological score indicative of depression at BDI, 50% of whom with active disease ($P=0.13$). Focusing on anxiety, 6 male patients (33.5%) scored pathologically at STAI-X1 and no female; 66% of them with active disease ($P=0.05$). Mean results of STAI-X2 indicated a slight overall trait anxiety (52.22 ± 17.96), with 7 patients (38.9%) reporting a pathological score (6 females); most of them (71%) with active disease ($P=0.017$). We indeed found an association between IGF-1 levels and STAI-X1 and STAI-X2 ($P=0.010$ and $P=0.008$, respectively) and between age and STAI-X1 and STAI-X2 ($P=0.046$ and 0.042, respectively). Considering cognitive function, mean results of both patients and controls resulted within the respective ranges of normality, yet the number of patients scoring pathologically was significantly higher vs controls, showing a deterioration in all domains explored except for constructional apraxia. No differences were found among pathological results and disease status or pituitary deficits, except for auditory learning (RAVLT-Immediate) and long-term verbal memory and (RAVLT-long-term), with hypopituitaric patients performing worse ($P=0.01$ and $P=0.01$ respectively). IGF-1 levels positively correlated only with the results of Corsi test indagating short term visuospatial memory ($P=0.014$). At prospective analysis, we registered an overall improving trend in neurocognitive performance scores over the follow-up period, especially from diagnosis to T3.
Conclusion
Our data confirmed the presence of psychological symptoms in acromegaly. We underlined the relation between active disease and cognitive impairment with a possible improvement after disease control.

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P125

Consensus and controversies on the diagnosis of GH-deficiency in children and adults - A Delphi survey by the GH research society

Mai C. Arlien-Søborg[1], Sally Radovick[2], Margaret Cristina da Silva Boguszewski[3], Martin Bidlingmaier[4], Gudmundur Johannsson[5], Andrew R. Hoffman[6] & Jens Otto Jørgensen[1]
[1]Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Denmark; [2]Robert Wood Johnson Medical School, United States; [3]University Hospital, Federal University of Parana, Curitiba, Brazil, Brazil; [4]Ludwig-Maximilians-University of Munich, Faculty of Medicine, Germany; [5]The University of Gothenburg, Sweden; [6]Stanford Medical Center, Division of Endocrinology, United States

Background
Growth hormone deficiency (GHD) is a rare disorder characterized by pronounced and symptomatic hypo secretion of growth hormone (GH) from the anterior pituitary gland. Biochemical tests are used as part of the diagnosis in both children and adults but controversies remain as regards whom, when, and how to test, and also how to interpret a given biochemical test result.
Aim
To map the current clinical practice of GHD diagnosing in children and adults.
Methods
A scientific committee (SC) composed of five members of the Growth Hormone Research Society (GRS) initiated a Delphi survey of the diagnosis of GH deficiency in children and adults. Dedicated pediatric ($n=18$) and adult ($n=25$) endocrinologists from fourteen different countries participated in the survey and rated their extent of agreement to 61 statements using a Likert-type-scale (1-7). Consensus was defined as $\geq$ 80% of panelists rating either ≥ 5 (agreement) or ≤ 3 (disagreement).
Results
Consensus was reached in 62% (38/61) of the statements. There was agreement to test for GHD in an appropriate clinical context such as neonates with persistent hypoglycemia and prolonged jaundice, growth deceleration and short stature in children, and overt pituitary disease in adults. Notwithstanding this, consensus was not reached regarding whether or not to test e. g. short children with obesity or adult patients without a classic phenotype. Low IGF-I levels were considered diagnostic in panhypopituitary children and adults. There was consensus to recommend the arginine stimulation test for the diagnosis of GHD in children whereas the insulin tolerance test (ITT) was recognized as the gold standard in adults. Controversy persisted regarding the utility of the macimorelin stimulation test in both children and adults. A stimulated GH cut-off < 3 µg/l was consistent with complete GHD in children, whereas assay-specific cut-offs were recommended in adults.
Conclusion
This Delphi survey reveals consensus (62%) but also considerable lack of consensus (38%) among clinical experts about diagnosing GHD in children and adults. Major areas of disagreement comprised both whom and how to test.

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P126

Replace: a randomized controlled trial on the effect of hydrocortisone or placebo in patients with reported symptoms of glucocorticoid-induced adrenal insufficiency after terminating prednisolone for polymyalgia rheumatic/giant cell arteritis

Anja Fenger Dreyer[1,2], Stina Willemoes Borresen[3,4], Simon Bøggild Hansen[5,6], Hajir Al-Jorani[1,2], Lise Sofie Bislev[5,6], Victor Brun Boesen[3,4], Louise Lehmann Christensen[1,2], Dorte Glintborg[1,2], Richard Christian Jensen[1], Nanna Thurmann Jørgensen[3,4], Marianne Klose[3,4], Marie Louise Lund[3,4], Jelena Stankovic[5,6], Randi Tei[5,6], Ulla Feldt-Rasmussen[3,4], Jens Otto Jørgensen[5,6] & Marianne Andersen[1,2]
[1]Odense University Hospital, Department of Endocrinology, Odense C, Denmark; [2]University of Southern Denmark, Department of Clinical Research, Faculty of Health Sciences, Odense C, Denmark; [3]Copenhagen University Hospital, Department of Endocrinology and Metabolism, Rigshospitalet, Copenhagen, Denmark; [4]Copenhagen University, Department of Clinical Medicine, Faculty of Health and Clinical Sciences, Copenhagen, Denmark; [5]Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus, Denmark; [6]Aarhus University, Department of Clinical Medicine, Aarhus, Denmark

Background
Glucocorticoid-induced adrenal insufficiency (GIA) may occur after termination of long-term glucocorticoid (GC) treatment. GIA is usually diagnosed by a short-synacthen-test (SST), but peak cortisol response to SST may not validly assess normalisation of the diurnal hypothalamic-pituitary-adrenal (HPA)-axis. In patients with polymyalgia rheumatic (PMR) and giant cell arteritis (GCA), we report at this meeting a surprisingly low prevalence of GIA of 1.6% after cessation of prednisolone treatment; whereas 33% of these patients reported symptoms of GIA (scores ≤ 85) according to the Addison's disease-specific quality-of-life questionnaire (AddiQoL-30) (ECE 2024 abstract ID: 5059). The primary study aim is to generate evidence-based guidance for management of GIA in patients using patient reported outcomes as a key tool for inclusion and outcome.

Methods
This is the first RCT to randomize patients with low AddiQoL-30 score after long-term GC use to hydrocortisone treatment or placebo. The REPLACE study is a multi-centre randomised, double-blinded, placebo-controlled study. Eligible patients have PMR and/or GCA and are in GC free remission for 2-12 weeks after long-term prednisolone treatment (>12 weeks). Patients are assigned to one of the study groups according to results of AddiQoL-30 and SST: All groups will participate in a standardized baseline visit. The RCT-group is randomized to either hydrocortisone or placebo for 16 weeks with repetition of baseline investigations at end of study.

RCT-group	AddiQoL-score ≤85 *or* 30 min. cortisol level >100 nmol/l and <420 nmol/l	$n=100$
Control-group 1	AddiQoL-score >85 *and* 30 min. cortisol level >420 nmol/l	$n=150$
Control-group 2	30 min. cortisol level ≤100 nmol/l regardless of Addi-QoL-score	$n=20$

Outcomes
Change in GIA symptom burden (AddiQoL-30) at 16-week follow-up is the primary outcome. Secondary outcomes are generic health-related QoL questionnaire scores (CushingQoL, SF-36v2, Single item Sleep Quality Scale, and the International Physical Activity Questionnaire-S7S). Participants will daily report on intercurrent illness and stress, and symptoms attributable to GIA, using a study smartphone application (app). Baseline and follow-up investigations of cardiovascular health, body composition, muscle function, and glucose homeostasis will be completed.
Ethics and dissemination
The REPLACE study is in accordance with the Declaration of Helsinki; registered at EudraCT (2020-006121-65) and publications will be according to the International Committee of Medical Journal Editors recommendations.
Funding
The REPLACE study is funded by the Novo Nordisk Foundation as part of a collaborative grant entitled 'DOUBLE EDGE – Characterization and mitigation of adverse effects of glucocorticoid treatment' (NNF20OC0063280).
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P127

Gonadotroph pituitary tumors: not always nonfunctioning
Anna Carretti[1,2], Mirela Diana Ilie[3], Alexandre Vasiljevic[4], Marie-Lise Jaffrain-Rea[5,6], Emmanuel Jouanneau[7] & Gerald Raverot[2]
[1]' Sapienza' University of Rome, Department of Experimental Medicine, Rome, Italy; [2]Reference Center for Rare Pituitary Diseases HyPO, 'Groupement Hospitalier Est' Hospices Civils de Lyon, Endocrinology Department, Bron, France; [3]Cancer Research Center of Lyon, Inserm U1052, CNRS UMR5286, Lyon, France; [4]Cancer Research Center of Lyon, Lyon 1 University, Pathology Department, Reference Center for Rare Pituitary Diseases Hypo, 'groupement Hospitalier Est' Hospices Civils de Lyon, Inserm U1052, Cnrs Umr5286, Lyon, France; [5]Neuromed Institute, Istituto di Ricovero e Cura a Carattere Scientifico, Pozzilli, Italy; [6]University of L'Aquila, Department of Biotechnological and Applied Clinical Sciences, L'Aquila, Italy; [7]Reference Center for Rare Pituitary Diseases HyPO, 'Groupement Hospitalier Est' Hospices Civils de Lyon, Neurosurgery Department, Bron, France

Gonadotroph pituitary tumors (GnPiT) account for ~40% of pituitary tumors surgically treated and 70-75% of non-functional pituitary tumors. Functional gonadotropin-secreting tumors are rare and clinical manifestations vary according to the age and sex of the patient. They are benign tumors which, due to their silent nature, can grow and invade surrounding structures, making complete resection impossible and leading to recurrence in ~30% of cases.
Objective
The aim of our study is to provide a comprehensive, up-to-date characterization of either clinically silent/whispering or functional GnPiT.
Patients and Method
Retrospective study of 151 adult patients (105 men and 48 women) with a histological diagnosis of GnPiT, operated at our referral pituitary center from January 2020 to December 2022. Clinical, hormonal, tumoral and pathological data were analyzed according to sex and age.
Results
Diagnosis was incidental in about half of patients. A different distribution of tumors based on age was found, with a normal distribution in male (median age 63 years (25-89)), and a bimodal one in female (median age 58 years (26-84)). Only one tumor showed a functioning hormonal secretion responsible of an ovarian hyperstimulation syndrome in a 40-year-old woman; while 8 tumors (1 F and 7 M) showed a possible, but clinically silent, secretory activity. FSH was elevated in all cases, accompanied by LH and testosterone in one. Hypersecretion did not cause a subsequent clinical picture, and tumors did not appear to behave differently compared to the non-secreting one. Four histological subtypes were described according to hormonal immunohistochemistry: FSH-LH ($n=96$), FSH ($n=41$), LH ($n=6$), non-immunoreactive (NIR; $n=8$). Sex-related distribution did not find relevant differences (FSH-LH: 65.62% M, 34.38% F; FSH: 75.60% M, 24.40% F; LH: 83.33% M 16.67%; NIR: 50% M, 50% F). No differences were found according to histological subtypes, especially regarding FSH and LH secretion. Spearman correlation analysis showed a weak, but significant, correlation between serum FSH and FSH staining (r: 0.21, p: 0.015), none between serum FSH and transcription factors SF1 and GATA3, and a weak, but significant, correlation between LH staining and GATA3 (r: 0.34, p: 0.0002).
Conclusion
Our results provide information possibly useful in future studies for a better understanding of the GnPiT subtype. Gonadotropins hypersecretion remains a rare finding and, when present, is mostly silent and not linked to specific pathological features. Moreover, a thorough pathological assessment did not highlight relevant differences among the four subgroups identified in this work.
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P128

Posterior pituitary tumours: a single institutional experience of 19 patients
Natalia Kremenevski[1], Yining Zhao[1], Coras Roland[2] & Michael Buchfelder[1]
[1]University of Erlangen-Nürnberg, Department of Neurosurgery, Erlangen, Germany; [2]University of Erlangen-Nürnberg, Institute of Neuropathology, Erlangen, Germany

Background
Posterior pituitary tumors (PPTs) present as clinically nonfunctioning space-occupying lesions of the sellar region. The diagnosis of PPTs is not possible on the basis of their clinical, radiological and biochemical features. Immunohistochemistry identifies them for their expression of TTF. They are virtually always mistakenly defined as one of the more common pituitary tumours. Due to their rarity, the long-term endocrine aspects and outcomes of PPTs are not well known.
Objective
The objective was to evaluate the clinical characteristics, surgical approaches, and survival of a single-center cohort of patients with PPTs who underwent surgical treatment at our institution.
Methods
19 patients (11 females and 8 males) with histologically confirmed PPTs were identified between the years 1982 and 2022 out of 8761 operated sellar lesions. Their data were retrospectively collected and analyzed.
Results
There were 3 pituicytoma (PC), 8 granular cell tumor (GCT), and 8 spindle cell oncocytoma (SCO) subtypes of what today all is called pituicytoma. The mean age at diagnosis was 58.65 ± 13.6 years (range 27-75). The most common presenting symptoms were visual disturbance and headache (47% each), followed by dizziness (26%) and decreased libido/erectile dysfunction (16%). Preoperative MRI scans were not predictive of PPTs. Preoperative endocrine dysfunction consisted of hypocortisolemia and hypogonadism (42% each), hyperprolactinemia and hypothyroidism (37% each). After surgery, corticotropic and gonadotropic dysfunction remained unchanged. A statistically significant reduction/normalization of prolactin levels was detected ($P<0.05$). Diabetes insipidus was observed in one patient preoperatively and in two patients postoperatively. The mean tumor volume was 2.14 ± 2.01 cm^3 (range 0.12-7.37). In most patients the surgery was performed through a transcranial approach (58%) and in 8 cases the transsphenoidal approach was used (42%). Gross total resection was achieved in 11 patients (58%). The mean follow-up in months was $58.89 \pm 43.13.5$ (median 63 [range 3-150]). Recurrence was observed in 3/19 (16%) patients.
Conclusion
PPTs are benign neoplasms and do not have specific presenting clinical, endocrinological and imaging findings. Histopathological examination with confirmation of TTF expression remains crucial in the diagnosis. The location and invasive growth with suprasellar tumour extension in this patient cohort makes them not amenable to total resection and more often dictates a transcranial approach as opposed to transsphenoidal surgery.
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P129

Usefulness of salivary cortisol in the diagnosis of adrenal insufficiency and evaluation of the hypothalamic-pituitary-adrenal axis

Pablo Fernández Velasco[1], Maria de la O Nieto de la Marca[1], Raquel Herrero Gómez[1], Paloma Pérez López[1], Beatriz Torres Torres[1], Daniel De Luis Román[1] & Gonzalo Díaz Soto[1]
[1]Hospital Clínico Universitario de Valladolid, Endocrinología y nutrición, Valladolid, Spain

Objective
This study aims to assess the utility of salivary cortisol (SC) in diagnosing adrenal insufficiency (AI) and to analyze the integrity of the hypothalamic-pituitary-adrenal axis. This involves evaluating cortisol rhythm, its correlation with plasma levels, and the impact of exogenous hydrocortisone (HC) substitution on SC determination.
Methods
A prospective study was conducted on all patients with suspected AI undergoing adrenocorticotropic hormone (ACTH) testing (ACTH-t) between 2014 and 2022 at the Endocrinology Department in an University Hospital. Ambulatory salivary cortisol rhythm was determined, and clinical and analytical variables were collected. Diagnostic performance of SC vs basal plasma cortisol (BC) was assessed using the area under the ROC curve (AUC), with ACTH-t results as the 'gold standard.' Correlation between SC and BC values was also determined.
Results
Sixty subjects (60.7% women, 42.9% evaluated for pituitary pathology) with a mean age of 50.7 ± 15.1 years were evaluated. Mean SC, BC, and ACTH levels were 0.378 ± 0.242 μg/dl, 11.3 ± 5.2 μg/dl, and 30.5 ± 45.8 pg/dl, respectively. 6.6% were excluded due to preanalytical contamination in SC determination. A moderate positive correlation ($r = 0.446$, $P < 0.001$) was found between SC and BC levels. The diagnostic yield of SC at 0800 hours was superior to BC (AUC = 0.804, $P < 0.01$ and AUC = 0.739, $P < 0.05$, respectively). CS values < 0.0975 μg/dl were diagnostic of AI, while values > 0.708 μg/dl ruled out AI, avoiding 21.4% of ACTH-t. However, SC rhythm determination at 13:00, 18:00, and 24:00 did not allow AI diagnosis (AUC = 0.202, 0.280, and 0.283, respectively). Determining SC in patients on HC treatment vs those without treatment demonstrated HC overdosage values at 13:00 (1.089 ± 1.120 vs 0.207 ± 0.227 μg/dl, $P < 0.01$), 18:00 (0.752 ± 0.971 vs 0.151 ± 0.130 μg/dl, $P < 0.01$), and 24:00 (1.069 ± 2.531 vs 0.094 ± 0.071 μg/dl, $P < 0.01$), except at 8:00 (0.274 ± 0.205 vs 0.409 ± 0.246 μg/dl, $P = 0.058$). Conclusions: Determination of SC at 0800 hours is a valid alternative for AI screening, showing good correlation with BC. Only 6.6% of the sample inadequately collected SC. In our population, values < 0.0975 μg/dl and > 0.708 μg/dl for SC confirmed and ruled out AI, respectively, preventing 21.7% of ACTH-t. SC determination at 13:00, 18:00, and 24:00 did not adequately identify patients with AI and showed overdose values in those on HC treatment.

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P130

Paradoxical responses to pasireotide in patient with cushing's disease

Anna Brona[1], Aleksandra Jawiarczyk-Przybyłowska[1], Aleksandra Zdrojowy-Wełna[1], Justyna Kuliczkowska-Płaksej[1] & Marek Bolanowski[1]
[1]Wrocław Medical University, Endocrinology, Diabetes and Isotope Therapy, Wrocław, Poland

69-year old male was diagnosed with non-secreting pituitary macroadenoma (25x 15x 15mm) in 2008. Patient underwent two transsphenoidal surgeries and stereotactic radiotherapy in 2008 and 2009. Tumor recurrence was noticed on MRI in 2016. In 2017 urgent right pterional craniotomy was performer due to right eyelid dropping with ocular nerves palsy. Despite surgery further growth of the tumor (32x 22x 31mm) was reported in 2018, followed by increased ACTH level and hypercortisolemia in 2019. It was decided to start therapy with pasireotide. Patient received 5 doses of pasireotide LAR between September 2019 and June 2020. In September 2019 cortisol level was 21μg/dl (3.7-19.4), and ACTH 107 pg/ml (0-46) before administration and increased up to 35.6μg/dl, and 176 pg/ml after it. This was the first time when paradoxical response was noticed. 2nd and 3rd doses were administered in October and in November 2019 without increase of cortisol or ACTH concentration and MRI showed marked regression of tumor one month later. 4th dose was administered in March and 5th dose in June 2020. There was no paradoxical response. Recurrence of hypercortisolemia and tumor progression were observed in February 2021. Cortisol level was 53.3μg/dl and ACTH 246 pg/ml. In March 2021 6th dose of pasireotide was administered. Then 2nd paradoxical response occured. Cortisol level increased up to 83.5μg/dl, and ACTH up to 392 pg/ml After metyrapone treatment cortisol concentration decreased and hydrocortisone was necessary. In April 2021 patient received 7th dose of pasireotide. Cortisol level was 10.2μg/dl and ACTH 149 pg/ml. After one week laboratory results confirmed 3rd paradoxical response to pasireotide (cortisol 59.3μg/dl and ACTH 186 pg/ml). In February 2022 cortisol level was very low (up to 4.6μg/dl) and ACTH decreased to 47.2 pg/ml. >MRI revealed marked regression of tumor mass. Pasireotide wasn't administered. In August 2022 it turned out that cortisol and ACTH concentration were increased (60.3μg/dl and 242 pg/ml). Severe hypercortisolemia was observed few weeks later despite metyrapone treatment. It was decided to administer pasireotide once again. In October 2022 patient received 8th dose and 4th paradoxical response occured. The rebounds in increase of cortisol were severe and required steroidogenesis inhibitors for few months. During this period the highest level of cortisol was 91μg/dl and ACTH 816 pg/ml. Treatment with pasireotide was considered as the emergency therapy. Pasireotide affects both tumor size and cortisol production and effects are likely to appear much earlier than after radiotherapy. Poor patient conditions and irregular growth of the tumor suggested against surgery.

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P131

Comparative efficacy and safety of osilodrostat vs metyrapone for the treatment of Cushing's syndrome – a matching-adjusted indirect comparison using LINC-3 and LINC-4

Rosario Pivonello[1], Beatrice Gueron[2], Conor Hickey[3], Emma Tyas[3], Grzegorz Binowski[4] & Fabian Schmidt[2]
[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]Recordati Rare Diseases, Puteaux, France; [3]Lumanity, London, United Kingdom; [4]MAHTA Intl., Warsaw, Poland

Objectives
Endogenous Cushing's syndrome (CS) is a rare, chronic condition that results in high morbidity, caused by prolonged exposure to elevated levels of circulating free cortisol. A previous comparative analysis showed osilodrostat increases the odds of complete response (CR; mean urinary free cortisol [mUFC] ≤ 1.0 x the upper limit of normal) at Weeks 12 and 36 vs metyrapone[1]; however, analyses were limited by small osilodrostat effective sample size (ESS; 25 patients). Therefore, we used pooled osilodrostat data from the LINC-3 and LINC-4 clinical trials ($n = 185$) to improve upon initial analyses of CR and discontinuation outcomes for osilodrostat vs metyrapone in CS.
Methods
The LINC-3/lINC-4 and PROMPT clinical trials investigated osilodrostat and metyrapone, respectively, in patients with endogenous CS. All LINC-3/lINC-4 patients and 90% of PROMPT patients had Cushing's disease. Unanchored matching-adjusted indirect comparisons were conducted using pooled LINC-3 and LINC-4 patient-level data and published summary data for PROMPT. CR at Weeks 12, 24 and 36; all-cause discontinuation and discontinuation due to treatment failure at Weeks 24 and 36 were analysed. Six baseline characteristics, identified as potential prognostic factors, were adjusted for: age, sex, time since diagnosis, mUFC, prior irradiation and prior surgery. Scenario analyses adjusted for race and explored an alternative categorization of mUFC. Scenario analyses also investigated a range of plausible discontinuation rates for six patients ineligible to enter the 6-month PROMPT extension at Week 12, but not considered discontinuations in the primary analysis.
Results
Populations were well balanced after matching; the ESS for the matched pooled osilodrostat population was 76 patients. Results suggested osilodrostat provides increased odds of CR vs metyrapone at Week 12 (odds ratio [OR]: 2.75; 95% confidence interval [CI]: 1.29, 5.88), Week 24 (OR: 3.28; 95% CI: 1.58, 6.84) and Week 36 (OR: 10.50; 95% CI: 1.84, 59.96), implying a greater proportion of patients experience normalized cortisol levels at these timepoints. Results are statistically significant as 95% CIs exclude 1. No evidence of a statistically significant difference between treatments for the discontinuation endpoints was found. Scenario analyses (described above) had consistent results.
Conclusion
Our analyses suggest osilodrostat increases the odds of achieving CR at Weeks 12, 24 and 36 vs metyrapone, implying osilodrostat is a more efficacious treatment option than metyrapone for normalizing cortisol levels in CS patients. These analyses improve upon previous comparisons by substantially increasing the osilodrostat ESS, providing consistent and more reliable results.
[1]Tyas E, *Endocr. abstr.*, 90. (2023) P132.

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P132

Is urine sαkl a potential biomarker in acromegaly?

Anica Pauline Gagliardo[1], Michael Haenelt[1], Júnia Ribeiro de Oliveira Longo Schweizer[1], Jun Thorsteinsdottir[2], Daniel Teupser[3], Jochen Schopohl[1], Sylvère Störmann[1], Martin Bidlingmaier[1] & Katharina Schilbach[1]
[1]LMU Klinikum, Medizinische Klinik und Poliklinik IV, München, Germany; [2]LMU Klinikum, Neurochirurgische Klinik und Poliklinik, München, Germany; [3]LMU Klinikum, Institut für Laboratoriumsmedizin, München, Germany

Background
Soluble alpha klotho (sαKL) is a peptide hormone, that has been shown to be elevated in serum of patients with uncontrolled acromegaly. One early pilot study suggested that sαKL is also detectable in urine from patients with acromegaly, and significantly drops after surgery. Notably, in this study, urine sαKL concentrations were undetectable in the control group, and fell consistently below the detection limit of the ELISA in postoperative patients in the acromegaly group. We previously found considerable impact of various preanalytical conditions on measured concentrations of urine sαKL, pointing to the need to define an appropriate pre-analytical process.
Aim
In this study, we evaluated urine sαKL collected under standardized conditions as a potential biomarker in a cohort with patients with acromegaly receiving a variety of therapy modalities as well as a healthy cohort.
Methods
Blood and corresponding spontaneous urine samples were collected from biochemically uncontrolled (IGF-I >1.3 times upper limit of normal ($\times$ULN); $n=20$) and controlled (IGF-I $<1.0\times$ULN; $n=31$) patients with acromegaly as well as from healthy subjects ($n=51$); Patients had a variety of therapy modalities. Serum was stored at -20°C and urine at -80°C. Anthropometric data and routine lab values were collected. SαKL was measured with a sandwich ELISA (IBL, Hamburg, Germany).
Results
No meaningful correlation could be established between urine sαKL and serum sαKL, IGF-I $\times$ ULN, IGFBP 3 $\times$ ULN, eGFR nor urine creatinine. A strong correlation was shown for urine sαKL and urine pH (Spearman's rho 0.770, $P<0.001$, $n=101$), with particularly low sαKL in samples with low pH. However, even after including only urine samples with pH greater or equal to 6.0, no correlation between the former mentioned parameters and urine sαKL was observed.
Conclusions
Interpretation of urine sαKL seems difficult at least. First, concentrations become very low or even undetectable in urine samples with a pH less than 6.0. Furthermore, even in samples with higher pH, concentrations of sαKL in urine do not correlate to serum concentrations. It is quite conceivable that additional factors impact urine sαKL concentration. Perhaps, more appropriate sampling conditions can be found. However, at present, our data do not support utilization of urine sαKL as a biomarker for growth hormone. In contrast, our data from this study further confirm serum sαKL correlates well with IGF-I.

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P133

Exploring the cardiovascular effects of recombinant human growth hormone therapy: a prospective study on endothelin-1 and asymmetric dimethyl arginine in adults with growth hormone deficiency

Maria Kościuszko[1,1], Angelika Buczyńska[2], Aleksandra Wiatr[2], Dorota Jankowska[3], Małgorzata Jacewicz-Święcka[1], Adam Krętowski[1] & Anna Popławska-Kita[1]
[1]Medical University of Białystok, Endocrinology, Diabetology and Internal Medicine, Białystok, Poland; [2]Medical University of Białystok, Clinical Research Center, Białystok, Poland; [3]Medical University of Białystok, Department of Biostatistics and Medical Informatics, Białystok, Poland

Adult growth hormone deficiency (GHD) is widely acknowledged for its association with heightened mortality, primarily linked to an increased risk of cardiovascular complications. Endothelin-1 (ET-1) is implicated in various cardiovascular conditions, including hypertension, atherosclerosis, and heart failure, where imbalances in its levels or signaling have been identified. Despite the distinct primary functions of growth hormone and endothelin within the body, both hormones assume a pivotal role in the intricate regulation of growth and developmental processes. Specifically, endothelin significantly contributes to the meticulous orchestration of blood flow regulation, exerting an indirect influence on the delivery of essential nutrients and oxygen to tissues. This intricate interplay carries profound implications for the sophisticated coordination of growth and metabolism within the organism. Furthermore, a critical non-traditional cardiovascular risk factor involves the heightened concentration of asymmetric dimethylarginine (ADMA), a potent inhibitor of nitric oxide synthase that contributes to vascular endothelial dysfunction. Elevated ADMA levels coincide with increased vascular tension, higher blood pressure, and the activation of numerous pro-atherogenic mechanisms. These include platelet aggregation, monocyte adhesion, smooth muscle cell proliferation, extracellular matrix expansion, and lipid accumulation in macrophages - elements that collectively contribute to the development of atherosclerosis. Consequently, this study aims to evaluate the effectiveness of recombinant human growth hormone (rhGH) in mitigating levels of ET-1 and ADMA in patients with GHD. The study focuses on assessing the efficacy of rhGH therapy in enhancing levels of ET-1 and reducing ADMA. The study encompassed 10 patients diagnosed with GHD who underwent a 12-month course of rhGH therapy. Measurements of ET-1 and ADMA levels were taken prior to the commencement of the therapy, at the 6-month mark, and at the conclusion of the 12-month period. Statistical analysis involved repeated-measures ANOVA and post hoc tests with Bonferroni correction.
Results
After 12 months of rhGH therapy, a significant decrease in the levels of ET-1 ($P=0.04$) was observed. Additionally, a statistically significant negative correlation between IGF-1 and ADMA levels were observed both after 6 and 12 months of therapy ($r=$-0.65, $P=0.02$; R-0.65, $P=0.01$, respectively). Post hoc tests confirmed significant differences between individual observation periods. The findings of this research suggest a potential link between growth hormone replacement therapy and a reduction in cardiovascular risk through its impact on ET-1 and ADMA levels. These results have the potential to contribute to the improvement of rhGH replacement therapy protocols, exerting a broader influence on the cardiovascular well-being of individuals undergoing such interventions.

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P134

Macroprolactin over time: Is there any point in rechecking it in people with a persistently elevated serum prolactin?

Adrian Heald[1,1], Syeda Hashimi[2], John Warner-Levy[1], Sudarshan Ramachadran[3], Ian Laing[4] & Mark Livingston[2]
[1]Salford Royal Hospital, Salford, Department of Endocrinology and Diabetes, Salford, United Kingdom; [2]Black Country Pathology Services, Walsall Manor Hospital, Walsall, United Kingdom, Department of Clinical Biochemistry, Wolverhampton, United Kingdom; [3]University Hospitals Birmingham NHS Foundation Trust, Sutton Coldfield, West Midlands, United Kingdom., Department of Clinical Biochemistry, Sutton Coldfield, United Kingdom; [4]Royal Preston Hospital, Preston, United Kingdom

Design
Macroprolactinemia may influence the interpretation of serum prolactin levels – a recognised phenomenon since 1978[1]. The degree of macroprolactinaemia over time is less well described. We determined how macroprolactin status (based on polyethylene glycol (PEG) precipitation varied by analysing serial measurements in hyperprolactinaemic individuals over nine years.
Patients and Measurements
Results from 1810 individuals were included. All serum total prolactin results (measured using Roche Cobas 8000 analyser) were extracted from the laboratory information system from 1 January 2012 to 1 April 2021, along with relevant patient demographic/test data. Samples with a macroprolactin screening test performed (on samples with prolactin >700 mu/l) were included in the main analysis.
Results
During the study period, 2782 macroprolactin checks were performed (12.5% of all prolactin tests) in 1810 (599 males/2183 females, median-age: 35, IQR:25-47, range:16-93 years) individuals. Multiple macroprolactin checks were carried out on 465 patients (1437 measurements) (see Table 1) with 94 patients (141 measurements) screening positive ($<60\%$ recovery). Only 19 patients (18 female) had at least one result above and one below the 60% screening cut-off. In terms of clinical details, six were on antidepressants/antipsychotics, four had a prolactinoma, one was pregnant, two were on an oral contraceptive pill (OCP) one person was on levothyroxine, and in five further clinical details were unavailable. 10 of these patients had results close to the 60% cut-off. 5 had clearly different results; 4 appeared to be outliers based on other results. In 7 cases the adjusted monomeric prolactin showed a potentially clinically significant difference.
Conclusions
In this study, only 19/465 patients appeared to change macroprolactin status based on a 60% PEG recovery cut-off. The majority of these 19 patients were on antipsychotic/antidepressant medication(s) or had a prolactinoma; In only 7

monomeric prolactin changed significantly. This suggests that once macroprolactin status has been determined, clinical decision-making is rarely affected by repeating it.

Table 1 Displays the number of macroprolactin (post-PEG % recovery) tests done for subjects over the study period

Number of tests	Subjects
1	1345
2	264
3	87
4	52
5	27
6	13
7	4
8	5
9	3
10	3
11	3
12	1
15	1
16	1
26	1

Reference
1. Heald, A., Blantern, E., Anderson, S., Radford, D., *et al*., Quantitative adjustment for macroprolactin is an integral part of laboratory assessment of hyperprolactinaemia. Experimental and Clinical Endocrinology & Diabetes 2012, 376–380.

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P135

Comprehensive clinical, transcriptomic, and functional relevance of the telomerase-shelterin system in pituitary tumors and craniopharyngiomas

Ana S. De la Rosa-Herencia[1,2,3,4], Miguel E. G-Garcia[1,2,3,4], Álvaro Flores-Martínez[1,2,3,4], María Ortega Bellido[1,2,3,4], Ignacio Gil-Duque[1,2,3,4], José H-Hernández[1,2,3,4], David Cano[5], Antonio Picó[6], Araceli García-Martínez[1,2,3], Justo P. Castaño[1,2,3,4], Manuel D. Gahete[1,2,3,4], María A. Gálvez-Moreno[1,4,7], Alfonso Soto-Moreno[5], Antonio C. Fuentes-Fayos[1,2,3,4] & Raúl M. Luque Huertas[1,2,3,4]
[1]Maimónides Biomedical Research Institute (IMIBIC), Córdoba, Spain; [2]University of Cordoba, Department of Cell Biology, Physiology and Immunology, Córdoba, Spain; [3]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Córdoba, Spain; [4]Reina Sofia University Hospital (HURS), Córdoba, Spain; [5]Hospital Universitario Virgen del Rocío (HUVR), Department of Neurosurgery, Seville, Spain; [6]Endocrinology & Nutrition Service, University Hospital, Alicante, Spain; [7]Service of Endocrinology and Nutrition, HURS, Córdoba, Spain

Intracranial Tumors comprise a diverse group of endocrine-related tumors [ERTs; e.g. craniopharyngiomas (CPs) and pituitary-tumors (PTs)], representing significant challenges for the diagnosis/prognosis/treatment of patients, their families and health systems due to their heterogeneity, associated neurological impairment and endocrine comorbidities. However, despite recent advances, the current treatment (e.g. surgery plus irradiation in CPs, pharmacological treatment with somatostatin/dopamine-agonists in PTs) originates adverse neurological effects, and drugs are not sufficiently effective in reducing the tumor mass size in a high proportion of cases. Therefore, the identification of novel therapeutic avenues to treat these devastating ERTs are urgently needed. Concretely, the Telomerase/Shelterin (TEL-SHEL) system, responsible for telomere maintenance, has been implicated in various cellular processes associated to cancer development/progression/aggressiveness. However, its interplay in the malignancy process of CPs and PTs remains poorly explored. Therefore, we aimed to analyze the: 1) expression of 17 critical TEL-SHEL components in CPs ($n=60$) and different PT types ($n=152$) compared to non-tumor pituitary tissues ($n=10$), using a microfluidic-array based on qPCR-technology; and 2) potential antitumor effects of modulating telomerase-activity and telomere-length through pharmacological modulation using BIBR1532 and *in vitro* cellula models. A profound dysregulation in the expression pattern of TEL-SHEL components was demonstrated in CPs and PTs. Notably, TERF2IP and TNKS were downregulated in CPs in three different human cohorts. Interestingly, enrichment analysis revealed a robust correlation between the low expression of TERF2IP and key cellular processes, such as the Wnt/β-catenin-pathway. Similarly, a significant alteration of the molecular profile TEL-SHEL was also observed in PTs, especially in somatotropinomas and corticotropinomas, but not in non-funcitoning PTs. Furthermore, BIBR1532-treatment showed a dose-dependent effect in different functional parameters in primary patient-derived cell-cultures and cell-lines [GH3 (somatotropinoma model) and AtT20 (corticotropinoma) models], including a reduction in cell-proliferation rates and stem-cell capacity. Altogether, we demonstrated a profound dysregulation of different key components of the TEL-SHEL system in CPs and PTs vs control samples, wherein some of these alterations may have clinical and/or functional relevance to improve the diagnosis/prognosis and management of these heterogeneous ERTs. Moreover, we demonstrated that the pharmacological modulation of the TEL-SHEL complex (using BIBR1532) exerted antitumoral effects in different ERTs, offering a clinically relevant opportunity that should be tested for use in humans.

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P136

Effect of oral urea on copeptin levels in healthy adults: a double-blind, randomized, placebo-controlled cross-over study

Sven Lustenberger[1], Cihan Atila[1], Sophie Monnerat[1], Julia Beck[1] & Mirjam Christ-Crain[1]
[1]Universitätsspital Basel, Endokrinologie, Diabetologie und Metabolismus, Basel, Switzerland

Background and Objectives
The differential diagnosis between arginine vasopressin (AVP) deficiency (AVP-D, formerly known as central diabetes insipidus) and primary polydipsia (PP) remains challenging. To date, the method with the highest diagnostic accuracy is osmotically-stimulated copeptin – a surrogate marker of AVP – using hypertonic saline infusion. However, this method is often limited to experienced hospitals, requires close monitoring, and may be cumbersome for patients. Therefore, an alternative simplified osmotic stimulation test would be highly desirable. It has been previously demonstrated that intravenous urea increases plasma osmolality and stimulates AVP release. However, no study investigated the effects of oral urea on copeptin levels.
Methods
The aim of this randomized double-blind placebo-controlled study was to investigate whether oral urea stimulates copeptin release in 22 healthy adults. Participants presented for two visits in the morning after an overnight food fasting and two-hour fluid fasting period. They received a single weight-adapted dose of oral urea (0.5 g/kg body weight; minimum 30g, maximum 45 g) and placebo in random order. Serum copeptin was measured at baseline and 30, 60, 90, 120, and 150 minutes after oral urea or placebo intake. The primary endpoint was the maximum increase in copeptin levels within 150 minutes after oral urea intake vs placebo.
Results
When stimulating with placebo, the median [IQR] copeptin level at baseline was 3.8 [2.9 – 6.6] pmol/l and remained stable after 120 minutes at 3.2 [2.8 – 5.6] pmol/l. In contrast, when stimulating with urea, the copeptin level at baseline was 4.6 [3.0 – 5.7] pmol/l and increased after 120 minutes to a maximum of 10.1 [7.2 – 11.6] pmol/l ($P < 0.001$).
Conclusion
Oral urea leads to an approximately two-fold increase in copeptin levels in healthy adults. Whether this applies to patients with PP and has the potential to discriminate them from patients with AVP-D remains uncertain and is currently being investigated.

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P137

Anastrazole in the treatment of a cabergoline-resistant male prolactinoma

Vittoria Favero[1,2], Andrea Saladino[3], Marcello Marchetti[3], Iacopo Chiodini[1,2] & Renato Cesare Cozzi[2]
[1]University of Milan, Department of Biotechnology and Translational Medicine, Milan, Italy; [2]Ospedale Niguarda Ca' Granda, Endocrinology Unit, Milan, Italy; [3]IRCCS Fondazione Istituto Neurologico Carlo Besta, Department of Neurosurgery, Milan, Italy

Introduction
Dopamine agonists are the first line treatment for prolactinomas. However, some patients may develop dopamine-agonist-resistant hyperprolactinemia, leading to surgery and/or radiotherapy. The persistence of hypogonadism requires testosterone replacement therapy which could theoretically reduce the efficacy of dopamine agonists due to the conversion of testosterone to estradiol, thus, in turn, increasing the resistance to dopamine agonists. Consequently, in these patients an anti-estrogen treatment has been advocated, but, to date, very few cases have been reported on the use of the anti-estrogen treatment in patients with prolactinomas.

Case report
We present the case of a 23-year-old man who presented with headache and visual impairment with bitemporal hemianopsia. Magnetic resonance imaging (MRI) of the pituitary revealed a large invasive intra- and supra-sellar pituitary adenoma. Prolactin levels were significantly elevated (3258 µg/l, normal values, nv: 5-25 µg/l), with low levels of booth testosterone (1.3 ng/ml, nv 2.4-9 ng/ml) and FT4 (0.82 pg/ml, nv 0.8-2.2 pg/ml). Treatment with cabergoline was initiated and gradually increased to 3 mg/week, with reduction in prolactin levels and improvement in visual field. After 12 months of therapy, the prolactin levels decreased to 352 mg/l, and due to the persistence of central hypothyroidism and hypogonadotropic hypogonadism, a replacement therapy with levothyroxine and testosterone was started. After starting testosterone treatment and obtaining low-normal testosterone levels, the prolactin levels increased to 551 mg/l. In addition, there was no significant reduction in the size of the pituitary lesion and the patient experienced more frequent headaches with a slight deterioration in visual field. Surgical intervention was then performed. Following surgery, the prolactin levels decreased to 88 mg/l and the MRI showed the persistence of an infra – and supra-sella adenoma remnant. However, in the subsequent years, despite continuing the treatment with cabergoline (3 mg/week), the prolactin levels gradually increased to 132 mg/l. Anastrozole 1 mg/daily was initiated, and, consequently, it was possible to reduce the cabergoline dose to 2 mg/week (by reducing the dose by 0.5 mg/week after 3 months and then by a further 0.5 mg/week after 12 months). A further decrease in prolactin levels to 55 µg/l and a shrinkage of the pituitary adenoma was then observed.
Conclusion
In cases of dopamine-agonist-resistant hyperprolactinemia, alternative treatment strategies may be required. In this case, the addition of anastrazole proved beneficial, resulting in improved hormonal control, tumor shrinkage, and better patient tolerability.

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Challenges in the management of invasive macroprolactinomas: cranio-dural defect requiring surgery after cabergoline treatment

Ioana Balinisteanu[1,2], Stefana Bilha[1,2], Anca Matei[1,2], Raluca Lepsa[2], Alexandru Florescu[1,2], Daniel Rotariu[1,3], Maria Christina Ungureanu[1,2] & Cristina Preda[1,2]
[1]' Grigore T. Popa' University of Medicine and Pharmacy, Endocrinology, Iaşi, Romania; [2]Sf. Spiridon County Hospital, Endocrinology, Iaşi, Romania; [3]Emergency Hospital Professor Doctor Nicolae Oblu, Iaşi, Romania

Introduction
Prolactinomas, prevalent among young women, are the most frequently encountered secreting pituitary tumors. Pituitary apoplexy is a rare and severe complication of prolactinomas, which manifests with rapid onset symptoms like severe headaches, visual disturbances, hormonal imbalances, requiring urgent medical care.
Case report
We report the case of a 46-year-old female patient with history of type 2 diabetes, early menopause (30 years old, without prior investigations) that presented in the Emergency Department for symptoms of intracranial hypertension. Head CT scan revealed a pituitary adenoma of 24 x 32 x 33 mm, that proved to be an invasive macroprolactinoma, therefore she was started on Cabergoline 2 mg/week. After one month, the patient returned to the emergency room with recurrence of intracranial hypertension and CSF (cerebrospinal fluid) rhinorrhea. Both CT scan and pituitary MRI were performed, showing pituitary apoplexy, with important pneumoencephaly, lysis of the sellar floor and the prolaps of the pituitary adenoma into the sphenoidal sinus. The ablation of the tumoral mass with the repair of the craniodural defect were performed and the treatment with Cabergoline was stopped. However, meningitis was confirmed and double antibiotherapy was administered, with favorable outcomes. Pathological examination confirmed the presence of a mixed pituitary neuroendocrine tumor, with immunohistochemistry positive for prolactin and GH. Six weeks postoperative, the patient reported residual CSF rhinorrhea, and the prolactin level was 107 ng/ml (normal values: 5-25 ng/ml). The 3 months follow-up confirmed the presence of pituitary insufficiency (central hypogonadism and hypothyroidism), with normal somatotroph axis function, while prolactin levels were persistently elevated (1310 ng/ml). Therefore, the patient was started on levothyroxine 50 mg/day and cabergoline 0.5 mg twice per week, with favourable outcomes (repeated prolactin after 1 month of Cabergoline = 29 ng/ml).
Conclusions
The initial high doses of Cabergoline could have led to the fast and severe shrinkage of the tumour, causing pituitary apoplexy. The persistence of the CSF rhinorrhoea long after the repair of the CSF leak is uncommon and rises the risk of meningitis. CT scan is best for determining CSF rhinorrhea, while MRI for the characteristics of pituitary adenoma. While Cabergoline is recommended as first-line treatment for macroprolactinomas > Knosp 2 according to the latest international Consensus, surgery is needed in the case of pituitary apoplexy complicated with CSF rhinorrhea. At the same time, repairing the cranio-dural defect is more important than the complete removal of the tumour.

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P139

Pitfalls in diagnosis of the pituitary stalk lesion: infundibulo-neurohypophysitis or germ cell tumor?

Salvatore Raia[1], Antonella Giampietro[1], Tommaso Tartaglione[1], Carmelo Caldarella[1], Mario Rigante[1], Marco Gessi[1], Liverena Lauretti[1], Pierpaolo Mattogno[1], Laura De Marinis[1], Alessandro Olivi[1], Alfredo Pontecorvi[1], Francesco Doglietto[1], Antonio Bianchi[1] & Sabrina Chiloiro[1]
[1]Fondazione policlinico universitario A. Gemelli IRCCS - Università Cattolica del Sacro Cuore

Introduction
Infundibulo-neurohypophysitis (INH) is an uncommon inflammatory disorder. Because of the location of inflammation, it selectively affects the neuropituitary and pituitary stalk. The differential diagnosis remains often challenging with neoplastic lesions, such as germ cell neoplasia, Langerhans cell histiocytosis, Erdheim-Chester Disease, metastasis. Our clinical case is emblematic for pitfalls in diagnosis of the pituitary stalk lesion
Case Report
A 18 years-old male patient was observed at our Center for Pituitary disease in July 2023, for pan-hypopituitarism due to a pituitary stalk lesion. The patient was also affected from Klinefelter syndrome. The patient medical history had started when he was 10 years-old with polyuria/polydipsia. On may 2021, the patient was admitted to another hospital, for asthenia, pubertal delay and persistence of polydipsia/polyuria. Pituitary hormone tests documented pan-hypopituitarism and diabetes insipidus. Hormonal replacement therapy with hydrocortisone, levothyroxine and desmopressin acetate was prescribed. Campimetry evaluation proved a bilateral hemianopsia. A pituitary and brain contrasted MRI proved a sellar and suprasellar lesion, suggestive for a germinoma. Pituitary biopsy was performed, resulting undiagnosed. Therefore, on June 2021, a second pituitary biopsy was conducted, with the detection of inflammatory infiltration of immune cells (B CD20+ and T CD3+), histiocytes and negative immunohistochemistry for c-Kit, PLAP, CD1a, SI 00, MPO, CD30, CD15. The patient was diagnosed for INH. On April 2022, the patient referred to another endocrinology department, where G4 immunoglobulins were dosed resulting normal, antinuclear antibodies were positive, and pituitary MRI showed unchanged the pituitary stalk lesion, and the empty sella due to previous pituitary biopsies. An 18- fluorodeoxyglucose (FDG) positron emission tomography computed tomography (PET-CT) showed a suprasellar tracer hyperaccumulation (SUV 23.2). Patient was treated with high dose corticosteroid therapy without a clinical and neuroradiology improvement. On October 2022, a pituitary MRI showed a reduction in size of the tissue sited in the suprasellar space, in absence of resolution of the campimetry deficit. The patient was referred to our Pituitary centre for an additional neurosurgical evaluation, for considering a third neurosurgical debulking. An endocrine evaluation confirmed the pan-hypopituitarism, the pituitary MRI showed unchanged the pituitary stalk lesion but a neuroradiological evaluation together with 18F-Fluorocholine PET-CT was suggestive for a germ cell tumor, then confirmed by histology.
Conclusion
Our case confirms the difficult in the differential diagnosis of pituitary stalk lesions, underlining the need of a multidisciplinary approach, through the application of clinical, molecular, pathology and imaging techniques, also considering the emerging role of functional imaging.

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P140

Elimination of fall in glucose during glucagon stimulation test does not completely abolish an increase in growth hormone and cortisol concentrations

Krzysztof Lewandowski[1,2], Joanna Kawalec[2], Wojciech Horzelski[3] & Andrzej Lewiński[1,2]
[1]The Medical University of Lodz, Department of Endocrinology & Metabolic Diseases, Lodz, Poland; [2]' Polish Mother's' Memorial Hospital Research Institute, Department of Endocrinology & Metabolic Diseases,

Lodz, Poland; [3]The University of Lodz, Department of Mathemathics & Computer Science, Lodz, Poland

Background
Precise mechanism(s) responsible for stimulation of growth hormone (GH) and cortisol during Glucagon Stimulation Test (GST) are not clear, but seem to be related to glucagon-induced fluctuations in glucose and/or insulin with an initial increase followed by a subsequent fall in glucose and insulin concentrations. We have endeavoured to assess whether elimination of fall in glucose concentrations during GST would obliterate any significant increase in GH and cortisol.
Subjects & Methods
We designed a cross-over study, where glucose, GH, cortisol and insulin were measured in six healthy subjects (age range 28-54, one male) during GST (0, 30, 60, 90, 120, 150 and 180 minutes), and subsequently in the same individuals, when a fall in glucose and insulin was prevented by infusion of 10% glucose that was started at 60 minutes after administration of intramuscular glucagon.
Results
As expected, administration of glucose prevented a fall in glucose and insulin concentrations observed during later time-points of GST (e.g. mean glucose at 180 minutes of GST 176.7 mg/dl vs 71.6 mg/dl, $P=0.001$, mean insulin 53.6 μU/ml vs 4.52 μU/ml, $P=0.003$). Despite that there was still an increase in GH concentrations though less pronounced than in cross-over controls ($GH_{glucose\ infusion}$: median lowest value 0.17ng/ml vs median maximal value 8.12 ng/ml, $P=0.04$, $GH_{cross\text{-}over\ controls}$: median lowest value 0.24 ng/ml vs median maximal value 15.12 ng/ml, $P=0.004$). The same applied to cortisol concentrations ($Cortisol_{glucose\ infusion}$: median lowest value 6.89 μg/dl vs median maximal value 15.15 μg/dl, $P=0.05$, $Cortisol_{cross\text{-}over\ controls}$: median lowest value 8.48 μg/dl vs median maximal value 19.75 μg/dl, $P=0.01$).
Conclusions
Fall in glucose concentrations during the second phase of GST contributes to stimulation of GH and cortisol secretion, but is not the only factor responsible for this phenomenon. Precise mechanisms involved in stimulation of GH and cortisol secretion during glucagon stimulation test still remain to be elucidated.

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P312

Maternal cortisol levels in pregnancy and intelligence quotient in children at 7 years of age. odense child cohort

Anja Fenger Dreyer[1,2], Tina Kold Jensen[3,4,5], Iben Have Beck[3], Dorte Glintborg[1,2], Niels Bilenberg[2,6] & Marianne Andersen[1,2]
[1]Odense University Hospital, Department of Endocrinology, Odense C; [2]University of Southern Denmark, Department of Clinical Research, Faculty of Health Sciences, Odense C; [3]University of Southern Denmark, Department of Clinical Pharmacology, Pharmacy and Environmental Medicine, Odense C, Denmark; [4]Odense University Hospital, Odense Child Cohort, Hans Christian Andersen Hospital for Children, Odense C, Denmark; [5]University of Southern Denmark, OPEN Patient data Explorative Network (OPEN), Odense C, Denmark; [6]University of Southern Denmark, Department of Child and Adolescent Mental Health Odense, Mental Health Services in the Region of Southern Denmark, Odense C, Denmark

Background
Maternal cortisol levels increase during pregnancy and prenatal cortisol exposure have been linked to cognitive function in childhood. Higher activity of the enzyme 11β-hydroxysteroid-dehydrogenase type 2 (11β-HSD2) downregulates the amount of maternal cortisol crossing the placenta by inactivation of cortisol to cortisone. In childhood, boys perform significantly poorer in tests of intelligence than girls.
Aim
To investigate associations between maternal 3rd trimester cortisol or cortisone and child IQ at 7-years-of-age, and to consider the impact of child sex.
Method
Odense Child Cohort is a prospective observational cohort study. In this current study, 943 mother-child dyads were included. Exposure was maternal 24 hour urine (u-) cortisol and cortisone, and fasting morning serum (s-) cortisol, obtained in 3rd trimester of pregnancy and measured by liquid chromatography–tandem mass spectrometry. Outcome was child intelligence at age 7 years assessed by trained psychologists using the Wechsler Intelligence Scale for Children version V. Estimations of full scale intelligence quotient (FSIQ) and verbal comprehension index (VCI) were calculated.
Results
Women carrying a boy had significantly lower s-cortisol levels than women carrying a girl (825 vs 865 nmol/l, $P=0.005$). Girls had a significant higher score in FSIQ (101.2 vs 98.2, $P<0.001$) and VCI (101.1 vs 98.9, $P=0.004$) compared to boys. In girls, levels of maternal u-cortisone were positively associated with VCI (B (95%-CI) = 6.2 (1.2; 11.2). In boys, maternal s-cortisol was negatively associated with FSIQ (B (95%-CI) = -3.9 (-6.5; -1.3)) and VCI (B (95%-CI) = -4.4 (-7.0; -1.9)). Child sex had a significant interaction with u-cortisone and s-cortisol in the associations.
Conclusion
Lower prenatal cortisol exposure of the fetus seems beneficial for cognitive development at 7-years-of-age. Girls were protected against high cortisol exposure via the inactivation of cortisol to cortisone by 11β-HSD2, while boys were more susceptible to high maternal cortisol levels. Child sex differences in prenatal cortisol exposure and cognitive development should be considered in future studies.

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P313

TGFBR3L gene expression and relevance for the gonadotroph non-functioning pituitary neuroendocrine tumours

Maren Wessel[1,2], Jens Petter Berg[3,4], Jens Bollerslev[1,3] & Nicoleta Cristina Olarescu[1,2,3]
[1]Section of Specialized Endocrinology, Department of Endocrinology, Oslo University Hospital (OUS), Oslo, Norway, Oslo, Norway; [2]Research Institute of Internal Medicine, Oslo University Hospital (OUS), Oslo, Norway; [3]Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; [4]Department of Medical Biochemistry, Oslo University Hospital (OUS), Oslo, Norway

Objective
Transforming growth factor beta receptor 3 like (TGFBR3L) has been recently described as a pituitary-specific membrane protein detected in a proportion of the gonadotroph cells in non-neoplastic and tumour tissue (1). Furthermore, mouse studies have indicated that TGFBR3L is an inhibin B co-receptor that regulates FSH levels (2). We hypothesized that TGFBR3L expression in gonadotroph non-functioning pituitary neuroendocrine tumours (NF-PitNETs) is related to clinical parameters as age, gender and tumour volume. Moreover, we aimed to decipher the possible function of this protein in tumorigenesis and hormone production in gonadotroph NF-PitNETs.
Methods
Gene expression of TGFBR3L was performed by RT-qPCR in immunohistochemically confirmed gonadotroph NF-PitNETs (SF1 and/or FSHβ/lHβ positive) in a cohort of prospectively included patients ($n=102$) diagnosed between 2014-2021. Clinical parameters as age, sex and tumour volume were recorded. RNA-sequencing was performed in a sub-cohort of 18 age and sex matched patients with high and low TGFBR3L gene expression ($n=9$ in each group). Posttranscriptional silencing of TGFBR3L by siRNA was performed in the LβT2 gonadotroph cell line and gene expression of FSHβ and LHβ were measured. Ongoing studies are performed on primary gonadotroph tumor cells isolated from gonadotroph NF-PiNETs.
Results
Of 102 patients 39 (32%) were women, age at diagnosis mean ± 1SD: 61 ± 14 years, tumour volume median (IQR) 5928 (3657-8717) cm3. TGFBR3L did not correlate to age, sex, and tumour volume. RNA-sequencing identified 1921 differentially expressed genes (DEGs) disclosing a distinct genetic profile associated with TGFBR3L expression, with 786 DEG up- and 1135 down-regulated genes. SF1/NR5A1, LHβ, GNRHR, ESR1, and SSTR3 were up-regulated in the high TGFBR3L group. Pathways analysis revealed an up-regulation of genes involved in the Notch signaling pathway along with downregulation of genes in the JAK/STAT pathway and partial suppression in the Wnt signaling pathway in the high-TGFBR3L group. Furthermore, pathways related to proliferation, cell survival and cell adhesion were differentially regulated between the groups. SiRNA-mediated suppression of TGFBR3L in LβT2 cells resulted in a significant increase in LHβ expression ($P=0.001$), without affecting FSHβ.
Conclusion
Although TGFBR3L gene expression is not related to primary clinical parameters, it is related to markers of gonadotroph cell differentiation. Analyses of the genes related to TGFBR3L expression and in vitro mechanistic studies may reveal distinct roles for this protein in NF-PitNETs pathogenesis.
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P314

A complex clinical scenario: chiari type ii malformation coexisting with suprasellar paraganglioma and associated succinate dehydrogenase subunit b (SDHB) genetic mutation

Stefano Testa[1,2], Erika Grossrubatscher[2], Paolo Dalino Ciaramella[2], Benedetta Zampetti[2], Vittoria Favero[1,2] & Iacopo Chiodini[1,2]
[1]University of Milan, Department of Biotechnology and Translational Medicine, Milan, Italy; [2]Ospedale Niguarda Ca' Granda, Endocrinology Unit, Milan, Italy

Introduction
Paragangliomas are rare neuroendocrine tumors, that manifest as painless, slow-growing masses, becoming evident only when symptoms of catecholamine overproduction or mass effects emerge. Paragangliomas exhibit a broad spectrum of characteristics, existing as solitary or multiple entities, and may be sporadic or hereditary. These tumors can be either benign or malignant and have origin in the sympathetic or parasympathetic tissues. Paragangliomas are commonly found in the pre-aortic and paravertebral sympathetic plexus or in the neck and head and they can be associated with hereditary syndromes, often linked to genes encoding different subunits of succinate dehydrogenase (SDHx). Carriers of SDHB gene mutations have the highest morbidity and mortality rates due to their malignant potential.
Case Report
We present the case of a 16-years-old female patient who had undergone neurosurgical intervention at birth due to Chiari malformation type II and myelomeningocele. The patient was referred for short stature and primary amenorrhea. A left wrist radiograph performed 5 months before indicated delayed skeletal maturation. Pituitary function tests were within normal range (FSH 6.4 mIU/ml, LH 7.5 mIU/ml, estradiol 34 pg/ml, TSH 2.1 mIU/l, FT4 11 pg/ml, 17-β-estradiol 67 pg/ml, cortisol 15 μg/dl, ACTH 35 pg/ml), except for reduced prolactin values (2 ng/ml). Surprisingly, a concurrent encephalic Magnetic Resonance Imaging (MRI), performed during the neurological follow-up, revealed a new left median-paramedian intra-suprasellar rounded lesion of 11 mm, hypointense in T1 and iso-hyperintense in T2, with features suggesting an uncertain nature. Based on the suspicion of astrocytoma or craniopharyngioma, a transnasosphenoidal surgery was performed six months later. The post-operative histologic examination was suggestive of paraganglioma, characterized by consistent morphologic and immunophenotypic features (focal CK+, S100+ in sustentacular cells, and diffuse synaptophysin+). Subsequently, the genetic examination revealed a variant in heterozygosity of exon 7 of the SDHB gene (c.688C>G), with a probable pathogenetic significance. The subsequent follow-ups indicated normal hypothalamic-pituitary-adrenal axis and the onset of menarche at 16.6 years. Postoperative pituitary MRIs confirmed no residual or recurrent disease. Further hormonal and radiological follow-ups were negative.
Conclusion
Despite advances, the imaging of paragangliomas remains challenging, with critical implications for the appropriate diagnostic-therapeutic approach and metastasis detection. The coexistence of paragangliomas and Chiari malformations has already been reported in patients with mutation of EPAS1 and neurofibromatosis type 1. This case suggests the need for further investigations into the genetic correlations of these two conditions, and highlights a possible role for SDHB gene mutations.

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Validation of baseline laboratory levels and a novel probability score in the diagnosis of patients with suspected arginine vasopressin deficiency (Central Diabetes Insipidus)

Cihan Atila[1], Irina Chifu[2], Juliana Drummond[3], Deborah Vogt[1], Martin Fassnacht[2], Bettina Winzeler[1], Julie Refardt[1] & Mirjam Christ-Crain[1]
[1]University of Basel, Endocrinology, Basel, Switzerland; [2]University of Würzburg, Würzburg, Germany; [3]Medical School of the Federal University of Minas Gerais, Belo Horizonte, Brazil

Introduction
Distinguishing arginine vasopressin deficiency (AVP-D, central diabetes insipidus) from primary polydipsia (PP) is challenging. The method with the highest diagnostic accuracy, hypertonic saline-stimulated copeptin, is often limited to experienced hospitals, requires close monitoring, and may be cumbersome for patients. A standardised, validated stepwise assessment and probability score to rule out AVP-D in the initial baseline evaluation is currently lacking.
Methods
This analysis includes two independent patient cohorts from two international multicentre studies undergoing the hypertonic saline stimulation test (HST). Eligible adults with polyuria (>50 mL/kg body weight/day) or known AVP-D were included. The final diagnosis was based on medical history, clinical symptoms, laboratory/imaging data, results of the HST and therapeutic response at a three-month follow-up. Primary aim was to assess the diagnostic potential of baseline laboratory levels and to develop a novel probability score. In the probability score, the overall best cut-off, high-sensitivity cut-off (defined as ≥95% sensitivity), and high-specificity cut-off (defined as ≥95% specificity) were derived in the first cohort (development), and their diagnostic performance was determined in the second cohort (validation). The final scoring scheme included: (baseline plasma sodium x osmolality)/100), baseline plasma copeptin (–50 points, if > 4.9pmol/l), nycturia [+30 points, if ≥3 times], onset of polyuria/polydipsia [+20 points, if sudden onset], drinking amount at night [30points, if >1L], presence of anterior pituitary deficiencies [+50points], previous pituitary surgery [+50points].
Results
In total, 299 patients were included between July 2013 and September 2022; 141 in the development cohort ($n=59$ [42%] AVP-D; $n=82$ [58%] PP) and 158 in the validation cohort ($n=69$ [44%] AVP-D; $n=89$ [56%] PP). For diagnosing AVP-D, a baseline plasma sodium of >145mmol/l provided 100% sensitivity (95%CI:100-100) and <135mmol 100% specificity (95%CI:100-100), and baseline plasma copeptin >5.6pmol/l resulted in 100% specificity (95%:CI 100-100). In the validation cohort, a probability score cut-off of 441 points provided the highest overall diagnostic accuracy of 86% (95%CI:73–94) and an area under the roc curve (AUC) of 91% (95%CI:87–96); the high-sensitivity cut-off of 415 points had a 93% sensitivity (95%CI:86-99), and the high-specificity cut-off of 461 points a 93% specificity (95%CI:88-98).
Interpretation
Our findings show that a plasma sodium <135mmol/l or a copeptin >5.6pmol/l rule out AVP-D, whereas a sodium >145mmoL/l can be used as a rule-in test. A novel probability score, including baseline laboratory values, clinical symptoms, and medical history, had high accuracy for identifying AVP-D without the need for any further stimulation testing.

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The pathogenic RET val804met variant in acromegaly: a new clinical phenotype?

Sabrina Chiloiro[1], Ettore Domenico Capoluongo[2], Flavia Costanza[1,3], Angelo Minucci[4], Antonella Giampietro[1], Amato Infante[5], Domenico Milardi[1], Claudio Ricciardi Tenore[4], Maria De Bonis[4], Simona Gaudino[5], Guido Rindi[6], Alessandro Olivi[7], Laura De Marinis[1], Alfredo Pontecorvi[1], Francesco Doglietto[7] & Antonio Bianchi[1]
[1]Catholic University of Sacred Heart, Endocrinology and Diabetology, Rome, Italy; [2]Federico II University, Department of Molecular Medicine and Medical Biotechnology, Naples, Italy; [3]Catholic University of Sacred Heart, Department of Endocrinology and Diabetology, Rome, Italy; [4]Catholic University of Sacred Heart, Unit of Molecular Diagnostics and Genomics, Department of Laboratory sciences and infectious diseases, Rome, Italy; [5]Fondazione Policlinico Universitario A. Gemelli, Department of Imaging, Radiation Therapy and Hematology, Università Cattolica del Sacro Cuore, Fonda-zione Policlinico Universitario Agostino Gemelli, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Rome, Italy; [6]Catholic University of Sacred Heart, Section of Anatomic Pathology, Department of Life Sciences and Public Health, Università Cattolica del Sacro Cuore, Rome, Italy; [7]Catholic University of Sacred Heart, Neurosurgery, Rome, Italy

Genetic discoveries improved the understanding of the etiology and pathogenesis of several diseases, including acromegaly. Germline mutations involving AIP, MEN1, CDKN1B, GPR101, PRKAR1A, and GNAS genes have been described in GH-secreting PitNETs, but realistically many genetic alterations have not been identified yet. Nowadays, RET mutations have not been reported in acromegaly, if not exclusively in the context of a multiple endocrine neoplasia (MEN). A 48-year-old patient was affected by a cavernous sinus and bone-invasive somatotropinoma, resistant to first- and second-line medical therapies. The patient was also diagnosed with left breast cancer and right breast fibroadenoma. According to the somatotropinoma aggressive behavior and cancer history, a genetic study for germline mutations was performed through a specific panel designed for Pit-NETs. To our knowledge, we describe the first acromegalic patient with the RET gene pathogenic variant (PV) (Class 5): c.2410G>A; p.Val804Met; rs79658334. The presence of RET fusions is well documented in breast cancers, but RET germline PVs have never been reported in breast cancer. After excluding all the other possible RET-associated pathologies, including MEN, we speculated that our patient could be affected by Hereditary Cancer-Predisposing Syndrome (HCPS) since the association with this PV is known in the literature. The patient's first-degree relatives underwent genetic screening for the same RET PV, resulting

positive in heterozygosity in the patient's father and daughter. Clinical, hormonal, and imaging assessment ruled out abnormalities until now, but the 25-year-old daughter was also diagnosed with right breast fibroadenoma. This finding supported the hypothesis that RET c.2410G > A PV may cause HCPS. The RET mutation may have induced constitutive activation of tyrosine kinase expressed also in the pituitary, enhancing GH production and somatotroph cell proliferation, according to the invasive growth and the poor response to treatments of the proband. Furthermore, the occurrence of breast tumors, in addition to the early onset in the young daughter, in the absence of other variants strongly associated with familial cancers, hints at the possibility that the RET PV may contribute to tumor susceptibility. In conclusion, our clinical case describes a new phenotype associated with RET PV, represented by an acromegalic woman with breast carcinoma, suggesting that also pituitary tumors should be considered in the landscape of HCPS. RET mutations may be considered for screening if NGS for well-established PitNET-associated gene mutations renders negative, in patients with aggressive tumors and suggestive clinical history.

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Relevance of USP8 mutations in the pathogenesis of pituitary tumours of the corticotroph lineage

Antonio Pico[1,2,3,4], Araceli Garcia-Martinez[1], Johana Sottile[1], Cristina Lamas[5,6], Elena Garcia[1,2,7], Maria Eugenia Torregrosa[1,2,8], María Niveiro[1,2,9], Javier Abarca[1,2,10] & Luís Miguel Valor[1]
[1]Instituto de Investigación Sanitaria y Biomédica de Alicante (ISABIAL); [2]Hospital General Universitario Dr. Balmis; [3]University Miguel Hernandez; [4]CIBERER; [5]Complejo Hospitalario Universitario de Albacete; [6], Endocrinology & Nutrition; [7], Radiology; [8], Clinical Analysis-Hormones; [9], Pathology; [10], Neurosurgery

Corticotroph tumours, comprising around 15% of pituitary tumours, express ACTH and other peptides originating from TPIT-lineage adenohypophyseal cells. Their tumorigenesis involves a complex interplay of genetic and epigenetic factors and hormonal and growth factor stimulation. Silent corticotroph tumours (SCT) share immunopositivity for ACTH and TPIT with functioning corticotroph tumours (FCT) but do not exhibit evidence of hypercortisolism. Despite their aggressive growth and high recurrence rates, the reasons for their failure to induce hypercortisolism remain speculative, focusing on factors like cell origin, sensitivity to hypothalamic stimulants, POMC cleavage, and cell cycle regulation. This study delves into the role of USP8 mutations in the pathogenesis of corticotroph tumours. USP8 is involved in the regulation of the epidermal growth factor receptor (EGFR) signalling pathway. USP8, when mutated, cannot properly regulate the ubiquitination and degradation of EGFR, and prolonged activation of EGFR due to impaired degradation can lead to sustained signalling, promoting increased POMC expression and subsequent ACTH secretion. Sanger sequencing was performed on 10 SCTs and 13 FCTs from a unique centre. Comprehensive analysis encompassed demographic, clinical, radiological, and genetic variables, including genes associated with ACTH processing, secretion, glucocorticoid receptor (GR) pathway, and the immune microenvironment. The results unveiled somatic USP8 mutations in 70% of SCTs and 30.8% of FCTs, all heterozygous and located in exon 14. Mutated tumours were more prevalent in younger individuals and women, smaller, less invasive, and exhibited heightened expression of ACTH-related genes (POMC, CHRH, AVPR1, TBX19, PCSK1/3, USB, CABLES1, EGFR). No significant changes were observed in genes related to ACTH degradation (PCSK2, PAM, CPE) or the GR pathway. In SCTs, mutated tumours displayed increased immune activity, as indicated by elevated PDL-1 expression. We also explored the expression of somatostatin receptor levels as potential therapeutic targets on these tumours. Both mutated SCTs and FCTs expressed higher levels of SSTR5 than non-mutated ones, and FCTs additionally expressed more SSTR2. In conclusion, USP8 mutations are prevalent in corticotroph lineage pituitary tumours, encompassing both silent and functioning variants. Mutated tumours exhibit a more differentiated profile, suggesting potential implications for diagnosis and targeted therapies.

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Circadian clock disruption impairs immune oscillation in chronic endogenous hypercortisolism: a multi-levels analysis from a multicenter clinical trial

Valeria Hasenmajer[1], Emilia Sbardella[2], Francesca Sciarra[1], Flavio Rizzo[1], Chiara Simeoli[3], Claudia Pivonello[4], Rosario Pivonello[4], Filippo Ceccato[5], Carla Scaroni[5], Giorgio Arnaldi[6], Riccardo Pofi[7], Alessia Cozzolino[1], Marianna Minnetti[1], Danilo Alunni Fegatelli[8], Simone Conia[9], Roberto Navigli[9], Daniele Gianfrilli[1], Mary Anna Venneri[1] & Andrea Isidori[1,10]
[1], Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy; [2], Rome, Italy; [3], Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Università Federico II di Napoli, Naples, Italy; [4], Dipartimento di Sanità Pubblica, Università Federico II di Napoli, Naples, Italy; [5], Endocrine Disease Unit, University-Hospital of Padova, Padova, Italy; [6], Division of Endocrinology and Metabolic Diseases, Department of Clinical and Molecular Sciences (DISCLIMO). Polytechnic University of Marche, Ancona, Italy; [7], Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, Oxford, United Kingdom; [8], Department of Public Health and Infectious Disease, Sapienza University of Rome, Rome, Italy; [9], Sapienza NLP, Department of Computer, Control and Management Engineering, Sapienza University of Rome, Rome, Italy; [10], Centre for Rare Diseases (Endo-ERN accredited), Policlinico Umberto I, Rome, Italy

Background
Glucocorticoids (GC) are potent entrainers of the circadian clock, however their effect on biological rhythms in human chronic exposure have been poorly studied. Endogenous hypercortisolism (Cushing's Syndrome, CS) is a rare condition, in which circadian disruption is sustained by a tumorous source of GC excess, offering the unique opportunity to investigate the *in vivo* chronic effects of GC.
Methods
In a 12-month prospective multicenter trial, the daily fluctuations in the number of circulating peripheral blood mononuclear cells (PBMCs) and the time-specific expression of clock-related genes were analyzed by RT-qPCR in a cohort of 68 subjects, 34 affected by CS and 34 age- and sex-matched controls. Rhythmicity algorithms and machine learning techniques were applied to the multi-level dataset.
Findings
Multiple, 6-points, daily sampling revealed profound changes in the levels, amplitude, and rhythmicity of several PBMCs populations. More specifically, total ($CD14^+$), intermediate ($CD14^+CD16^+$) and non-classical ($CD14^+CD16^{++}$) monocytes increased, while classical ($CD14^{++}CD16^-$) monocytes decreased, all normalizing after remission, except for a persisting dampening of the amplitude of their daily variations. On the other hand, the decrease in total ($CD3^+$) and $CD4^+$ lymphocytes and the increase in $CD8^+$ lymphocytes only partially restored after CS remission, while regaining similar amplitude compared to controls. Mesor of total $CD56^+$ NK cells and all NK cells subsets were significantly reduced in CS as well. Clock gene analyses in isolated PBMCs showed a significant flattening of circadian oscillation of PER1, PER2, PER3, PRF1 and TIMELESS expression, and a paradoxical increase in the amplitude of PER genes after remission. In the active phase, the JTK_CICLE algorithm revealed a loss of rhythmicity of all genes which were circadian in the PBMCs of controls. Most, but not all, regained physiological oscillation after remission. Machine learning revealed that while combined time-course sets of clock-genes were highly effective in separating patients from controls, immune profiling was efficient even as single time-points.
Interpretation
In conclusion, the oscillation of circulating immune cells is profoundly altered in CS patients, representing a convergence point of circadian rhythm disruption, metabolic and steroid hormone imbalances. Machine learning techniques proved the superiority of immune profiling, over parameters such as cortisol, anthropometric and metabolic variables, and gene expression analysis, to identify CS activity.

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Natural history of rathke's cleft cysts. a retrospective analysis of a fifteen centers experience in spain

Edelmiro Luis Menendez Torre[1,2,3], Alba Gutierrez Hurtado[1], Ana Irigaray[4], Patricia Martin Rojas[5], Inmaculada González Molero[6], Almudena Vicente[7], Marta Araujo[8], Cindy Idobro[8], Rocio Villar Taibo[9], Betina Biagetti[10], Alfonso Soto-Moreno[11], Manel Mateu Salat[12], Fernando Guerrero[13], Maria Dolores Moure Rodriguez[14], Miguel Paja Fano[15], Fernando Cordido[16], Pedro Iglesias[17], M Dolores Ollero[18] & Ana Aulinas Maso[19]
[1]Central University Hospital of Asturias, Endocrinology and Nutrition, Oviedo, Spain; [2]Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain; [3]University of Oviedo, Oviedo, Spain; [4]Navarra Hospital Complex - Navarra Hospital, Pamplona, Spain; [5]La Paz University Hospital, Madrid, Spain; [6]Hospital Regional Universitario de Málaga, Málaga, Spain; [7]Hospital General Universitario de Toledo, Toledo,

Spain; [8]Ramón y Cajal Hospital, Madrid, Spain; [9]Santiago Clinic Hospital CHUS, Santiago de Compostela, Spain; [10]Vall d'Hebron University Hospital, Barcelona, Spain; [11]Virgen del Rocío University Hospital, Sevilla, Spain; [12]Institut de Recerca Sant Pau, Barcelona, Spain; [13]Bellvitge University Hospital, L'Hospitalet de Llobregat, Spain; [14]University Hospital of the Crosses, Barakaldo, Spain; [15]Basurto University Hospital, Bilbo, Spain; [16]University Hospital of A Coruña, A Coruña, Spain; [17]Hospital Universitario Puerta de Hierro, Majadahonda, Spain; [18]Navarra Hospital Complex - Navarra Hospital, Endocrinology and Nutrition, Pamplona, Spain; [19]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Objective
To evaluate the natural history of Rathke's cleft cysts (RCC).
Materials and Methods
A multicenter retrospective clinical practice study of adult patients with radiologically diagnosed RCCs since 2000 in 15 tertiary hospitals (SPAIN-QBR study) with a diameter greater than 5 mm, in whom non-surgical follow-up was decided.
Results
A total of 177 patients were followed for 65.8 ± 42.3 months. The mean age was 42.8 ± 18.1 years, significantly ($P<0,01$) lower than that of other patients who underwent surgery (48.0 ± 16.4 years). The larger diameter was between 6 and 10 mm in 84 patients (49.7%), 11-20 mm in 86 patients (48.5%), and >20 mm in 11 patients (6.2%). Suprasellar extension was present in 44 (24.9%) and cavernous sinus extension in 3 (1.7%). The largest MRI tumor diameter remained stable or decreased in 133 patients (75.1%) and increased in 44 patients (24.9%). None of the baseline tumor or patient characteristics predicted the evolution of tumor size. During follow-up, 7 patients (3.9%) underwent surgery, in one case by patient decision without previous change, in three 3 cases after clinical events (two cases due to visual changes and one due to hormonal changes) and in another three patients because of significant growth observed on MRI with risk of chiasmatic involvement. Surgery was performed at 27, 43, 55, 80, 84, and 105 months after diagnosis. (Table 1) When baseline clinical covariates were included in a regression model, the only predictor of the need for surgery was the degree of hormonal involvement at baseline.
Conclusion
After a mean of 5 years of follow-up, 24% of patients experienced some increase in RCC size, but without clinical significance. Only 3% needed surgery, which was more likely in those with more hormonal involvement at diagnosis.

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Impact of clinical and treatment characteristics on HR-QoL in patients with prolactinoma - cross-sectional analysis of a dutch multicenter prospective cohort study

Ingrid Zandbergen[1], Iris Pelsma[2], Wouter van Furth[1] & Nienke Biermasz[2]
[1]Leiden University Medical Center, Neurosurgery, Leiden; [2]Leiden University Medical Center, Endocrinology and Metabolism, Leiden

Introduction
Patients with prolactinomas suffer from a wide range of symptoms, of which the effect on health-related quality of life (HR-QoL) needs further investigation. Moreover, the first-line treatment for patients with prolactinomas, dopamine agonists (DAs), albeit being effective in lowering prolactin levels, might further hamper HR-QoL due to side effects. To assess the impact of symptoms and treatment modality on HR-QoL, a cohort of patients with prolactinoma was cross-sectionally investigated.
Methods
Baseline clinical characteristics, symptoms (measured using the PRO-CTCAE, and HADS questionnaire), treatment outcomes, and HR-QoL (measured using the SF-36 questionnaire) of 210 DA treated (DAT) patients (mean age 49.4 ± 15.4 years; 122 females (58.1%)), and 106 patients not treated with DA (mean age 40.9 ± 12.9 years; 87 females (82.1%)) are described in this Dutch multicenter prospective observational cohort study.
Results
Current prolactin levels -available for 229 patients- were elevated above the sex upper limit of normal in 54/210 DAT patients (34.8%), and in 52/106 patients not treatment with DA (70.3%, $P<0.001$). Galactorrhea was reported more frequently by 13/44 (29.5%) patients not treated with DA *vs* 15/119 (12.6%) DAT patients ($P=0.011$), and was more frequently reported by female patients (25.0% vs 1.8%, $P<0.001$). Side effects of DA treatment – reported by 155/210 DAT patients – were gastro-intestinal (GI) tract symptoms (total 63/155 (40.6%), males 14/68 (20.6%) *vs* females 49/87 (56.3%), $P<0.001$); fatigue (total 77/155 (50.0%), males 22/68 (32.4%) vs females 55/86 (64.0%), $P<0.001$), and concentration loss (total 41/155 (26.6%)). DA treatment did not influence risk for anxiety (36/143 *vs* 18/65, $P=0.747$) and depression (30/144 *vs* 17/65, $P=0.394$), and was not different in males and females. All HR-QoL domains, bar physical functioning and pain, were lower in patients with prolactinoma compared to the Dutch population (General Health domain 55.0 ± 14.5 in patients with prolactinoma *vs* 70.7 ± 20.7 in the Dutch population, $P<0.001$). Female patients had lower domain scores on Social Functioning (68.4 ± 29.0 vs 77.9 ± 26.1, $P<0.025$), Fatigue (48.4 ± 22.8 vs 59.9 ± 22.0, $P<0.001$), and Pain (77.0 ± 26.3 vs 85.3 ± 18.9, $P<0.025$).
Conclusions
Based on this cross-sectional analysis of the Dutch national cohort of patients with prolactinomas, 66.5% of patients were currently treated with DA. Despite DA treatment, a proportion of patients had prolactin levels above the ULN. Significant sex differences for most outcomes of interest (i.e. current treatment, current tumor size, symptoms at present) were observed, necessitating further research into sex differences in patients with prolactinoma. Moreover, HR-QoL was significantly affected in patients with prolactinoma, highlighting the impact of the prolactin-producing tumor.

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Apelin and copeptin levels in patients with chronic SIAD treated with empagliflozin – a secondary analysis of the SANDx trial

Sophie Monnerat[1], Nikolaos Drivakos[1,2], Fiona A. Chapman[3,4], Neeraj Dhaun[3,4], Julie Refardt[1] & Mirjam Christ-Crain[1,5]
[1]University Hospital Basel, Department of Endocrinology, Diabetology and Metabolism, Basel, Switzerland; [2]Hospital Center of Biel, Department of Nephrology, Biel, Switzerland; [3]Queen's Medical Research Institute, BHF/University of Edinburgh Centre for Cardiovascular Science, Edinburgh, United Kingdom; [4]Royal Infirmary of Edinburgh, Department of Renal Medicine, Edinburgh, United Kingdom; [5]University of Basel, Department of Clinical Research, Basel, Switzerland

Introduction
Glucose-induced osmotic diuresis and free water loss induced by the SGLT2 inhibitor empagliflozin effectively increase sodium levels in patients with a chronic syndrome of inappropriate antidiuresis (SIAD) where arginine vasopressin (AVP) levels are inappropriately increased in relation to osmolality. The hormone apelin opposes the actions of AVP in salt and water homeostasis and administering exogenous apelin increases sodium levels in rats with SIAD. In patients with type 2 diabetes mellitus and heart failure, apelin levels increased after a 6-month treatment with dapagliflozin. We aimed to investigate whether an increase in plasma apelin level may contribute to the therapeutic efficacy of empagliflozin in chronic SIAD.
Methods
Post-hoc secondary analysis of a double-blind, crossover, placebo-controlled trial performed from 12/2017 to 08/2021 at the University Hospital Basel, Switzerland, investigating the effect of a 4-week treatment with empagliflozin 25 mg/day as compared to placebo in 14 outpatients with chronic SIAD. The primary objective was to investigate the effect of empagliflozin on apelin levels. Secondary objectives included the effect of empagliflozin on copeptin levels and on the apelin/copeptin ratio. Absolute changes in apelin, copeptin and their ratio were compared using a paired Wilcoxon signed-rank test. The relationship between apelin and sodium levels was investigated by computing Spearman correlation coefficients.
Results
Fourteen patients, 50% female, with a median [IQR] age of 72 years [65–77] were included in the analysis. Median apelin levels were 956 pmol/l [853, 1038] at baseline. Median [IQR] apelin absolute changes were 102 [1, 166] pmol/l and 82 [-47, 199] pmol/l ($P=0.677$) at the end of the placebo and empagliflozin phase respectively. Baseline apelin levels did not correlate with baseline sodium levels ($\rho = 0.34$, $P=0.282$), nor did their absolute changes at week 4 ($\rho = -0.007$, $P=0.974$). Median copeptin levels were 2.6 [2.2, 4.5] pmol/l at baseline and increased by 0.2 [-0.1, 0.6] pmol/l and 0.6 [0.3, 0.9] pmol/l ($P=0.069$) over the placebo and empagliflozin phase, respectively. Median apelin/copeptin ratio was 369 [147, 503] at baseline and increased by 8 [-97, 36] and decreased by 4 [-72, 32] ($P=0.266$) during the placebo and empagliflozin phase, respectively.
Conclusion
Treatment with empagliflozin in patients with chronic SIAD did not lead to significant changes in either apelin or copeptin levels, or the apelin/copeptin ratio. Our findings suggest that the efficacy of empagliflozin in SIAD is not due to an alteration in plasma apelin concentration.

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Minimum data set for global monitoring of the safety and efficacy of growth hormone replacement in adults - an expert group recommendation

Suet Ching Chen[1], Faisal Ahmed[2], Deno Andrews[3], Beverly M.K. Biller[4], Cesar Luiz Boguszewski[5], Jillian Bryce[6], Minglu Chen[7], Peter Clayton[8], Maria Fleseriu[9], Judith Gebauer[10], Ken Ho[11], Jens Otto Jørgensen[12], Xiaoping Luo[13], Bradley Miller[14], Sebastian Neggers[15], Lars Savendahl[16], Katharina Schilbach[17], Christian J. Strasburger[18], Yutaka Takahashi[19], Diana Vitali[20], Kevin Yuen[21], Andrew Hoffman[22] & Gudmundur Johannsson[23]

[1]Office for Rare Conditions, University of Glasgow, Developmental Endocrinology Research Group, Royal Hospital for Children, Paediatric Endocrinology, Glasgow, United Kingdom; [2]Office for Rare Conditions, University of Glasgow, Developmental Endocrinology Research Group, Royal Hospital for Children, Paediatric Endocrinology, Glasgow, United Kingdom; [3]ICOSEP, Chicago, United States; [4]Neuroendocrine & Pituitary Tumor Clinical Center, Massachusetts General Hospital, United States; [5]SEMPR, Endocrine Division, Federal University of Parana, Brazil; [6]Office for Rare Conditions, University of Glasgow, United Kingdom; [7], Office for Rare Conditions, University of Glasgow, Glasgow, United Kingdom; [8]University of Manchester, Manchester, United Kingdom; [9]Pituitary Center, Departments of Medicine and Neurological Surgery, Oregon Health & Science University, Portland, United States; [10]Department of Internal Medicine I, University Hospital of Schleswig-Holstein, Lubeck, Germany; [11]The Garvan Institute of Medical Research and St. Vincent's Hospital, Sydney, Australia; [12]Aarhus University Hospital, Aarhus, Denmark; [13]Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [14]Division of Endocrinology, Department of Pediatrics, University of Minnesota Medical School, M Health Fairview Masonic Children's Hospital, Minneapolis, United States; [15]Dept. of Internal Medicine section Endocrinology and Pituitary Center Rotterdam, Rotterdam, Netherlands; [16]Dept. of Womeńs and Childreńs Health, Karolinska Institutet, Stockholm, Sweden; [17]Medizinische Klinik und Poliklinik IV, Faculty of Medicine, LMU Munich, Munich, Germany; [18]Dept. of Endocrinology and Metabolic Disorders, Charite universitaetsmedizin, Berlin, Germany; [19]Department of Diabetes and Endocrinology, Nara Medical University, Nara, Japan; [20]SOD Italia, Rome, Italy; [21]Departments of Neuronedocrinology and Neurosurgery, Barrow Pituitary Center, Barrow Neurological Institute, University of Arizona College of Medicine, Phoenix, United States; [22]Dept. of Medicine, Stanford University School of Medicine, Stanford, United States; [23]Department of Endocrinology, Sahlgrenska University Hospital and Institute of Medicine, Sahlgrenska, Sahlgrenska, Sweden

Introduction
Growth hormone (GH) replacement therapy is safe and confers significant benefits in body composition, bone health, cardiometabolic risk factors, and quality of life in adults with GH deficiency. However, longer term safety and efficacy data are limited by the lack of consistency in data collection between studies. The study aim was to develop a simple global register by standardising and developing a minimum data set (MDS) to facilitate international collection of safety and efficacy data.
Methods
This study was undertaken by the Adulthood GHD Expert Working Group (EWG) in GloBE-Reg, the Global Registry for Novel Therapies in Rare Bone and Endocrine Conditions (https://globe-reg.net/). Seventeen international clinical experts from 10 countries and two representatives from patient organisations participated in this initiative using published methodology for the grading system of MDS in childhood-onset GHD (cGHD) (doi: 10.1159/000533763). Inclusion criteria required $>70\%$ consensus for importance as defined for the MDS, provided $<50\%$ of the group deemed the item difficult to collect. The development of the finalised MDS took place over four months, which included two virtual meetings among the EWG members.
Results
A total of 190 data fields compiled from routine clinical practice of the EWG and fields in the cGHD MDS were graded. Of these, 111 items fulfilled the criteria for importance whilst 117 items were deemed easy to collect. Combining the criteria for importance and ease of data collection, 86 items fulfilled the criteria for MDS. Six items were excluded as one was redundant, another was a calculated field and four were designated as core data. Several fields such as adherence and patient reported outcomes while important, were considered difficult to assess objectively in routine clinical settings. Following detailed discussions, twenty items unrelated to safety and efficacy of GH therapy were removed, with the remaining 60 items merged into the finalised MDS recommendation of 43 items.
Conclusion
In summary, GloBE-Reg has developed a MDS suitable for monitoring the long-term safety and effectiveness of GH replacement therapy in adults during routine clinical practice world-wide. Such data harmonisation that bridges the monitoring of safety and efficacy of growth hormone therapy across the age span in patients of different healthcare settings will be pivotal in facilitating longer term surveillance and improving patient outcomes.

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Predictors of corticotroph tumour recurrence after surgical resection

Prishila Fookeerah[1,2], Winny Varikatt[3,4], Meena Shingde[3,4], Mark Dexter[4,5], Sue Lynn Lau[1,2] & Mark McLean[1,2]

[1]Westmead Hospital, Diabetes and Endocrinology, Sydney, Australia; [2]Western Sydney University, School of Medicine, Sydney, Australia; [3]Westmead Hospital, Tissue Pathology and Diagnostic Oncology, Sydney, Australia; [4]University of Sydney, Westmead Clinical School, Sydney, Australia; [5]Westmead Hospital, Neurosurgery, Sydney, Australia

Background
Corticotroph tumours are a heterogenous group of pituitary neuroendocrine tumours (PitNETs) in terms of their histological type, clinical presentation and tumour behaviour. These tumours are overrepresented in recurrent PitNETs and pose an important clinical and therapeutic challenge[1]. Although risk factors such as radiological invasion and elevated proliferative markers have been identified for PitNET recurrence, an improvement in proposed prognostic models is necessary to optimise management and monitoring of corticotroph tumour after surgical resection[2]. We compared recurrent and non-recurrent corticotroph tumours to assess differences in clinical and histological parameters.
Methods
51 consecutive corticotroph PitNETs resected from 2011 to 2018 and archived at Westmead Hospital were reviewed in a retrospective study. All tumours were characterised using transcription factor and hormonal immunohistochemistry. Corticotroph PitNETs were identified by positive TPIT expression. Clinical, radiological and histological characteristics of recurrent tumours were compared with cases without recurrence. 5 cases were excluded due to lack of adequate follow up data.
Results
Twelve cases (26%) had radiological or biochemical recurrence with mean time to detection of 45 months (range 12-144). Proportion of sparsely granulated subtype was similar in both groups(75% vs 76.5%, $P=0.69$). There was no significant difference in the proportion of silent and functioning corticotroph tumours between the two groups (58.3% vs 67.6% silent and 41.7% vs 32.4% functioning, $P=0.72$). Maximum tumour diameter at presentation was greater for tumours that later recurred (25.4 vs 17.2mm, $P=0.046$). Radiological or histological invasion was more frequent in recurrent tumours, though not statistically significant (42.9% vs 30%, $P=0.67$). Recurrent tumours were more likely to have a visible residual tumour after first resection (66.7% vs 20.6%, $P=0.01$). Presence of tumour remnant after surgery was associated with recurrence (OR 7.42, 95% CI 1.72 to 32.05, $P=0.0072$). The 12 recurrent tumours required a total of 24 separate interventions. Of these, 66.7% were repeat surgery, 16.7% radiotherapy, 12.5% medical therapy and 9.5% bilateral adrenalectomy. 33.3% of recurrent tumours expressed SSTR5.
Conclusion
Persistent tumour remnant after surgery may be an important predictor of corticotroph PitNET recurrence requiring further therapeutic intervention. Silent corticotroph tumours or sparsely granulated subtype did not predict recurrence in our study.
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Drug-induced hyperprolactinemia and granulomatous mastitis: a case report and literature review

Mohammed Alenazi[1], Sarah Howse[1] & Syed Imran[1]

[1]Dalhousie University, Division of Endocrinology and Metabolism, Halifax, Canada

Background
Granulomatous mastitis (GM) is a rare inflammatory condition of the breast typically affecting women during postpartum period. GM can mimic inflammatory breast cancer and only be reliably distinguished through histopathology. While there is no generally accepted treatment for GM, therapeutic options include - antibiotics, wide surgical excision, and corticosteroids.
Clinical Case
A 54-year-old female presented to her family physician with with a warm, erythematous lump on the right breast. She was prescribed a 7-day course of antibiotics and referred to the infectious disease clinic. A subsequent biopsy confirmed acute and chronic granulomatous inflammation and gram-positive cocci. She responded to the antibiotic therapy, but her symptoms recurred and was prescribed a 2-month course of doxycycline but her GM symptoms failed to resolve. She had an over 10-year history of hyperprolactinemia thought to be due to chronic opioid therapy and was referred to Endocrinology for further assessment. Serum prolactin (PRL) level had ranged between 63 to 81 µg/l (5-25 µg/l) and the sella MRI was normal. The patient declined to stop opioid therapy and considering the possibility of PRL-induced GM, she was prescribed cabergoline 0.5 mg once weekly. Her GM symptoms rapidly resolved and she has remained asymptomatic.
Discussion
This case represents a rare occurrence of acute on chronic GM in the setting of longstanding drug-induced hyperprolactinemia. A review of literature revealed three other cases of drug-induced hyperprolactinemia associated with GM and four cases were prolactinoma. The underlying etiological role of PRL in GM is not fully understood, but it is believed to have immunomodulatory effects, potentially triggering an inflammatory response in the breast tissue. This report emphasizes the importance of considering hyperprolactinemia in the diagnosis and treatment of GM, particularly in cases of recurrent GM.

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Cyclic cushing's syndrome: a diagnostic challenge

Ioanna Tsironi[1], Labrini Papanastasiou[1], Athanasios Fountas[1], Eirini Kaliakatsou[1], Kostis Karachalios[1], Panagiota Christou[2], Stelios Tigas[2], Miltiadis Gravvanis[3] & Athina Markou[1]
[1]'G. Gennimatas' General Hospital of Athens, Unit of Endocrinology and Diabetes Center, Athens, Greece; [2]University Hospital of Ioannina, Department of Endocrinology, Ioannina, Greece; [3]G. Gennimatas' General Hospital of Athens, Radiology Department, Athens, Greece

Introduction
Cyclic Cushing's syndrome is a rare disease characterized by episodes of cortisol hypersecretion followed by periods of normal cortisol secretion, ranging from days to months. We report a case of cyclic Cushing's syndrome whose diagnosis was delayed for years.
Case presentation
A 50-year-old female with a 16-year history of non-Hodgkin's lymphoma was referred to the Endocrinology Unit due to suspected hypercortisolemia. She had a 2-year history of hirsutism, supraclavicular fat pads, irritability, and insomnia. During her first admission, ACTH-dependent hypercortisolemia [midnight serum cortisol: 404.5 nmol/l, cortisol levels post-dexamethasone suppression test (DST) 127.42 nmol/l, ACTH: 14.3 pg/ml] was confirmed. Patient was, also, diagnosed with osteoporosis, arterial hypertension, and dyslipidemia. Pituitary MRI was performed and a 4 mm lesion on the left side of the gland was identified. CRH and DDAVP stimulation tests were performed which were both indicative of Cushing's disease. Given, however, the size of the pituitary lesion, an inferior petrosal sinus sampling (IPSS) was scheduled. Patient was re-admitted 2 weeks later for the IPSS, and, interestingly, her hormonal investigations were found to be normal [24h urinary free cortisol levels (31.5 mg/24h, NR < 80), midnight serum cortisol (118 nmol/l), and cortisol post-DST levels (29.3 nmol/l)]. Because of the conflicting results between the later and the previous admission, the above-mentioned tests were repeated 1 month later, which, this time, confirmed hypercortisolemia [24h urinary free cortisol levels (178 mg/24h, NR < 80), midnight serum cortisol (300 nmol/l), and cortisol post-DST levels (218 nmol/l)]. Taking into account the results of the hormonal tests, the presence of a pituitary microadenoma, and the patient's sex, a working diagnosis of cyclical Cushing's disease was made. To confirm the diagnosis, two days later, an IPSS with desmopressin stimulation was performed but ACTH-dependent hypercortisolemia was not detected indicating disease shift to another inactive phase. A second IPSS with desmopressin stimulation was performed 1 month later, with the patient's disease being in active phase, as demonstrated by elevated midnight serum cortisol levels for 2 consecutive days prior to IPSS, and the results were consistent with left-sided pituitary ACTH hypersecretion. Subsequently, a transsphenoidal pituitary surgery was successfully performed and the patient's Cushing's disease is currently on remission.
Conclusion
Our case demonstrates that the diagnosis of cyclic Cushing's syndrome is particularly challenging. During a period of inactivity, tests may be negative. However, if the clinical suspicion is high, follow-up with repeated screening tests are suggested to establish the final diagnosis.

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Deciphering microenvironment interactions during age-related pituitary tumour onset and through orthotopic mouse pre-clinical model

Álvaro Flores-Martínez[1,2], Marie Chanal[1], Marine Daura[1], Alexandre Vasiljevic[1,3], Radu Bolbos[4], Jean-Baptiste Langlois[4], Gerald Raverot[1,5] & Philippe Bertolino[1]
[1]Inserm U1052, CNRS UMR5286, Cancer Research Center of Lyon, Lyon 1 University., Lyon, France; [2]Maimónides Biomedical Research Institute (IMIBIC)/Reina Sofía University Hospital (HURS)/University of Cordoba, Department of Cell Biology, Physiology and Immunology, Córdoba, Spain; [3]Pathology Department, Reference Center for Rare Pituitary Diseases HyPO, 'Groupement Hospitalier Est' Hospices Civils de Lyon, Bron, France; [4]CERMEP-Life Imaging Center, Lyon, France; [5]Endocrinology Department, Reference Center for Rare Pituitary Diseases HyPO, Groupement Hospitalier Est' Hospices Civils de Lyon, Bron, France

Rationale
Pituitary tumours (PiTs) are a common and heterogeneous group of benign, slow-growing intracranial neoplasms arising from the sellar region. While recent advances have improved our knowledge of their cellular composition and the contribution of their tumour microenvironment (TME), most of PiT subtypes lack effective therapeutic treatments. Moreover, the mechanisms that occur in the early stage of PiT initiation remain to be elucidated partly due to the limited number of identified driver-mutations.
Objectives
Here, we aim to i) evaluate the consequences of pituitary tumorigenesis initiation on the remodelling of the native anterior pituitary microenvironment and ii) further model the dynamics of the functional interaction that exists between pituitary tumour cells and their microenvironment.
Approaches
We employed two main strategies based on: (1) the characterisation of the TME in spontaneous pituitary lesions found in aged mice and, (2) the development of an orthotopic mouse-model in which pituitary tumour cells were injected in the anterior pituitary gland.
Results
We confirmed that spontaneous lesions can be found in the anterior pituitary gland of aged mice. At the age of 20 months, we observed that 61.5 % of C57bl/6 mice ($n = 8/13$) developed histological abnormalities. While only one tumour could be found, all other lesions were characterized by the presence of a moderate cell hyperplasia in areas with haemorrhages associated with the presence of siderophages. All lesions showed matrix remodelling, as demonstrated by their reduced reticular fibre network. The spatial distribution of endocrine cells was also impacted compared to control animals. Additionally, we developed a novel preclinical model based on the orthotopic injection of tumour cells in the anterior pituitary. Using this setup, we evaluated the growth of injected tumour-cells through MRI to define early and late stages of tumour progression. This preclinical model was validated with gonadotroph (αT3, LβT2), corticotroph (AtT-20) and lacto-somatotroph (GH3) rodent cells. Then, we addressed the state of the anterior pituitary environment and evaluate the presence of endothelial and myeloid cells, as well as the network of reticulin fibres in early and advanced grafted-tumours.
Conclusion
Taken together, our results support that the native environment of the anterior pituitary is subjected to a remodelling during the onset of spontaneous PiTs. Also, preliminary observations using our orthotopic approach confirmed the usefulness of this preclinical model for studying the cellular interactions between the PiT cells and their TME.

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High prevalence of vertebral fractures associated with age, GH, and bone mineral density in patients with acromegaly

Chen Shuaiming[1], Li Jing[1], Wang Chun[1], Tan Huiwen[1], An Zhenmei[1], Yu Yerong[1] & Li Jianwei[1]
[1]West China Hospital, Sichuan University, Department of Endocrinology & Metabolism, Chengdu, China

Objective
Studies have demonstrated that patients with acromegaly have compromised bone health and an increased risk of vertebral fractures (VFs). However, the prevalence of VFs in Chinese patients with acromegaly has not been investigated by far. This study aimed to evaluate the prevalence and determinants of VFs in patients with acromegaly in a tertiary hospital in China.
Methods
We enrolled patients diagnosed with acromegaly consecutively at West China Hospital between January 2021 and December 2023, and excluded patients with plurihormonal PIT-1 positive pituitary adenoma. Supine and lateral thoracolumbar spine X-ray was performed to detect vertebral morphometry, and Genant's semi-quantitative criteria was applied to determine VFs.
Results
We enrolled 74 participants (48 females/26 males) in total, and found that 38 patients (51.4%) had VFs, with the majority of fractures being multiple (65.7%) and moderate/severe (63.2%). Patients with VFs were older (median age 55 vs 39 years old), and had higher parathyroid hormone (5.45 pmol/l vs 4.77 pmol/l) and apnea hypoventilation index (43.3 times/hr vs 13.9 times/hr) than the non-fractured patients. In addition, more fractured females developed menopause compared with non-fractured females (72.7% vs 26.9%, $P=0.002$). Patients with VFs had slightly decreased bone mineral density (BMD) in spine, femoral neck and total hip by dual-energy X-ray absorptiometry, and dramatic lower BMD in spine by quantitative computed tomography compared with those without VFs (121.4 g/cm3 vs 171.6 g/cm3, $P<0.005$). However, growth hormone (GH) level was higher in patients without VFs. The insulin-like growth factor-1, beta-C-terminal telopeptide and total type I collagen N-terminal propeptide were not comparable in the two groups. Nevertheless, binary logistic regression analysis showed that GH level (OR 1.018; 95% CI, 1.000-1.035; $P=0.050$) and age $\geq$ 50 years/menopause (OR 4.462; 95% CI, 1.489-13.368; $P=0.008$) were two independent predicting factors of VFs.
Conclusion
This study indicates a high prevalence of VFs among patients with acromegaly in China for the first time. Findings in our study also remind us of the need to evaluate bone health in patients with acromegaly, especially in those with higher GH level, older age, or female patients with menopause.

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Cytological, immunological and radiological predictors of the efficacy of first-generation somatostatin receptor ligands (fg-SRLs) in patients with acromegaly

Evgeny Pronin[1], Mikhail Antsiferov[1,2], Alexey Petraikin[3], Vyacheslav Pronin[1,2], Tatiana Alekseeva[1], Anastasia Lapshina[4], Lilia Selivanova[4], Anna Khoruzhaya[3] & Safi Tamaeva[5]
[1]Endocrinological dispensary, Moscow Health Department; [2]Russian Medical Academy of Continuing Professional Education, Ministry of Health of Russian Federation; [3]Scientific and Practical Clinical Center for Diagnostics and Telemedicine Technologies, Moscow Health Department; [4]National Medical Research Center for Endocrinology, Ministry of Health of Russian Federation; [5]I. M. Sechenov First Moscow State Medical University (Sechenov University), Ministry of Health of Russian Federation

Taking into account heterogeneity of somatotrophic tumors (STs), intragroup differential diagnostics is of practical importance, since it allows to predict scenario of acromegaly clinical course, as well as the efficacy of secondary drug therapy (DT).
The aim of this study was to determine prognostic power of cytological, immunological&radiological predictors of sensitivity/resistance to fg-SRLs in patients with pure somatotropinomas.
Materials and Methods
A retrospective morphological&radiological analysis was carried out in 83 (30m) patients who achieved/did not achieve [IGF-1 index (IGF-1/ULN) >1] acromegaly control against background of long-term secondary DT by fg-SRLs. Immunohistochemical analysis (IHA) included determination of antibodies to GH, Ki-67, CAM5.2, SSTR2& 5. Proportion of cells with presence of fibrous bodies (FB) was ranked according to scores 1-3 (1 – absence, 2 – $<70\%$ of cells, 3 – $>70\%$ of cells). Additionally, MRI recordings were reanalyzed with quantification of relative tumor signal intensity (RTSI) by comparing the area of interest with gray matter of the brain on T2-weighed MRI (T2-WI). Data obtained were compared with final results of fg-SRLs treatment.
Results
IHA revealed immunophenotypes of densely&sparsely granulated somatotrophic tumor (DGST&SGST) were identified in 41&42 patients, respectively. Microscopy with H&E staining identified several cytological variants of pure somatotropinomas. Among DGSTs,19 (46%) patients had eosinophilic tumors (ETs),22 (54%) – mixed tumors of eosinophilic&chromophobic cells [intermediate type of tumors (ITTs)]. Among SGSTs,29 (66%) patients had chromophobic tumors (CTs),11 (27%) – ITTs and 2 (7%) – ETs. ETs were distinguished by larger number of secretory cells and SSTR2 expression, as well as by smaller initial tumor volume, low proliferative activity and minimal presence of FB in cells. CTs, on the contrary, were distinguished by their larger size, low SSTR2 expression, higher proliferative activity and pronounced presence of FB in cells. ITTs demonstrated intermediate characteristics of expression varying degrees depending on affiliation with DGSTs/SGSTs. When assessing RTSI, it was shown ETs demonstrated hypointense, ITTs – isointense and CTs – hyperintense signal on T2-WI. As for DT results, with similar initial values of IGF-1 index, maximum dose and treatment duration, patients with ETs, ITTs&CTs had drug remission, partial&complete resistance to fg-SRLs, respectively (Table).
Conclusion
Determination of RTSI on T2-WI adds to IHA data, allows to clarify clinicopathological characteristics of STs and identify patients who are known to be sensitive/resistant to fg-SRLs treatment.

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Daytime sleepiness and health-related quality of life in patients with childhood-onset craniopharyngioma

Laura Verena Mann-Markutzyk[1], Julia Beckhaus[1,2], Jale Oezyurt[3], Carsten Friedrich[1] & Hermann Müller[1]
[1]University Children's Hospital, Carl von Ossietzky Universität Oldenburg, Department of Pediatrics and Pediatric Hematology / Oncology, Klinikum Oldenburg AöR, Oldenburg, Germany; [2]Carl von Ossietzky Universität Oldenburg School VI - School of Medicine and Health Sciences, Division of Epidemiology and Biometry, Oldenburg, Germany; [3]Carl von Ossietzky Universität Oldenburg School IV - School of Medicine and Health Sciences, Biological Psychology Lab, Department of Psychology, Oldenburg, Germany

Background
Adamantinomatous craniopharyngioma (CP) is a rare embryonal malformation originating from remnants of the craniopharyngeal duct and located in the sellar and/or parasellar area. Overall survival rates are high (92%), but frequently quality of life (QoL) is severely impaired in patients with CP involving hypothalamic structures. Tumor- and/or treatment-related hypothalamic lesions result in disturbances of circadian rhythms including increased daytime sleepiness.
Patients and Methods
After a median follow-up interval of 10 years (range: 1-39 years), 119 patients (63 female / 56 male) with CP, recruited in KRANIOPHARyNGEOM 2000/2007 and KRANIOPHARyNGEOM Registry 2019 between 2000 and 2022, were analysed for daytime sleepiness by Epworth scale (ES) and for QoL by EORTC QLQ-C30 questionnaire.
Results
CP patients ($n=85$) with pathologically increased ES score (ES score >12) had worse QoL ($P=0.003$), when compared with CP patients with normal ES score ($n=34$). Pathologically increased daytime sleepiness (ES score) was negatively

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	Tumor volume (cm^3)	Antibodies to GH (%)	Ki-67 (%)	% cells with FB (scores)	SSTR2 (IRS scores)	RTSI on T2-WI (%)	IGF-1 index baseline	IGF-1 index final
ET	2.6±5.9	86.7±12.7	3.9±2.2	1.2±0.4	10.8±2.3	-27.0±15.5	3.1±1.0	0.95±0.34
ITT	3.8±5.7	73.1±29.1	4.5±3.4	1.9±0.8	8.7±3.5	-4.0±20.8	2.7±0.9	1.14±0.56
CT	10.1±11.6	36.7±16.5	8.9±5.4	2.9±0.4	5.7±3.6	20.6±22.9	2.7±0.9	1.65±0.8
p	$p^{1-2}=0.48$ **$p^{1-3,2-3}<0.05$**	**<0.05**	$p^{1-2}=0.495$ **$p^{1-3,2-3}<0.05$**	**<0.05**	**<0.05**	**<0.05**	N/A	$p^{1-2}=0.3458$ **$p^{1-3,2-3}<0.05$**

correlated with QoL ($r = -0.395$; $P < 0.001$). Surgical hypothalamic lesions (71% of patients) were associated with higher ES scores, wheras such impact could not be observed for presurgical hypothalamic involment of CP (73% of patients).
Conclusion
As increased daytime sleepiness plays an important role for QoL in survivors of CP, treatment of disturbances of circadian rhythms with medication such as central stimulating agents is recommended. For prevention of increased daytime sleepiness, hypothalamus-sparing surgical treatment startegies should be considered as state of the art in patients with CP.

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A case of type 2 diabetes masked by insulinoma

Adrian Li[1] & Samira Khalilova[2,3]
[1]Princess Royal University Hospital, United Kingdom; [2]Princess Royal University Hospital, Diabetes and Endocrinology, Orpington, United Kingdom; [3]

Introduction
Insulinomas are the most common functioning endocrine neoplasms of the pancreas. 53% of patients are diagnosed within five years of experiencing their first symptoms. Surgical resection is the primary treatment modality. However, patients awaiting surgery or who are not surgical candidates have achieved symptomatic relief from medical therapy. Cases of insulinoma masking diabetes has been described but are rare and diabetes often presents following surgery. Here, we describe a case of insulinoma diagnosed four years after symptom onset with unmasking of type 2 diabetes mellitus following initiation of medical treatment.
Clinical case
An 89-year-old woman presented with severe hypoglycaemia, having been found by relatives in bed with neuroglycopenic symptoms. Capillary blood glucose was 1.4 mmol/l. She was given intramuscular Glucagon by paramedics. Upon further questioning, the patient reported having one to two similar episodes of hypoglycaemia per month over the past four years, which she was self-correcting at home or by help of the ambulance service. Pituitary, liver and renal profiles were within normal limits. During the admission, the patient underwent a prolonged fasting test. Although nadir blood glucose achieved was 2.5mmol/l due to significant symptom, hypoglycaemia screen revealed high level of C-peptide 2885 pmol/l (370-1470) though normal insulin(64 pmol/l) and beta-hydroxybutyrate levels (0.1 mmol/l) at hypoglycaemia episode. CT pancreas revealed a 14.5 mm enhancing nodule on the body of the pancreas consistent with a neuroendocrine tumour, which was confirmed by MRI imaging. After discussion at the MDT, the patient was started on diazoxide 50 mg TDS. A dotatate-PET scan was arranged and she was listed for surgery. Blood glucose was in range after starting diazoxide. However, the patient was readmitted after one month with hyperglycaemia (37.1 mmol/l), fever, cough and bilateral pitting oedema. Diazoxide was held and she was commenced on oral antihyperglycaemic agents, and then eventually switched to insulin management. Unfortunately, the patient deteriorated during the admission and passed away.
Discussion
Our case highlights the challenges with the diagnosis of insulinoma and how insulinoma can mask undiagnosed type 2 diabetes. This also highlights the importance of continuing glucose monitoring after starting medical management for insulinoma, even if stable glycaemia is initially achieved.
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Pituitary involvement in familial hemophagocytic lymphohistiocytosis type 5 associated with homozygous mutation in the syntaxin-binding protein-2 gene (STXBP2)

Thin San[1], Diane Bray[1] & Jana Bujanova[1]
[1]University Hospital Southampton NHS Foundation Trust, Department of Diabetes and Endocrinology, Southampton, United Kingdom

35y male presented with extreme fatigue and symptomatic hypogonadism. He had history of multiple infections since childhood due to combined immunodeficiency syndrome and hypogammaglobulinemia, autoimmune haemolytic anaemia, sensorineural deafness, cytopenias, acute hepatitis with hepatosplenomegaly. Liver biopsy (age 15y) showed chronic hepatitis with necrosis. In 2020 (age 32y) he underwent bone marrow biopsy for progressive pancytopenia demonstrating hypercellularity, but no evidence of hemophagocytosis or malignancy. Historical notes revealed history of short stature and delayed puberty presumed to chronic illness (normal pituitary MRI, LH <0.07 iu/l, FSH 0.9 iu/l, testosterone 0.3 nmol/l (10-27.6) and IGF-1 44 mg/l (75-580) at 14y). Brief testosterone replacement at 18y was followed by spontaneous recovery of gonadal axis and pubertal progression to TV 15ml, G5, PH4. Participation in 100,000 Genomes Project at age 32y designed to identify rare genetic disorders through whole genome sequencing revealed homozygosity for STXBP2 c. 1247-1G $>$C pathogenic variant consistent with Familial Hemophagocytic Lymphohistiocytosis type 5 (FHL5), tying up previous issues. On examination he had small stature, hypogonadal appearance, testicular volume 15 mls, height 157 cm, weight 48 kg.
Results
LH 0.5 iu/l, FSH 0.3 iu/l, testosterone <0.4 nmol/l, prolactin 802 mu/l (55.4-276), IGF-1 2.4 nmol/l (9.3-30.7), cortisol-436 nmol/l, fT4 9.2 pmol/l (7.7-15.1), Hb 76 g/l (130-170), platelets 46×10^9/l (150-400), WBC 1.3×10^9(4-11). Patient had no symptoms of arginine vasopressin deficiency (AVP-D). Pituitary MRI showed thickening and enhancement of infundibulum extending to hypothalamus and floor of third ventricle. Anterior gland looked normal and posterior bright spot was absent. Testosterone replacement was commenced with excellent symptomatic response. Macimorelin test to confirm growth hormone (GH) deficiency followed by GH replacement was planned but is delayed due to recent admission with decompensated liver disease.
Discussion
FHL 5 is a rare genetic hyperinflammatory syndrome caused by an uncontrolled immune response mediated by T-lymphocyte, natural killer cells and activated macrophages and infiltration of several organs by activated lymphocytes and macrophages. Pituitary involvement is well reported in other types of histiocytic disorders such as Langerhans cell histiocytosis, but rarely in familial or acquired HLH. The lack of AVP-D symptoms here is unusual. Partial hypopituitarism in this case could have contributed at least partially to significant pancytopenia and it will be interesting to observe, if his cell count improves with hormone replacement. Results three months after staring testosterone showed rise in Hb (76 to 93 g/l), but no change in platelet and white cell count to date.

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P332

Sarcoma of the sphenoid sinus occurring 34 years after fractionated sellar 60Cobalt radiotherapy for acromegaly

Ana Maria Prunariu[1], Mihaela Popescu[2], Sergiu Stoica[3], Mariana Costache Outas[3], Anda Dumitrascu[1] & Monica Livia Gheorghiu[4]
[1]CI Parhon National Institute of Endocrinology, Bucharest, Romania; [2]University of Medicine and Pharmacy of Craiova & Clinical Emergency County Hospital, Craiova, Romania; [3]Brain Institute, Monza Hospital, Bucharest, Romania; [4]C Davila University of Medicine and Pharmacy & CI Parhon National Institute of Endocrinology, Bucharest, Romania

Introduction
Treatment options for acromegaly include surgery or radiation to remove or reduce the size of the tumor and medication to help normalize the hormone levels. While improving the prognosis, patients with acromegaly treated with radiotherapy are at risk of long-term development of secondary malignancies (1-2% at 10-20 years). We report the case of a 55-year old woman diagnosed with high-grade sarcoma of the sphenoid sinus developed 34 years after receiving 60Cobalt external beam radiation therapy for acromegaly.
Case report
The patient was diagnosed with acromegaly from a pituitary macroadenoma at 18 years (1986) and underwent 60Cobalt high voltage fractionated sellar irradiation in 1989 (total dose 6000 r), after which she was treated with Bromocriptine from 1989 to 2014 or a combination of Bromocriptine and Sandostatin LAR from 1998 to 2008. Apart from the modest and stable clinical picture of acromegaly she was asymptomatic, with a slowly decreasing pituitary mass (1.7 to 1.2 cm), but persistently elevated IGF1 levels (1.5 – 1.7 $\times$ ULN). In October 2023 she presented for a recent evidence of asymptomatic tumor increase, without hypopituitarism: a sellar mass of 3/3/1.9 cm, with large infrasellar extension, predominantly on the left side, involving the cavernous segments of the internal carotid arteries and apparently with a large extension into the sphenoidal sinus (Knosp 3b). IGF1 was $1.7\times$ULN. She began treatment with Lanreotide Autogel 120 mg monthly and underwent transsphenoidal surgery. Postsurgery she had a small residual tumor in the left cavernous sinus and stable GH hypersecretion ($1.7\times$ULN) with central hypocortisolism. Histopathology revealed a high-grade

(grade 3) sarcoma of the sphenoid sinus (leiomiosarcoma type). She was referred to an oncologist for radiation therapy but the treatment was postponed. A repeat MRI 2 months after surgery revealed a large invasive and erosive sellar and perisellar inhomogeneous mass (4.4/4.7/4.2 cm). The patient started stereotactic fractionated radiation therapy and was planned for chemotherapy.
Conclusion
Our case fulfills the diagnostic criteria of radiation-induced tumors: it occurred within the irradiated field, a sufficient latency period elapsed between irradiation and secondary tumor occurrence (>30 years) and the secondary tumor was proven to be of a different histological type from the original one. Clinicians should be vigilant about the possibility of post-radiation cranial sarcoma development (notably after conventional radiotherapy), suggested in this case by a tumor re-growth long-term after radiotherapy for acromegaly, not associated with a correspondent increase in hormonal activity.

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P333

Additive effect of combined treatment with the small peptide GH receptor antagonist, AZP-3813, and the somatostatin analog, octreotide, in decreasing IGF1 levels in the rat

Guillaume Ravel[1], Corentin Berardet[1], Clémentine Chalmey[1], Haruaki Kurasaki[2], Tatsuya Tomiyama[2], Patrick Reid[2], David Duracher[1], Rakesh Datta[3], Myriam Aouadi[1] & Michael Culler[3]
[1]Amolyt Pharma, Écully, France; [2]PeptiDream Inc, Kawasaki City, Kanagawa, Japan; [3]Amolyt Pharma, Cambridge, Massachusetts, United States

While somatostatin analogs (SSA) are the primary medical therapy for treatment of acromegaly, they fail to normalize insulin-like growth factor 1 (IGF1) levels in the majority of patients when used as monotherapy. Even in patients with controlled IGF1, growth hormone (GH) levels can remain elevated and induce symptoms by interacting with GH receptors throughout the body. AZP-3813 is a 16-amino acid, bicyclic peptide GH receptor antagonist (GHRA) which has been demonstrated to potently decrease IGF1 in both rats and dogs. To examine the effect of adding AZP-3813 to SSA treatment to decrease IGF1, 8-week old, male, Sprague Dawley rats were implanted subcutaneously with Alzet model 2002 minipumps containing either vehicle or the SSA, octreotide (OCT), at a dose of 20µg OCT/kg/day. Blood samples for IGF1 measurement were collected before, and 48 and 72 hours after pump implantation. Immediately following the 72-hour blood collection, rats from both infusion groups were injected subcutaneously with either vehicle or AZP-3813 at 0.3, 1, 3, 10 or 30 mg/kg ($n=7$/group). A subsequent blood sample was collected 24 hours after the injection of vehicle or AZP-3813, which also corresponded to 96 hours after pump implantation. Plasma levels of IGF1 were assessed by radioimmunoassay. Seventy-two hours after initiating OCT infusion, IGF1 was decreased by -10 ± 3.6%, as compared to baseline, while vehicle-infused rats showed a 2 ± 2.8% increase. Injection of AZP-3813 into the vehicle-infused rats produced a dose-related decrease in IGF1 that was significantly different from baseline with doses from 3 to 30 mg/kg, decreasing IGF1 by -13 ± 2.8 to -29 ± 2.0%, respectively. When AZP-3813 was injected into OCT-infused rats, a clear, additive effect was observed with the same 3 to 30 mg/kg doses of AZP-3813 now producing a dose-related decrease in IGF1 ranging from -23 ± 3.3 to -38 ± 3.4%. The magnitude of the decrease in IGF1 obtained with the 3 mg/kg dose of AZP-3813 combined with OCT infusion was not statistically different from the decrease in IGF1 obtained with the 30 mg/kg dose of AZP-3813 alone in vehicle-infused rats; thus, demonstrating a 10-fold increase in the effectiveness of AZP-3813 when combined with OCT. These results demonstrate the enhanced efficacy of AZP-3813 in decreasing IGF1 when combined with the SSA, OCT, and support the development of AZP-3813 as an add-on treatment for patients inadequately controlled with SSA monotherapy.

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P334

Prognostic value of the pituitary apoplexy score for predicting hormonal and visual recovery of patients with pituitary apoplexy: results from a spanish multicentric study

María Noelia Sánchez Ramírez[1], Carlos Perez[2], Igor Paredes[3], Alberto Acitores Cancela[4], Pablo García Feijoo[2], Cristina Álvares Escolá[5], María Calatayud[6], María Soledad Librizzi[6], Alfonso Lagares[3], Víctor Rodríguez Berrocal[4,7] & Marta Araujo Castro[1,8]
[1]University Hospital Ramón y Cajal, Department of Endocrinology and Nutrition, Madrid, Spain; [2]University Hospital La Paz, Department of Neurosurgery, Madrid, Spain; [3]University Hospital 12 de Octubre, Department of Neurosurgery, Madrid, Spain; [4]University Hospital Ramón y Cajal, Department of Neurosurgery, Madrid, Spain; [5]University Hospital La Paz, Department of Endocrinology, Madrid, Spain; [6]University Hospital 12 de Octubre, Department of Endocrinology, Madrid, Spain; [7]University Hospital Puerta del Sur, Department of Neurosurgery, Madrid, Spain; [8]Institute for Biomedical Research Ramón y Cajal, Department of Endocrinology and Nutrition, Madrid, Spain

Aim
Evaluate the predictive value of the Pituitary Apoplexy Score (PAS) for predicting hormonal and visual recovery after surgery or conservative management of patients with pituitary apoplexy (PA).
Methods
Multicenter retrospective study of patients presenting with clinical PA in three Spanish tertiary hospitals between 2008 and 2022. The PAS was calculated following the UK Pituitary Apoplexy Guidelines Development Group evaluation grid.
Results
A total of 71 patients with PA were included, with a median age of 60 years and 67.6% were male. Most patients had macroadenomas, with the exception of one with microadenoma. A total of 33 cases had a PAS ≥3 and 25 ≥4. Only 16 patients had a Glasgow Coma Scale lower than 15 at diagnosis. There were 20 patients with visual loss, 17 with diplopia and 13 with visual loss and diplopia. Of the whole cohort, 61 patients underwent pituitary surgery and 10 were conservatively managed. After surgery or conservative treatment, 38.5% of the 52 patients with hormonal deficits at diagnosis recovered the pituitary function and 61.2% of the 49 patients with visual involvement at diagnosis had a normal visual function. Based on ROC curve, the optimal threshold in the PAS to identify those patients with a lower probability of visual recovery was 3, and for hormonal recovery was 4. Patients with PAS ≥3 had larger tumors (30.3 ± 9.49 vs 23.7 ± 12.80 mm, $P=0.019$) and panhypopituitarism was four times more common (OR 4.0, 95% CI 1.32 to 12.15) than in patients with PAS <3. The proportion of patients who underwent conservative management did not differ between patients with PAS ≥3 and PAS <3. Patients with a score ≥3 had a probability of non-visual recovery 3.8 times higher than those with a score <3 (OR 3.8, 95% CI 1.01 to 13.96). These differences lost significance after adjusting by tumor size (adjusted OR 3.68, 95% CI 0.96 to 14.07). No differences in the rate of hormonal recovery (OR 0.61, 95% CI 0.19 to 1.93) nor in the rate of visual normalization (OR 0.69, 95% CI 0.22 to 2.19) were observed between patients with a PAS ≥4 and PAS <4.
Conclusion
PAS score equal or greater than 3 seems more accurate than the classical threshold of 4 to identify those patients with PA with a lower chance of visual recovery after surgical/conservative management. This association is related to a larger tumor size in patients with PAS score exceeding 2.

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P335

Cardiovascular disease and gender differences in non-functioning pituitary tumors: preliminary data of a prospective study

Elisa Sala[1], Veronica Lotito[1,2], Giulia Carosi[1], Giulia Del Sindaco[1,2], Roberta Mungari[1], Arianna Cremaschi[1], Angela Pagnano[1,2], Alessandra Mangone[1,2], Emanuele Ferrante[1] & Giovanna Mantovani[1,2]
[1]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [2]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

Background
In the last few decades, the association between pituitary disorders and cardiovascular disease has been demonstrated. Furthermore, the importance of gender as a non-modifiable risk of factor is increasingly emerging.
Methods
We retrospectively analyzed data of 112 patients diagnosed with nonfunctioning pituitary tumor (NFPT) attending the outpatient clinic at our tertiary center. In this study we report only preliminary data of the retrospective analysis, while a subsequent prospective analysis is ongoing.
Results
In our cohort of patients (51M/61F; mean age 58 ± 16 years), males showed a more aggressive presentation with a significantly higher number of macroadenomas and of tumors needing surgery than females ($P=0.04$ and $P=0.03$, respectively). Concerning the presence of pituitary deficits as well, they were significantly more frequent in males compared to females (central hypothyroidism: 45% vs 16%, $P=0.03$; hypogonadism with exclusion of menopausal state:

47% vs 16%, $P<0.01$), hypoadrenalism: 37% vs 19%, $P=0.05$; GH deficiency: 35% 11%, $P<0.01$). In the whole group, 46 patients (41%) had hypertension, 11 (9.8%) cardiovascular ischemic disease while cerebrovascular disease appeared only in 3 (2.6%) patients. Diabetes mellitus was diagnosed in 10 patients (9%), 42 patients (37.5%) presented dyslipidemia, 12 patients (11%) obesity. Comparing male and females, we found a significantly higher presence of cardiovascular morbidities in the male group compared to the female one (hypertension, cardiovascular events and cerebrovascular events, for all $P<0.05$), while concerning metabolic comorbidities no differences were found. Comparing our data to the general Italian population in the same age range we did not find any difference in the female group, while in the NFPT male group a significantly higher percentage of cardiovascular events and hypertension compared to the general population was found ($P=0.04$ and $P=0.01$ respectively; data reported by the Italian National Institute of Statistic - ISTAT).

Conclusion

Our data confirmed that the presence of NFPT is related to cardiovascular complications. In particular, our data showed that NFPT in males have a more aggressive presentation compared to females both in endocrinological and cardiovascular comorbidities. We interestingly reported that males with NFPT present a greater risk of hypertension and cardiovascular disease than the general population of the same age, suggesting the need for a targeted approach with greater surveillance in this specific group of patients.

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P336

Evaluation of new prognostic clinicopathological classification of pituitary adenomas proposed by trouillas *et al*. in patients with giant pituitary adenomas

Barbara Buchalska[1], Wiesław Bonicki[1], Maria Maksymowicz[2] & Jacek Kunicki[1]

[1]The Maria Sklodowska-Curie National Research Institute of Oncology, Department of Neurosurgery, Warsaw, Poland; [2]The Maria Sklodowska-Curie National Research Institute of Oncology, Department of Pathology, Warsaw, Poland

Introduction

In 2013 Trouillas *et al*. reported a new prognostic clinicopathological classification of pituitary adenomas. This classification analyses the impact of the intensity of proliferation and invasiveness of the tumor on patients' prognosis. The aim of the study was to review this new classification in giant pituitary adenomas (GPAs) treated with endoscopic transsphenoidal approach.

Material and methods

The study is a retrospective analysis of a series of 176 patients (66 women and 110 men) treated from the 2007 to 2023 by the endoscopic transsphenoidal surgeries for GPAs (>40mm). The mean age of the patients was 57.0 years (20-81 years), and the mean follow up period was 7.5 years (0-16 years). The patients were divided into the control group without the evidence of disease (EoD) and the study group with EoD.

Results

In the group with EoD the most commonly observed were grade 2a tumors (71.7%), followed by grade 1a (13.3%), 2b (12.4%), and 1b (2.7%). In the control group (with favorable outcomes – no EoD) grades 2a and 1a were reported in similar numbers of patients (46.0% and 41.3% respectively), followed by grade 2b and 1b (both observed in 6.3% of patients). Overall, more invasive or proliferative tumors classified either as grade 2a or 2b were observed in the group with EoD (OR=2.97 and OR=2.09 respectively, $P<0.001$).

Conclusion

Our results indicate that the new classification proposed by Trouillas *et al*. is a reliable tool in predicting prognosis of patients with GPAs.

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P337

Clinical and radiological predictive factors of dopamin agonist resistance in prolactinoma

Sandra Pekic Djurdjevic[1,2], Marko Stojanovic[1,2], Mirjana Doknic[1,2], Dragana Miljic[1,2], Toplica Milojevic[3], Mihailo Milicevic[1,3], Aleksandar Stanimirovic[1,3], Vuk Scepanovic[1,3], Emilija Manojlovic Gacic[1,4], Ivana Cekic[2], Ivan Jevtic[2], Zvezdana Jemuovic[2], Marina Nikolic Djurovic[1,2], Danica Grujicic[1,3], Vera Popovic[1] & Milan Petakov[1,2]

[1]Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [2]Clinic for Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Center of Serbia, Department of Neuroendocrinology, Belgrade, Serbia; [3]Clinic for Neurosurgery, University Clinical Center of Serbia, Belgrade, Serbia; [4]Institute of Pathology, Belgrade, Serbia

Background

A subset of patients with prolactinomas does not respond satisfactorily to first-line medical therapy with dopamine agonists (DA). DA resistance is defined as failure to normalize prolactin (PRL) levels and/or to achieve ≥50% reduction in maximal tumor diameter under maximally tolerated doses (or a weekly cabergoline dose of ≥3mg). The predictive factors for DA resistance are male gender and tumor invasiveness.

Aim

To characterize patients with DA resistant prolactinoma patients.

Methods

We retrospectively analysed clinical, hormonal and radiological features, management and outcome of DA therapy of 527 patients with prolactinoma who were treated at the Department of Neuroendocrinology of a tertiary hospital between 2005 and 2023.

Results

Thirteen prolactinoma patients with cabergoline resistance were identifed (2.5%). The mean age at diagnosis was 36.5±3.3years (range: 17-64) and seven patients (53.8%) were male. PRL level at baseline was 70.110±41.425mIU/l (range: 1796-505.978). The average tumor size was 27.3±7.0mm (range: 9-58), ten (76.9%) were macroadenomas. Of ten macroadenomas, all were invasive and three were giant tumors (>40mm). Males had larger tumors than females (40.0± 6.8mm vs 10.3±0.9mm; $P<0.001$) and higher PRL levels at baseline (137.562±75.700 vs 2657±380mIU/l; $P<0.01$) Prolactinomas were graded as KNOSP-3 in 2 (15.4%), and KNOSP-4 in 3 (23.1%) patients, more frequent in males ($P<0.01$). The mean maximal cabergoline dose was 4.1±0.4 mg/week (range: 3-7), higher in males (5.0±0.6 mg/week vs 3.0±0.8 mg/week; $P<0.01$). The median follow-up was 86.8±17.0months (range: 18-233). Nine patients were treated only with cabergoline in escalating doses, two underwent transsphenoidal surgery combined with cabergoline, one underwent surgery and radiotherapy combined with cabergoline and one patient was treated with all these modalities plus temozolomide. PRL level after therapy (only cabergoline, or multimodal therapy) was 9383±7099mIU/l (range: 400-94.000). Two patients developed apoplexy during cabergoline therapy and two patients had nasoliquorrhea. One patient treated with multimodal therapy and temozolomide died after eighth operation. At the last visit five patients had controlled PRL levels and most of them had a stable tumor size.

Conclusion

The prevalence of cabergoline resistance in our series was around 2.5%. Our data support a male gender, large tumor size and tumor invasiveness as the risk factors for DA resistance. We were able to control 5/12 (41.6%, 1 patient died) of resistant prolactinomas. Resistant prolactinomas usually require a multi-modal treatment strategy.

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Efficacy of pasireotide treatment in acromegaly: a systematic review and meta-analysis

Turkan Aliyeva[1], Juliana Muniz[2], Gustavo Meira[3], Sarah Firdausa[4] & Lubna Mirza[5]

[1]Özel Koru Hastanesi, Internal Medicine, Ankara, Turkey; [2]Kliniken Schmieder Heidelberg, Heidelberg, Germany; [3]Universidade Católica de Brasília - Câmpus Taguatinga, Brazil; [4]Syiah Kuala, Indonesia; [5]Norman Regional Hospital, Norman, United States

Background

Acromegaly is an uncommon chronic endocrine disorder which is associated with considerable comorbidities. Many patients fail to achieve biochemical control with current medical therapies, including surgery and first-generation somatostatin analogs. We aimed to perform a systematic review and single-arm meta-analysis to evaluate the efficacy of the multi-receptor ligand somatostatin analog Pasireotide in patients with acromegaly.

Methods

We systematically searched PubMed, EMBASE, and Cochrane databases for studies that assessed the efficacy of Pasireotide in patients with acromegaly and reported the outcomes of (1) biochemical control and its composite indicators; (2) normalized IGF-1 level and (3) GH< 2.5 mg/l. Random effect models were used for all Statistical analysis, which were conducted using R software. Heterogeneity was assessed with I2 statistics.

Results

We included twelve studies with a total of 664 patients: eight clinical trials and four observational cohorts. The overall population consisted of 67% of

inadequately controlled acromegaly patients. In a pooled analysis, the biochemical control rate was 30% (95% CI: 16; 49). The frequency of normalization of IGF-1 and reduction of GH level were 45% (95% CI: 33; 57) and 34% (95% CI: 24; 45) respectively. A long-term effect (>12 months) of Pasireotide on biochemical control was observed, with a rate of 45% (95% CI: 26; 65). The most commonly reported adverse events were hyperglycemia in 42% (95% CI: 25; 59) and gastrointestinal disturbances in 41% (95% CI: 16; 71) of patients. Moreover, Pasireotide treatment was associated with a 31% (95% CI: 22; 41) incidence of new-onset diabetes mellitus.

Conclusion

Our findings suggest that Pasireotide has superior efficacy in patients with acromegaly. Although a high rate of hyperglycemic adverse events and diabetes mellitus related to treatment were observed, most of them were manageable.

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P339

T2-weighted MRI signal intensity of a somatotroph PitNETs-assessed with quantitative and qualitative methods- how our predictions are verified in the histopathological examination?

Magdalena Godlewska[1], Anna Grochowska[2], Anna Bogusławska[1], Grzegorz Zielinski[3], Dariusz Adamek[4], Maria Maksymowicz[5], Alicja Hubalewska-Dydejczyk[1] & Aleksandra Gilis-Januszewska[1]
[1]Jagiellonian University Medical College, Department of Endocrinology, Cracow, Poland; [2]Jagiellonian Uniersity Medical College, Department of Radiology, Cracow, Poland; [3]Military Institute of Medicine, Department of Neurosurgery, Warsaw, Poland; [4]Jagiellonian University Medical College, Department of Pathomorphology, Cracow, Poland; [5]Maria Sklodowska-Curie National Research Institute of Oncology, Department of Cancer Pathomorphology, Warsaw, Poland

Aim

To investigate T2-signal intensity (SI) and histopathological characteristics of the somatotroph PitNETs (S-PitNET).

Methods

41 out of 109 consecutive patients with newly diagnosed acromegaly and available histopathological results were included. 36 results contained the electron microscope examination. Tumors were divided into 3 SI groups: hyperintensive (HyPER), isointensive (ISO) and hypointensive (HyPO). SI was assessed qualitatively using Visual Method (visual comparison between S-PitNET and white and grey matter of the temporal lobe (WM and GM, respectively) and quantitatively by measurement of SI within the Region of Interest in the solid part of S-PitNET and in the WM and GM. Relative Signal Intensity (rSI, calculated ratio of S-PitNET's SI and the SI of GM) ≤ 0.8 classified S-PitNET as HyPO, >0.8 but <1.2 as ISO, ≥ 1.2 as HyPER. Three Tissue Method classified tumors with SI equal or lower to WM as HyPO, with SI equal or higher than GM as HyPER, while the remaining tumors were classified as ISO.

Results

31.7% of tumors expressed only GH, 17.1% co-expressed GH and PRL, other S-PitNETs expressed GH and at least one hormone other than PRL (the most frequent combination: GH, PRL, alpha subunit). We found no differences between HyPER, ISO and HyPO in hormone expression. In electron microscope 58.3% of tumors were classified as densely granulated, 27.8% as sparsely granulated and 13.9% as bihormonal. According to Visual Method and rSI HyPER and ISO had both dense and sparse granulation. Bihormonal tumors presented as HyPO (60-80%) and ISO (20- 40%). According to Three Tissue Method, no HyPO specimens had sparse granulation. Ki-67 $<1\%$ was the most frequent diagnosis among all tumors. None of the HyPO had Ki-67 $\geq 3\%$. Detailed results are depicted in Table 1.

Table 1. Results of electron microscope verification

Tumor type	Densely granulated	Sparsely granulated	Bihormonal	
		Visual Method		
HyPER	72.7%	27.3%	0%	$P=0.159$
ISO	50%	41.7%	8.3%	
HyPO	53.8%	15.4%	30.8%	
		rSI		
HyPER	71.4%	28.6%	0%	$P=0.514$
ISO	52.9%	35.3%	11.8%	
HyPO ($n=12$)	58.3%	16.7%	25%	
		Three Tissue Method		
HyPER	64.7%	29.4%	5.9%	$P=0.056$
ISO	53.8%	38.5%	7.7%	
HyPO	50%	0%	50%	

Conclusion

Tumors manifesting as HyPER or ISO are verified in histopathological examination as both densely and sparsely granulated, regardless of SI assessment method. No HyPO tumor had sparse granulation. Interestingly, no bihormonal tumor presented as HyPER.

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Improvements in diabetes and hypertension were sustained over long-term osilodrostat treatment in patients with Cushing's disease: A pooled analysis of LINC 3 and LINC 4

Rosario Pivonello[1], Maria Fleseriu[2], John Newell-Price[3], Monica Gadelha[4], Richard Auchus[5], Richard Feelders[6], Andre Lacroix[7], Shimatsu Akira[8], Przemysław Witek[9], Marie Bex[10], Andrea Piacentini[11], Alberto Pedroncelli[12,13] & Beverly M.K. Biller[14]
[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]Oregon Health & Science University, Pituitary Center, Departments of Medicine and Neurological Surgery, Portland, OR, United States; [3]University of Sheffield, School of Medicine and Population Health, Sheffield, United Kingdom; [4]Medical School and Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Neuroendocrinology Research Center, Endocrinology Section, Rio de Janeiro, Brazil; [5]University of Michigan, Department of Pharmacology and Division of Metabolism, Endocrinology and Diabetes, Ann Arbor, MI, United States; [6]Erasmus Medical Center, Department of Internal Medicine, Endocrine Section, Rotterdam, Netherlands; [7]Centre hospitalier de l'Université de Montréal, Montreal, Canada; [8]Omi Medical Center, Kusatsu, Japan; [9]Medical University of Warsaw, Department of Internal Medicine, Endocrinology and Diabetes, Warsaw, Poland; [10]University Hospitals Leuven, Department of Endocrinology, Leuven, Belgium; [11]Recordati SpA, Milan, Italy; [12]Recordati AG, Basel, Switzerland; [13]Camurus AB, Lund, Sweden; [14]Massachusetts General Hospital, Neuroendocrine and Pituitary Tumor Clinical Center, Boston, MA, United States

Introduction

Diabetes mellitus (DM) and hypertension are common comorbidities that pose significant clinical burden in Cushing's syndrome patients and may be improved by normalising cortisol. In two Phase III trials (LINC3 [NCT02180217]; LINC4 [NCT02697734]), osilodrostat, a potent oral 11β-hydroxylase inhibitor, provided reductions in cortisol and improved clinical manifestations of hypercortisolism in most Cushing's disease (CD) patients. Here, we describe changes in glycaemic parameters and blood pressure (BP) in a pooled patient population, according to baseline hypertensive and diabetic status.

Methods

LINC3 comprised a 48-week (W) core phase, including an 8W randomised-withdrawal phase for eligible patients. LINC4 included an initial 12W, double-blind, randomised, placebo-controlled period, then 36W of open-label osilodrostat. Both studies included an optional extension. Baseline DM was defined as prior diagnosis, taking antidiabetic medication, HbA_{1c} $\geq 6.5\%$, and/or fasting plasma glucose (FPG) ≥ 126 mg/dl. Baseline hypertension was defined as prior diagnosis, taking antihypertensive medication, and/or systolic/diastolic BP (SBP/DBP) $>130/>90$mmHg. Data were pooled in a secondary exploratory analysis for all patients with data at baseline and W72; periods whereby patients received placebo are excluded. No formal statistical testing was performed; all analyses are descriptive.

Results

Of patients with baseline DM ($n=84/210$; 40.0%), mean (SD) FPG and HbA_{1c}, respectively, decreased from 90.9 (17.3) mg/dl and 5.8 (0.8)% at baseline to 87.1 (9.9) mg/dl and 5.4 (0.6)% at W72 for those not receiving antidiabetic treatment during the study, and decreased from 118.1 (33.5) mg/dl and 6.9 (1.0)% at baseline to 102.7 (27.6) mg/dl and 6.1 (0.8)% at W72 in those receiving antidiabetic medication. Higher baseline FPG and HbA_{1c} was associated with greater improvements at W72, demonstrated by a negative correlation between change in FPG and HbA_{1c} from baseline to W72 and baseline FPG and HbA_{1c} ($r=-0.60$ and -0.68, respectively; $P<0.0001$). Most patients ($n=174/210$; 82.9%) had baseline hypertension. ~50% of patients with baseline SBP >130mmHg had SBP ≤ 130mmHg at W72, and ~60% with baseline DBP >90mmHg had DBP ≤ 90mmHg at W72. Higher baseline SBP/DBP was associated with greater improvements at W72, demonstrated by a negative correlation between change in SBP/DBP from baseline to W72 and baseline SBP/DBP ($r=-0.69/-0.64$; $P<0.0001$).

Conclusion

DM severity and prevalence of hypertension reduced over long-term osilodrostat treatment. Patients with higher baseline FPG, HbA_{1c}, SBP and DBP experienced the greatest reductions in these parameters at W72. These findings highlight the importance of treating hypercortisolism to improve comorbidities in CD patients.

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P341

A case of meningitis mimicking pituitary macroadenoma

Natalia Ostrowska-Mrozowska[1], Sonia Kaniuka-Jakubowska[1], Olivia Cyran-Stańczak[1] & Renata Świątkowska-Stodulska[1]
[1]Department of Endocrinology and Internal Medicine, Faculty of Medicine, Medical University of Gdansk, Poland,

The spectrum of lesions in the sellar and parasellar region includes a wide range of diseases, from the most common adenoma to various non-adenomatous lesions i.a. empty sella syndrome, stroke and congenital conditions. We identified a case of meningitis in which the images initially suggested the presence of a pituitary macroadenoma. The 45-year-old patient without chronic diseases was admitted to the Department of Neurology due to severe headaches and vomiting that had woken him up the night before. Neurological examination showed no signs of focal CNS damage, meningeal symptoms were negative. A non-contrast CT brain revealed in the sellar region a heterogeneous, hypodense lesion 18x18mm. The diagnostics were extended to head MR which showed a mass in the sella 22x19x19mm, with a heterogeneous high signal, intensity, focally in the central and slightly peripheral part, enhanced after contrast administration. A suspicion of pituitary macroadenoma or Rathke's pouch was made. Additionally, the image of dura mater suggested meningitis and inflammatory changes in the nasal sinuses. CSF analysis revealed lymphocytic or viral meningitis. The patient reported the deterioration of vision in the right eye and the temporal disturbances in visual field examination in this eye were confirmed. Blood tests revealed increased inflammatory markers, intravenous antibiotics were initiated, leading to a favourable clinical outcome. Initial analysis of pituitary function revealed normal low morning cortisol concentration (166nmol/l) with a normal ACTH concentration (25.7 pg/ml) preserved other pituitary axes, however, the supplementation of the hydrocortisone has been implemented. The patient was referred to our department. Pituitary MR was performed which confirmed previous intrasellar and parasellar meningitis, complicated by bleeding into the encapsulated space in the sella and post-hemorrhagic areas in the suprasellar and intrasellar region; intrasellar lesions had decreased from 21mm to 5mm. The sellar diaphragm remained in post-inflammatory conglomerates with the optic chiasm, which remained deformed and pulled strongly downwards. The optic chiasm showed a heterogeneous increase in T2 weighted signal. In this situation, there were no indications for neurosurgery. In subsequent follow-up imaging examinations, further regression of the sellar region lesions occurred, with no progression in the involvement of the optic nerves. This case illustrates an atypical type of meningitis mimicking a pituitary macroadenoma. This proves that due to the complex nature of pituitary diseases, most patients require coordinated care. It shows the need for an integrated, multidisciplinary approach to the diagnosis, assessment and treatment of patients with pituitary disorders.

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P342

Is histological subtyping important in the prognostication of acromegaly?

Prishila Fookeerah[1,2], Winny Varikatt[3,4], Mark Dexter[4,5], Sue Lynn Lau[1,2] & Mark McLean[1,2]
[1]Westmead Hospital, Diabetes and Endocrinology, Sydney, Australia; [2]Western Sydney University, School of Medicine, Sydney, Australia; [3]Westmead Hospital, Tissue Pathology and Diagnostic Oncology, Sydney, Australia; [4]University of Sydney, Westmead Clinical School, Sydney, Australia; [5]Westmead Hospital, Neurosurgery, Sydney, Australia

Background
Pituitary neuroendocrine tumours (PitNETs) that cause acromegaly are often collectively categorised as 'growth hormone (GH) secreting adenomas'. The 2022 WHO classification however identifies 7 histological variants that can secrete GH: densely granulated somatotroph (DGST), sparsely granulated somatotroph (SGST), mammosomatotroph (MST), mixed somatotroph and lactotroph (MSLT), mature plurihormonal PIT1 (MPPT), immature PIT1 (IPT) and acidophil stem cell (ASCT) tumours. Although differences in clinical behaviour have been outlined in studies comparing select tumour subgroups, there is currently insufficient evidence to include tumour histotype in therapeutic or prognostic algorithms for acromegaly. We analysed all tumour variants of acromegaly to assess differences in clinical characteristics.
Methods
We conducted a retrospective assessment of all PitNETs resected from 2011 to 2018 at Westmead Hospital. Tumour specimens underwent assessment for expression of transcription factors, co factors, anterior pituitary hormones, cytokeratin and somatostatin receptor (SSTR) 2 and 5 using immunohistochemistry. All PitNETs were then assigned a morphological subtype according to the 2022 WHO classification. Variants that can cause acromegaly were selected. Multilineage PIT1 and SF1 tumours (MPST) were identified as an eighth distinct subtype that causes acromegaly and included in our analysis. Correlation was sought with clinical data from medical records.
Results
Of the 47 tumours, 40 (85.1%) had clinical or biochemical acromegaly at presentation. Tumour size differed by histological type; SGSTs (mean diameter 23.4 $\pm$5.9mm) larger than DGSTs (13 $\pm$7.1mm, $P=0.03$) or MSTs (11.8 $\pm$ 7.6mm, $P=0.002$). The number of therapeutic interventions after initial surgery was not different between SGST and MST groups (1.11 $\pm$0.93 vs 1.00 $\pm$0.82, $P=0.40$), but was lower for the MPST group (0.29 $\pm$0.49, $P=0.03$ vs SGST). At 3 months after surgery, normalisation of IGF-1 was achieved in a higher proportion of MPST than SGST (66.7% vs 14.3%, $P=0.05$). 17 PitNETs (42.5%) required treatment with somatostatin receptor ligands (SRL), 29.4% were SGST and 29.4% were MST. Over a mean follow up duration of 75 months, tumour regrowth or recurrence was observed in 25% of SGST and 40% of IPT, but was not seen with any other variants. Proportion of 'high-risk' variants (SGST and IPT) needing radiotherapy was higher than other groups combined (42.9% vs 9.1%, $P=0.01$).
Conclusion
Our data suggests that there are differences in clinical behaviour and outcome among histological variants that cause acromegaly. Tumour histotype potentially has a role in directing individualised management plans for acromegaly and may be useful for prognostication.

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P343

Comparative analysis of giant and 'nearly giant' pituitary adenomas

Barbara Buchalska[1], Wiesław Bonicki[1], Maria Maksymowicz[2] & Jacek Kunicki[1]
[1]The Maria Sklodowska-Curie National Research Institute of Oncology, Department of Neurosurgery, Warsaw, Poland; [2]Maria Sklodowska-Curie National Research Institute of Oncology, Department of Pathology, Warsaw, Poland

Introduction
Giant pituitary adenomas (GPAs) are traditionally defined as the tumors with the greatest diameter at or above 40 mm. However, some clinical series of GPAs include tumors with maximal diameter of 35 to 40 mm, and those tumors can be named 'nearly giant' pituitary adenomas (nearly GPAs). The treatment of GPAs is challenging and has a higher risk of complications due to the size and complex anatomical relations. This study was conducted to compare GPAs and nearly GPAs treated in The Maria Sklodowska-Curie National Research Institute of Oncology.
Material and methods
The study is a retrospective analysis of case series of GPAs and nearly GPAs treated with an endoscopic transsphenoidal approach in The Maria Sklodowska-Curie National Research Institute of Oncology from 2007 to 2023. The first study group included 176 patients with GPAs (66 women, 110 men), and the second group comprised 32 patients with nearly GPAs (6 women, 26 men). The mean age of patients at the time of surgery and observation time in the first group were 57.0 and 7.5 years, respectively, and in the second group 54.9 and 6.7 years.
Results
Patients with nearly GPAs had total resections more frequently (75.0%) compared to patients with GPAs (42.0%). The most common histopathologic diagnosis was the gonadotroph adenoma in both groups. GPAs more commonly showed invasion of the adjacent structures (73.3%) than nearly GPAs (46.9%). The treatment of GPAs was more often associated with complications. Moreover, patients with GPAs experienced serious complications (hematoma, hydrocephalus, coma, death), which were not observed in the nearly GPAs group.
Conclusion
GPAs differ significantly from nearly GPAs in clinical and morphological aspects. The diagnosis of a pituitary adenoma with a maximum diameter above 40 mm is associated with a poorer prognosis and should prompt a more intense treatment.

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P344

Growth hormone potently stimulates fibroblast activation protein activity and collagen turnover – a prospective study in newly diagnosed patients with acromegaly before and after treatment

Amanda Bæk[1,2], Anne Kathrine Pedersen[2], Mai Arlien-Søborg[1], Niels Jessen[2], Mette Bjerre[1,3] & Jens Otto Jørgensen[1]

[1]Aarhus University, Department of Clinical Medicine - The Department of Endocrinology and Diabetes, Aarhus, Denmark; [2]Aarhus University, Department of Clinical Medicine - SDCA-Steno Diabetes Center Aarhus, Aarhus, Denmark; [3]Aarhus University, Department of Clinical Medicine - Medical Research Laboratory, Aarhus, Denmark

Background
GH potently stimulates collagen turnover which underlies its anabolic effects on bone in children, whereas it may promote fibrosis in adults. Fibroblast activation protein-α (FAPα) is involved in collagen turnover by its collagen-cleaving and fibroblast-stimulating activity, which predominantly is expressed in association with fibrosis. FAPα also cleaves and inactivates fibroblast growth factor 21 (FGF21), a multi-faceted metabolic hormone. We have previously recorded elevated FAPα protein levels in uncontrolled acromegaly but it remains to be studied if FAPα activity is GH-dependent.
Aim
To prospectively measure serum FAPα levels and activity, FGF21, and collagen turnover biomarkers in patients with acromegaly at time of diagnosis and after treatment.
Methods
Using immunoassays and an activity assay, we measured FAPα levels and activity, total and intact FGF21, PINP, PIIINP and CTx in serum from 15 acromegaly patients before and after treatment.
Results
Serum FAPα protein levels (μg/l) and enzymatic activity (RFU/min) decreased by 35% (101.7 ±9.4 [before] vs 63.1 ±5.9 [after] (mean ±SEM); $P<0.001$) and 34% (373.2 ±26.5 [before] vs 248.3 ±14.9 [after]; $P<0.0001$) after treatment, respectively. Serum PINP, PIIINP and CTx levels decreased by 60% ($P<0.001$), 69% ($P<0.01$) and 53% ($P<0.001$) after treatment, respectively. The change in FAPα protein levels before and after treatment correlated positively with the change in FAPα activity before and after treatment ($r=0.74$; $P<0.01$).
Conclusion
1. Our study document for the first time that GH stimulates FAPα activity in human subjects *in vivo*.
2. The concomitant increase in markers of collagen turnover and the lack of change in FGF21 suggest that GH-driven FAPα activity predominantly involves collagen breakdown.
3. FAPα is a novel and promising biomarker of GH/IGF-I activity and may be causally linked to GH-induced fibrosis.

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P345

Expression pattern of select cell proliferation and apoptotic markers in non-functioning pituitary adenomas predictive of tumour growth/recurrence: a pilot project

Andrea Hebb[1], Sidney Croul[2], Jae Han[1], Emad Massoud[3], Lisa Tramble[4], Syed Imran[4] & David Clarke[1]
[1]Dalhousie University, Division of Neurosurgery; [2]Dalhousie University, Division of Pathology; [3]Dalhousie University, Division of Otolaryngology-Head and Neck Surgery; [4]Dalhousie University, Division of Endocrinology & Metabolism

Introduction
While there is a significant risk of recurrence in nonfunctioning pituitary adenoma (NFPA) after surgery, it is challenging to predict which NFPAs will recur based solely on routine histopathology. To better understand markers of recurrence, we assessed the established tumor markers linked to aggressive tumor behavior including X-linked IAP (XIAP), the most potent inhibitor of the apoptosis protein family, vascular epithelial growth factor (VEGF) which facilitates angiogenesis and tumour cell proliferation as well as leptin.
Purpose
The purpose of this pilot study was to determine if the expression pattern of select cell proliferation and apoptotic markers in NFA is predictive of tumour quiescence and growth/recurrence compared to normal pituitary tissue in a clinical population.
Methods
Informed consent was obtained from patients during a clinic visit. Tissue microarrays were constructed from paraffin-embedded tissue microarrays (representing pituitary tissues from growing or stable tumours, or normal controls). Immunohistochemical staining using mouse anti-human XIAP monoclonal antibody (BD Biosciences); VEGF monoclonal antibody (Dako); leptin polyclonal antibody (R & D systems) and leptin receptor (Abcam) was completed. Slides were analyzed using Aperio Image Scope-pathology slide viewing software. Chi square and Fishers exact test ($P<0.05$) were employed.
Results
Tissue samples from 98 patients with NFA (52 males) were analyzed. TMA analysis of normal pituitary tissue ($n=24$) revealed low levels (weakly positive) of XIAP relative to VEG-F, leptin, and leptin-receptor. VEG-F levels and leptin were moderately positive, while staining for leptin receptor strongly positive in normal pituitary tissue ($P<0.0001$). XIAP levels in overall tumor tissue revealed moderate and strongly positive staining of XIAP relative to the low staining present in normal pituitary tissue ($P<0.00001$). VEGF levels in overall tumor tissue were moderately positive in normal pituitary tissue and weakly positive in tumor tissue ($P<0.00001$). The pattern of leptin and receptor staining in normal tissue was moderately to strongly positive while there was more variability amongst tumor samples ($P<0.05$). Analyses are ongoing to correlate the pattern of staining with clinical and tumor variables.
Conclusion
Preliminary data show altered expression of markers in tumors compared with normal pituitary tissue. Further clinical data are being analyzed to assess the impact of these changes on recurrence.

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P346

Incidence of nephrogenic diabetes insipidus during prolonged sevoflurane sedation in the intensive care unit: a retrospective analysis and predictive model

Joost Glissenaar[1], Bastiaan Sol[2], Karel Van Eeckhout[1], Lynn De Mey[3], Bert Bravenboer[4], Kurt Barbé[5] & Jeroen M.K. de Filette[6]
[1]University Hospital of Brussels, Anesthesiology and Perioperative Medicine, Brussels, Belgium; [2]AZ Alma, Endocrinology, Eeklo, Belgium; [3]University Hospital of Brussels, Nuclear Medicine, Brussels, Belgium; [4]University Hospital of Brussels, Endocrinology, Brussels, Belgium; [5]Free University Brussels (VUB), Research group Biostatistics and Medical Informatics, Brussels, Belgium; [6]CHU Brugmann, Endocrinology, Brussels, Belgium

Study Objective
Sevoflurane is a halogenated inhalational anesthetic increasingly used in the intensive care unit (ICU) for its potentially beneficial effects in patients with acute respiratory distress syndrome. However, safety data on prolonged sevoflurane sedation are lacking and cases of diabetes insipidus (DI) have been observed. The objective of this study was to assess the incidence and risk factors of DI during prolonged sevoflurane sedation.
Design & Setting
A single-center retrospective analysis in the ICU of the University Hospital of Brussels (March 2013 - March 2021).
Patients
One hundred and six (106) ICU patients receiving prolonged sevoflurane sedation were divided into three groups: 1) no DI, 2) suspected for DI (polyuria >40ml/kg/24h and hypernatremia >145 mmol/l but without available urine sampling) and 3) confirmed DI (polyuria and hypernatremia with urine osmolality <300 mOsm/kg [complete DI] or between 300-600 mOsm/kg [partial DI]).
Measurements
The electronic medical records of the University Hospital of Brussels were retrospectively explored. Logistic regression modelling was used to build a predictive model for DI in patients with prolonged sevoflurane sedation.
Main Results
Twenty-two (22/106; 20.8%) patients developed polyuria-hypernatremia. DI was suspected in 13 patients (12.3%) but could not be confirmed due to the absence of urine sampling. DI was confirmed in 9 patients (8.5%), of which 5 were partial and 4 complete. Desmopressin test was performed in 5/9 patients of which none responded, diagnostic for nephrogenic DI. Sevoflurane was administered for a median duration of 96, 155 and 166 hours (p 0.003), at a median end-tidal concentration of 1.11, 1.25 and 1.22% (p 0.09), respectively. The variables identified in the logistic regression model were: higher sevoflurane end-tidal concentration (p 0.02), longer sevoflurane exposure time (p 0.07) and admission for COVID-19 (p 0.16). A cutoff value of >3 for the linear discriminator was predictive for suspected/confirmed DI.
Conclusion
DI occurs frequently during prolonged sevoflurane sedation in the ICU. Intensive care physicians should be vigilant for the development of polyuria-hypernatremia. Monitoring of plasma osmolality, sodium, creatinine, and urine output is advisable for early detection of DI in this setting. This study established a model for DI associated with prolonged sevoflurane sedation, including longer sevoflurane use, higher end-tidal concentrations and COVID-19 infection.

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P347

Safety profile of growth hormone replacement (GHr) in GH deficient patients during transition period treated for intracranial tumors and malignancy in childhood- Single center expirence

Mirjana Doknic[1,2], Mihajlo Curcic[2], Marko Stojanovic[1,2], Tatjana Milenkovic[3], Vera Zdravkovic[2,4], Maja Jesic[2,4], Slaana Todorović[3], Mihailo Milicevic[2,5], Aleksandar Stanimirovic[2,5], Vuk Scepanovic[2,5], Katarina Mitrović[2,3], Rade Vukovic[2,3], Dragana Miljic[1,2], Sandra Pekic Djurdjevic[1,2], Ivana Cekic[1], Ivan Jevtic[1], Emilija Manojlovic Gacic[2,6], Danica Grujicic[2,5], Milan Petakov[1,2] & Ivan Soldatovic[2,7]
[1]University Clinical Centre of Serbia - Clinic for Endocrinology, Diabetes and Metabolic Diseases, Neuroendocrine Department, Belgrade, Serbia; [2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [3]Mother and Child Health Care Institute of Serbia'Dr Vukan Cupic', Belgrade, Serbia; [4]University Children's Clinic 'Tirsova', Belgrade, Serbia; [5]Clinic for Neurosurgery, University Clinical Centre of Serbia, Belgrade, Serbia; [6]Institute for Pathology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [7]Institute of Medical Statistics and Informatics, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Introduction
Considering the mitogenic potential of GH and IGF1, the safety profile of growth hormone therapy since the beginning of its use has been debated. From that point of view, adolescents in transition to adulthood who were treated in childhood for endocranial tumors or malignancies require special caution.
Patients and Methods
In a monocentric, observational, retrospective cross-sectional study spanning 18 years, we analyzed 251 childhood onset growth hormone deficiency - COGHD patients (16-25 years old, 181 males) at time-point of pediatric to adult endocrine care transfer and over transition period on GHr. Fifty-three subjects experienced childhood-onset cranial tumor or acute lymphoblastic leukemia-ALL (TUM, 21.1%). Other patients had congenital (CON, 46.2%) or idiopathic COGHD (32.6%). Craniopharyngiomas predominated among TUM group (39.6%), followed by germinoma (15.2%), Langerhans cell histiocytosis (11.3%), medulloblastoma (9.4%), astrocytoma and ALL (each 5.6%), pituitary pseudotumor (TSH hyperplasia-3.8%), PNET, ganglioglioma, hamartoma, thalamic tumor, and malignant triton tumor (1.8% each). We monitored possible tumor recurrence using cranial MRI and hematological evaluation every 12 months in TUM group. Monitoring for recurrent lesions on GHr also extended to 6 of CON patients who underwent non-cranial childhood surgery due to benign tumors of kidney (2), skin (2) adrenals (1) or mediastinum (1).
Results
Median age of patients at time of transfer from pediatrics was 18.1 ± 3.3 years. Patients with persistent GHD (65.8%) continued GHr in daily doses of 0.5 ± 0.2 mg (range 0.3-1.4 mg) with follow-up IGF-I maintained mid-ranged. Duration of GHr during childhood was 5.7 ± 4.9 years (1-16 years), while during the transition period it was 3.6 ± 1.9 years (1-7 years). We detected papillary carcinoma of the thyroid gland in a male patient who had the experience of thalamic germinoma treated by surgery and radiotherapy at the age of 18. He started GHr (0.3 mg daily) at the age of 22 and stopped 3 years later after a malignant thyroid tumor was discovered. His brother was also treated for cranial germinoma and the same mutation on the KRAS gene was proven in both of them. During GHr no benign tumors regrowth was detected in the CON group.
Conclusion
In 53 patients with tumor-related COGHD, we monitored the safety of GH therapy in the transition period. Through follow-up, we detected papillary thyroid carcinoma in a patient previously treated for cranial germinoma. Patients should be carefully monitored on GH treatment due to the possibility of developing not only the recurrence of the tumor causing GHD, but also secondary neoplasms.

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P348

Diabetes insipidus and cerebral malaria: a rare etiology to be considered

Mariana Lopes-Pinto[1] & Ema Paula Ricca Lacerda Nobre M Caetano[1]
[1]Unidade Local de Saúde de Santa Maria, Hospital de Santa Maria, Endocrinology Department, Lisbon, Portugal

Background
Cerebral malaria may present with altered cognition, severe hemolysis, renal and metabolic dysfunction. The endocrine abnormalities induced by malaria include: hypoglycemia, hypocalcemia, hypercortisolism and compromised pituitary function due to sequestration of drepanocytes in hypothalamo-pituitary portal microvasculature.
Aim
To raise awareness for the risk of pituitary dysfunction in severe malaria.
Case
A previously healthy 22 years old woman was admitted at the emergency department with fever, rigors, vomiting and altered cognition after a flight from Guinea. Malaria was suspected and *P.falciparum* parasitemia was of 3% at admission. Anemia, pulmonary edema, acute renal lesion (maximum creatinine 9.2 mg/dl (N:0.5-0.9)), thrombocytopenia, hyperbilirubinemia, hypocalcemia and elevated inflammatory markers were present. She had a normal head CT scan. After quinine and doxiciclin treatment a generalized cognition and hematologic improvement was followed by acute renal lesion KDIGO 3, with oliguria and uremia requiring hemodyalisis. Spontaneous miction was followed by prompt increase in urinary output reaching a maximum of 4.9L without fluids or diuretics. After fluid treatment, negative fluid balance reached -5.5L (urinary output 15.5L), followed by dehydration and sinusal tachycardia. The progression and duration of polyuria raised suspicion of diabetes insipidus (DI). Hypotonic polyuria was confirmed, serum osmolality ranged between 269-277mOsmol/Kg (N: 275-298), and sodium levels between 136-138 mmol/l (N:135-145). Low basal copeptin level (1.14pmol/l) was suggestive of central DI and a therapeutical trial with desmopressin was started and titrated up to 0.6 mg/day with clinical improvement. Pituitary function was assessed and elevated ACTH 135.6 pg/ml (N: 7.2-63.3) and 0800 hours cortisol of 23.2 mg/dl required further study. Lack of suppression in 1mg dexamethasone suppression test (18.4 mg/dl) was documented and a sellar MRI obtained. No pituitary adenomas were present, but a neurohypophysis with right deviation and hypersignal in T2 of 'imprecise meaning' was described. The hypercortisolism was admitted as a result of hospitalization and acute disease, and was resumed after hospital discharge. After two weeks, desmopressin was stopped without relapse of polyuria, and normal sodium and osmolality levels were documented in urine and serum evaluation, as previously described in DI due to malaria.
Conclusion
In conclusion, cerebral malaria may present with compromised pituitary function, such as diabetes insipidus, requiring prompt diagnosis and treatment.

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Prolactin-related challenges in two critical moments of womens' life: postpartum and menopause

Catarina Silvestre[1], Tânia Matos[1], Daniela Dias[1], Filipa Serra[1], Pedro Marques[1,2] & Inês Sapinho[1]
[1]Hospital CUF Descobertas, Lisboa, Portugal; [2]Catholic University of Portugal, Lisboa, Portugal

Introduction
Prolactin is involved in lactation and reproduction. Endocrinologists should be familiar with physiological effects of prolactin in women, particular in key moments: breastfeeding and menopause. We aimed to report two females with unusual prolactin-related challenges: the first case corresponds to a postpartum woman with normoprolactinemia and breastfeeding problems; the second case concerns a menopausal woman with a prolactinoma who developed hot flashes following normalization of prolactin levels.
Clinical cases
A 32 year-old woman was referenced 2 months after delivery of her first child, after evaluation by a Lactation consultant. She sought help for not being able to exclusively breastfeed since the birth, with no let-down reflex/draught. She had two normal serum prolactin measurements (14.3 and 8.3ng/ml, normal range <25). Her baseline pituitary function was normal. She was advised to breastfeed on full-demand, mainly at night, to increase her lactation function. A 50 year-old woman was diagnosed with a macroprolactinoma after complaining of headache, although she had a secondary amenorrhea since 26 years-old-not previously investigated. At diagnosis, she had elevated prolactin levels at 2500ng/ml, and low LH and FSH levels at 0.36 and 5.26 mUI/ml, respectively; remaining pituitary function was normal. Pituitary MRI showed a 3.6 cm-cystic pituitary mass with cavernous sinus invasion compressing the optic chiasm. She initiated cabergoline, with good biochemical and structural response. Within 6 months on cabergoline, prolactin levels normalized, with a concomitant increase of LH/FSH levels up to the range for a postmenopausal woman, respectively 19.27 and 34.31 mUI/ml. At this point in time, the patient started to report menopause-like symptoms, particularly hot flashes, which she never experienced before, even when she became amenorrheic.
Conclusion
Despite the fact that lactation is a well-known cause of secondary hyperprolactinemia, normal prolactin levels can be found in breastfeeding women. Since delivery and during breastfeeding, serum prolactin levels may slowly decline over time; also serum prolactin peaks throughout the day in breastfeeding women, and

correlate with moments of suckling stimulation. With the second case, we learned that hyperprolactinemia contributed to abolishment of menopause-related hot flashes, due to gonadotropin/GnRH suppression. Although hot flashes in menopausal women are classically attributed to estrogen deficiency, this case suggested that elevated FSH/lH may also play a role. This may be due to proximity of hypothalamic GnRH neurons with thermoregulatory neurons, explaining a possible association of pulsatile LH-release and occurrence of hot flashes.

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P350

Assessment of insulin resistance and its associated factors in women with hypopituitarism

Salma Salhi[1], Ibtissem Oueslati[1], Emna Talbi[2], Kacem Ben Fradj[2], Ahmed Mezioud[2], Meriem Yazidi[1], Moncef Feki[2] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia; [2]La Rabta University Hospital, Laboratory of Biochemistry, Tunis, Tunisia

Introduction
Insulin resistance (IR) is prevalent in patients with hypopituitarism receiving conventional replacement therapy. Recognizing and addressing IR in women with hypopituitarism is crucial for comprehensive patient management and prevention of other metabolic complications. The aims of this study were to determine the prevalence of IR and to assess its associated factors in women with hypopituitarism.
Methods
This was a monocentric cross-sectional study including 50 patients with complete anterior hypopituitarism secondary to Sheehan's syndrome (SS) and 50 age, and body-mass index (BMI)-matched women controls. Participants underwent physical examination and laboratory tests including fasting blood glucose and baseline insulin. Homeostatic Model Assessment of IR (HOMA-IR) index was calculated using the following formula: [Fasting Blood Glucose (mmol/l) $\times$ Basal Insulin (mIU/l)] / 22.5. IR was defined by an HOMA-IR index $\geq$ 2.4.
Results
The mean age was 62.2 $\pm$ 9.4 years in women with SS and 60.6 $\pm$ 8.4 years in controls ($P=0.385$). The mean BMI was 29.6 $\pm$ 6.0 kg/m^2 in patients and 30.0 $\pm$ 5.0 kg/m^2 in controls ($P=0.741$). The baseline insulin level was significantly higher in women with SS than in controls (respectively: 15.0 $\pm$ 11.6 µIU/ml vs 10.6 $\pm$ 5.5 µIU/ml, $P=0.030$). The HOMA-IR index was significantly higher in patients than in controls (respectively: 3.4 $\pm$ 3 vs 2.4 $\pm$ 1.2, $P=0.017$). The prevalence of IR was 38% in patients and 56% in controls ($P=0.070$). In patients with SS, factors associated with IR included age $\leq$ 62 years (OR=4.43, IC95%: 1.26-15.48, $P=0.016$), family history of obesity (OR=3.78, IC95%: 1.01-14.17, $P=0.042$), BMI $\geq$30 kg/m^2 (OR=1.21, IC95%: 1.06-1.40, $P=0.004$), body-fat ratio $\geq$ 30% (OR=1.13, IC95%: 1.02-1.26, $P=0.021$), and waist circumference $\geq$94 cm (OR=1.86, IC95%: 1.40-2.47, $P=0.009$). However, the risk of IR was not associated with the diagnostic delay of SS, disease duration, GH levels, FT4 levels, levothyroxine dose, daily or cumulative dose of hydrocortisone, and oestrogen-progesterone therapy.
Conclusions
Women with hypopituitarism had a significantly higher insulin levels and HOMA-IR ratio than controls. However, the prevalence of insulin resistant was comparable in the two groups. Age, family history of obesity, BMI, body fat ratio, and waist circumference were positively associated with IR.

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P351

ER stress causes variable ACTH production and secretion in corticotroph tumour cells

Merisa Abusdal[1,2,3], Jens Petter Berg[3,4], Maria Walewska[1], Hemaseh Bideli[1], Jens Bollerslev[1,3] & Nicoleta Olarescu[1,2,3]
[1]Section of Specialized Endocrinology, Department of Endocrinology, Oslo University Hospital (OUS), Oslo, Norway; [2]Research Institute of Internal Medicine, Oslo University Hospital (OUS), Oslo, Norway; [3]Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; [4]Department of Medical Biochemistry, Oslo University Hospital (OUS), Oslo, Norway

Objective
Cushing's disease is caused by hypercortisolism due to adrenocorticotropic hormone (ACTH) hypersecretion from functioning pituitary adenomas (FCA). Endoplasmic reticulum (ER) protein processing is important for hormone production and is upregulated in FCA as shown previously. ER protein processing can be disturbed by ER stress. We hypothesized that ACTH production and secretion can be inhibited by agents that cause ER stress by attenuating ER protein processing.
Methods
Cells from the AtT-20 mouse pituitary corticotroph tumor cell line and primary cells isolated from FCA were treated for 6 and 24 hours with 50-µM-Hsp90 inhibitor 17-N-allylamino-17-demethoxygeldanamycin (17-AAG, tanespimycin) and 250 nM of the sarco- and endoplasmatic reticulum Ca-ATPase inhibitor thapsigargin (Tg) to induce ER stress. The stimulation was followed by gene and protein expression analyses, and ACTH measurement in culture media and cell lysate.
Results
In AtT-20 cells, gene expression involved in ER protein processing, including CALR, GRP78, GRP94, UGGT1 were significantly upregulated by Tg and 17-AAG at 24 h compared with controls. Tg increased all unfolded proteins signalling pathway responses (ATF4, IRE1 and ATF6) at both 6 and 24 h, whereas 17-AAG increased only ATF4 at 6 h, and IRE1 at 24 h, and no effect was observed on ATF6. The ratio of s/uXBP1, member of IRE1 pathway, was downregulated by 17-AAG at both time points ($P<0.001$ for both), suggesting that the cells are in recovery phase from ER stress. POMC gene expression was downregulated by Tg at both 6 and 24 h ($P<0.0001$, both), whereas 17-AAG was upregulated at 6 h ($P=0.0497$). At 24 h, Tg decreased secreted ACTH in media by 24% in AtT-20 cells ($P<0.0001$) and 32% in primary cells ($P<0.0001$) compared with controls. However, 17-AAG increased secreted ACTH by 64% ($P=0.0052$) with marked response variation between FCA patients' tumor cells. No effect of 17-AAG was observed in AtT-20 cells. Intracellular ACTH level in both cell types showed no change by Tg, while 17-AAG increased it in AtT-20 by 17% ($P=0.0075$) and by 38% in primary cells ($P=0.0354$).
Conclusion
ER stress may disturb ACTH production and secretion from the corticotroph tumour cells. The broad induction of ER stress by Tg effectively reduced ACTH production and secretion. On the contrary, targeted ER stress induced by 17-AAG showed increased ACTH production and secretion by FCA primary cells, possibly by inducing ER compensatory mechanisms.

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P510

Plasma apelin levels in patients with polyuria-polydipsia syndrome undergoing copeptin stimulation tests

Chiara Bizzozero[1], Sophie Monnerat[1], Fiona Chapman[2], Neeraj Dhaun[2], Julie Refardt[1] & Mirjam Christ-Crain[1]
[1]University Hospital Basel, Department of Endocrinology, Diabetology and Metabolism, Basel; [2]Royal Infirmary of Edinburgh, Department of Renal Medicine, Edinburgh, United Kingdom

Introduction
In polyuria-polydipsia syndrome (PPS) the differentiation between arginine vasopressin deficiency (AVP-D) and primary polydipsia (PP) remains challenging and a stimulation test is required. Apelin is an endogenous hormone that antagonises AVP and seems to play an important role in regulating salt and water homeostasis. The dynamic of apelin plasma levels in patients with PPS undergoing copeptin stimulation tests is unknown.
Methods
Post-hoc secondary analysis of the multicentric randomised cross-over diagnostic CARGOx study (NCT03572166) performed from 09/2018 to 12/2022. Apelin levels from patients with PPS included at the University Hospital Basel were measured upon stimulation with hypertonic saline and arginine infusions. The primary objective was to compare the changes in plasma apelin levels during copeptin-stimulation tests among patients with PPS. Secondary objectives included comparing changes in the apelin/copeptin ratio and comparing the diagnostic ability of apelin, copeptin and their ratio.
Results
Of the 38 patients enrolled at the University Hospital of Basel, 23 (60%) patients had PP and 15 (40%) patients had AVP-D. At baseline median [IQR] apelin levels were 1079 [912, 1225] and 910 [756, 1039] and apelin/copeptin was 336 [218, 336] and 426 [369, 509] in PP and AVP-D respectively. During the hypertonic saline stimulation test, apelin decreased by -241 [-326, -124] and -47.2 [-198, 5.86] ($P=0.022$) and apelin/copeptin ratio decreased by -300 [-425, -235] and -69 [-150, -15] in PP and AVP-D respectively ($P=0.001$). The AUC [95%-CI] to differentiate PP from AVP-D was 97.1% [90.5, 100] for copeptin, 49.3% [30.4, 68.1] for apelin and 95.6 [87.2, 100] for apelin/copeptin ratio. During the arginine stimulation test, apelin decreased in PP by -39.2 [-96.4, 39.8] and increased in AVP-D by 25.8 [2.8, 113.0] ($P=0.1$), and apelin/copeptin ratio decreased by -188 [-326, -68] and -59 [-171, 8] in PP and AVP-D respectively ($P=0.034$). The

AUC [95%-CI] was 97.1% [79.6, 98.0] for copeptin, 60.5% [39.8, 80.0] for apelin and 83.0% [67.0, 95.3] for apelin/copeptin ratio.
Conclusion
Our findings suggest that apelin and apelin/copeptin ratio decrease during hypertonic infusion to a greater extent in patients with PP as compared to patients with AVP-D. Copeptin remains the best marker to differentiate AVP-D from PP upon hypertonic saline and arginine stimulation. Whether apelin would provide greater diagnostic accuracy using other provocation tests should be further investigated.

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Assessment of GH/IGF1 axis in relation to pituitary volume and MRI intensity in subjects with obesity: A controlled, cross-sectional, observational study

Gabriele Veroi[1], Dario De Alcubierre[1], Davide Masi[1], Rebecca Rossetti[1], Maria Elena Spoltore[1], Elena Gangitano[1], Mikiko Watanabe[1], Stefania Mariani[1], Lucio Gnessi[1] & Carla Lubrano[1]
[1]Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza University of Rome, Rome, Italy

Background
It has been reported that some Magnetic Resonance Imaging (MRI) pituitary findings may reflect specific endocrinological alterations, as in the case of adult-onset growth hormone deficiency (GHD), which has already been associated with lower MRI-derived pituitary height and volume in pediatric patients.
Purpose
The objective of this study was to investigate potential associations between pituitary morphology and signal intensity on MRI with GH secretory function in a cohort of patients with varying degrees of adiposity.
Methods
We conducted a retrospective observational study on 297 patients (235 females, median age 46 years, IQR: 20 years), admitted to our institution between January 2015 and December 2023, who had signs and symptoms suggestive of GHD. Our cohort included 243 patients with obesity and 54 age- and sex- matched controls. We assessed GH-IGF1 axis and pituitary morphology with MRI. To quantify the mean and standard deviation (SD) of pituitary signal intensity, we used Horos software, employing T2-weighted sequences and gray matter intensity as a normalizer. In addition, we measured pituitary height and calculated pituitary area in coronal section as a surrogate for pituitary volume.
Results
In the entire study population, we found an inverse correlation between BMI and pituitary area (r=-0.357, P=.000), height (r=-0.406, P=.000) and normalised pituitary signal intensity (r=-0.197, P=0.05). Patients with obesity showed significantly lower pituitary height and area (P=.000) along with a higher prevalence of empty sella (X2= 13.996, P=.000) compared to controls. Regarding GH secretory capacity, we found a direct correlation between the area under the curve of the GHRH+arginine test and pituitary area (r = 0.479, P= .000) and height (r=0.513, P=.0.00) and a negative correlation with BMI (r= -0.481, P=.000). Finally, by fitting ROC curves, we identified cut-offs for pituitary area (lower than 27.8 mm^2, AUC= 0.696, P=.000) and pituitary height in coronal scan (lower than 3.1 mm, AUC= 0.729, P=.000) as predictors of GHD with a sensitivity of 69% and 72% and specificity of 61% and 62%, respectively. After stratifying the cohort by the degree of adiposity, we showed a progressive reduction in GH secretory capacity and pituitary size from the control group to gradually higher degrees of obesity (P=.000 for all parameters).
Conclusion
Consistent with current evidence, our study demonstrates that patients with obesity have impaired GH-IGF1 axis and reduced pituitary size compared to controls, suggesting a close relationship between pituitary morphology and functional capacity.

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P512

Transsphenoidal surgical treatment of symptomatic rathke's cysts. results, follow-up, and recurrence rates

Edelmiro Luis Menendez Torre[1,2,3], Alba Gutierrez Hurtado[4], M Dolores Ollero[5], Patricia Martin Rojas[6], Inmaculada Gonzalez-Molero[7], Marta Araujo Castro[8], Cindy Idobro[8], Maria Dolores Moure Rodriguez[9], Betina Biagetti[10], Pedro Iglesias[11], Miguel Paja Fano[12,13], Rocio Villar Taibo[14], Alberto Pena Dubra[14], Almudena Vicente[15], Fernando Guerrero[16], Fernando Cordido[17], Ana Aulinas Maso[18], Manel Mateu Salat[18] & Alfonso Soto-Moreno[19]
[1]Central University Hospital of Asturias, Endocrinology and Nutrition, Oviedo, Spain; [2]Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain; [3]University of Oviedo, Oviedo, Spain; [4]Central University Hospital of Asturias, Oviedo, Spain; [5]Navarra Hospital Complex - Navarra Hospital, Pamplona, Spain; [6]La Paz University Hospital, Madrid, Spain; [7]Hospital Regional Universitario de Málaga, Málaga, Spain; [8]Ramón y Cajal Hospital, Madrid, Spain; [9]Hospital Universitario de Cruces, Barakaldo, Spain; [10]Vall d'Hebron University Hospital, Barcelona, Spain; [11]Puerta de Hierro Majadahonda University Hospital, Majadahonda, Spain; [12]Basurto Hospital, Bilbao, Spain; [13]Basurto University Hospital – OSI Bilbao-Basurto, Endocrinology; [14]Santiago Clinic Hospital CHUS, Santiago de Compostela, Spain; [15]Hospital General Universitario de Toledo, Toledo, Spain; [16]Bellvitge University Hospital, L'Hospitalet de Llobregat, Spain; [17][CHUAC] University Hospital of A Coruña, A Coruña, Spain; [18]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [19]Virgen del Rocío University Hospital, Sevilla, Spain

Aim
To evaluate the efficacy of transsphenoidal surgery in patients with Rathke cleft cysts (RCCs), and recurrence rates after follow-up
Methods
A multicenter retrospective clinical practice study in patients with RCCs operated through transsphenoidal route and followed in 15 tertiary hospitals (SPAIN-QBR study) during 64.0 ± 49.0 months.

Table 1. Pre and post-surgery clinical alterations

	Pre-surgery	Post-surgery	
Visual field defects	39 (47.1%)	12 (14.3%)	P<0,001
Neurologic alterations	5 (5.9%)	2 (2.2%)	ns
Headache	44 (4.4%)	6 (6.7%)	P<0,001
Diplopia	3 (3.5 %)	2 (2.2%)	ns
Any pituitary deficiency	41 (48.2%)	50 (58.8%)	P<0,001

Table 2. Complications of surgery

Increased anterior pituitary damage	21 (24.7 %)
Permanent arginine vasopresin deficiency	13 (15.3%)
Reinterventions	11 (12.9 %)
Cerebrospinal fluid leakage	8 (9.4%)
Meningitis	4 (4.7 %)
Intracranial hemorrhage	2 (2.4%)
Abscess	1 (1.2 %)
Mortality	1 (1.2%)

Results
A total of 85 patients with a diagnosis of RCCs underwent transsphenoidal surgery, 62 (72.9%) due to secondary clinical symptoms and 23 (27,1 %) for risk of chiasmatic compression. Most surgeries were endoscopic (74 patients) and only 11 were microscopic. Men represented 30.6% (n=26 of the cases) and 59 (69.4%) were women. The mean age was 47±19 years for men and 47±16 years for women. After surgery visual field alterations and headache improved in more than 67% of the patients but the number of patients with hormonal deficiencies increased due to new cases of arginine vasopresin deficiency (Table 1). Other complications can be seen in table 2. Total resection was achieved in 58 % of patients and after a long follow-up (64.0 ± 49.0 months) growth of cysts was seen in nine patients (10.6%) and only one required new surgery.
Conclusion
In patients with symptomatic Rathke cleft cysts, transsphenoidal surgery achieves an improvement in signs and symptoms due to mass-effect with low rate of complications. However, up to 11% of the cases may experience recurrence during follow-up; thus, long-term follow-up is recommended after surgery.

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P513

Novel mutations causing pachydermoperiostosis - hormonal and phenotypic alterations

Maria Stelmachowska-Banaś[1], Sayka Barry[2], Ishita Angurala[2], Tom Rice[2], Kesson Magid[2], Ana Carreira[2], Ashutosh Rai[2], Amy Evans[2], Mark Bollington[2], Vaishali Kaur[3], Cristina Alina Silaghi[4], Alan McGregor[5], Kudakwashe Mandisodza[5], Jayaprakash Sahoo[6], Rahul Gupta[7], Kishore Behera[8], Ayan Roy[9], Ian Carr[10], Paul Loughrey[11], Pinaki Dutta[3] & Márta Korbonits[2]
[1]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland; [2]Centre for Endocrinology, William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom; [3]Postgraduate Institute of Medical Education and Research, Department of Endocrinology,

Chandigarh, India; [4]Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, Department of Endocrinology, Cluj-Napoca, Romania; [5]College of Health Sciences, Parirenyatwa Group of Hospitals Harare, University of Zimbabwe, Department of Medicine, Harare, Zimbabwe; [6]Jawaharlal Institute of Postgraduate Medical Education & Research, Department of Endocrinology, Puducherry, India; [7]All India Institute of Medical Sciences, Department of Endocrinology and Metabolism, Bhopal, India; [8]All India Institute of Medical Sciences, Department of Endocrinology, Bhubaneswar, India; [9]All India Institute of Medical Sciences, Department of Endocrinology, Kalyani, India; [10]University of Leeds, Molecular Medicine Unit, Leeds, United Kingdom; [11]Patrick G Johnston Centre for Cancer Research, Queen's University, Belfast, United Kingdom

Background
Pachydermoperiostosis (primary hypertrophic osteoarthropathy, PHO) is a rare genetic disease characterised by clinical signs and symptoms which may overlap with acromegaly (pachydermia, hyperhidrosis and enlargement of hands and feet). In the majority of cases, the disease is due to biallelic loss-of-function variants in either of two genes, *SLCO2A1* and *HPGD* playing an important role in prostaglandin metabolism. Although PHO patients are often referred to endocrinologists, a detailed hormonal assessment is not available for these patients.
Patients and methods
Patients ($n=16$, all males), referred to endocrinology centres with a possible diagnosis of acromegaly and eventually diagnosed with PHO, were assessed for biochemical and hormonal abnormalities. Acromegaly was excluded based on normal IGF-1 concentration and/or GH suppression during an oral glucose tolerance test (OGTT). Sanger sequencing for *HPGD* and *SLCO2A1* variants on peripheral blood DNA was performed. The identified variants on both genes were classified using the American College of Medical Genetics classification guidelines.
Results
The mean ($\pm$ standard deviation) age at PHO diagnosis was 27.8 years $\pm$11.3 (range 9-43 years). Digital clubbing and periostosis were present in all patients. Arthralgia of large joints was present in 15/16 patients (94%), periarticular oedema in 13/16 (81%), pachydermia in 14/16 (88%) and facial features suggesting acromegaly in 12/16 (75%). Further characteristic features included eyelash trichomegaly (10/16 patients), blepharoptosis (9/16), high-arched palate (9/15), gastrointestinal symptoms (7/16), gingival hypertrophy (1/16) and marfanoid habitus (2/16). All tested patients ($n=13$) suppressed GH on OGTT <1.0 µg/l, but 4 (31%) did not supress GH <0.4 µg/l. Nine patients (57%) had abnormally low serum IGF-1 level and the other three patients (19%) had IGF-1 levels in the lower quartile of the reference range. While testosterone and prolactin levels were normal, oestradiol concentration was increased above the normal range in eight patients (62%). Two families harboured homozygous *HPGD* changes (one of these is a novel variant). Ten families had 12 different pathogenic/likely pathogenic variants in *SLCO2A1* (eight novel variants). Eight kindreds had homozygous change while two kindreds had compound heterozygous mutation. Two patients from two different kindreds had no identifiable pathogenic/likely pathogenic variant in *HPGD* or *SLCO2A1*. Their phenotype was not different from the other patients.
Conclusion
Low IGF-1 and elevated oestradiol levels are typical features for patients with both *HPGD* or *SLCO2A1* mutations while analysing the data of 14 kindreds with PHO carrying nine novel and five known pathogenic/likely pathogenic genetic variants.

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P514

A Novel CDKN1B mutation in multiple endocrine neoplasia type 4

Christina Millou[1], George Chrousos[2] & Amalia Sertedaki[3]
[1]University Hospital Coventry & Warwickshire, Endocrinology Diabetes and Metabolism, coventry, United Kingdom; [2]University Research Institute of Maternal and Child Health and precision medicine, National and Kapodistrian University of Athens, Athens, Greece; [3]Division of Endocrinology, Diabetes and Metabolism, Aghia Sophia Children's Hospital ENDO-ERN Center for Rare Paediatric Endocrine Diseases, National and Kapodistrian University of Athens, Athens, Greece

Multiple endocrine neoplasia (MEN) includes a group of autosomal dominant disorders, associated with the development of a variety of endocrine and non-endocrine manifestations. MEN4 is a rare and the latest reported type in the spectrum of the MEN syndromes. MEN4 was discovered initially in rats (MENX) and later in humans. It is caused by germline and somatic mutations in the cyclin-dependent kinase inhibitor 1B (CDKN1B) tumor suppressor gene, which encodes nuclear protein p27 (IFI27), a key regulator of cell cycle progression. The most common phenotype of MEN4 is primary hyperparathyroidism (PHPT), followed by pituitary adenomas and rarely NETs. MEN4 and MEN1 syndromes have similar phenotypes. However, in MEN4 the disease manifestations appear later in life, associated with an improved life- expectancy and a different prevalence. We present an adult woman with MEN4 who presented with a non-functioning pituitary adenoma, an adrenocortical adenoma causing mild Cushing syndrome, a parathyroid adenoma associated with mild PHPT and benign intestinal polyps. We identified that she is harboring a novel heterozygous CDKN1B gene pathogenic variant, p.Lys96GInfsTer 29.

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P515

Body weight in acromegaly – does it make any difference?

Sonia Kaniuka-Jakubowska[1], claire higham[2,3], Jessica Davis[4], Tara Kearney[5], Paul Loughrey[6,7], Aisha Elamin[8], Daniel Flanagan[9], Mariusz Kaszubowski[10], John Ayuk[11,12], Steve M Orme[13] & John Wass[14]
[1]Faculty of Medicine, Medical University of Gdansk, Department of Endocrinology and Internal Medicine, Gdansk, Poland; [2]The Christie Hospital NHS Foundation Trust, Department of Endocrinology, Manchester, United Kingdom; [3]The University of Manchester, Division of Cancer Sciences, Manchester, United Kingdom; [4]Society for Endocrinology, Bristol, United Kingdom; [5]Salford Royal Foundation Trust, Department of Endocrinology, Salford, United Kingdom; [6]Queen's University Belfast, Patrick G Johnston Centre for Cancer Research, Belfast, United Kingdom; [7]Royal Victoria Hospital, Belfast Health and Social Care Trust, Regional Centre for Endocrinology and Diabetes, Belfast, United Kingdom; [8]Sheffield Teaching Hospitals NHS Foundation Trust, Department of Endocrinology, Sheffield, United Kingdom; [9]University Hospital Plymouth, Department of Endocrinology, Plymouth, United Kingdom; [10]Faculty of Management and Economics, Gdansk University of Technology, Department of Economic Sciences, Gdansk, Poland; [11]Birmingham Health Partners, Centre for Endocrinology, Diabetes and Metabolism, Birmingham, United Kingdom; [12]Queen Elizabeth Hospital Birmingham, Department of Endocrinology, Birmingham, United Kingdom; [13]St James's University Hospital, Leeds Teaching Hospitals NHS Trust, Department of Endocrinology, Leeds Centre for Diabetes and Endocrinology, Leeds, United Kingdom; [14]Oxford University Hospitals NHS Foundation Trust, Department of Endocrinology at the Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, United Kingdom

Introduction
IGF-1 dependence on sex is a well-known fact; however, whether IGF-1 is also influenced by body weight is still questionable, and the mechanism of a potential relationship between GH, IGF-1 and body weight is not fully explained. The effect of gender (or rather oestrogens) on IGF-1 is visible in acromegaly - women are diagnosed at an older age than men (approximately 4 years) (potentially by suppressive effect on the axis of GH-IGF-1). The aim of the study was to assess whether BMI is a factor influencing the age of diagnosis of acromegaly - potentially by influencing (like oestrogens) the GH-IGF-1 relationship.
Materials and Methods
In a retrospective analysis of the UK Acromegaly Register (UKAR, 22 centres, 1997-2017) we enrolled 1136 patients (53.4% males) with available BMI results, which were reported +/- 2 years before diagnosis. We assessed the correlation between gender, BMI and age of diagnosis, age of first symptoms, diagnostic delay and the number of treatments in our selected group.
Results
We found, that that females are significantly older at diagnosis of acromegaly than males (approximately 4.3 years, $p<0.001$). However, there was no correlation between BMI and age of diagnosis ($p=0.072$). There was also no correlation between BMI and age of first symptoms ($r=0.0947$, $P=0.002$) and the time between first symptoms and diagnosis ($r=0.0065$; $p=0.835$). Patients with a higher BMI did not receive more treatment modalities in their course of follow-up ($r=-0.0491$; $p=0.150$).
Conclusions
BMI does not influence the age of diagnosis of acromegaly as the gender does. If oestrogens are responsible for a delay in diagnosis, it is probably by influencing the GH-IGF-1 axis - which is not visible in the BMI and age at diagnosis relationship. Mechanisms other than GH-IGF-1 should be considered when assessing differences in IGF-1 for different BMI. on behalf of the UKAR Steering Group 2024

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Cytokeratin 18: An early biomarker of increased liver fibrosis in newly diagnosed acromegaly

Meric Coskun[1], Halit Nahit Sendur[2], Afruz Babayeva[1], Mahi Nur Cerit[2], Ethem Turgay Cerit[1], Mehmet Muhittin yalcin[1], Alev Eroglu Altinova[1], Mujde Akturk[1], Mehmet Ayhan Karakoc[1] & Fusun Balos Toruner[1]

[1]Gazi University, Faculty of Medicine, Endocrinology and Metabolism, Ankara, Turkey; [2]Gazi University, Faculty of Medicine, Radiology, Ankara, Turkey

Purpose
The liver is known to be protected from steatosis under the influence of high GH/IGF-1. Cytokeratin 18 (CK18) and insulin-like growth factor binding protein 7 (IGFBP7) increase in liver steatosis and fibrosis. Whether decreasing lipid content completely protects the liver from metabolic alterations and the response of CK18 and IGFBP7 to liver changes in acromegaly is unknown.
Methods
This single-center, multidisciplinary, cross-sectional study included 23 patients with newly diagnosed acromegaly and 46 age, sex, body mass index (BMI) and waist circumference (WC)-matched healthy controls. Liver steatosis was assessed using tissue attenuation imaging (TAI), and stiffness, indicative of fibrosis, was assessed using shear wave elastography (SWE). Serum IGFBP7 and CK18 were studied by ELISA.
Results
The acromegaly group had significantly lower liver steatosis ($P=0.006$) and higher liver stiffness ($P=0.004$), serum IGFBP7 ($P=0.048$) and CK18 ($P=0.005$) levels than the control group. The presence of fibrosis ($P=0.012$) was significantly higher in the acromegaly group than in the control group. Moreover, CK18 was positively correlated with liver stiffness, WC, HOMA-IR, HbA1c, and triglyceride. In the acromegaly group, liver steatosis was negatively correlated with GH level. Stepwise multiple linear regression analysis revealed that BMI ($P=0.008$) and CK18 ($P=0.015$) were independent risk factors for increased liver stiffness.
Conclusion
This study showed that newly diagnosed acromegaly had low hepatic steatosis with a protective effect of GH, and metabolic changes caused an increase in liver fibrosis. Additionally, elevated CK18 in patients with acromegaly may be an early biomarker of increased liver fibrosis due to metabolic alterations.

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Management of prolactinomas before, during and after pregnancy: results from the italian association of clinical endocrinologists (AME) survey

Irene Gagliardi[1], Rita Indirli[2,3], Maria Rosaria Ambrosio[1] & On behalf of AME Pituitary Disorders Committee[4]
[1]University of Ferrara, Section of Endocrinology, Geriatrics and Internal Medicine, Department of Medical Sciences, Ferrara, Italy; [2]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [4]Italian Association of Clinical Endocrinologists, Rome, Italy

Background
Prolactinomas are the most common functioning pituitary adenomas and are mostly diagnosed in fertile women. Dopamine-agonists (DAs) have always represented the cornerstone of prolactinoma treatment in terms of hormonal control and tumor shrinkage. Recent guidelines suggest surgery as an alternative option in selected cases after a joint evaluation with an expert surgeon. Prolactinoma management in women seeking fertility and during pregnancy remains challenging, and areas of uncertainty are still present, especially concerning drug safety. The management should be personalized. Herein, we present the results of a cross-sectional survey conducted among Italian endocrinologists, focusing on managing prolactinomas in fertile women and during pregnancy.
Methods
Italian Association of Clinical Endocrinologists members were invited to participate in an online anonymous survey. 578 responded to the survey (61% women, equal distribution between 30-50 and 50-70 years of age).
Results
88% of responders declare to be acquainted with prolactinoma management, and they almost systematically provide counseling on fertility and pregnancy to women of reproductive age. The choice of first-line therapy (DAs vs surgery) is influenced by pregnancy desire (80%) and adenoma size (84%). In particular, 34% of participants opt for surgery in macroadenomas, 22% discuss the choice with the patient in microadenomas, and 77% prefer medical therapy in microadenomas. In women under medical therapy and seeking pregnancy, most clinicians continue the ongoing DAs; 22% switch from cabergoline to bromocriptine, while 18% discontinue therapy. Once pregnancy is confirmed, 58% of participants may continue DAs in selected cases. Great heterogeneity can be observed in prolactinoma management during pregnancy: according to 25% of respondents, women need clinical follow-up. Conversely, nearly 20% require visual field testing only in case of new-onset visual impairment. More than half of responders require prolactin measurement during pregnancy. Finally, 39% advise against vaginal delivery in macroprolactinomas, but the majority do not generally discourage breastfeeding. After delivery and breastfeeding, only half of the participants systematically reassess prolactin concentrations and repeat magnetic resonance imaging before restarting DAs.
Conclusion
Prolactinoma management in fertile-age women is still a challenge in clinical practice. Clinical, hormonal, and ophthalmological follow-ups are largely heterogeneous among endocrinologists. Moreover, a lack of compliance with current guidelines emerged concerning DAs therapy in women seeking fertility and during pregnancy, indications for delivery modalities, and the need for prolactin re-evaluation before restarting DAs. An effort is required from endocrinological societies to spread knowledge about prolactinomas in reproductive-age women and promote management uniformity among endocrinologists.

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Long-term pharmacotherapy of giant prolactinomas

Vaclav Hana[1], Manuela Vaněčková[2], Michal Krsek[1], Mikuláš Kosák[1], Jana Ježková[1], Václav Hána jr.[1], Adela Krausova[1], Pavel Diblík[3], Pavel Kuthan[3], Petr Sklenka[3], David Netuka[4], Václav Masopust[4], Martin Májovský[4] & Roman Liščák[5]
[1]First Faculty of Medicine, Charles University, 3rd Department of Internal Medicine, Prague, Czech Republic; [2]First Faculty of Medicine, Charles University, Department of Radiodiagnostics, Prague, Czech Republic; [3]First Faculty of Medicine, Charles University, Department of Ophtalmology, Prague, Czech Republic; [4]First Faculty of Medicine, Charles University, Department of Neurosurgery, Prague, Czech Republic; [5]Hospital Na Homolce, Department of Stereotactic and Radiation Neurosurgery, Prague, Czech Republic

Giant prolactinomas (GPs) are prolactin secreting pituitary adenomas (PitNETs) $\geq$4 cm, usually with prolactinaemia over 1000 mg/l and without co-secretion of other hormones.
Aims
evaluation of long term treatment of GPs, the effect of D2 agonists and of different doses on prolactinaemia, tumour shrinkage and complications.
Patients and methods
33 patients (27 males, 82%) diagnosed with GP in our department between 1997 - 2020 and subsequently on pharmacotherapy (cabergoline, bromocriptine, terguride) as a first line treatment. Mean age was 41.7 years (range 23 - 71 years). The follow-up ranged 30 months - 23 years. Tumor size was evaluated as the largest diameter (LD) on MRI. Fast tumor shrinkage was considered as LD regression $\geq$20% in less than 6 months. Fast prolactin normalisation was considered when in $<$6 months.
Course of pharmacotherapy and Results
24 patients were on pure D2 agonist pharmacotherapy and 9 had to undergo a surgery during the course of therapy (3 rhinorhea, 3 symptomatic intratumoral bleeding and 3 partial resistance). Three patients underwent stereotactic radiosurgery. The largest tumor was 53x76x65 mm. Suprasellar progression was present in all patients. Dominating clinical signs were visual field defect (26), headache (16), hypogonadism (12). Initial prolactin levels were 250 - 45 500 mg/l. In 3 patients were $<$1000 mg/l. Tumor shrank in all patients. Fast shrinkage was present in 22/29 (76%) evaluated patients. Slow regression in 7 (24%). Visual field defects improved/normalised in 25/26. Prolactinaemia decreased in all patients and normalised in 31/33. Prolactin normalised on pure pharmacotherapy in $<$6 months in 14/24, in 6-12 months in 2/24, in $>$12 months in 6/24 patients and never normalised in 2. Different effects of pharmacotherapy on prolactin normalisation and shrinkage were observed. Eleven patients had both fast normalisation of prolactin and shrinkage; 12 slow normalisation of prolactinaemia, but fast shrinkage; 5 normalised prolactin quickly, but shrinkage was slower. Slow decrease of both was in 1.
Conclusion
Pharmacotherapy of GPs was fully effective as monotherapy in 73%. Complications (rhinorhea, bleeding, resistance) needed neurosurgery (27%) and/or radiosurgery. Fast prolactin normalisation was observed in 71%. Shrinkage of GPs was observed in all and fast in 76%. Discrepance between speed of biochemical and graphical regression is frequently observed and patience is required. High initial D2 agonist doses (cabergoline 3.5mg weekly) led to faster prolactin normalisation, but not to faster shrinkage. Regression of hypogonadism was observed in 39%.
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Machine learning in differential diagnosis of ACTH-dependent hypercortisolism

Zhanna Belaya[1], Olga Golounina[1], Kirill Voronov[2], Alexander Solodovnikov[2,3], Liudmila Rozhinskaya[1], Galina Melnichenko[1], Natalia Mokrysheva[1] & Ivan Dedov[1]
[1]Endocrinology Research Centre, Moscow, Russian Federation; [2]Statandocs LLC, yekaterinburg, Russian Federation; [3]Ural State Medical University, yekaterinburg, Russian Federation

Objective
To develop a non-invasive method of differential diagnosis for ACTH-dependent hypercortisolism using machine learning methods based on clinical data analysis.
Materials and methods
This is a single-center study of a retrospective cohort to predict the probability of EAS among patients with ACTH-dependent hypercortisolism using artificial machine learning algorithms. Patients were randomly stratified into 2 samples: training (80%) and test (20%). Eleven machine learning algorithms were used to develop predictive models: Linear Discriminant Analysis, Logistic Regression, elastic network (GLMNET), Support Vector machine (SVM Radial), k-nearest neighbors (kNN), Naive Bayes, binary decision tree (CART), C5.0 decision tree algorithms, Bagged CART, Random Forest, Gradient Boosting (Stochastic Gradient Boosting, GBM).
Results
The study included 223 patients (163 women, 60 men) with ACTH-dependent hypercortisolism, of which 175 patients had Cushing's disease (CD), 48 had EAS. As a result of preliminary data processing and selection of the most informative signs, the final variables for the classification and prediction of EAS were selected: morning ACTH level, potassium level (the minimum value of potassium in the active stage of the disease), 24-h urinary free cortisol, late-night serum cortisol, late-night salivary cortisol, the largest mesurement of pituitary adenoma according to MRI. The best predictive ability in a training sample of all trained machine learning models for all three final metrics (ROC-AUC (0.867), sensitivity (90%), specificity (56.4%)) demonstrated a model of gradient boosting (Generalized Boosted Modeling, GBM). In the test sample, the AUC, sensitivity and specificity of the model in predicting EAS were 0.920; 77.8% and 97.1%, respectively.
Conclusion
The GBM machine learning algorithm is useful to differentiate patients with EAS and CD based on basic clinical results and can be recommended as primary screening of patients with ACTH-dependent hypercortisolism.

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Use of artificial intelligence to predict survival of patients with acromegaly: is it really better?

Cem Sulu[1], Serdar Sahin[1], Hande Ozkaya[1] & Pinar Kadioglu[1]
[1]Cerrahpasa Medical Faculty Hospital, Turkey

Aim
To identify the causes and predictors of mortality in acromegaly patients diagnosed, treated, and followed in the Pituitary Center of Istanbul University-Cerrahpasa over the last three decades using machine learning (ML) models.
Methods
The study sample consisted of 607 consecutive patients diagnosed with acromegaly at Cerrahpasa Faculty of Medicine during the period 1990 – 2023. The main inclusion criteria were age $>$ 18 years and a clear-cut diagnosis of acromegaly according to standard criteria at the time of presentation. There were 556 alive patients (91.6%) and 51 deceased patients (8.4%), indicating a class imbalance. Synthetic Minority Over-sampling Technique (SMOTE) was applied due to imbalanced data. Minimum Redundancy Maximum Relevance (mRMR) and Recursive Feature Elimination (RFE) methods were used to select features. Logistic Regression, Random Forest, and XGBoost models were used to generate feature importance. The accuracy of the models were assessed through 4-fold cross validation and precision used as the performance metric. The importance of potential predictors were measured by SHAP values.
Results
Of 607 patients, 42% ($n=257$) were male. The median age at diagnosis and last visit were 40 [32–50] and 54 [45–64] years, respectively. The median follow up duration was 99 [40–150] months. Macroadenoma, cavernous invasion, and hypopituitarism was present in 66.9%, 8.5%, and 10.7% of the patients at diagnosis, respectively. Transsphenoidal surgery (TSS) was the initial treatment in 90.3% of the patients with a success of achieving remission in 28.7%. After TSS, 16.1% of patients received additional radiotherapy and 57.1% received postoperative drug treatment. Somatostatin receptor ligands (SLAR) was the most common drug and 36.1% of the patients were SLAR resistant. At last visit, 22% of the patients had active disease. Hypertension was the most common comorbidity (37.2%), followed by diabetes mellitus (36.4%), cardiovascular disease (CVD) (15.7%), colon polyps (12.2%), and malignancy (10%). Thyroid carcinoma was the most common malignity (5.03%), followed by gastrointestinal cancers (1.6%). The main cause of death was CVD (41.2%) and malignities (21.6%). XGBoost had the highest accuracy and precision scores. Top-ranked features in XGBoost model with decreasing importance were malignity and cardiovascular disease.
Conclusion
Malignity and cardiovascular diseases are important causes of morbidity and mortality in patients with acromegaly. ML models may a better understanding of patients' mortality risk, assisting healthcare professionals to tailor management strategies.

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Assessing long-term safety and efficacy of osilodrostat in prior- and new-use patients with endogenous cushing's syndrome: a 1-year real-world interim analysis of the non-interventional, multinational LINC 6 study

Frederic Castinetti[1], Eliza Geer[2], Beverly Biller[3], Richard Feelders[4], Maria Fleseriu[5], Rosario Pivonello[6], Martin Reincke[7], Antoine Tabarin[8], Jeannie Le Mouhaër[9], Julia Stermenska[10], Mario Maldonado[10] & Irina Bancos[11]
[1]Aix Marseille University, INSERM, La Conception Hospital, Assistance Publique Hôpitaux de Marseille, Marseille Medical Genetics, Department of Endcrionology, Marseille, France; [2]Memorial Sloan Kettering Cancer Center, Multidisciplinary Pituitary and Skull Base Tumor Center, New york, Ny, United States; [3]Massachusetts General Hospital, Neuroendocrine and Pituitary Tumor Clinical Center, Boston, MA, United States; [4]Erasmus Medical Center, Department of Internal Medicine, Endocrine Section, Rotterdam, Netherlands; [5]Oregon Health & Science University, Pituitary Center, Departments of Medicine and Neurological Surgery, Portland, United States; [6]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [7]Ludwig-Maximilians-Universität München, Munich, Germany; [8]CHU de Bordeaux, Bordeaux, France; [9]Recordati Rare Diseases SpA, Paris, France; [10]Recordati AG, Basel, Switzerland; [11]Mayo Clinic, Division of Endocrinology, Metabolism and Nutrition, Rochester, United States

Introduction
Potent 11β-hydroxylase inhibitor osilodrostat provides cortisol level control in patients with Cushing's syndrome (CS), as demonstrated by the LINC clinical development programme in Cushing's disease (CD) patients.[1] We report data from year 1 of the prospective observational LINC6 study (NCT05382156), evaluating long-term safety and efficacy of osilodrostat in CS patients during 3 years of routine clinical practice.
Methods
Irrespective of prior osilodrostat use, adult patients with endogenous CS are being enrolled in countries where osilodrostat is approved and available (USA and Europe). Incidence of osilodrostat-related adverse events (AE) and serious AEs (SAE) is the primary endpoint. Secondary endpoints include change in mean urinary free cortisol (mUFC), serum cortisol and late-night salivary cortisol (LNSC). AEs are recorded at baseline and each visit. Outcomes were separately analysed in patients with prior (any time before study entry) and new osilodrostat use. We report changes for patients with baseline and month (M) 3 assessments. All assessments are descriptive.
Results
The safety population (received ≥ 1 osilodrostat dose) comprises 94/106 enrolled patients: CD, $n=78$; non-CD CS, $n=16$ (adrenal adenoma, $n=3$; adrenal hyperplasia, $n=3$; ectopic, $n=9$; other, $n=1$). For prior and new users, mean (SD) age was 53.0 (12.8), $n=71$ and 54.0 years (12.7), $n=23$, respectively; 73.2% and 60.9% were female; median (min–max) on-study osilodrostat exposure and dose were 6.0M (0.1–13.9) and 5.0 mg/day (1.0–60.0), and 2.7M (0.7–9.2) and 5.7 mg/day (2.0–50.0), respectively. Seven prior and five new users reported 33 and 11 treatment-related AEs, most commonly (>1 occurrence) acute adrenocortical insufficiency, diarrhoea, dizziness (each 3/33, 9.1%) and vomiting (2/33, 6.1%) in prior users, and vomiting (2/11, 18.2%) in new users. In both groups, most AEs were mild or moderate. Two patients discontinued because of five treatment-related AEs (worsening hypertension, uncontrolled blood pressure and dizziness, $n=1$, prior user; nausea and vomiting, $n=1$, new user). SAEs occurred infrequently, in 2.8% of prior ($n=2/71$) and 17.4% of new ($n=4/23$) users. At M3, mUFC, serum cortisol and LNSC were normalised in 72.7% ($n=8/11$), 70.0% ($n=14/20$) and 54.5% ($n=6/11$) of prior users, and in 66.7% ($n=2/3$), 66.7% ($n=4/6$) and 33.3% ($n=1/3$) of new users.

Conclusion
Building on Phase III trial evidence (LINC3, NCT02180217; LINC4, NCT02697734), preliminary results from real-world clinical settings show that osilodrostat is generally well-tolerated in endogenous CS patients and provides control of cortisol production in most prior and new osilodrostat users.
Reference
Fleseriu M *et al*. *Lancet Diabetes Endocrinol* 2021;9:847–75
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Beyond idiopathic arginine vasopressin deficiency: unveiling its etiology after over a decade

Patricia-Maria Anton[1], Serban Radian[1,2], Căpăţînă Cristina[1,2] & Cătălina Poiană[1,2]
[1]National Institute of Endocrinology 'CI Parhon', Pituitary and Neuroendocrine Disorders, Bucharest, Romania; [2]University of Medicine and Pharmacy 'Carol Davila', Bucharest, Romania

Introduction
Arginine vasopressin deficiency (AVP-D) is a rare disorder with diverse etiologies. Approximately 30% of cases are labelled idiopathic, often associated with an underlying autoimmune process. This case report presents a previously presumed idiopathic AVP-D, revealing its aetiology after more than a decade of follow-up.
Case presentation
A 19-year-old male presented in 2012 with symptoms of AVP-D and non-pruritic papular skin lesions on the limbs. Hormonal evaluation confirmed complete AVP-D, and Desmopressin treatment was started. Pituitary MRI revealed the absence of physiologic hyperintense signal of the posterior pituitary on T1-weighted images and a moderate pituitary stalk thickening (PST), with an anteroposterior diameter of 3 mm at the level of the optic chiasm and 2 mm at the pituitary gland insertion, along with a transverse diameter of 5.1 mm, exhibiting a round shape. Thoracic radiography showed normal findings. The dermatological evaluation considered both guttate psoriasis and pityriasis rosea Gilbert as possible diagnostics, and treatment with erythromycin and corticosteroids was recommended, with remission of the skin lesions. After two years of follow-up, hypogonadotropic hypogonadism developed (FSH < 0.2 mU/ml, LH = 0.84 mU/ml, Testosterone = 0.17 ng/ml), and testosterone substitution was given. Additionally, the IGF-1 levels were lower than the sex- and age-specific limits (IGF-1 = 89.2 ng/ml, RR 197-333). Serial pituitary MRIs indicated stable stalk thickness until 2022 when an increase was noted (transverse diameter 5.9 mm). In the same year, abdominal pain, cough and weight loss of 16 kg in 6 months led to the presumed diagnosis of sclerosing cholangitis (SCH) in the context of cystic fibrosis. SCH progressed to severe liver cirrhosis, necessitating transplantation. The patient received Tacrolimus 3 mg/day and oral Methylprednisolone 6 mg/day. Subsequently, considering the presumed diagnosis, a pulmonary consultation was performed, ruling out the diagnosis of cystic fibrosis. Nine months post-transplantation, endocrinological reassessment in the absence of testosterone substitution showed remission of hypogonadism (LH = 4.82 mU/ml, FSH = 2.63 mU/ml, Testosterone = 3.75 ng/ml). The coexistence of SCH, pulmonary cysts and AVP-D raised the suspicion of Langerhans cell histiocytosis (LCH), confirmed by immunohistochemistry on the hepatic specimen. The patient was referred to a haematologist for appropriate treatment.
Conclusion
Regular, long-term follow-ups for AVP-D and PST patients, assessing 'risk' organs, remain essential. A definitive diagnosis for biopsy-worthy conditions may enhance early detection and optimise care. The intriguing observation of hypogonadism reversibility prompts exploration of immunosuppression impact. Following LCH treatment, while diabetes insipidus is usually irreversible, a reduced desmopressin requirement can be anticipated.
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Characterization of patients stopping GH therapy for childhood-onset growth hormone deficiency in belgium - luxemburg

Boutsen Laure[1], Thomas Muriel[2], Staels Willem[3], Lysy Philippe[4], Becker Marianne[5], Anne Rochtus[6], Boros Emese[7], Kathleen De Waele[8], Hilde Dotrement[9], Parent Anne-Simone[10], Daniel Klink[11], Chivu Olimpia[12], Massa Guy[13], Beckers Dominique[1], sylvia Depoorter[14], Reynaert Nele[15], Logghe Karl[16] & Jean De Schepper[17]
[1]CHU UCL Namur, Pediatric Endocrinology, yvoir, Belgium; [2], Brussels; [3]UZ Brussel, Brussels; [4]Cliniques Universitaires Saint-Luc, Brussels, Belgium; [5]Luxembourg, Luxembourg, Luxembourg; [6]UZ Leuven, Leuven, Belgium; [7]Hôpital Universitaire des Enfants Reine Fabiola, Brussels, Belgium; [8]UZ Gent, Gent, Belgium; [9]UZ Antwerpen, Edegem, Belgium; [10]CHU de Liège, Liège, Belgium; [11]ZNA Koniging Paola Kinderziekenhuis, Antwerpen, Belgium; [12]Clinique CHC MontLègia, Liège, Belgium; [13]Jessa Ziekenhuis, Hasselt, Belgium; [14]AZ Sint-Jan, Brugge, Belgium; [15]Ziekenhuis Oost-Limburg, Genk, Belgium; [16]AZ Delta, Roeselare, Belgium; [17]UZ Brussel, Pediatric Endocrinology, Brussel, Belgium

Background
Growth hormone deficiency (GHD) in children comes in different etiologies and can be either isolated or combined with other pituitary hormone deficiencies. The diversity in GHD types and the variable duration of GH therapy complicate assessments of long-term treatment outcome. We characterized GHD patients at the end of GH therapy in Belgium and Luxemburg and evaluated height and adiposity outcomes in relation to GHD type.
Methods
Anthropometric and clinical characteristics of children with GHD who stopped GH therapy between January 2019 and December 2021 were retrieved from the binational BeLUX database (BELGROW).
Results
In total, 179 (119 male and 60 female) patients stopped GH therapy after a median (P10; P90) duration of 6.8 (2.6; 12.9) years. Eight patients received GH therapy for less than 2 years. In total, 113 (63 %) patients had isolated GHD and 66 (37%) combined GHD. Forty-five had congenital GHD (i.e., identified structural or genetic cause), 45 acquired and 89 (50%) idiopathic. All diagnostic categories showed male preponderance (>66 %). Isolated GHD was most prevalent in idiopathic GHD (93.3 % vs 44.2 % in congenital vs 22.2 % in acquired GHD). Ten patients stopped GH therapy before 13 years of age. Ninety -two male and 25 female patients stopped GH therapy after the age of 16 years at a mean (SD) height of 171.2 (7.3) cm and 159.5 (8.9) cm, respectively. Their mean (SD) height (-1.05 (1.0) vs -1.11 (1.48)) and BMI (0.06 (1.65) vs 0.18 (1.5)) z-scores were comparable. In this subgroup older than 16 years, the 66 patients with isolated GHD had significantly ($P = 0.016$) lower height z-scores than the 51 patients with combined GHD (-1.28(1.06) vs.-0.78 (1.13). Mean height and BMI z-scores at the end of GH therapy in patients > 16 years were similar between congenital ($n = 29$), acquired GHD ($n = 32$) and idiopathic GHD ($n = 56$), while mean duration of GH therapy was longest in congenital GHD (9.78 (4.3) vs 6.9 (3.8) vs 6.46(3.7) year; $P = 0.001$).
Conclusion
In GHD patients stopping GH therapy in BeLUx, we see a two-fold male preponderance and 1.7-fold preponderance of isolated GHD. Less than 6 % discontinue GH therapy before 13 years or receive less than 2 years of treatment. In those discontinuing GH therapy after 16 years of age, the height was superior in patients with combined GHD.
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Differences in the efficacy of second-line therapies on the biochemical control of acromegaly in patients with GH secreting pituitary neuroendocrine tumors (Pit-NETs) and GH and PRL cosecreting Pit-NETs

Marta Araujo Castro[1], Almudena Vicente[2], Fernando Cordido[3], Edelmiro Luis Menendez Torre[4], Eider Pascual-Corrales[1], Eva Venegas Moreno[5], Rogelio García Centeno[6], Rocio Villar Taibo[7], Fernando Guerrero[8], Pablo Abellán Galiana[9], Felicia A Hanzu[10], Carmen Fajardo-Montañana[11], Cristina Novo[12], Rosa Camara[13], Maria Dolores Aviles Perez[14], Mónica Marazuela[15], Betina Biagetti[16] & Manel Puig-Domingo[17]
[1]Ramón y Cajal Hospital, Endocrinology & Nutrition, Madrid, Spain; [2]Hospital Universitario de Toledo, Endocrinology & Nutrition, Toledo, Spain; [3]Hospital Universitario de Coruña, Coruña, Spain; [4]Hospital Universitario Central de Asturias, Asturias, Spain; [5]Hospital Universitario Virgen del Rocío, Sevilla, Spain; [6]Hospital Gregorio Marañón, Madrid, Spain; [7]Hospital Santiago de Compostela, Spain; [8]Hospital Universitari de Bellvitge., Spain; [9]Hospital Universitario de Castellón, Spain; [10]Hospital Clinic de Barcelona, Spain; [11]Hospital Ribera, Spain; [12]Hospital Virgen de las Nieves, Spain; [13]Hospital Universitario La Fe, Spain; [14]Hospital Universitario San Cecilio., Spain; [15]Hospital Universitario la Princesa, Spain; [16]Hospital Universitario Vall d'Hebrón, Spain; [17]Hospital Germans Trias i Pujol, Spain

Aim
To evaluate the efficacy of second-line therapies in patients with acromegaly caused by a GH and PRL cosecreting pituitary neuroendocrine tumor (GH&PRL-Pit-NET) and those caused by a GH-Pit-NET.
Methods
A multicenter retrospective clinical practice study of 679 patients with acromegaly in follow-up in 33 tertiary hospitals (ACRO-SPAIN study). For this analysis, only patients on treatment with pasireotide or pegvisomant in monotherapy or in combination with other drugs were included ($n=150$; 22.1%). Patients were classified in two groups: GH-Pit-NET if PRL levels were normal ($n=122$) and GH&PRL-Pit-NET when evidence of hyperprolactinemia and immunohistochemistry (IHC) for GH and PRL was positive or if PRL levels were >100ng/dl regardless of the PRL IHC ($n=28$).
Results
A total of 150 patients with acromegaly accomplish the inclusion criteria. A total of 124 patients were treated with pegvisomant and 49 with pasireotide at any time **(Table 1).** The median time of treatment was of 30.8 months (IQR = 15.9-58.2) with pasireotide and 100 months (IQR = 34.4-138.5) with pegvisomant. No differences in IGF1 control with pasireotide neither with pegvisomant were observed between GH&PRL-Pit-NETs and GH-Pit-NETs **(Table 1).** All GH&PRL-Pit-NET cases treated with pasireotide ($n=6$) and 82.6% ($n=19/23$) of the cases treated with pegvisomant normalized PRL levels. No differences in the rate of IGF1 control between pegvisomant (in monotherapy or combined with dopamine agonists) vs pasireotide (in monotherapy or combined with dopamine agonists) were detected in patients with GH&PRL-Pit-NET (84.9% vs 66.7%, $P=0.178$). Neither in the rate of PRL control (80% vs 100%, $P=0.234$). **Table 1**. Differences in the acromegaly presentation and in the response to second-line medical therapies between GH-Pit-NETs and GH&PRL-Pit-NETs
Conclusion
GH&PRL-Pit-NETs are invasive tumors and present at a younger age than GH-Pit-NETs. However, no differences in the rate of IGF-1 biochemical control with second line therapies were observed between both groups.

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P525

Pituitary apoplexy during the SARS-CoV-2 pandemic. role of acute covid-19 and covid vaccination

Fanny Valsecchi[1,2], Alberto Vassallo[1,2], Marco Losa[3,4], Stefano Frara[1,2], Pietro Mortini[3,4] & Andrea Giustina[1,2]
[1]Vita-Salute San Raffaele University, Institute of Endocrine and Metabolic Sciences, Milan, Italy; [2]IRCCS Ospedale San Raffaele, Endocrinology Unit, Milan, Italy; [3]Vita-Salute San Raffaele University, Chair of Neurosurgery, Milan, Italy; [4]IRCCS Ospedale San Raffaele, Departments of Neurosurgery and Gamma Knife Radiosurgery, Milan, Italy

Background
Pituitary apoplexy (PA) is a rare endocrine and neurosurgical syndrome characterized by pituitary hemorrhage/infarction. SARS-CoV-2 infection and vaccination have been described as possible risk factors for PA, but the real impact of COVID-19 burden on PA epidemiology is still unknown.
Purpose
To investigate the incidence of PA in the pandemic period during exposure to SARS-CoV-2 infection and vaccination and possible peculiar clinical characteristics of COVID-related PA.
Methods
Of retrospectively evaluated 581 consecutive patients who underwent transsphenoidal surgery (TNS) at Neurosurgery Department of IRCCS San Raffaele Hospital between Jan 2017 and Dec 2022, 21 were diagnosed with PA. Patients were divided into pandemic (Jan2020-Dec2022) and pre-pandemic groups (Jan2017-Dec2019). Data on known risk factors for PA, clinical presentation signs/symptoms, radiological and pituitary hormonal status at inpatient evaluation and 6 months after surgery were collected. During the pandemic, a SARS-CoV-2 nasopharyngeal swab was obtained at hospital admission in all patients.
Results
Patients with PA had a mean age of 53.9 ± 14.8 years, a mean BMI of 26.6 ± 3.77 kg/m^2 and were more frequently males (14/21). Number of TNS procedures decreased by 16.7% from pre- to pandemic with similar incidence of PA (12 - 3.8%- vs 9 -3.4%-, respectively). Between the two groups, there were no differences among known risk factors for PA ($P=0.95$), clinical presentation ($P=0.82$), radiological ($P=0.128$) and hormonal ($P=0.21$) status at PA onset. Only pathophysiological difference was that in the pandemic group 3 patients (33%) were highly suspect for COVID-19-related PA: of them 1 experienced PA during hospitalization for SARS-CoV-2 pneumonia and 2 within 8 weeks after mRNA SARS-CoV-2 vaccination. Moreover, during pandemic a significantly better hormonal axes recovery (58.3% vs 22.2%, $P=0.002$) and also a trend toward a prompter neurological improvement at six-month follow-up ($P=0.091$) was observed.
Conclusion
Overall PA incidence was not increased during the SARS-CoV-2 period although data highlight that one third of the patients operated for PA during the pandemic had relevant COVID-19-related issues. This finding may represent paradigm shift in pathogenesis and clinical course of PA in pandemic era although data may be interpreted with caution possibly either overestimating (a casual association can not be excluded) or even underestimating (less severe cases may not be operated upon and shifted to conservative medical treatment) the impact of COVID-19 on PA. Multicenter collaborative studies enrolling a higher number of patients are needed to confirm our results.

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Epidemiology of hypothalamic obesity in craniopharyngioma and other rare sellar and suprasellar tumors

Julian Witte[1], Bastian Surmann[1], Manuel Batram[1], Markus Weinert[1], Mathias Flume[2], Nicolas Touchot[3], Julia Beckhaus[4,5], Carsten Friedrich[4] & Hermann Müller[4]
[1]Vandage GmbH, Bielefeld, Germany; [2]Gene Access GmbH, Dortmund, Germany; [3]Rhythm Pharmaceuticals, Boston MA, United States; [4]University Children's Hospital, Carl von Ossietzky University Oldenburg, Klinikum Oldenburg AöR, Department of Pediatrics and Pediatric Hematology / Oncology, Oldenburg, Germany; [5]Carl von Ossietzky University Oldenburg, Division of Epidemiology and Biometry, Oldenburg, Germany

Background
Hypothalamic obesity (HO) is defined as abnormal weight gain resulting in severe persistent obesity due to physical, tumor- and/or treatment related damage of the hypothalamus. The HO epidemiology is poorly understood. We developed a database algorithm supporting the standardized identification of tumor/treatment-related HO (TTR-HO) patients.
Methods
The algorithm is used to estimate incidence rates of TTR-HO patients in the German healthcare context from a representative claims database ($n=5.42$ million) covering 2010-2020. Patients were identified based on surgery/radiotherapy procedures and HO-associated tumor diagnoses ($n=3,976$). TTR-HO was defined by incident obesity and validated based on incident diabetes insipidus diagnosis and desmopressin prescription within a twelve-month period after surgery/radiotherapy. Uncertainty due to algorithm definitions is explored in sensitivity analyses.

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Table 1. Differences in the acromegaly presentation and in the response to second-line medical therapies between GH-Pit-NETs and GH&PRL-Pit-NETs

	GH-Pit-NET ($n=122$)	GH&PRL-Pit-NET ($n=28$)	P value
CLINICO-RADIOLOGICAL DATA AT ACROMEGALy DIAGNOSIS			
Age (years)	46.2±16.03	38.0±13.77	0.017
Knosp>2 ($n=118$)	51.7% ($n=47/91$)	74.1% ($n=20/27$)	0.039
EFFICACy OF SECOND-LINE MEDICAL THERAPIES (IGF normalization)			
Pasireotide monotherapy or combined with DA ($n=43$)	66.7% ($n=24/36$)	71.4% ($n=5/7$)	0.806
Pasireotide monotherapy ($n=24$)	69.6% ($n=16/23$)	100% ($n=1$)	0.512
Pasireotide+DA	61.5% ($n=8/13$)	66.7% ($n=4/6$)	0.829
Pegvisomant monotherapy or combined with DA/f-SRL ($n=118$)	84.4% ($n=81/96$)	77.3% ($n=17/22$)	0.423
Pegvisomant monotherapy ($n=45$)	85.7% ($n=30/35$)	80% ($n=8/10$)	0.660
Pegvisomant+f-SRL ($n=43$)	79.5% ($n=31/39$)	100% ($n=4$)	0.315
Pegvisomant+DA ($n=20$)	86.7% ($n=13/15$)	60% ($n=3/5$)	0.197
Pegvisomant+pasireotide ($n=6$)	40% ($n=2/5$)	100% ($n=1$)	0.273

DA = dopamine agonists; f-SRL = first generation somatostatin receptor ligands

Results
Estimated annual incidence of TTR-HO in Germany is between 0.7 and 1.7 cases per 1,000,000 persons (2019 prevalence: $n=1,262$ patients). With observed cases in all age groups, two HO-incidence peaks are identified: children/young adults aged 10-14 years and adults aged 40-44 years. Most frequent HO-validated tumor diagnoses are benign sellar/suprasellar tumors (6.1/1,000,000 persons over nine-years), including tumors of the craniopharyngeal duct (3.1/1,000,000), neoplasms of the pituitary gland (4.1/1,000,000), and nonspecific brain tumors of endocrine glands (2.4/1,000,000).
Conclusion
This is the first real-world database analysis of TTR-HO epidemiology, refining current estimates of HO-epidemiology and early patient identification. A more comprehensive characterization of HO patients, along with a better understanding of its clinical implications, will be crucial in developing optimal treatment strategies to improve patient outcomes.

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P527

Soluble alpha klotho concentrations are resistant to short-term stimulation and suppression of growth hormone

Junia Ribeiro de Oliveira Longo Schweizer[1], Katharina Schilbach[1], Olivia Tausendfreund[1], Michael Haenelt[1], Anica Gagliardo[1], Jochen Schopohl[1], Michael Drey[1] & Martin Bidlingmaier[1]
[1]Ludwig Maximilians University, LMU Klinikum; Med. Klinik und Poliklinik IV, München

Background
Serum soluble alpha klotho (sαKL) is a circulating protein which had been shown to be very high in active acromegaly, and significantly reduced after disease control. Therefore, sαKL has been suggested as a new biomarker for growth hormone (GH) excess. In this study, we aimed to evaluate the impact of short-term stimulation and suppression of GH and acute modulation of glucose metabolism on sαKL concentrations.
Methods
Serum sαKL was measured by ELISA (IBL, Hamburg, Germany). Samples were collected during GHRH-Arginine test (0, 30, 60, 90 and 120 min.) in geriatric patients without GH deficiency ($n=9$, 72-94 years, 5 males) and in a cohort of patients with proven GH deficiency (GHD, $n=10$, 22-71years, 5 males). We also evaluated sαKL in healthy participants ($n=22$, aged 22-52 year, 8 males) during oral glucose tolerance test (OGTT: 0,30,60,90,120 and 180 min.).
Results
As expected, GH concentrations (mean ± SD, ng/dl) significantly increased during GHRH-Arginine test in participants without GHD (baseline: 0.78 ± 0.48 vs $_{peak}$GH: 14.7 ± 7.8, $P<0.05$) but not in patients with GHD (baseline: 0.36 ± 0.5 vs $_{peak}$GH: 1.26 ± 1.1, $p>0.05$). Neither in aged patients without GHD (baseline sαKL: 668 ± 174 vs $_{120min}$sαKL: 654 ± 168, $p>0.05$) nor in patients with GHD (baseline: 831 ± 221 vs $_{120min}$sαKL:827 ± 271, $p>0.05$) sαKL concentrations (mean ± SD, pg/ml) varied significantly during GHRH-Arginine test. During OGTT, GH concentrations decreased, and glucose and insulin increased, but sαKL concentrations did not change significantly ($p>0.05$ for all comparisons).
Conclusion
In contrast to chronic GH excess in acromegaly, sαKL concentrations are not significantly affected by short-term stimulation and suppression of GH. Furthermore, acute elevation of glucose and insulin do not significantly impact sαKL concentrations in healthy subjects.

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Predictors of diabetes remission after surgery in patients with acromegaly. a series of 604 cases

Eider Pascual-Corrales[1], Betina Biaggeti[2], Mónica Marazuela[3], Manel Puig-Domingo[4], Víctor Rodríguez Berrocal[5], Ana Irigaray[6], Cristina Novo[7], María Calatayud[8], Ignacio Bernabeu[9], Cristina Álvarez Escolá[10], Carmen Tenorio Jimenez[7], Inmaculada Gonzalez-Molero[11], Pedro Iglesias[12], Concepción Blanco[13], Maria Paz de Miguel Novoa[14], Elena López-Mezquita Torres[15], Cristina Lamas[16], Ana Aulinas Maso[17], Paola Gracia Gimeno[18], José María Recio[19], Miguel Antonio Sampedro Núñez[3], Miguel Paja Fano[20], Maria Dolores Moure Rodriguez[21], Carmen Fajardo-Montañana[22], Fernando Cordido[23], Edelmiro Luis Menendez Torre[24], Juan Carlos Percovich[25], Rogelio García Centeno[25], Rosa Camara[26], Felicia A Hanzu[27], Almudena Vicente[28], Laura Gonzalez Fernandez[25], Fernando Guerrero[29], M Dolores Ollero[6] & Marta Araujo Castro[1]
[1]Hospital Universitario Ramón y Cajal, Endocrinology and Nutrition, Madrid, Spain; [2]Hospital Universitario Vall de Hebrón, Endocrinology and Nutrition, Barcelona, Spain; [3]Hospital Universitario La Princesa, Endocrinology and Nutrition, Madrid, Spain; [4]Hospital Universitario Germans Trias i Pujol, Endocrinology and Nutrition, Spain; [5]Hospital Universitario Ramón y Cajal, Neurosurgery, Madrid, Spain; [6]Complejo Hospitalario de Navarra, Endocrinology and Nutrition, Pamplona, Spain; [7]Hospital Universitario Virgen de las Nieves, Endocrinology and Nutrition, Granada, Spain; [8]Hospital Universitario 12 de Octubre, Endocrinology and Nutrition, Madrid, Spain; [9]Hospital Universitario de Santiago de Compostela, Endocrinology and Nutrition, Santiago de Compostela, Spain; [10]Hospital Universitario La Paz, Endocrinology and Nutrition, Madrid, Spain; [11]Hospital Regional Universitario de Málaga, Endocrinology and Nutrition, Málaga, Spain; [12]Hospital Universitario Puerta de Hierro, Endocrinology and Nutrition, Madrid, Spain; [13]Hospital Universitario Príncipe de Asturias, Endocrinology and Nutrition, Madrid, Spain; [14]Hospital Clínico San Carlos, Endocrinology and Nutrition, Madrid, Spain; [15]Hospital Universitario Clínico San Cecilio, Endocrinology and Nutrition, Granada, Spain; [16]Hospital Universitario De Albacete, Endocrinology and Nutrition, Albacete, Spain; [17]Hospital de la Santa Creu i Sant Pau, Endocrinology and Nutrition, Barcelona, Spain; [18]Hospital Royo Villanova, Endocrinology and Nutrition, Zaragoza, Spain; [19]Hospital Universitario de Salamanca, Endocrinology and Nutrition, Salamanca, Spain; [20]Hospital Universitario de Basurto, Endocrinology and Nutrition, Bilbao, Spain; [21]Hospital de Cruces, Endocrinology and Nutrition, Bilbao, Spain; [22]Hospital Universitario de La Ribera, Endocrinology and Nutrition, Valencia, Spain; [23]Complejo Hospitalario Universitario A Coruña, Endocrinology and Nutrition, A Coruña, Spain; [24]Hospital Universitario Central de Asturias, Endocrinology and Nutrition, Oviedo, Spain; [25]Hospital Universitario Gregorio Marañón, Endocrinology and Nutrition, Madrid, Spain; [26]Hospital Universitario La Fe, Endocrinology and Nutrition, Valencia, Spain; [27]Hospital Universitario Clinic, Endocrinology and Nutrition, Barcelona, Spain; [28]Hospital Universitario de Toledo, Endocrinology and Nutrition, Toledo, Spain; [29]Hospital Universitario de Bellvitge, Endocrinology and Nutrition, Barcelona, Spain

Aim
To investigate the impact of pituitary surgery on glucose metabolism and to identify predictors of diabetes remission after surgery in patients with acromegaly.
Methods
A national multicenter retrospective study of acromegaly patients undergoing transsphenoidal surgery for the first time at 33 tertiary Spanish hospitals (ACRO-SPAIN study, $n=604$) was performed. Surgical remission was evaluated according to the 2000 and 2010 criteria. Glucose metabolism and metabolic control were evaluated before, within 3 months after surgery and at the long-term follow up (last available visit).
Results
A total of 604 acromegaly patients were included in the study with a median follow up of 91 months (IQR 45-163). The mean age was 47.8 ± 14.0 years and 58.9% ($n=356$) were women. At baseline, 23.8% of the patients had type 2 diabetes mellitus (T2DM) with a median of glycated hemoglobin (HbA1c) levels of 6.9% (IQR 6.4-7.9) and of fasting plasma glucose (FPG) levels of 143 mg/dl (IQR 124-169). We observed a positive correlation between IGF-1 levels at acromegaly diagnosis and FPG($r=0.16$, $P<0.001$) and HbA1c($r=0.18$, $P=0.001$) levels. No correlation between initial GH levels and FPG or HbA1c levels was found. In the multivariate analysis, an older age(OR 1.02 per each in increase in year, 95%CI 1.00-1.05), having dyslipidemia(OR 5.26, 95%CI 2.82-9.79) and higher IGF-1 levels (OR 1.30 per each increase in standard deviation above the upper limit of normal, 95%CI 1.05-1.60) were associated with a greater prevalence of T2DM. At the last follow-up visit after surgery, 53.4% of the patients achieved surgical remission based on the Cortina criteria and 41.4% based on the 2010 criteria. A significant improvement in FPG and HbA1c levels was observed in the global cohort, being greater in the group of T2DM patients($P<0.001$). No differences in the rate of reduction of HbA1c or FPG levels were observed between patients pretreated and not pretreated with first generation somatostatin receptor ligands; neither between patients cured of acromegaly after surgery and those who did not. After surgery, 21.3% of the T2DM patients, 56.7% of them with surgical remission of acromegaly(2010criteria), experienced diabetes remission. The cure of T2DM was more common in older patients(HR 1.77), when surgical cure was achieved(HR 2.10) and when anterior pituitary function was not affected after surgery(HR 3.38).
Conclusion
Glucose metabolism improved in patients with acromegaly after surgery, especially in T2DM patients. The remission of T2DM was more frequent in patients with older age, with surgical cure and preserved anterior pituitary function after surgery.

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P529

A peculiar case of ectopic ACTH-syndrome – multiple challenges during diagnostic and therapeutic workup

Annamária Kövesdi[1,2], Judit Tőke[1,3], Katalin Eitler[1,4], Gergely Kiss[1,5], Nóra Nyilas[1,6], Bálint Scheich[1,7] & Miklós Tóth[1,8]
[1]Semmelweis University; [2]Semmelweis University, Department of Internal Medicine and Oncology; [3]Semmelweis University, Budapest, Department of Internal Medicine and Oncology; [4]Semmelweis University, Budapest, Department of Surgery, Transplantation and Gastroenterology; [5]Semmelweis University, Budapest, Department of Radiology, Medical Imaging Centre; [6]Semmelweis University, Budapest, Department of Neuroradiology, Medical Imaging Centre; [7], Semmelweis University, Budapest, Department of Pathology and Experimental Cancer Research; [8], Semmelweis University, Budapest, Department of Internal Medicine and Oncology

Case description
A 32-year-old male patient was treated with remdesivir and high-dose steroid for severe COVID-19 pneumonia in an ICU for one month. He was later diagnosed with steroid-induced diabetes mellitus. An endocrinological consultation raised the possibility of endogenous Cushing's syndrome. He was then referred to our department for further investigation of suspected Cushing's syndrome (CS). The patient presented with typical physical signs and symptoms of CS. Severe ACTH-dependent hypercortisolism was diagnosed. The high dose dexamethasone test, the marked ACTH response to iv. desmopressin and a pituitary microadenoma revealed by MRI suggested Cushing's disease. However, chest CT showed a 1 cm mass compatible with a pulmonary NET in the left S7. In the first phase of investigations, the origin of the ACTH-dependent CS was equivocal. All of the non-invasive tests argued for the pituitary source of ACTH excess. Because of the high radiological suspicion of pulmonary NET, and despite the results of the traditional hormone tests, both our pituitary and pulmonary boards suggested pulmonary surgery as a first-line intervention. Thus, a segmentectomy was performed; histology confirmed a typical bronchial carcinoid with intense ACTH expression. Postoperatively, persisting hypercortisolism was proved, necessitating an inferior petrosal sinus sampling (IPSS). IPSS excluded CD and unambiguously confirmed the ectopic nature of ACTH secretion. Unfortunately, all the postoperative imaging modalities, including ^{18}FDG-PET-CT and Tc-99m-Tektrotyd SPECT/CT, were negative, suggesting an occult residual metastatic tumour. ^{68}Ga-DOTATOC-PET-CT was suggested; however, the patient could not afford it. Metyrapone, followed by osilodrostate, was started. Severe resistant hypercortisolism persisted, leading to pathological vertebral compression fractures, despite 6 months of treatment with osilodrostate in a daily doses of up to 2x15 mg. However, no metastatic lesion could be identified. We decided to perform a bilateral total adrenalectomy, which resulted in a prompt resolution of hypercortisolism. The localization of suspected metastatic tumour(s) is still uncovered.

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P530

The analgesic effect of pasireotide in aggressive, giant pituitary neuroendocrine tumors-case series

Karol Ciszek[1], Anna Bogusławska[1], Maria Aleksandra Komisarz-Calik[1], Alicja Hubalewska-Dydejczyk[1] & Aleksandra Gilis-Januszewska[1]
[1]Chair and Department of Endocrinology, Jagiellonian University, Medical College, Cracow, Poland

Pasireotide is a a synthetic polypeptide second-generation somatostatin analogue that can be used in the treatment of GH- and ACTH- secreting pituitary neuroendocrine tumors (PitNETs), however, there are single reports of pasireotide treatment in other subtype of PitNETs. We present a case series of aggressive, giant PitNETs treated with pasireotide alone or as multimodal therapy.
Case 1
A 33-year-old male reported to the Clinic due to severe headaches and vomiting. In MRI pituitary mass 33×39×55 mm and a cerebral oedema were revealed. TSS with external ventricular drainage were performed. Histopathology results showed densely granulated silent corticotroph adenoma subtype 1, Ki67 < 1%. After 3 months, MRI showed tumour progression to 39×40×30 mm. Two emergency TSS followed by stereotactic radiotherapy were performed. Combined therapy with cabergoline and temozolomide was introduced. Due to sever headaches pasireotide was introduced. After 18 months, stabilization of the disease was observed with complete remission of headaches.
Case 2
A 59-year-old male underwent transsphenoidal surgery (TSS) ten years ago due to severe headaches and visual deficits. Histopathology results showed partially acidophilic adenoma (FSH- LH- GH- ACTH- PRL-). Control MRI showed tumour regrowth - 56×56×89 mm mass invading local structures. The patient was qualified for radiotherapy, to which he did not consent. Due to the progression of symptoms, temozolomide and pasireotide were introduced. After 5 months, significant improvement in headaches and vision was observed. In MRI stable pituitary mass was noted.
Case 3
A 59-year-old male presented with severe headaches and life-threatening tumour mass effect. In MRI a 48x48x33mm mass was observed. The patient underwent two non-radical TSS, 4 cycles of pasireotide, and cyberknife treatment. Histopathology showed gonadotroph PitNET, Ki < 67%. MRI showed tumour shrinkage to 45×46×29 mm, with persistent severe headaches. The patient was re-qualified for pasireotide treatment.
Case 4
A 17-year-old male with dopamine resistant giant prolactinoma underwent after recent two non-radical surgeries presented in the clinic due to daily severe headaches and peripheral vision loss. In control MRIs progressing mass 38×34×33 mm invading local structures was observed. Due to worsening of the symptoms, pasireotide was introduced resulting in a decrease of headaches and improvement in vision. The tumour size remained stationary.
Conclusion
Our study demonstrates the clinical potential and the efficacy of pasireotide treatment in aggressive, giant PitNETs. The therapy alone, or in combination has a potential role to reduce the tumour size, decrease the headaches, and allows the stabilization of the disease.

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P531

Potential antitumoral effects through modulation of VEGF-A splicing in rat somatotroph and lactotroph pituitary tumoral cells

Donatella Treppiedi[1], Sonia Di Bari[2], Federica Mangili[1], Giusy Marra[2], Anna Maria Barbieri[2], Federico Arlati[2], Marco Locatelli[3,4], Andrea Lania[5,6], Erika Peverelli[1,2] & Giovanna Mantovani[1,2]
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [2]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [3]University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy; [4]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Neurosurgery Unit, Milan, Italy; [5]IRCCS Humanitas Research Hospital, Endocrinology, Diabetology and Medical Andrology Unit, Milan, Italy; [6]Humanitas University, Department of Biomedical Sciences, Milan, Italy

Alternative splicing is a crucial mechanism of gene regulation and this process can be dysregulated in cancer. In pituitary tumors (PitNETs), alteration in the serine/arginine-rich splicing factors (SRSFs) has been reported. Newly synthetized SRSFs are phosphorylated by serine-arginine protein kinase 1 (SRPK1) to facilitate their nuclear import. In response to extracellular stimuli SRPK1 may translocate to the nucleus as well to hyperphosphorylate SRSFs and favor their interaction with mRNA and the initiation of alternative splicing. SRPK1 is considered a proto-oncogene and its inhibition by small molecule inhibitors have shown antitumoral effects via the SRPK1-SRSF1-VEGF-A pathway modulation in different cancer types, however, so far, no studies have been carried out in the pituitary. This project aims to explore the role of SRPK1 inhibitors SRPIN340 and SPHINX31 in pituitary somato-lactotroph tumoral cells (GH4 and MMQ cells) by looking at the VEGF-A alternative splicing regulation, and to investigate SRPK1 protein expression levels in GH-secreting PitNETs. First, an abolishment of the EGF-mediated SRPK1 nuclear translocation in GH4 cells upon 10μM SRPIN340 incubation was observed by immunofluorescence experiments. This data, along with immunoblot results showing a reduction of phosphorylation of SRSFs induced by SRPIN340 and SPHINX31, demonstrated the efficacy of these compounds in impairing SRPK1 activity. SRPIN340 reduced cell proliferation (-38.9(43.9)%, p $0 < 0.05$ vs basal at 1μM), cell migration (-65(46.3)%, $P < 0.001$ vs basal at 10μM) and induced cell apoptosis (+40.5(26.6)%, $P < 0.05$ vs basal at 10 μM), in GH4 cells. Similar results were obtained in MMQ cells and comparable effects between SRPIN340 and SPHINX31 were observed in both cell lines. Moreover, both SRPIN340 and SPHINX31 reduced PRL secretion in MMQ cells (-30.2(49)% $P < 0.05$ vs basal, -39.2(18)% $P < 0.001$ vs basal, at 10μM SRPIN340- and SPHINX31-treated cells, respectively). In addition, the pro-angiogenic and pro-mitotic VEGF-A_{164a} transcript isoform was significantly decreased by both inhibitors in GH4 cells (-61(33.5)% $P < 0.05$ vs basal, -55(20.5)% $P < 0.05$ vs basal, in SRPIN340- and SPHINX31-treated cells, respectively). Finally, SRPK1 was expressed at variable levels in 14 GH-secreting PitNETs. Interestingly, an overexpression of SRPK1 was found in GH-secreting PitNETs tissues whose corresponding primary cultures were *in vitro* resistant to octreotide in terms of GH suppression (0.09(0.31) vs 0.02(0.03), $P < 0.05$ vs *in vitro* responder group). In conclusion, SRPK1 inhibition may represent a novel strategy to exert antitumoral effects in

somato-lactotroph tumoral cells via SRPK1-SRSF1-VEGF-A pathway regulation. Further studies are needed to investigate the role of SRPK1 as a potential marker of octreotide responsiveness in GH-secreting PitNETs.

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Electronic health technologies for comprehensive acromegaly management. preliminary data from a single center experience

Giulia Carosi[1], Giulia Del Sindaco[1,2], Elisa Sala[1], Alessandra Mangone[1,2], Roberta Mungari[1], Arianna Cremaschi[1], Emanuele Ferrante[1] & Giovanna Mantovani[1,2]
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [2]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy

Background
Acromegaly is a chronic disease which causes multiple impairments that negatively affect daily life. Telemedicine is proving to be useful in diagnosing and treating these disabling aspects, including psycho-physical comorbidities, which are difficult to investigate during conventional visits.
Aim of the study
To improve the management of acromegaly, both in cured and active disease, through the use of telemedicine technologies in addition to conventional visits, tailoring individual healthcare pathways.
Methods
We conducted a prospective study in patients with a diagnosis of acromegaly. We randomly assigned to participants a web-based email system (electronic Health Device group or 'eHD group'). For 12 months, this group received periodic questionnaires that explored different areas such as adherence to therapy, quality of life, psychological and disease-specific symptoms (e.g. Acromegaly Quality of Life Questionnaire 'AcroQoL', Epworth Sleepiness Scale 'ESS', Beck-Depression-Inventory-II 'BDI-II'). Additionally, all patients underwent conventional on-site clinical assessments. Data collected were stored on a dedicated portal and statistically analysed.
Results
We enrolled 60 acromegalic patients (50% in the eHD group and 50% controls), 50/60 completed the study. Females were 56% and mean age was 59.6 years. Sex distribution and age were comparable in the two groups. Patients in the eHD group actively answered questionnaires for a mean time of 4 months (range = 2-11), with higher compliance for monthly and trimestral questionnaires as compared to weekly ones (adherence of 91%, 88%, and 64%, respectively). Periodical questionnaires in eHD group revealed that some patients experienced severe clinical deterioration, which required specialist consultation during the study (e.g. BDI-II results showed that two patients experienced severe depression and two patients suffered from obstructive sleep apnea according to ESS results). At baseline, 70% of the participants were on medical treatment for acromegaly (pegvisomant or somatostatin analogues) and 30% were on remission. At the end of the study, biochemical disease control improved in 20% of the eHD group vs 8% of controls ($P = 0.42$). A worsening was observed in 8% of participants in the control group only ($P = 0.53$) and disease was stable in the remaining patients. Data collected from the eHD group showed a high adherence to medical therapy for acromegaly (95%, both with pegvisomant and somatostatin analogues).
Conclusion
our preliminary data indicates that telemedicine may be used to monitor and manage symptoms, personalize follow-up, and promote treatment compliance, thereby improving the clinical management of acromegaly.

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The relations between serum growth hormone, seminal plasma growth hormone, and sperm count in acromegaly patients

Ebru Cicek[1], Cem Sulu[1], Serdar Sahin[1], Hamdi Ozkara[1], Hande Ozkaya[1], Rosario Pivonello[2] & Pinar Kadioglu[1]
[1]Cerrahpasa Medical Faculty Hospital, Turkey; [2]University of Naples Federico II, Napoli, Italy

Aim
To investigate the relationship between serum growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels, seminal plasma GH and IGF-1 levels, and sperm parameters in acromegalic patients.
Methods
A cross-sectional study was conducted on 24 acromegaly patients (acromegaly group), 11 non-functioning adenoma (NFA) patients (NFA group), and 16 healthy men (control group). Seminal plasma GH and IGF-1 levels were measured. Semen parameters and seminal plasma hormone levels were compared. Mediation analysis using SPSS PROCESS macro was performed to evaluate the relations between serum and seminal plasma GH/IGF-1 levels and sperm parameters.
Results
Acromegaly group had higher levels of serum GH (0.475 IQR[0.245 -0.770] mg/l) compared to NFA (0.08 IQR[0.054 - 0.260] mg/l) and control groups (0.08 IQR[0.03 - 0.159] mg/l) ($P < 0.001$). Although seminal plasma GH levels were higher in acromegaly group (114 $\pm$ 82 pg/ml) than NFA (43 $\pm$ 19 pg/ml) and control groups (61 $\pm$ 39 pg/ml) ($P = 0.004$), seminal plasma IGF-1 showed no difference among groups ($P = 0.203$). The serum GH was positively correlated with seminal plasma GH ($r = 0.530$, $P < 0.001$). The mediation analyses showed that serum GH directly affected sperm count ($\beta = 80.2$, $P = 0.0026$), and this effect was not mediated by an increase in seminal plasma GH ($\beta = 0.06$, $P = 0.720$).
Conclusion
The findings of this study suggest that sperm count may be negatively affected in acromegalic patients despite intact hypothalamic-pituitary-gonadal axis, and this association could be linked to elevated serum GH levels rather than increased seminal plasma GH. While our study provided important preliminary data regarding the seminal plasma GH and IGF-1 levels, the underlying the specific effects of seminal plasma GH and IGF-1 on testicular function of acromegaly patients require more in-depth research.

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Implications of somatotroph axis in the behaviour of silent corticotroph tumours

Cristina Guillen[1,2,3], Johana Sottile[1], Elena García-Garrigós[1,2,2,4], Maria Eugenia Torregrosa[1,2,5], Maria Niveiro[1,2,6], Javier Abarca[1,2,7], Luis Valor[1] & Antonio Pico[1,2,3,8,9]
[1]Instituto de Investigación Sanitaria y Biomédica de Alicante (Isabial), Endocrinology & Nutrition, Alicante, Spain; [2]Hospital General Universitario Dr. Balmis, Radiology; [3], Endocrinology & Nutrition; [4], Radiology; [5], Clinical Analysis-Hormones; [6], Pathology; [7], Neurosurgery; [8]University Miguel Hernandez, Clinical Medicine, Alicante; [9]Ciberer, Neuroendocrinology

Silent corticotroph tumors (SCT) represent a distinct subtype of pituitary tumors (PT) known for their potential aggressiveness, surpassing other silent PTs like gonadotroph tumors (SGT). Despite their aggressive clinical behavior, the mechanisms underlying their aggressiveness remain unclear. Recent studies in various cancers, such as breast cancer, have implicated the IGF1 axis in the presence of metastases. This study aims to investigate some components of the somatotroph axis in a cohort of 31 SCTs and a control group of 67 SGTs, all monitored in a PTOCE since 2012. Demographic, biochemical, and radiological variables were analyzed, alongside the expression (quantitative PCR) of GH, GHRH, and somatostatin subtype receptors ($sst_{1,2,3,5}$). Results showed that SCT patients were predominantly women and younger compared to SGT patients. While tumor size and invasion percentages showed no significant differences between groups, SCTs exhibited a significantly higher Signal Intensity Ratio (SIR) and increased proliferation (Ki67 qPCR), along with a higher recurrence rate than SGTs. Cortisol levels were comparable, but SCTs displayed significantly elevated levels of ACTH and, notably, IGF1 compared to SGTs. SCTs had significantly higher expression of sst2, and lower expression of sst3, with no significant differences in the expression of GH, GHRH, and $sst_{1,5}$ between the two groups. In conclusion. Elevated levels of ACTH and IGF1 in SCTs underscore the intricate interplay between the somatotroph and corticotroph axes. These findings suggest a potential crosstalk mechanism that contributes to the unique characteristics of SCTs, influencing their aggressiveness and clinical course and offering a more tailored and effective therapeutic approach

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Assessment of endothelial dysfunction in cushings syndrome

Tugce Apaydin[1], Ceyda Dinçer yazan[2] & Dilek Gogas yavuz[2]
[1]Alanya Alaaddin Keykubat University Training Hospital, Endocrinology and Metabolism, Antalya, Turkey; [2]Marmara University Faculty of Medicine, Endocrinology and Metabolism, Istanbul, Turkey

Introduction
Cushingˋs Syndrome (CS) is associated with endothelial dysfunction and premature atherosclerosis, which occurs due to hypercortisolism itself and associated comorbidities including diabetes and hypertension. Advanced glycation end products (AGE) are heterogeneous compounds produced endogenously from the non-enzymatic glycation of proteins, lipids, and nucleic acids, leading to the activation of various stress-induced transcription factors through the stimulation of oxidative stress, and pro-inflammatory mediators such as cytokines and acute phase proteins, and consequently causes vascular dysfunction. Cardiovascular disease is the main cause of mortality in subjects with CS, and endothelial dysfunction is an early parameter for cardiovascular risk. With the hypothesis that hypercortisolemia in CS may itself lead to endothelial dysfunction by increasing AGE production, we aimed to evaluate microvascular function in CS with carotid intima-media thickness (CIMT) and to investigate the relationship between endothelial dysfunction and AGE.
Methods
Forty patients with active CS and 56 age- and sex-matched subjects without known inflammatory disease were enrolled in this cross-sectional study. Measurement of CIMT was performed by a single blind vascular sonographer using Doppler USG. Serum AGE and carboxymethyl lysine (CML) levels were measured by ELISA.
Results
Age, gender, BMI, the frequency of diabetes mellitus and hypertension were similar in the CS and control groups. While 65% of cases had pituitary Cushingˋs disease ($n=26$), the remaining 14 cases were adrenal CS (35%). CIMT was higher in CS than in the control group (0.615 ± 0.076 mm vs 0.517 ± 0.152 mm; $P<0.001$), but CML and AGE levels were similar in both groups ($p>0.05$). After adjustment for diabetes and hypertension, CIMT was still higher in CS but there were no significant differences between the CS and control groups in terms of CML and AGE levels ($p>0.05$). According to univariate regression analysis, there was no statistically significant association between CIMT and CML, AGE levels.
Discussion
CIMT, an early predictor of subsequent cardiovascular events or mortality, was increased in subjects with CS. Large-scale studies are needed to make definite conclusions about the effect of AGE levels on CIMT.

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P536

Prevalence of steatosis and cardio-metabolic complications in a cohort of adult patients with growth hormone deficiency: a cross-sectional study

Alessandro Risio[1], Eriselda Profka[1,2], Giulia Rodari[1,2], Giovanna Oberti[3], valeria citterio[1], Valentina Collini[1], Federico Giacchetti[2], Anna Ludovica Fracanzani[3,4], Rosa Lombardi[3,4], Giovanna Mantovani[1,2] & Claudia Giavoli[1,2]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Unit of Internal Medicine and Metabolic Diseases, Milan; [4]University of Milan, Department of Pathophysiology and Transplantation, Milan

Introduction
Adults with growth hormone deficiency (AGHD) have increased prevalence of hepatic steatosis (HS) that might be improved by growth hormone replacement therapy (rhGH). However, data on this topic are conflincting and scanty. Aim: to evaluate prevalence of HS, organ-specific distribution of adipose tissue and cardiovascular impairment in AGHD.
Methods
cross-sectional collection of clinical, biochemical and instrumental data (abdominal ultrasound, fibroscan, assessment of epicardial fat, supra-aortic trunks ultrasound and body composition through bio impedence) in AGHD.
Results
Fifty subjects (M/F 25/25, median age 54.5 years, IQR 46-65, median disease duration 14 years, IQR 9-21 years) were consecutively enrolled. Among them, 32/50 patients were currently on rhGH (median dose 2.4 mg/week, IQR 1.2-5.2, duration 15.6 ± 8.2 years). In the whole cohort, 37/50 patients showed HS (74% vs around 20% in the worldwide general population), with 38% prevalence of moderate and severe forms and 6% of hepatic fibrosis. The prevalence of carotid plaques was 32% and of increased epicardial fat was 27.7%. Prevalence of hypertransaminasemia was higher in untreated than treated AGHD (27.8% vs 3.2%, $P=0.02$). Although not statistically significant, possibly due to sample size, untreated patients showed higher prevalence of steatosis (15/18, 83% vs 22/32, 69%), cardiovascular events (4/18, 22.2% vs 1/32, 3.1%), increased epicardial fat (41.2% vs 20%), and carotid plaques (44% vs 25%) than treated ones, with a negative association between rhGH dose and intima-media thickness ($P=0.02$). No difference was found in median age ($P=0.27$) an sex ($P=0.56$) between the two groups. Lastly, AGHD with HS were compared to a cohort of 42 patients with non-alcoholic fatty liver disease (NAFLD). Despite a similar prevalence of hypertension, atherosclerosis and dyslipidemia, AGHD showed lower fat mass (33.2%, IQR 25.2-38.5% vs 40.2%, IQR 35.7-45.6, $P<0.001$) and lower prevalence of metabolic syndrome (36.1% vs 66.7%, $P=0.01$) and diabetes (5.4% vs 23.8%, $P=0.02$). Interestingly, AGHD were younger than NAFLD patients (53.4 ± 15.8 years vs 64.5 ± 12.2 years, $P=0.001$).
Conclusion
HS, carotid atherosclerosis and increased epicardial fat are highly prevalent in AGHD. When compared with NAFLD patients, AGHD with HS, though younger and with lower percentage of fat mass and metabolic syndrome, showed a similar prevalence of hypertension, atherosclerosis and dyslipidemia. These findings suggest a pathogenetic role of GHD in the development of metabolic complications, while the higher prevalence of hepatic derangement in untreated AGHD supports a possible impact of rhGH. We ought to confirm our findings by comparing them with age and sex- matched NAFLD patients.

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P537

Panhypopituitarism and diabetes mellitus in a woman with HIST1H1E syndrome

carlien de herdt[1] & De Block Christophe[1]
[1]Antwerp University Hospital, Endocrinology, diabetology and metabolism, Edegem, Belgium

Introduction
HIST1H1E syndrome is a rare disorder caused by a de novo gene mutation encoding for histone H1-4 affecting a whole range of cellular processes. The phenotype is dominated by neurodevelopment disorders and facial deformities. Endocrinopathies and diabetes mellitus are not the main clinical features. The case of a woman with HIST1H1E syndrome associated with diabetes mellitus and panhypopituitarism is presented.
Case presentation
A 19-year-old woman was referred to the endocrinology department because of primary amenorrhea and absence of secondary sexual characteristics. At the age of 12 years she was diagnosed with HIST1H1E syndrome. Growth curve was not available and height at the moment of consultation was 156 cm and BMI 20 kg/m^2. Pituitary function revealed central hypothyroidism, hypogonadotropic hypogonadism and low IGF-1. GH deficiency was confirmed with an insulin tolerance test. Cortisol deficiency was excluded and there were no arguments for AVP deficiency. Reviewing a blood sample at the age of 9 years, a normal thyrotropic axis was measured. MRI of the pituitary was normal. X-ray of the hand showed an almost closed growth plate. Bone density showed osteoporosis. The blood sample showed hyperglycaemia with an HbA1c of 13.9% (128 mmol/mol) and low c-peptide (0.08 nmol/l). Insulin therapy was started.
Conclusion
HIST1H1E syndrome is rare as only 52 cases have been described in the literature. Endocrinopathies are rarely associated with this syndrome as only 6 previous cases had hypothyroidism. In 2023 the first case of a young girl with HIST1H1E syndrome and short stature due to panhypopituitarism (TSH, LH/FSH, GH deficiency) was published. MRI showed a hypoplastic pituitary gland. We present the second case of a woman with panhypopituitarism (TSH, LH/FSH, growth hormone deficiency), associated with HIST1H1E syndrome after presenting with primary amenorrhea. Corticotropic axis is preserved in both cases. We hypothesize the dysfunctional histones lead to a PROP1-related combined pituitary hormone deficiency. However, it is unclear why the other published cases did not show hypopituitarism except for these cases concern children and pituitary deficiency may not have already developed. Diabetes mellitus type 2 has previously been described in only one 19-year-old woman with HIST1H1E syndrome. Our case has an impaired insulin secretion questioning the possible association of the pathogenic histone variants with loss of β cell function. Given the rareness of this syndrome, it is however uncertain if clinical features as hypopituitarism and diabetes mellitus are related to the dysfunctional histones or are incidental findings.

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Patient with granulomatous hypophysitis in the course of granulomatosis with polyangiitis (GPA) misdiagnosed as craniopharyngioma

Monika Piasecka[1], Anna Lewczuk-Myślicka[1], Łukasz Obołończyk[2], Sonia Kaniuka-Jakubowska[1] & Renata Świątkowska-Stodulska[1]
[1]Medical University of Gdansk, Department of Endocrinology and Internal Medicine, Gdansk, Poland; [2]Institute of Maritime and Tropical Medicine, Medical University of Gdansk, Depatrment of Occupational, Metabolic and Internal Medicine, Gdynia, Poland

Introduction
Idiopathic granulomatous hypophysitis (IGH) is a rare inflammatory disease that may present with radiological changes in the pituitary gland. Diagnosis with non-specific syndromes becomes challenging. Secondary causes of granulomatous hypophysitis include tuberculosis, sarcoidosis, syphilis, Langerhans cell histiocytosis, GPA, and Rathke's cleft cyst rupture. GPA is a multisystem disease, characterized by necrotizing small-vessel vasculitis, mostly affecting the lung, kidneys, ears, nose, and throat, but potentially it can involve any organs. Pituitary involvement in GPA is rare, estimated occurrence is about 1 % of all cases.
Case description
The history of the 18-year-old woman began a few months before admitting to our Department, with a throbbing headache and dropping the right eyelid. Her CT revealed no pathology, however in head MR the sellar mass (12x14x14mm) was described. Additionally, mucosal changes filling almost completely the left maxillary sinus and the ethmoid on the left side were found. The lesion was described as craniopharyngioma. Four months later pituitary MR demonstrated a sellar lesion ($17\times21\times11$ mm) with compression of the optic chiasm. The pituitary gland could not be delineated in the sellar region. Mucosal thickening was observed in all sinuses. It has been described again as intrasellar and suprasellar mass which might correspond to a craniopharyngioma. Additional tests revealed high antinuclear antibodies ANA titer, positive anti-RNP/Sm antibodies, and antibodies against B centromeres and DFS 70. Due to the positive result of the Schrimer test, the suspicion of Sjögren's syndrome was raised. During the next month, the patient's clinical status deteriorated. She reported fever, fatigue, and headache, along with nausea and vomiting, occurring mostly in the morning. She underwent transsphenoidal resection of the pituitary region mass. After the surgery the pituitary hormonal assessment was done, confirming panhypopituitarism. Despite the surgical procedure and the hormonal replacement therapy, the patient's general condition did not improve as it was expected. The obtained pathomorphological results indicated granulomatous inflammation. Once the histopathologic diagnosis was established, the patient underwent further tests for systemic granulomatous disease. GPA was diagnosed based on recurrent sinusitis, and positive autoantibodies c-ANCA.
Conclusion
The correct diagnosis is essential to avoid surgical treatment, which is not recommended in pituitary GPA. Publications present satisfactory responses to steroid and immunosuppressive treatment. It is important to keep in mind the rare causes of damage of the sellar region and not neglect of coexisting symptoms even those not specific to pituitary diseases.

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COVID-19 and hyponatremia: from possibility to probability

Kristina Steiner[1], Silvija Canecki-Varžić[1,2], Ema Schönberger[1,2], Romana Marušić[2,3], Klara Ormanac[1,2] & Ines Bilić-Ćurčić[1,2]
[1]Clinical Hospital Center Osijek, Department of Endocrinology, Osijek, Croatia; [2]Faculty of Medicine Osijek, Osijek, Croatia; [3]General Hospital Vukovar, Department of Internal Medicine, Vukovar, Croatia

Introduction
Hyponatremia is the most common electrolyte imbalance in hospitalized patients and frequent finding in intensive care units. Hyponatremia is characterized with serum sodium values less than 135 mmol/l and defined by the ratio of total sodium and total body water. It presents with lethargy, confusion, neuromuscular excitability, hyperreflexia, stupor and even coma. In addition to neurological signs and symptoms, assessment of hyponatremia is based on severity and duration. There are several etiological factors leading to hyponatremia, so diagnosis and treatment present a challenge in everyday clinical practice.
Case report
In this case report we present a 71-year-old woman who presented herself to the emergency department due to weakness. Besides general fatigue, she reported a tingling sensation in the whole body and flatulence which lasted for 3-4 days. She has been vomiting lately. No other neurological symptoms have been observed. Based on her previous medical documentation we ascertain that due to similar symptoms, she has visited the emergency department several times. In her medical history, she has been treated with indapamide due to arterial hypertension, and a month ago she was treated for COVID-19. In physical examination, euvolemia was present, with normal vital parameters. An initial examination was performed and severe hyponatremia was verified with a serum sodium level of 110 mmol/l. Urine analysis showed an osmolality of 406 mOsmol/kg and sodium level of 45 mmol/l, X-ray examination was described as normal. Endocrinological workup excluded adrenal insufficiency and hypothyroidism, thus the diagnosis of SIADH was the most probable one. Additional investigation of medical records revealed that a month ago, while being treated due to COVID-19 patient had unrecognized serum sodium levels of 127 mmol/l and 116 mmol/l, respectively. In the emergency department, hyponatremia was corrected by intravenous administration of 3% NaCl for 20 minutes, with an increase in serum sodium by 4mmol/l. The patient was hospitalized and the gradual increase in serum sodium levels was monitored with fluid withdrawal to 800 mL per day which led to complete recovery and correction of electrolyte disbalance.
Conclusion
In this case report we intended to emphasize how important it is to recognize hyponatremia in COVID-19 patients, which can be caused by two mechanisms: SIADH due to Interleukin-6 induced non-osmotic release of vasopressin or loss of Na due to diarrhea and vomiting. Distinguishing between the two is essential for timely and correct treatment to avoid severe hyponatremia that can have potentially fatal consequences.

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P540

Pituitary apoplexy – a tertiary centre experience

Matej Rakusa[1,2], Roman Bošnjak[3] & Tomaž Kocjan[1,2]
[1], Department of Endocrinology, Diabetes and Metabolic Disease, University Medical Centre Ljubljana, Ljubljana, Slovenia; [2]Department of Internal Medicine, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia; [3], Department of Neurosurgery, University Medical Centre Ljubljana, Ljubljana, Slovenia

Background
Pituitary apoplexy (PA) is a rare, potentially life-threatening endocrine emergency, due to abrupt pituitary haemorrhage and/or infarction, usually within a pituitary adenoma. PA most commonly presents with severe headache, visual and oculomotor activity disturbances, nausea/vomiting and/or altered mental status. The outcome is variable and difficult to predict. Most proposed risk factors are hypertension (HTN), diabetes mellitus (DM), and anticoagulant treatment. Optimal management of PA is still controversial due to rarity of the condition.
Aim
To assess the characteristics and the outcomes of our patients with PA.
Material and methods
We retrospectively analysed medical records of patients with PA managed at the national tertiary care centre from 2010 to 2023. We collected data for adenoma size, hormone deficiency, visual and oculomotor activity disturbances at the time of presentation and after at least 3 months later. We also checked for operative treatment or spontaneous reduction of adenoma when not operated on, presence of HTN, DM or anticoagulant treatment.
Results
Sixteen patients (11 males, 68,8%) of median age 66,5 (IQR 20) with PA were identified during the studied period. At presentation, 14 of them (87,5%) had adrenocorticotropic and 15 (93,8%) thyrotropic deficiency, 7 (43,8%) had hyponatremia, and 2 (12,5%) developed diabetes insipidus (DI). Median sodium was 134 (IQR 7,25) mmol/l, overall. Visual disturbances were present in 6 (37,5%) and oculomotor palsy in 10 (62,5%) patients. Eight (50%) patients were treated surgically, including all 6 patients with visual disturbances. Visual field improvement was noted in all patients and oculomotor palsy resolved completely. HTN was present in 6 (37,5%), DM in 4 (25%) patients, while two (12,5%) patients received anticoagulant treatment. Median adenoma size was 22,5 (IQR 12,50) mm. There was no statistically significant difference in adenoma size between surgically and conservatively managed patients ($P=0{,}162$). Adenoma decreased in size in 4 (50%) patients without surgery. The adenoma shrinkage was statistically significant from median 18,5 (IQR 9,75) mm to 13 (IQR 7,50) mm ($P=0{,}044$). At follow-up, 12 (75%) had adrenocorticotropic and thyrotropic deficiency, 11 (68,8%) also had secondary hypogonadism, 7 (43,8%) had low IGF-1, 4 (25%) patients had low prolactin levels. Six (37,5%) patients had DI, including 4 after surgery. Multiple hormonal deficiencies were more common in surgically managed patients.
Conclusion
Our observations suggest that conservative management of PA is feasible in carefully selected milder cases without important visual deficit. Further studies on optimal stratification of PA patients are needed.

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P541

Complications of transphenoidal surgery for non-producing pituitary adenomas are not related to pretended surgical goals or surgical experience

Miguel Paja Fano[1], Fernando Guerrero[2], Dolores Moure[3], Felicia Hanzu[4], Betina Biagetti[5], Almudena Vicente[6], Rosa Cámara[7], Andreu Simó[8], Jose Recio[9], Rocío Villar[10], María Calatayud[11], Silvia Aznar[12], Marta Araujo-Castro[13], Soledad Librizzi[13], Angeles Gálvez[14], Guillermo Serra[15], Dolores Ollero[16], Ana Irigaray[16], Ana Delgado[17], Paola Parra[18], Patricia Martín[19], Fernando Muñoz[20], Anna Aulinas[21], Rogelio García[22], Isabel Ortiz[23], Tomás González-Vidal[24], Cristina Crespo[25], Aina Raventós[26], Javier Abarca[27] & Alfonso Soto[28]
[1]Basurto University Hospital, Endocrinology; [2]Hospital Universitari de Bellvitge, Endocrinology; [3]Hospital Universitario de Cruces, Endocrinology; [4]Hospital Clinic Barcelona, Endocrinology; [5]Hospital Universitario Vall de Hebron, Endocrinology; [6]Complejo Hospitalario de Toledo, Endocrinology; [7]Hospital Universitari i Politècnic la Fe, Endocrinology; [8]Hospital Universitario Mutua de Terrassa, Endocrinology; [9]Hospital Universitario de Salamanca, Endocrinology; [10]Complejo Hospitalario Universitario de Santiago, Endocrinology; [11]Hospital Universitario 12 de Octubre, Endocrinology, Madrid, Spain; [12]Complejo Hospitalario Universitario de Albacete, Endocrinology, Madrid, Spain; [13]Hospital Universitario Ramon y Cajal, Endocrinology; [14]Hospital Reina Sofía, Endocrinology; [15]Hospital Son Espases, Endocrinology; [16]Hospital Universitario de Navarra, Endocrinology; [17]Hospital Universitario de Burgos, Endocrinology; [18]Hospital Universitario La Paz, Endocrinology; [19]Patricia Martín, Endocrinology; [20]Hospital Sant Pau -Hospital del Mar, Neurosurgery; [21]Hospital Sant Pau, Endocrinology; [22]Hospital Gregorio Marañón, Endocrinology; [23]Hospital Universitario Virgen de las Nieves, Neurosurgery; [24]Hospital Universitario Central de Asturias, Endocrinology; [25]Hospital Universitario Río Hortega, Endocrinology; [26]Hospital German Trías i Pujol Badalona, Endocrinology; [27]Hospital General Universitario de Alicante, Neurosurgery; [28]Hospital Virgen del Rocío, Endocrinology

Surgical factors, in particular a higher volume of operations and a dedicated neurosurgeon, are considered the main determinants of surgical complication rates in transsphenoidal surgery (TSS). We evaluated postoperative complications in a large series of TSS for non-producing adenomas included in TESSPAIN, a retrospective multicenter nationwide registry. All TSS performed at the 29 participating centers between 2018 and 2022 were included. Globally, 1421 non-producing pituitary adenomas were included, representing 50,.5% of all TSS in these centers. An expert endocrinologist reviewed the feasibility of total pituitary adenoma resection in each case, and assessed outcome and permanent complications, including reoperation for bleeding or CSF leak, infection, anterior pituitary damage, permanent ADH deficiency, venous thromboembolism, cerebrovascular accident, death, cranial oculomotor or optic nerve damage, and others (including pneumocephalus, regrowth with second surgery and vasospasm). The most common reason for performing a TSS was optic nerve damage, which occurred in 615 cases (43.3%). Slightly more than half of the adenomas were considered amenable to total resection (n:759; 53.4%), which was achieved in 616 cases (81.2%). A quarter of the cases (n:355) had permanent surgical complications, the most common being additional antehypophyseal damage, which was reported in 16,8% of cases. Permanent ADH deficiency occurred in 91 cases (6.4%). Immediate reintervention due to bleeding, CSF leakage or vasospasm was required in fifty patients (3.5%). Forty-five cases (3.2%) presented with CSF leak on admission and 14 patients (1.0%) suffered cranial nerve damage as a complication of surgery. There were nine deaths related to TSS (0.63%), five cerebrovascular accidents and four thromboembolic events. The overall complication rate was not correlated with the number of surgeons performing TSS (mean rate: 25.9 ± 16.9% vs 24.2 ± 13.2% between centers with one or two dedicated neurosugeons vs more neurosurgeons; p: 0.77), nor with the total volume of TS surgeries during the study period (p: 0.91), nor with the number of non-producing pituitary adenomas operated on (p: 0.54). Only the rate of permanent ADH deficiency showed a trend towards a negative correlation with the cure rate of producing adenomas at the center evaluated (p: 0.08; r: -0.334). In conclusion, the rate of surgical complications reached 25% in a large series of TSS for non-producing pituitary adenomas, without apparent relation to surgical volume, number of neurosurgeons, or surgical goal of complete resection. These findings may be explained by the fact that more experienced centers assumed the most difficult cases and planned a stricter resection.

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DXA-derived lumbar bone strain index corrected for kyphosis is associated with vertebral fractures in acromegaly

Simona Jafaar[1,2], Giacomo Cristofolini[1,2], Emanuela Morenghi[1,3], Luca Rinaudo[4], Maria Francesca Birtolo[1,2], Elisa Sala[5], Emanuele Ferrante[5], Roberta Mungari[5], Elisabetta Lavezzi[2], Lorenzo Leonardi[6], Pasquala Ragucci[6], Fabio Massimo Ulivieri[7], Luca Balzarini[6], Giovanna Mantovani[5,8], Andrea Lania[1,2] & Gherardo Mazziotti[1,2]
[1]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy; [2]IRCCS Humanitas Research Hospital, Endocrinology, Diabetology and Andrology Unit, Rozzano, Italy; [3]IRCCS Humanitas Research Hospital, Biostatistics Unit, Rozzano, Italy; [4]Tecnologie Avanzate S.r.l, Turin, Italy; [5]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [6]IRCCS Humanitas Research Hospital, Department of Radiology, Rozzano, Italy; [7]Casa di Cura la Madonnina, Bone Metabolic Unit, Milan, Italy; [8]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy

The bone strain index (BSI) is a marker of bone deformation based on a finite element analysis inferred from dual X-ray absorptiometry (DXA) scans, that has been proposed as a predictor of fractures in osteoporosis. BSI value represents the average equivalent strain in a skeletal site, assuming that a higher strain level (higher BSI) indicates a lower bone's resistance to loads with consequent higher risk of fractures. BSI index is usually calculated for specific loading condition (e.g. standing for the lumbar site), but for particular reasons the load may vary due to external conditions (e.g. load bearing) or spine. These conditions possibly affecting BSI have been frequently described in patients with acromegaly. We aimed to investigate the association between lumbar BSI and vertebral fractures (VFs) in acromegaly. Twenty-three patients with acromegaly (13 males, mean age 58 years; three with active disease) were evaluated for morphometric VFs, trabecular bone score (TBS), bone mineral density (BMD) and lumbar BSI, the latter being corrected for the kyphosis as measured by low-dose X-ray imaging system (EOS®-2D/3D). In particular, for each degree increase of the sagittal Cobb angle, the force applied to the upper surface of the vertebra was increased by approximately 6% according to uncompensated position and the information derived from the lateral image coming from EOS device. Impaired TBS (i.e., TBS <1.310), low BMD (i.e., BMD T-score $\leq$-1.0 SD) at either skeletal site and pathological lumbar BSI (i.e., BSI ≥ 2.4) were found in 10 (43.50%), 13 (56.50%) and 6 (26.09%) patients, respectively. Patients with pathological lumbar BSI showed more frequently impaired TBS as compared to those with normal lumbar BSI (83.30% vs 29.40%; $P=0.05$), without differences in age, duration of active disease, serum IGF-I values, current medical therapies of acromegaly, coexistent hypopituitarism, previous treatment with bone-active drugs and low BMD at either skeletal site. Lumbar BSI was significantly higher in patients with VFs (*13 cases*) as compared to those without fractures (2.26, 95%C.I. 1.3-5.7 vs 1.85, 95%C.I. 1.16-2.22; $P=0.040$). 6 out of 13 (46.15%) patients with VFs had pathological BSI, whereas all patients without VFs had normal BSI ($P=0.019$). Patients with VFs had also more frequently impaired TBS vs patients without VFs (61.50% vs 20.00%; $P=0.04$). In conclusion, lumbar BSI corrected for kyphosis could be proposed as integrated parameter of spine arthropathy and osteopathy in acromegaly helping the clinicians in identifying patients predisposed to VFs.

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Presentation and treatment response in men with micro, macro or giant prolactinoma

Stefan Matei Constantinescu[1], Orsalia Alexopoulou[1] & Dominique Maiter[1]
[1]Cliniques universitaires Saint-Luc (UCLouvain), Department of Endocrinology and Nutrition, Bruxelles, Belgium

Introduction
Men with prolactinoma often present with larger tumors than women. Whether giant prolactinomas ($\geq$4 cm, GP) present differently and achieve the same outcomes as non-giant macroprolatinomas (1-3.9 cm, MP) or microprolactinomas ($<$1 cm, mP) is not clearly established.
Methods
We report retrospective data from a monocentric cohort of 129 men with prolactinoma and we compare baseline characteristics and treatment response in patients with different tumor sizes. We excluded patients with very small tumors (maximal diameter $<$5mm or PRL initially $<$45 mg/l).
Results
Among the 129 patients, 25 (19%) harbored a GP (median PRL 9270 mg/l; size range: 40-60 mm), 83 (64%) had MP (median PRL 776 µg/l; 10-39mm), and 20 (15%) had mP (median PRL 103 µg/l; 5-9.9mm). The mean age at presentation was similar in the three subgroups (41 ± 17, 45 ± 17 and 45 ± 16 years in the mP, MP and GP groups, respectively; NS). BMI and testosterone levels also did not differ significantly between the groups. Mean testosterone concentration at diagnosis was 6.3, 6.2 and 4.7nmol/l for mP, MP and GP, respectively. Patients with GP and MP

suffered from more visual field deficits (60% and 24% respectively) than those with mP (0%, $P<0.001$). The same was true for cavernous sinus invasion ($P<0.001$), ACTH deficit ($P=0.036$) and TSH deficit ($P<0.001$). However, the frequency of LH deficit was similar in the three groups (mP 94%, MP 82%, GP 96%, $P=0.132$). The prevalence of gynecomastia was significantly higher ($P<0.01$) in mP (68%) than in MP (25%) or GP men (16%), although the prevalence of decreased libido or erectile dysfunction was similar in all three groups. The need for surgery during follow-up was significantly more important in GP (44%) than MP (31%) or mP (5%, $P=0.015$). At last follow-up, normal prolactin was achieved in 80% of mP patients, 68% of MP patients, and in only 40% of GP patients ($P=0.010$). At last follow-up more patients in the GP (65%) and MP (38%) group suffered from persistent hypogonadism than mP patients (20%) ($P=0.008$). The same was true for TSH deficit ($P<0.001$) and ACTH deficit ($P=0.067$).
Conclusion
In men, 83% of prolactinomas at diagnosis reach a size of 1 cm or more and 19% reach or exceed 4 cm. Interestingly, patients with mP more often present with gynecomastia than those with MP or GP, despite similar age, BMI and testosterone levels, perhaps leading to earlier diagnosis. Endocrine outcomes and resistance to treatment worsen with increasing tumor diameter.

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A case of sporadic metastatic medullary cancer with distant metastases and negative RET mutation

Samira Khalilova[1,1] & Adrian Li[1]
[1]Princess Royal University Hospital, United Kingdom

Introduction
Medullary thyroid cancer accounts only 1% to 4% of thyroid cancer cases (1). 25% of cases are familial secondary to germline RET mutation, while the remaining 75% are sporadic and also harbour a somatic RET mutation in more than half of all cases. Up to 15–20% of patients will present with distant metastatic disease. The standard treatment for MTC is total thyroidectomy and dissection of cervical lymph node compartments. Post-operative levels of serum calcitonin $>$ 150 ng/l generally indicate distant metastases. We present a case of sporadic RET-negative medullary cancer with distant metastases.
Clinical case
72 y.o man referred for thyroid USS with neck swelling and supraclavicular lymph node enlargement in March 2023. USS revealed left sided conglomerate of the slightly hypoechoic nodules with internal calcifications measuring up to 51 mm in diameter (U4/5) and rounded lymph node in the left neck measuring 1.6x9.2x11 mm. FNA confirmed suspicious for malignancy (Thy4). CT neck showed extracapsular extension focally anteriorly to the SCM and extensive lymph nodes extending from level 2-6 on the left. After discussion at MDT calcitonin level has been checked which showed 12100 ng/ml. Meanwhile screen for pheochromocytoma, hyperparathyroidism and RET-gene was negative. Subsequently, patient underwent total thyroidectomy with level 6 lymph adenectomy and bilateral neck dissection in June 2023. Repeated calcitonin level in September 2023 showed calcitonin 7380. MRI liver in October 2023 showed multiple bilobar liver metastases which were Dotate-PET negative, but positive on FDG-PET scan. Furthermore, both PET scans showed positive uptake in the left supraclavicular fossa, which is concerning for residual/metastatic disease. Latest calcitonin level is 8770 and after MDT discussion there is plan for tyrosine kinase inhibitors therapy.
Discussion
Medullary thyroid cancer is a rare thyroid cancer with high mortality rate requiring multidisciplinary approach. Our case represent challenges in diagnosis and ongoing care of the patients with medullary cancer. While surgical management is a main treatment approach for medullary cancer, metastatic and recurrent cases can be treated with new treatment modalities, like thyrosine kinase inhibitors.

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Effects of recombinant growth hormone treatment on metabolic fitness, body composition and echocardiographic parameters in a population of patients with overweight or obesity and adult GH deficiency

Maria Elena Spoltore[1], Davide Masi[1], Rebecca Rossetti[1], Gabriele Veroi[1], Maria Ignazia Curreli[1], Mariangela Peruzzi[2], Valentina Ventimiglia[1], Giorgia Maria Baldazzi[1], Elena Gangitano[1], Mikiko Watanabe[1], Stefania Mariani[1], Lucio Gnessi[1] & Carla Lubrano[1]
[1]Sapienza University of Rome, Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Rome, Italy; [2]Sapienza University of Rome, Department of Clinical Internal, Anaesthesiological and Cardiovascular Sciences, Rome, Italy

Introduction
Adult growth hormone (GH) deficiency has been associated with the onset of sarcopenic obesity, reduced bone mineral density, and the progression of metabolic syndrome, often accompanied by the accumulation of ectopic fat at the epicardial level and changes in echocardiographic measures.
Objective and Design
This prospective pilot study aimed to assess the impact of recombinant human GH (rhGH) replacement therapy on glyco-metabolic parameters, body composition, and echocardiographic measures within a cohort of patients presenting both obesity/overweight and adult GH deficiency (aGHD). Inclusion criteria were as follows: age between 18 and 65, BMI $\geq$ 25 kg/m^2, peak GH secretion post GHRH + arginine stimulation test $<$ 4.2 ng/ml, and either partially or entirely empty sella turcica. Exclusion criteria included pregnancy/lactation, presence of active neoplasia, alcohol dependence, tobacco use, and medication potentially influencing the hypothalamic-pituitary axis.
Results
Our study involved 13 patients with obesity/overweight and aGHD (5 males, 8 females, mean age: 57.15 $\pm$ 6.29 years). Following enrollment, patients underwent rhGH replacement therapy and assessments were conducted at baseline (T0), after 6 months (T1), and after 12 months (T2), involving anthropometric, biochemical, DEXA-based body composition, and echocardiographic evaluations. At T1 and T2, notable reductions in waist/hip ratio ($P=0.05$), trunk fat ($P=0.03$), and trunk fat/low limb lean mass ratio ($P=0.05$) were observed, indicating substantial improvements in fat distribution. Concurrently, positive alterations were noted in cardio-metabolic risk markers, including reduced systolic blood pressure ($P<0.003$), total cholesterol/HDL cholesterol ratio ($P<0.004$), and increased HDL cholesterol levels ($P=0.05$). Moreover, a decrease in epicardial adipose tissue, indexed ventricular mass, interventricular septal thickness, and left ventricular posterior wall thickness was evident ($P=0.04$), with a tendency toward enhancement in left ventricular ejection fraction and telediastolic diameter.
Conclusion
The presence of GHD exacerbates cardiovascular risks in patients with overweight/obesity. Treatment with rhGH in our study cohort demonstrated improvements in adipose tissue distribution, lipid profiles, and notable effects on specific echocardiographic parameters. Notwithstanding, our study's limitations encompass a small sample size and a 12-month follow-up duration. Future investigations with expanded cohorts and extended follow-ups up to 36 months are planned. If substantiated, these results could advocate for rhGH replacement therapy in aGHD individuals with obesity/overweight to mitigate cardiometabolic risks and enhance cardiac structure and function.

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Pregnancy in a lady with pre-existing cyclical cushing's disease

Cheuk Wah Ho[1]
[1]United Christian Hospital, Hong Kong

A 35-year-old lady presented in Feb 2022 for lower limb weakness for 2 months, easy fall and amenorrhoea for 6 months. Her potassium was 2.4mmol/l. Clinically, she had moon face and proximal muscle weakness. Her workup showed metabolic alkalosis, renal loss of potassium and high 24-hour urine free cortisol (UFC) 825 nmol/l (24-140), which was 5.9x above the upper limit of normal (ULN). The paired baseline ACTH and morning cortisol were 22.1 and 469nmol/l respectively. 1mg ONDST was 580nmol/l. 8mg DST was suppressible. CRH and DDAVP stimulation test respectively confirmed Cushing's disease. MRI pituitary showed 3mm hypoenhancing lesion on the right of the pituitary gland. IPSS was done in 10/2022 with successful cannulation and confirmed Cushing's disease (CD). Serial monthly 24-hour UFC showed cortisol was 21, 208, 612nmol/l. Cyclical CD was suspected. The patient resumed spontaneous monthly menses and got pregnant due to misunderstanding. At 9th gestational week (GW), 24-hour UFC was 8.7x above ULN with muscle weakness. As she was having active CD, TSS at second trimester was advised. Before surgery, cabergoline and enoxaparin were given. 24-hour UFC reduces to 6.5x ULN on cabergoline 1.5mg 2x/week. TSS was done at 17 GW. Specimen was stained positive for prolactin, GH and ACTH. Cabergoline and potassium was stopped post-operatively. Stress dose of hydrocortisone was given then tapered to replacement dose. After TSS, the 24-hour UFC was at 2x ULN. The patient sustained left distal fibula fracture after stepping on uneven ground at GW 33+ weeks. She had preterm premature rupture of membrane the next day. A healthy baby was delivered weighing 1.97 kg and was observed in the neonatal ICU. It

was finally discharged home at 23 days old, weighing 2.51 kg. The patient was on hydrocortisone replacement. She is planned to reassess for any cortisol excess after 3 months. Up to 2021, 62 cases of CD complicated pregnancy are reported. The risk of maternal complication such as pre-eclampsia, gestational hypertension, gestational diabetes and risk of fetal complication including preterm birth, low birth weight, intrauterine death are higher in active CD. Therefore, TSS at the second trimester was advised in this patient. Secondly, it is difficult to assess for any remission after surgery. As the cortisol level is higher in normal pregnancy up to 2-3x ULN, the usual reference for CD remission cannot be applied. Thirdly, as this patient had cyclical CD, the periodically near normal cortisol level may not indicate a remission.

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The protean manisfestations of erdheim-chester disease

Shyam Seshadri[1], Adrian Jennings[1] & Manoj Thomas[1]
[1]The Queen Elizabeth Hospital Foundation NHS Trust, Department of Endocrinology, Kings Lynn, United Kingdom

A 43-year-old female presented to the endocrine clinic with a 6-month history of polyuria and polydipsia. Investigations revealed a raised prolactin and a water deprivation test confirmed cranial diabetes insipidus. Subsequent pituitary MRI showed a likely pituitary microadenoma which however on further radiology review was thought to represent a hypothalamic/stalk lesion measuring up to 5 mm. She was commenced on intranasal desmopressin and cabergoline initially. Repeat MRI 2 years and 5 years post initial scan showed unchanged appearances to the stalk lesion. The patient found good symptom relief with desmopressin. A decision was made to stop cabergoline as this was not thought to be related to her stalk lesion. The patient had intermittent breathlessness which was investigated by lung function and a CT which did not show any interstitial lung disease but picked a borderline decreased transfer factor and low iron levels. The patient then subsequently developed intermittent haematuria which was investigated by a CT scan which showed mesenteric panniculitis and borderline mesenteric lymph nodes. Laparoscopic biopsy confirmed panniculitis with fibrosis while immunohistochemistry showed only a small number of IgG4 cells. A year later patient presented with features of an acute ischemic stroke from which she made an uneventful recovery. Over the next 2 years patient developed bilateral knee pain which appeared to get progressively worse. X-rays of her knees and a subsequent CT picked up expansile bony lesions in the distal femur and proximal tibia. She was investigated by haematology including a bone marrow biopsy which ruled out any plasma cell dyscrasias or metastases. The patient underwent a distal femoral biopsy which confirmed xanthomatous histiocyte infiltration of the trabecular bone and marrow spaces in keeping with a diagnosis of Erdheim-Chester disease. The patient had also noticed yellow deposits on her neck and face which appeared to have worsened subsequently. She was seen by dermatology who suspected large xanthelasma plaques and biopsy of the neck lesions confirmed the above diagnosis. A DNA analysis revealed an activating BRAF mutation, p. (Val600Glu) which is reported in more than 50% of patients with Erdheim-Chester disease which is a rare form of non-Langerhans-cell histiocytosis with the propensity to involve the following organs in decreasing order of frequency, namely long bones, maxillary sinus, large vessels, retroperitoneum, heart, lungs, central nervous system, skin, pituitary gland, and orbit. Our patient had endocrine manifestations preceding her eventual diagnosis a decade later.

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Effects of MIA-602, GHRH receptor antagonist, on emotional disorders in mice

Maria Loreta Libero[1,2,3], Lucia Recinella[1], Andrew V. Schally[4], Roberto Salvatori[5], Luigi Brunetti[1] & Sheila Leone[1]
[1]D'Annunzio University of Chieti - Pescara, Department of Pharmacy, Chieti, Italy; [2]Instituto Maimónides de Investigación Biomédica de Córdoba, Córdoba; [3]University of Cordoba, Córdoba; [4]University of Miami Leonard M. Miller School of Medicine, Division of Medical/Oncology and Endocrinology, Miami, United States; [5]The Johns Hopkins University School of Medicine, Department of Medicine, Division of Endocrinology, Diabetes and Metabolism, Baltimore, United States

The role of growth hormone-releasing hormone (GHRH) in brain function has been suggested. Recent behavior studies by our group clearly demonstrate a powerful anxiolytic and antidepressant-like effects of a novel growth hormone releasing hormone (GHRH) antagonist of MIAMI class, MIA-690, probably related to modulatory effects on the inflammatory and oxidative status [1]. Our investigation in this work was focused on the potential beneficial effects of MIA-602, another recently developed GHRH antagonist on emotional disorders and examined how mood disorders are related to the endocrine system. In this context, the effects induced by MIA-602 were also analyzed in comparison to vehicle-treated mice with GH deficiency due to generalized ablation of the GHRH gene (GHRH knock out (GHRHKO)). The beneficial effect of MIA-602 on inflammatory and oxidative status and synaptogenesis resulting in anxiolytic and antidepressant-like effects could be related by increases of nuclear factor erythroid 2-related factor 2 (Nrf2) and of brain-derived neurotrophic factor (BDNF) signaling pathways in the hippocampus and prefrontal cortex. MIA-602 exhibited antinflammatory and antioxidant effects in ex vivo and *in vivo* experimental models, inducing anxiolytic and antidepressant-like behavior in mice subcutaneously treated for 4 weeks. Moreover, immunohistochemical and Western blot analyses suggested an evident activation of Nrf2, HO1, and NQO1 in the prefrontal cortex of both +/+ mice treated with MIA-602 (+/+ MIA-602) and homozygous GHRHKO (−/− control) animals. Finally, we also found significantly decreased COX-2, iNOS, NFkB, and TNF-α gene expressions, as well as increased P-AKT and AKT levels in +/+ MIA-602 and −/− control animals compared to +/+ mice treated with vehicle (+/+ control). We hypothesize that the generalized ablation of the GHRH gene leads to a dysregulation of neural pathways, which is mimicked by GHRH antagonist treatment.

[1] Recinella, L. *et al*. Antinflammatory, antioxidant, and behavioral effects induced by administration of growth hormone-releasing hormone analogs in mice. *Sci Rep* **10**, 732 (2020).

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Effects of glucagon-like peptide-1 analogs on prolactin: a randomized, double-blind, placebo-controlled crossover trial

Cyrill Müller[1], Sophia Lengsfeld[1], Leila Probst[1], Fabienne Baur[1], Emara Yara[1], Laura Werlen[1], Deborah Vogt[1], Cemile Bathelt[1] & Bettina Winzeler[1]
[1]University Hospital Basel, Endocrinology, Diabetes & Metabolism, Basel, Switzerland

Background
Research indicates that prolactin, a hormone linked to lactation, may influence the brain's reward system by interacting with dopamine. GLP-1 analogues, prescribed for diabetes and obesity, are known for their appetite-suppressant effects. With GLP-1 receptors found in mood and reward-related brain regions, a potential role of GLP-1 in reward regulation is suggested. A knowledge gap exists regarding the interaction between GLP-1 and prolactin in the context of the reward system. This study aims to explore this gap by investigating changes in prolactin on GLP-1 analogue and placebo treatment.
Methods
This is a predefined secondary analysis of a single-center, randomized, double-blind, placebo-controlled, crossover trial conducted at the University Hospital Basel in Switzerland. We enrolled 26 healthy eugonad men of normal weight (BMI 18.5-25 kg/m^2 or BMI 25.1-30 kg/m^2 and waist circumference $<$102 cm), aged between 18 and 50 years. Participants were randomized to a 4-week treatment of the GLP-1 analogue dulaglutide 1.5 mg/week and placebo in random order. We evaluated the changes in prolactin from baseline to week 4 in dulaglutide and placebo treated participants using paired t-tests.
Results
Between May 2021 and February 2022, 24 out of 26 randomized participants completed the study. Median age at inclusion was 24.5 years old (IQR [21.0, 29.0]), median BMI was 23.9 kg/m^2 (IQR [22.2, 25.0]). The average change in prolactin levels from baseline to 4 weeks of dulaglutide was -31.1 mU/l (SD 87.0 mU/l) and +44.6 mU/l (SD 113.1 mU/l) on placebo (estimated differences in prolactin levels from baseline to end of treatment under dulaglutide and under placebo -75.68 mU/l (95% CI: [-158.68, 7.33])).
Conclusion
In healthy men, dulaglutide led to a decrease in prolactin levels after 4 weeks of dulaglutide compared to placebo. These preliminary results support the hypothesis that GLP-1 analogues may interact with the dopamine-prolactin pathway.

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P141

Copeptin and oxytocin in MDMA-induced hyponatremia:incidence and severity, mechanisms of action, and the effect of fluid restriction

Cihan Atila[1], Isabelle Straumann[1], Patrick Vizeli[1], Julia Beck[1], Sophie Monnerat[1], Friederike Holze[1], Matthias Liechti[1] & Mirjam Christ-Crain[1]
[1]University of Basel, Basel, Switzerland

Importance
3,4-Methylenedioxymethamphetamine (MDMA, 'ecstasy') is a trending recreational drug but also has potential to enter clinical practice. Acute hyponatremia is a serious complication arising from ingesting even a single dose of MDMA. The assumed aetiology is a vasopressin release inducing the syndrome of inappropriate anti-diuresis combined with increased thirst causing polydipsia and thus water intoxication.
Methods
Pooled analysis of experimental MDMA-sessions of four placebo-controlled cross-over trials in 96 healthy participants conducted at the University Hospital Basel, Switzerland. The aim was to investigate the incidence and severity of hyponatremia after a single dose of MDMA, underlying mechanisms of action, and potential effect of fluid restriction on lowering the risk of hyponatremia. Single oral dose of 100 or 125 mg MDMA. 81 participants were not restricted to fluid intake, while in 15 participants, fluid intake was controlled. Plasma oxytocin, copeptin (surrogate marker of vasopressin), and sodium were measured repeatedly within 360 minutes after drug intake.
Results
At baseline, the mean (SD) sodium level was 140 mmol/l ($\pm$3) and decreased in response to MDMA by 3 mmol/l ($\pm$3), leading to hyponatremia in 31%(n=33/96) of the participants. Among hyponatraemic participants, the mean sodium level was 133 mmol ($\pm$2). In participants not restricted to fluid intake, at baseline, the plasma sodium was 140 mmol/l ($\pm$3) and decreased in response to MDMA by 4 mmol/l ($\pm$3), leading to hyponatremia in 41% (n=33/81). In contrast, in participants restricted to fluid intake, at baseline, the plasma sodium was 141 mmol/l ($\pm$1) and decreased only slightly in response to MDMA by 1 mmol/l ($\pm$2), leading to no hyponatremia (n=0/15), suggesting that fluid restriction significantly prevented hyponatremia (P=0.002). At baseline, plasma oxytocin was 87 pg/ml ($\pm$45) and increased in response to MDMA by 474 pg/ml ($\pm$309). At baseline, plasma copeptin was 4.9 pmol/l ($\pm$3.8) and only slightly decreased in response to MDMA by 0.3 pmol/l ($\pm$1.1). The decrease in sodium levels was significantly correlated with the increase in oxytocin (r=-0.4; P<0.001), while no correlation was observed between the change in sodium and copeptin (r=-0.1; P=0.220).
Conclusion
We report a high incidence of acute and mainly mild hyponatremia in response to MDMA, which can effectively be prevented by fluid restriction. Hyponatremia is associated with acute strong oxytocin but not copeptin release - this challenges the current hypothesis of direct vasopressin release and rather indicates that the increase in oxytocin mimics the effect of vasopressin in the kidneys due to close structural homology.

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Decoding desire: a neurofunctional exploration of distressing low sexual desire reveals sexually dimorphic brain responses

Jovanna Tsoutsouki[1], Natalie Ertl[1,2], Edouard G Mills[1], Matt B Wall[1,2], Layla Thurston[1], Lisa Yang[1], Tia Hunjan[1], Maria Phylactou[1], Paul Bassett[3], Bijal Patel[1], Jonathan Howard[2], Ali Abbara[1], David Goldmeier[4], Alexander Comninos[1,5] & Waljit Dhillo[1,5]
[1]Imperial College London, Section of Endocrinology and Investigative Medicine, United Kingdom; [2]Invicro London, London, United Kingdom; [3]Statsconsultancy Ltd, Amersham, United Kingdom; [4]Imperial College Healthcare NHS Trust, Jane Wadsworth Sexual Function Clinic, London, United Kingdom; [5]Imperial College Healthcare NHS Trust, Department of Endocrinology, London, United Kingdom

Background
Distressing low sexual desire, termed Hypoactive Sexual Desire Disorder (HSDD), affects 10% of women and 8% of men. The established 'top-down' neurofunctional model of HSDD in women suggests that in response to erotic cues, excessive activation of higher-level cognitive brain regions (involved in introspection/self-monitoring) suppresses lower-level sexual brain centres, thereby impeding normal sexual function. By contrast, the neurodysfunction in men with HSDD remains to be fully characterised and crucially unlike in women, there are currently no licensed therapies. Herein, we report the first direct comparison of the neural bases of HSDD in women and men.
Methods
32 premenopausal women with HSDD [mean age $\pm$ SD(y) 29.2 $\pm$ 6.7] and 32 men with HSDD [age 37.9 $\pm$ 8.6] underwent a task-based functional MRI (fMRI) measuring sexual brain activity during erotic vs control (exercise) videos. Participants completed psychometric questionnaires before and after the fMRI scan, providing functional relevance for the brain activity changes.
Results
Women displayed significantly greater activation in higher-level cortical regions (e.g. inferior frontal gyrus, superior frontal gyrus) and lower-level limbic brain regions (e.g. amygdala, striatum, thalamus) in response to erotic videos, compared to the men. Lower activation in lower-limbic sexual regions in women correlated with more severe HSDD, which along with a hyperactivation in the inferior-frontal gyrus relative to the men, supports the 'top-down' mechanism underlying HSDD in women. By contrast, men exhibited lower activation in both higher-cortical and lower-limbic regions, but greater activation than the women in the visual cortex in response to erotic videos. Hence, a heightened sensitivity to visual erotic cues in men might not be effectively relayed to the limbic system. In women only, hypothalamic hyperactivation in response to erotic videos correlated with 'increased heartbeat' (r=0.5, P=0.001), and 'tingling all over' (r=0.6, P<0.001), while higher striatal activation correlated with feeling more 'stimulated' (r=0.4, P=0.001) and 'genital tingling' (r=0.6, P<0.001) on the psychometric questionnaires. Crucially, these findings were specific to erotic stimuli as no differences were identified in the control comparison (exercise > baseline contrast).
Discussion
This is the first study to directly compare the neural bases of distressing low sexual desire in women and men. While supporting the 'top-down' mechanism of HSDD in women, it suggests a different neurodysfunctional process in men with HSDD, highlighting a potential functional disconnection between sensory/attention and sexual centres. Our findings have key clinical implications as they identify a sexual dimorphism in the neural bases of low sexual desire relevant to the escalating development of therapeutics for patients with HSDD.

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Receptor-mediated internalisation of the long-acting growth hormone analogue somapacitan in comparison with recombinant human growth hormone and pegvisomant

Matthäus Brandt[1], Elena Kassianidou[1], Carsten Behrens[1] & Peter Thygesen[2,2]
[1]Novo Nordisk A/S, Måløv, Denmark; [2]Novo Nordisk A/S, Rare Endocrine Disorders, Maaloev, Denmark

Growth hormone receptor (GHR) internalisation plays a crucial role in GHR activation and signalling by controlling the availability of the receptor for binding growth hormone (GH), regulating the intensity and duration of the GH signal, initiating unique signalling pathways, and maintaining homeostasis in the GH signalling pathway. GHR internalisation occurs mainly through clathrin-mediated endocytosis. Upon GH binding, the GHR undergoes ubiquitination, which is a signal for internalisation. The GHR is then included in clathrin-coated pits and internalised into early endosomes. From here, GHR can be recycled back to the plasma membrane. Here we present a quantitative study of the internalisation of human GH, the long-acting GH analogue somapacitan and the GHR antagonist pegvisomant using human GHR-expressing baby hamster kidney fibroblasts (BHK21). Human GH, somapacitan and pegvisomant were conjugated with Alexa Fluor 647 dye to follow the internalisation. Receptor internalisation could be observed for all three compounds in the concentration range 0.005–10 nM. Cells were fixated at predetermined timepoints from 0–4 hours and fluorescence determined for each combination of time point and concentration level. Internalisation was reduced in the presence of a non-labelled competitor showing that uptake is specific to the receptor. The results showed that all three compounds were internalised by the GHR. The internalisation rate was highest for human GH followed by somapacitan and with pegvisomant having the slowest rate. Addition of non-labelled pegvisomant to cells together with labelled human GH or somapacitan showed a displacement effect of pegvisomant of both compounds on the GHR with a stronger effect on somapacitan. While the competition effect for GH is higher at 4 hours after addition of pegvisomant compared to 24 hours, the displacement effect for somapacitan lasted for 24 hours. In conclusion, somapacitan undergoes receptor-mediated internalisation by the GHR at a slower rate than human GH, but faster than pegvisomant. Somapacitan is more easily displaced from the GHR by pegvisomant compared to human GH.

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Adopted transgender subjects are over represented and have a different psychosocial profile than their non-adopted counterparts: a case-control study

Iris Yaish[1], Yona Greenman[1,2] & Karen Tordjman[1,2,2]
[1]Tel Aviv Sourasky Medical Center, Institute of Endocrinology, Metabolism and Hypertension, Tel Aviv, Israel; [2]Tel Aviv University, Sackler Faculty of Medicine, Internal Medicine, Tel Aviv, Israel

Background and Aim
We previously demonstrated (1) that in our transgender clinic, adoptees are significantly overrepresented compared to the general population, suggesting early life traumas may play a role in the etiology of transgenderism. We had also shown a large preponderance (close to 80%) of female sex-assigned-at-birth (SAB), and a trend for presenting for treatment at an older age than non-adopted subjects. In the current study we aimed to further characterize this subgroup by comparing them to contemporary, non-adopted matched control subjects.
Subjects and Methods
Between 01.05.2014 and 31.12.2022, 671 new adult subjects presented to our center for gender-affirming hormonal treatment (GAHT), 14 of whom were adoptees (2.09%). These were matched in a 1:4 for age and SAB, with non-adopted transgender subjects from the same cohort. The 2 groups were compared for multiple psychosocial and life-style characteristics. Comparisons of categorical variables were performed by cross-tabulation statistics.
Results
By design, the current age of subjects (25.0 $\pm$ 6.1 y] range 20-40), and the age at initiation of GHAT (22 y [IQR 20-27.5]), were identical, but so was the mean age of dysphoria onset (10 y, range 3-30); 77.1% were transgender men. Groups did not differ with respect to their marital status, altogether 75.7% were single, none had biological children. Adoptees came from families with significantly higher socioeconomic status (SES), 28.6% from high SES vs none among controls. Despite this, none of the adoptees had any college education vs 28.3% of the controls ($P=0.028$). Employment rate, however, was generally similar in both groups at 72.1% of the cohort. Adoptees tended to carry a psychiatric co-morbidity more often (57.1% vs 28.6%, $P=0.061$). The number of psychiatric co-morbidities was also higher among adoptees (0.38 per subject vs 0.79, $P=0.042$). Among non-adopted subjects 62.2% were still living with their parents, as opposed to only 21.4% of adoptees ($P=0.013$). Lastly, adoptees were more often smokers (57.1% vs 16.4%, $P=0.004$), and cannabis users (21.4% vs 1.9%, $P=0.028$).
Conclusion
Adoptees are not only overrepresented among the transgender population treated at our center, but they also have a more fragile psychosocial profile despite coming from higher SES families. These observations might shed some light into the etiology of transition among adoptees that should prompt further exploration. Additionally, they should heighten the attention of clinicians to the vulnerability of this special population.
1. Yaish I, Keltch G, Greenman y, Kolitz T, Tordjman K. doi: 10.1210/jendso/bvad114.2065

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European survey of diagnosis and management of the polycystic ovary syndrome: full report on the ESE PCOS special interest group's 2023 questionnaire

Sarantis Livadas[1], Bulent Yildiz[2], George Mastorakos[3], Alessandra Gambineri[4], Duarte Pignatelli[5], Francesco Giorgino[6], Marianne Andersen[7], Barbara Obermayer-Pietsch[8] & Djuro P. Macut[9]
[1]Athens Medical Centre, Athens, Greece; [2]Hacettepe University School of Medicine, Division of Endocrinology and Metabolism, Department of Internal Medicine, Ankara, Turkey; [3]Aretaieion Hospital, Faculty of Medicine, National and Kapodistrian University of Athens, Unit of Endocrinology, Diabetes Mellitus and Metabolism, Athens, Greece; [4]University of Bologna, Unit of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [5]Centro Hospitalar e Universitário de S. João, Department of Endocrinology, Porto, Portugal; [6]University of Bari Aldo Moro, Section of Internal Medicine, Endocrinology, Andrology and Metabolic Diseases, Department of Precision and Regenerative Medicine and Ionian Area, Bari, Italy; [7]Odense University Hospital, Department of Endocrinology, Odense, Denmark; [8]und Universitätsklinik für Frauenheilkunde & Geburtshilfe Medizinische Universität Graz, Universitätsklinik für Innere Medizin, Klinische Abteilung Endokrinologie und Diabetologie, Graz, Austria; [9]Faculty of Medicine, University of Belgrade, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Belgrade, Serbia

Background
Although polycystic ovary syndrome (PCOS) constitutes a common endocrinopathy, there are several issues which confuse clinicians during everyday practice.
Objective
To define the current status of knowledge of the full spectrum of PCOS among European endocrinologists.
Methods
A detailed questionnaire comprising 41 items covering various aspects of diagnosis and management of women with PCOS was shared via web among members of European Society of Endocrinology.
Results
505 European endocrinologists (64% females), with a mean age of 47 $\pm$ 11.6 years answered the questionnaire. Rotterdam criteria were used by 85% of endocrinologists. The most frequent age at referral was between 20-40 years (87.1%). A quarter of doctors have access to mass spectrometry for the evaluation of androgen levels. Extended metabolic profile was part of workup by the vast majority, but there was significant uncertainty regarding the diagnosis of chronic anovulation. Diabetes, gestational or type 2, was considered a major consequence for women with PCOS and screening is carried out regardless of BMI status. Lifestyle modification and metformin are considered a standard approach of all participants and oral contraceptives are a standard therapeutic modality, but there is significant discrepancy on the duration of treatment.
Conclusions
Rotterdam diagnostic criteria are currently an established diagnostic approach within the European endocrine community. This updated survey showed an advance in using steroid profiling for diagnosis and strong position on recognizing PCOS as a metabolic condition with potential broader consequences. Therapeutic aspects are currently changed into the need for more lifestyle intervention involvement and the use of metabolic therapies either as monotherapy or in combination with standard hormonal compounds.

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The role of menstrual cycle changes in the evaluation of women's reproductive, sexual and mental health – lessons learned from the covid-19 pandemic

Kristina Saravinovska[1], Ljiljana Marina[1], Neda Delic[2], Antoan Stefan Sojat[1], Nevena Radonjic[3], Sladjana Mihajlovic[4], Milan Lackovic[4], Ilija Gunjic[5], Tijana Petkovic[1], Natalija Antic[1], Emilija Jankov[2], Zorana Arizanovic[1], Miomira Ivovic[1] & Svetlana Vujovic[1]
[1]Clinic of Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, National Centre for Infertility and Endocrinology of Gender, Belgrade, Serbia; [2]Faculty of Medicine, University of Belgrade, Belgrade; [3]Upstate Medical University, Department of Psychiatry and Behavioral Sciences, Syracuse, United States; [4]Clinical Hospital Centre "Dragisa Misovic, Department of Obstetrics and Gynecology, Belgrade, Serbia; [5]Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia

Introduction
It has been shown that women with a previous Sars-CoV-2 infection have long-lasting menstrual cycle (MC) changes.
Aim
To investigate the MC changes and their relationship with women's reproductive, sexual and mental health disturbances during the COVID-19 pandemic.
Methods
Anonymous survey about reproductive, sexual and mental health was shared with women of reproductive age between May 2022 and November 2023. All women used MC diary while filling out the survey. Surveys were stratified based on RT-PCR/Antigen test Results Positive (CP) or negative (CN). All reported changes in CP referred to time after the Sars-CoV-2 infection and in CN to a pandemic timeframe in general.
Results
1270 women completed the survey. Based on inclusion, exclusion, and complete data availability 676 surveys were taken into the final analysis. 186/28% CN-mean age 29.8 $\pm$ 9.2, mean BMI 22.6 $\pm$ 3.8 kg/m^2, and 490/72% CP, mean age 29.6 $\pm$ 9, mean BMI 22.4 $\pm$ 3.8 kg/m^2, no difference in age or BMI between the groups ($P>0.05$). When compared to CN, 365/74.5% CP had MC changes ($P<0.001$), with 3 different MC patterns detected. 33/6.7% CP had a triad (TR1) - shortening of MC length (sMC), heavier menstrual bleeding (HMB) and PMS worsening (wPMS) ($P=0.003$); 25/5.1% CP had a different TR (TR2) - sMC, wPMS and painful menstrual bleeding (pMB) ($P=0.006$); 17/3.5% CP reported a tetrad (TT) - sMC, HMB, wPMS and pMB ($P=0.034$). 63/14% CP with MC changes reported decreased libido ($P<0.001$). When compared to CN, 226/46% CP reported low mood ($P<0.001$) and 125/25% CP poor sleep ($P=0.015$). 109/22% CP reported difficulty accessing healthcare as the main stressor

($P=0.002$). 137/38% CP reported that the MC changes are still present ($P<0.001$) - mean duration 308 days. 208/47% of all surveys reported being vaccinated which had no effect on MC changes ($P>0.05$). 244/49.8% CP reported gaining weight with a median of 5 kg which had no effect on MC changes ($P>0.05$). In CP, TR1 was the predictor of decreased libido ($R^2$0.044, $P<0.001$, OR 4.25, 95% CI = 1.942-9.3) and poor sleep ($R^2$0.02, $P=0.008$, OR 2.629, 95% CI = 1.282-5.390) and TR2 was the predictor of low mood ($R^2$0.026, $P=0.004$, OR 3.947, 95% CI = 1.548-10.062). In CP, Sars-CoV2 was the predictor of MC changes ($P<0.0001$, B = 1.577, OR 4.838; 95% CI = 3.29-7.09).

Conclusion

Sars-CoV-2 causes long-term MC changes and patterns associated with low mood, poor sleep, and decreased libido. Tracking MC is an easily accessible tool that provides a simple and cost-effective method, making it easy to detect potential health changes.

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P147

Revised adolescent PCOS criteria: implications for women's metabolic well-being

Maria Nowak-Ciołek[1], Julia Stachowiak[1], Katarzyna Krok[1], Julia Sokal[1], Zaneta Malczyk[2] & Agnieszka Zachurzok[2]

[1]Medical University of Silesia, Students' Scientific Association at the Department of Pediatrics, Zabrze, Poland; [2]Medical University of Silesia, Department of Pediatrics, Zabrze, Poland

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies in women. In recent years revised diagnostic criteria for PCOS in adolescent females were disseminated. These new criteria notably encompass the specification of irregular menstrual cycles and hyperandrogenism, with the exclusion of polycystic ovarian morphology. In our study, we aimed to verify whether the clinical presentation of adolescent patients meeting the new criteria is associated with an increased risk of metabolic disorders in adulthood.

Methods

We conducted a retrospective analysis of the medical records of adolescent patients in a singular medical center scrutinizing individuals with PCOS (meeting adolescent or Rotterdam criteria). Subsequently, after 4 to 11 years from the first visit, 35 women were reassessed with 19 meeting the new criteria as adolescents (study group, SG) and 16 serving as controls (CG) – not meeting adolescent criteria. Comprehensive blood tests encompassed assessments of alanine aminotransferase (ALT), aspartate aminotransferase (AST), lipids, insulin, and glucose. A concurrent clinical assessment complemented the laboratory analyses. Statistical analyses were conducted utilizing Student's T-test and Pearson's correlation.

Results

In SG, 8 out of 19 individuals (42%) are afflicted with obesity as opposed to CG comprising 4 (25%) individuals living with obesity. The disparity in BMI values between the groups in this cohort did not attain statistical significance (SG 30.3 ± 8.9 kg/m^2 vs CG 26.4 ± 6.6 kg/m^2; $P=0.16$). However, analyzed data revealed a significant increase in BMI between the first and second assessment in SG ($\Delta=2.0\pm3.7$ kg/m^2; $P=0.03$), which was not observed in CG ($\Delta=1.4\pm3.9$ kg/m^2; $P=0.17$). Other significant differences were identified in AST(SG 23.4 ± 5.9 U/l vs CG 19.3 ± 3.6U/L; $P=0.02$), ALT (SG 24.0 ± 14.2U/L vs CG 15.9 ± 6.2U/l; $P=0.04$), and insulin levels (SG 13.0 ± 8.5uIU/ml vs CG 7.9 ± 3.8uIU/ml; $P=0.03$). There was no significant difference in lipids and glucose levels between the groups. The study further unveiled a significant correlation in SG between testosterone levels during adolescence and glucose levels in adulthood ($r=0.91$, $P<0.05$).

Conclusion

Our study on PCOS patients, diagnosed using adolescent criteria, reveals a significant increase in BMI within the SG over time. Despite non-significant BMI differences between SG and CG, notable variations in AST, ALT, and insulin levels were observed in SG. These findings emphasize the importance of addressing and managing of PCOS during adolescence to mitigate potential metabolic risks in adulthood.

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P148

Use of combined oral contraceptive pills in women with and without PCOS: A longitudinal population-based cohort study

Maria Forslund[1,2], Johanna Melin[3], Deborah Loxton[4], Helena Teede[2], Anju Joham[2] & Chau Thien Tay[2]

[1]Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Department of Obstetrics and Gynecology, Gothenburg, Sweden; [2]Faculty of Medicine, Nursing and Health Sciences, Monash University, Monash Centre for Health Research & Implementation, Melbourne, Australia; [3]University of Helsinki, Department of Obstetrics and Gynecology, Helsinki, Finland; [4]University of Newcastle, Centre for Women's Health Research, Callaghan NSW, Australia

Objective

Combined oral contraceptive pills (COCP), primarily used for contraception; are also indicated in other conditions including polycystic ovary syndrome (PCOS). Evidence on the prevalence and patterns of COCP use in PCOS compared to those without the condition are unknown, and studies in unselected populations, especially longitudinally, are very limited. The aim of this study was to examine prevalence and patterns of COCP use in women with PCOS, compared to the background population and to explore patterns of use in different subgroups by age and BMI.

Study design

Women born 1973-78 were randomly selected and included in the Australian Longitudinal Study of Womeńs Health (ALSWH), $n=$ 981 women with and 13 266 women without PCOS. They were followed during a 25-year period.

Results

Altogether, more than 70% of all women had used COCP at some point. More women with than without PCOS reported ever having used COCP (77% vs 71%, $P<0.001$). However, cross-sectionally at different ages, use was less common in women with PCOS (at mean age 25 years 43% vs 51%; 31 years 31% vs 37%). Usage rates decreased with age in both groups. In the subgroup with BMI ≥30 kg/m^2, women with PCOS were more likely to use COCP than women without PCOS at different ages (mean age 25 years 16% vs 9%; 31 years 20% vs 8%; 42 years 5% vs 3%, respectively, $P<0.001$).

Conclusion

COCP usage was common among all women, more common overall in PCOS, but duration of use appeared shorter in PCOS. COCP usage was also more common among women with PCOS in the subgroup with obesity. Considering the increased indications and the increased metabolic risks associated with PCOS, there is a clear need for high-quality studies on COCP use in women with PCOS, to inform a risk-benefit assessment.

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P149

The impact of testosterone on TLR expression in transgender men

Hüseyin Cihan[1], Özge Güngör[2], Gökçen Ünal Kocabaş[3], Esma Pehlivan Köroğlu[3], Kübra Gülpınar[3], Erhan Parıltay[2], Fatma Ömür Ardeniz[4], Bettina Winzeler[1] & Banu Şarer yürekli[3]

[1]University Hospital of Basel, Department of Endocrinology, Basel, Switzerland; [2]University Hospital of Ege, Department of Medical Genetics, Izmir, Turkey; [3]University Hospital of Ege, Department of Endocrinology, Izmir, Turkey; [4]University Hospital of Ege, Department of Allergy and Immunology, Izmir, Turkey

Background

Sex based differences in the immune system are well-documented in the literature. The influence of sex on the immune system is primarily attributed via chromosomal and sex hormone mediation. Cis men generally exhibit a weaker immune response compared to cis women. This contrast extends to various immune-mediated diseases, where cis men show a higher incidence of cancer but fewer autoimmune diseases than cis women. Testosterone is part of gender affirming masculinizing hormone therapy. Transgender men often take testosterone to align with their gender identity. Despite the safety of testosterone use in this population, limited data exist regarding its effects on the immune system in transgender men. Questions persist about whether the immune modulation in transgender men on testosterone aligns with their assigned sex at birth or if a unique modulation occurs.

Methods

This study conducted between October 2022 and November 2023, as a prospective observational study involving 21 healthy transgender men with XX chromosomes. All participants were testosterone-naïve at baseline. Over a 6-month period, participants underwent routine clinical care, with testosterone levels targeted towards cis-men ranges. Immunological, hormonal, and biochemical parameters were assessed. TLR receptor expressions were measured on whole blood using real-time PCR at baseline and 6 month. β-actin and GAPDH served as housekeeping control genes.

Results

At the 6-month assessment, changes in TLR expressions were evaluated, revealing noteworthy alterations. TLR2, TLR3, TLR6, TLR10, CD14 and MD2 displayed varying degrees of modulation. Of particular interest, TLR8 exhibited a significant

decrease expression from 3.5 [3.1, 4.3] to 2.6 [1.2, 3.3] ($P = 0.0016$), a similar decrease was also observed for TLR10 from 6.2 [5.3, 6.7] to 4.7 [3.5, 5.4] ($P < 0.001$).
Conclusion
This study sheds new light on the intricate dynamics of immune modulation in transgender men undergoing testosterone therapy, revealing specific alterations in TLR expressions. The statistically significant changes observed for TLR8 and TLR10 suggest a nuanced impact of testosterone on immune markers and once again demonstrates the immunosuppressive mechanism of testosterone. This study advances our understanding of hormone therapy's immunological effects in transgender individuals. Furthermore, these findings can offer the potential to deepen comprehension of immune variations between genders, extending beyond the scope of transgender health.

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P150

Prevalence of polycystic ovary syndrome in women with prediabetes

Cem Sulu[1], Hande Ozkaya[1], Taner Damci[1], Fahrettin Kelestimur[2] & Mustafa Gonen[1]
[1]Cerrahpasa Medical Faculty Hospital, Turkey; [2]yeditepe University Hospital, Turkey

Objective
To determine the frequency of polycystic ovary syndrome (PCOS) in women with prediabetes compared to control women.
Methods
Digital screening and tele-interviews remotely excluded 3218 out of 3465 consecutive women applied for routine check-up. In-person assessments were performed on 247 women, excluding 49. Final analyses included 198 premenopausal women without endocrine disorders (other than prediabetes and PCOS) or conditions affecting gonadal functions. Prediabetes and PCOS were determined according to American Diabetes Association and Rotterdam criteria, respectively.
Results
One-hundred women had prediabetes and 98 women had normoglycemia. The frequency of PCOS were 21% and 19.4% in prediabetes and control groups, respectively ($P = 0.860$). PCOS frequency was 32% in impaired glucose tolerance (IGT) only subgroup. Prediabetes group had higher insulin-like growth factor-1(IGF–1) levels and lower anti-Müllerian hormone (AMH) levels ($P = 0.013$ and $P = 0.016$ respectively). Insulin levels were correlated with testosterone, antral follicle count (AFC), and ovarian volume only in prediabetes group ($P < 0.05$ for all). Mediation model in prediabetes group showed that insulin levels increased testosterone levels both directly, and indirectly through increasing IGF-1 levels ($b = 0.4$, $P = 0.0006$).
Conclusion
While risk of PCOS was not increased in overall prediabetes group, a trend for an increased risk in IGT only subgroup was noteworthy. Positive correlation of insulin levels with testosterone levels, AFC, and ovarian volume being only found in prediabetes group suggested that prediabetes might render ovaries susceptible to the PCOS-like changes induced by insulin. The lower AMH levels in prediabetes group, indicating diminished ovarian reserve, implied that even mild hyperglycemia might have deleterious effects on ovaries. The glucotoxicity of prediabetes on ovaries merits further attention.

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P151

Thyroid autoimmunity can negatively influence placental angiogenic factors and hormone secretion

Kamila Tańska[1], Piotr Glinicki[1,2], Beata Rebizant[3], Wojciech Zgliczyński[1] & Małgorzata Gietka-Czernel[1]
[1]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland; [2]Centre of Postgraduate Medical Education, EndoLab Laboratory, Warsaw, Poland; [3]Centre of Postgraduate Medical Education, Department of Obstetrics, Perinatology and Neonatology, Warsaw, Poland

Introduction
Thyroid autoimmunity (TAI) commonly defined as the presence of thyroperoxidase antibodies (TPOAbs) and/or thyroglobulin antibodies (TgAbs) affects up to 15 percent of women of reproductive age and is a well-known risk factor of pregnancy loss. One of the possible explanations of obstetrical complications might be the disturbed process of placentation caused by thyroid antibodies. To test this hypothesis, we evaluated placental hormonal function and placental angiogenic factors in women with TAI.
Materials and methods
91 hypothyroid pregnant women and 39 healthy pregnant controls were enrolled to the study. Patients were divided into two groups: positive for TPOAbs/TgAbs ($n = 58$) and negative for TPOAbs/TgAbs ($n = 33$). All hypothyroid women were diagnosed before pregnancy or at the 1st trimester of pregnancy and treated with L-thyroxine to maintain TSH < 2.5 mIU/l. Maternal thyroid function tests (TSH,fT4,fT3) were established every month throughout pregnancy and angiogenic placental factors: proangiogenic placental growth factor (PlGF), and 2 antiangiogenic factors: soluble vascular endothelial growth factor receptor 1 (sFlt-1), soluble endoglin (sEng) as well as placental hormones: estradiol, progesterone, and human chorionic gonadotropin were determined at each trimester.
Results
Obstetrical and neonatal outcomes did not differ between the groups. TAI negatively impacted placental hormone secretion. Group 1 characterized by lower estradiol concentration compared to group 2 in the 1st trimester: 1682.00 vs 2440.00 pg/mL, $P = 0.016$ and lower progesterone concentration compared to controls in the 2nd trimester: 37.00 vs 50.25 ng/mL, $P = 0.003$. Thyroid autoimmunity was connected with unfavorable placental angiogenic factors profile. Antiangiogenic sEng was higher in group 1 than in group 2 in all three trimesters (1st trimester: 6.79 ± 2.18 vs 5.73 ± 1.41, $P = 0.026$, 2nd trimester: 5.81 ± 1.76 vs 4.68 ± 0.75, $P = 0.022$, 3rd trimester: 7.80 vs 5.60 ng/mL, $P = 0.003$). In group 1 positive correlation between TPOAbs and sFlt-1 in the 3rd trimester: rho = 0.31, $P = 0.040$, and negative correlation between TgAbs and estradiol in the 3rd trimester, and between TgAbs and PIGF in 1st trimester was found (rho = -0.29, $P = 0.043$, and rho = -0.27, $P = 0.037$, respectively).
Conclusion
Our preliminary results suggest that thyroid autoimmunity can negatively influence placental development and function, but further research is needed.

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P152

Comparative analysis of pain characteristics in women with and without endometriosis

Lana Oren[1], Lijamol Thoppil[1], George Mkheidze[1], Yaron Meerzon[2], Salome Kaldani[1] & Lela Tandashvili[3]
[1]Tbilisi State Medical University, T'bilisi, Georgia; [2]Georgian American University (GAU), T'bilisi, Georgia; [3]Aversi Clinic, T'bilisi, Georgia

Objective
Endometriosis is a condition marked by presence of endometrial tissue outside the uterus, causing inflammation, adhesions, and pelvic structural changes.[1] Despite its impact on women's quality of life, endometriosis symptoms are viewed as nonspecific, overlapping with other gynecological diseases and are normalized [2], all contributing to a long delay in diagnosis. This cross-sectional study aimed to address these issues by analysing distribution and intensity of chronic pain in laparoscopically confirmed endometriosis patients compared to other gynecological conditions and healthy controls. Compared the severity of cyclic pain between the three cohorts, explored correlations between rASRM staging and common endometriosis pain symptoms (cyclic pain, dyspareunia, dyschezia, and dysuria), and assessed the impact of lifestyle factors (coffee consumption, exercise intensity) on the intensity of chronic pain.
Methods
237 participants were categorized into endometriosis ($n = 76$), other gynecological conditions ($n = 60$), and healthy controls ($n = 101$). Participants provided data by completing a custom questionnaire, including an interactive body map for chronic pain localization.
Results
Women with endometriosis exhibited a higher chronic pain intensity and broader distribution compared to other gynecological conditions or healthy individuals, particularly in the abdomen, pubic, lower back, anterior thighs, and gluteal regions. Similarly, cyclic pain was significantly elevated in endometriosis compared to the other cohorts. Additionally, no significant correlation was found between rASRM staging and the severity of common endometriosis pain symptoms. Finally, lifestyle factors showed no clear associations with chronic pain severity in endometriosis patients.
Conclusion
This study provides insights into the complex landscape of chronic pain in endometriosis, as it revealed higher pain intensities and distribution compared to other gynecological conditions. The findings contribute to a deeper understanding of pain patterns, diagnostic considerations and reconfirm the limitations of the rASRM classification system.
1. Bulletti C, Coccia ME, Battistoni S, Borini A. Endometriosis and infertility. J Assist Reprod Genet 2010;27(8):441–7.

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	Chest	Abdomen	Pubic	Anterior Hands	Anterior legs	Upper back	Lower back	Gluteal	Posterior Hands	Posterior Legs
ANOVA p-value	**0.0211**	**<0.0001**	**<0.0001**	0.4768	**<0.0001**	0.0527	**0.0164**	**0.0002**	0.1191	**0.0487**
Endometriosis vs Other Gynecological conditions p-value	0.3870	**0.0017**	**<0.0001**	>0.9999	**0.0010**	>0.1085	**0.0455**	**0.0036**	>0.2894	0.9233
Endometriosis vs Healthy p-value	**0.0166**	**<0.0001**	**<0.0001**	>0.6713	**<0.0001**	>0.9999	**0.0336**	**0.0003**	0.1761	**0.0433**
Other Gynecological Conditions vs Healthy p-value	>0.9873	>0.9999	>0.2654	>0.9999	>0.9999	>0.0778	>0.9999	>0.9999	>0.9999	>0.6921

2. Surrey E, Soliman AM, Trenz H, Blauer-Peterson C, Sluis A. Impact of Endometriosis Diagnostic Delays on Healthcare Resource Utilization and Costs. Adv Ther 2020;37(3):1087–99.

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P153

Sexual function, quality of life and gender-related differences in patients with well-differentiated neuroendocrine tumors

Rossella Mazzilli[1], Virginia Zamponi[1], Roberta Modica[2], Cristiano Scandurra[3], Camilla Mancini[1], Franz Sesti[4], Tiziana Feola[4], Elisa Giannetta[4], Nelson Mauro Maldonato[3], Annamaria Colao[2] & Antongiulio Faggiano[1]
[1]Sapienza University of Rome, Department of Clinical and Molecular Medicine, Rome, Italy; [2]Federico II University of Naples, Department of Clinical Medicine and Surgery, Naples, Italy; [3]University of Naples Federico II, Department of Neuroscience, Reproductive Sciences, and Dentistry, Naples, Italy; [4]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy

Introduction
Neuroendocrine neoplasms (NEN) represent a group of rare neoplasms characterized by wide heterogeneity in terms of biological characteristics and clinical behavior. Despite their increasing relevance in the oncology field, health-related quality of life (HRQoL) and sexual function remain poorly investigated.
Aim
To investigate sexual function in patients affected by NEN; to evaluate the impact of clinical severity (presence or absence of metastases and tumor grade), heterogeneity (location of primary tumor and presence or absence of endocrine syndrome) and NEN therapies on sexual function and HRQoL; to study the possible correlation between these features and biochemical and psychological parameters.
Materials & Methods
In this cross-sectional, multicenter study, patients with a new diagnosis of gastroenteropancreatic (GEP) or bronchial NEN, aged 18 to 75 years, were recruited. Tumor severity, clinical heterogeneity, therapies performed were valuated. Through validated questionnaires, data about sexual function, sex-related distress, HRQoL, anxiety and depression were also collected. Furthermore, blood concentrations of LDL, glucose, HbA1c, and sex hormones were measured.
Results
To date, a total of 50 patients (28 men and 22 women) has been included. The mean age was 59.2 and 58.7 years, respectively. Of them, 71.6% were GEP, 33.4% bronchial; furthermore, 73.7% of patients were on systemic therapy, 35.0% had a metastatic form and 21.1% had an endocrine syndrome. The prevalence of erectile dysfunction (ED) was 60.7% (17/28) and the prevalence of female sexual dysfunctions (FSD) was 50.0% (11/22), without significant gender differences regarding the prevalence of dysfunctions and sex-related distress ($P=$ 0.5). Furthermore, only 17.9% (5/28) of men were satisfied with their sexual life, compared to 31.8% of women (7/22; $P=0.32$). A different impact of tumor severity on men and women was found; while tumor grading mainly influenced sexual function in men ($P=$ 0.001), the presence of metastases would seem to be the most impacting factor on sexual function in women ($P=$ 0.023). Higher levels of sexual distress reported higher glucose levels and greater perceived psychological distress, as well as a lower HRQoL (P = 0.039, $r=$ 0.45). Furthermore, only female sexual function was related with LDL values ($P=0.03$, $r=0.8$).
Conclusion
These results highlighted the relationship between NEN clinical severity, sexual dysfunction, and sex-related distress, suggesting that more attention should be paid to sexual function and distress in the clinical management of NEN patients, including female population, to promote better QoL and minimize psychological distress.

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Aromatase inhibitors and abrupt increase obesity rates among in males during puberty

Rezo Jamburia[1], Tekle Bakhtadze[1], Shota Janjgava[1], Ana Davitashvili[1], Natia Goletiani[1], Medea Zhgenti[1] & Elene Giorgadze[1]
[1]National Institute of Endocrinology - ენდოკრინოლოგიის ეროვნული ინსტიტუტი, Tbilisi, Georgia

Even in the presence of normally circulating androgens, the imbalance between estrogen and androgen in males between the prepubertal and pubertal periods may have an impact on male reproductive function. While there are many variables that affect how each person reaches puberty at different times, boys who are becoming more obese have higher aromatase activity. This enzyme turns testosterone into estradiol permanently, which lowers testosterone levels and raises estrogen levels. It has been observed that aromatase inhibitors enhance boys' pubertal condition and increase height prediction in boys of short stature. The study aims to establish the safety and efficacy of aromatase inhibitors in pediatric male patients with hypoestrogenic hypogonadism, as well as the relevance of analysis in interpreting the rise in obesity and the advantages of treatment among children. A retrospective investigation was carried out on guys between the ages of 12 and 17 who were in the process of puberty and had a confirmed diagnosis of hypoestrogenism along with symptoms of delayed puberty. Information was taken from medical records who visited the clinic between 2020 and 2023. A BMI-for-age percentile calculation was made using CDC growth charts as a guide. Three groups comprised us: The first group, consisting of fifty-five patients, underwent lifestyle modification, A second group of fifty-five individuals received aromatase inhibitors in conjunction with lifestyle modification, Third Group: fifty-five patients where used Life style modifation with Placebo. Findings: We examined 165 boys' medical records. In 2021, out of the 35 patients that underwent evaluation, 34% were overweight, 54% were obese, and 12% had severe obesity. In 2022, out of the 54 individuals that underwent evaluation, 35% were overweight, 43% were obese, and 22% had severe obesity. As of 2023, out of the 76 patients that underwent evaluation, 31% were overweight, 46% were obese, and 23 severely obese. Following a half-year of therapy, the II group experienced a statistically significant rise in testosterone and a statistically significant drop in estradiol. The same outcomes were observed for HOMA-IR, metabolic indices, and pubertal development.
Conclusions
Recent research indicates that the prevalence of obesity and the metabolic syndrome is correlated with the increase in hypoestrogenic, hypogonadotropic teenagers. Aromatase inhibitors are more beneficial when used in this type of patient, although more controlled research is required to confirm the safety and effectiveness of aromatase inhibitors in juvenile patients.

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P207

Diagnosis experiences in an international sample of lean women with PCOS

Melissa Masters[1], Kenlee Dropping[1], Amie Parry-Jones[2] & Rachel Sinley[1]
[1]Metropolitan State University of Denver, Department of Nutrition; [2]No Affiliation

Background
Polycystic Ovary Syndrome (PCOS), an endocrine disorder affecting 9-18% of reproductive-aged women, impacts all body types including those with a normal body mass index (BMI) often termed lean or atypical PCOS. This study aimed to investigate the diagnosis experience in an international sample of lean women with PCOS.
Methods
Participants were recruited from social media sites aimed at women with PCOS. Eligibility criteria included being ≥18 years of age, having a prior diagnosis of PCOS, and having a self-reported BMI ≤25 kg/m^2. Survey questions were adapted from previously published research. Categorical data were analyzed as count and proportions. Chi-squared tests were conducted to test for associations between various factors and satisfaction with the diagnosis experience. Strengths of associations were further assessed using Cramer's V coefficients. Post-hoc analysis was conducted using adjusted standardized residuals. Statistical significance was set at $P<0.05$. Qualitative data was analyzed utilizing an inductive thematic approach.
Results
Participants ($n=150$) represented 31 countries. Approximately 49.0% reported PCOS diagnosis experience dissatisfaction, 72.8% disagreed that there is adequate information about lean PCOS and 80.2% disagreed that health professionals have adequate knowledge about lean PCOS. Significant associations were found between length of time to diagnosis and diagnosis satisfaction ($P=0.001$, X2= 18.133, df=4, Cramer's V=0.258) as well as number of medical professionals seen and diagnosis satisfaction ($P<0.001$, X2=18.095, df=2, Cramer's V= 0.362). The top three PCOS concerns reported included irregular menstrual cycles (72.0%), hormone imbalance (64.7%), and anxiety (49.3%). Online blogs, support groups or forums (69.3%) and social media sites (48.7%) were the primary sources participants turned to for PCOS information. Qualitative analyses revealed the following primary theme across all questions: participants received limited information from providers about PCOS management. Secondary themes included participants reporting the need to conduct their own research on the condition and a focus on weight throughout the diagnosis process. Participants reported feeling that providers dismissed PCOS as a possible diagnosis, or focused on weight management in the treatment plan, despite their normal BMI. Overall, the diagnosis experience was reported to be an emotional journey.
Conclusions
This study demonstrates that the diagnosis experience in lean women with PCOS includes high feelings of dissatisfaction and is an emotional journey. The results of this study highlight opportunities for improvement in PCOS healthcare given and received worldwide, including in patients with lean PCOS. Future research should further examine lived experiences of women with lean PCOS.

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The impact of motivational interviews and hospitalization in themanagement of obesity associated infertility

Dijana Jankovic[1], Kristina Saravinovska[1], Neda Delic[2], Antoan Stefan Sojat[1], Ilija Gunjic[3], Miomira Ivovic[1], Tijana Petkovic[1], Natalija Antic[1], Dragana Mitrovic[1], Suzana Mutavdzic[4], Zorana Arizanovic[1], Svetlana Vujovic[1] & Ljiljana Marina[1]
[1]Clinic of Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Centre, National Centre for Infertility and Endocrinology of Gender, Belgrade, Serbia; [2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [3]Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia; [4]General Hospital of Novi Pazar, Department of Psychiatry, Novi Pazar, Serbia

Introduction
The interplay between obesity and hormones has a profound impact on women's reproductive health, reducing the likelihood of successful conception.
Methods
We performed a 6-month longitudinal study. The inclusion criteria were: women aged 20-40 with infertility, regular anovulatory menstrual cycles, BMI 35-40 kg/m^2, unrelated to other diseases. 30 eligible women were categorized into three groups: Group 1 (G1) received motivational interviews, hospitalizations, and nutritionist check-ups; Group 2 (G2) underwent hospitalization and nutritionist check-ups, while Group 3 (G3) served as the control without any interventions.
Results
G1-mean age 32.2±5.5, mean starting BMI (BMI1) 35.6±6.4 kg/m^2, G2-mean age 36.4±4.1, mean BMI1 38.2±4.9 kg/m^2, G3-mean age 33.7±4.9, mean BMI1 35±1.0 kg/m^2, with no difference in age or BMI between the groups ($P>0.05$). After 6 months, G1 lost 15.5±7.4% of their initial body weight (BW) i.e 14.5±9.09% of the BMI1, G2 lost 10.9±8.07% BW i.e. 11.05±8.2% BMI1, G3 lost 0.38±1.8% BW i.e. 0.41±1.08% BMI1 ($P<0.0001$). When compared based on percentage of BMI loss, there was a difference between G1-G3 ($P<0.001$), G1-G2 ($P<0.01$), but no difference between G2-G3 ($P>0.05$). When compared based on percentage of BW loss, there was a difference between G1-G3 ($P<0.0001$), G2-G3 ($P=0.02$), but no difference between G1-G2 was observed ($P>0.05$). After 6 months, only in G1 progesterone reached ovulatory levels 10.88± 8.72 nmol/l ($P<0.05$), where in G2/8.6±5.9 nmol/l and G3/3.4± 1.65 nmol/l, this effect was absent ($P<0.05$). Progesterone levels were significantly higher in G1 than in G3 ($P=0.034$) although there was no difference between the groups G1 and G2 ($P>0.05$) and G2 and G3 ($P>0.05$). The number of hospitalizations with motivational interview was a linear predictor of percentage of weight loss ($P<0.0001$, B=3.785, 95% CI 2.08-5.48, OR 4.553).
Conclusion
The motivational interview emerges as a promising and effective method with a significant role in the reduction of excessive body weight. The combined approach of motivational interviews and hospitalization presents a synergistic strategy in the comprehensive treatment of obesity and its associated reproductive health challenges.

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Early response with fezolinetant treatment of moderate-to-severe vasomotor symptoms associated with menopause in women considered unsuitable for hormone therapy: phase 3b daylight study

Angelica Lindén Hirschberg[1], Céline Bouchard[2], Antonio Cano[3], Katrin Schaudig[4], Karla Martins[5], Kentaro Miyazaki[6], Xi Wu[7] & Xuegong Wang[7]
[1]Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden; [2]Clinique de Recherche en Santé de la Femme, Quebec City, Canada; [3]University of Valencia, Valencia, Spain; [4]Hormone Hamburg, Hamburg, Germany; [5]Astellas Pharma Europe Ltd, Addlestone, United Kingdom; [6]Astellas Pharma Inc., Tokyo, Japan; [7]Astellas Pharma Global Development, Northbrook, IL, United States

Introduction
There is a need for well tolerated and effective nonhormonal therapies for vasomotor symptoms (VMS) associated with menopause. Fezolinetant is a nonhormonal, selective neurokinin 3 receptor antagonist that is approved for the treatment of moderate-to-severe VMS associated with menopause.
Objective
To assess how early a response to fezolinetant in frequency and severity of moderate-to-severe VMS was observed in the 24-week placebo-controlled DAyLIGHT study.
Methods
Daylight (NCT05033886) was a phase 3b, randomised, double-blind, 24-week placebo-controlled study. Participants were women aged ≥40 to ≤65 years with moderate-to-severe VMS who were unsuitable for hormone therapy (HT) based on four categories - contraindications, caution (prior medical history), stoppers (lack of efficacy, side effects, or medical advice), or averse (made informed choice not to take HT after discussion with clinician) - and randomised 1:1 to placebo or fezolinetant 45 mg once daily. The primary endpoint was mean change in daily VMS frequency of moderate-to-severe episodes from baseline to week 24. Mean change in VMS severity (key secondary endpoint) and safety were also assessed.
Results
Overall, 453 women were enrolled (placebo $n=226$; fezolinetant $n=227$), including HT contraindicated (51, 11%), caution (165, 36%), stoppers (69, 15%), and averse (168, 37%). Participants treated with fezolinetant 45 mg had a greater reduction from baseline in the daily mean change in frequency of moderate-to-severe VMS compared with placebo during the first week of treatment (day 7 least squares [LS] mean difference: –2.20; 95% CI: –2.78, –1.61; $P<0.001$). VMS frequency consistently decreased from days 1 to 6, with the strongest decrease during the first 3 days. Participants treated with fezolinetant 45 mg had a greater reduction from baseline in the daily mean change in VMS severity compared with placebo from days 2 to 7 (day 7 LS mean difference: –0.17; 95% CI: –0.23, –0.10; $P<0.001$). Improvements in VMS frequency and severity were sustained through week 24. No safety signals of concern were apparent for the 45 mg fezolinetant dose through week 24.

Conclusions
Daylight is the first study of fezolinetant to investigate efficacy vs placebo over 24 weeks. Fezolinetant 45 mg was efficacious and well tolerated for moderate-to-severe VMS in women considered unsuitable for HT. An effect on VMS frequency was seen as early as day 1 and maintained through the 24-week placebo-controlled period, demonstrating a rapid onset of action and sustained efficacy with fezolinetant treatment.

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Renal 11β-hydroxysteroid dehydrogenase type 2 is of central importance for 11-oxygenated androgen biosynthesis and is disrupted in chronic kidney disease

Maria Tomkins[1,2], Tara McDonnell[1,2], Leanne Cussen[1,2], Michael S Sagmeister[3], Imken Oestlund[4], Fozia Shaheen[3], Lorraine Harper[3], Rowan S Hardy[3], Angela E Taylor[3], Lorna C Gilligan[3], Wiebke Arlt[3,5,6], Marie McIlroy[1], Declan de Freitas[7], Peter Conlon[7], Colm Magee[7], Mark Denton[7], Conall O'Seaghdha[7], Jacky Snoep[4], Karl Heinz-Storbeck[4], Mark Sherlock[1,2] & Michael W O'Reilly[1,2]
[1]Royal College of Surgeons in Ireland, Academic Division of Endocrinology, Department of Medicine, Dublin, Ireland; [2]Beaumont Hospital, Department of Endocrinology, Dublin, Ireland; [3]University of Birmingham, Institute of Metabolism and Systems Research, United Kingdom; [4]Stellenbosch University, Department of Biochemistry, Stellenbosch, South Africa; [5]MRC Laboratory of Medical Sciences, London, United Kingdom; [6]Institute of Clinical Sciences, Imperial College London, London, United Kingdom; [7]Beaumont Hospital, Department of Nephrology, Dublin, Ireland

11-oxygenated androgens are a group of adrenal-derived C19 steroids that require activation in peripheral tissues. 11β-hydroxysteroid dehydrogenase type 2 (HSD11B2) has been shown *in vitro* to be essential for 11-oxygenated androgen activation, converting 11β-hydroxyandrostenedione (11OHA4) to 11-ketoandrostenedione (11KA4), the direct precursor of the potent androgen 11-ketotestosterone (11KT). As the kidney is the major site of HSD11B2 expression, we hypothesized that patients with chronic kidney disease (CKD) would have reduced 11-oxygenated androgen activation due to impaired renal HSD11B2 activity. In this cross-sectional multicentre cohort study of patients with CKD and healthy controls, serum and urinary multi-steroid profiling by liquid chromatography-tandem mass spectrometry (LC-MS/MS) was performed to measure 11-oxygenated androgens, classic androgens and glucocorticoids. Serum and urinary cortisol/cortisone ratios, previously established as validated surrogate markers of HSD11B2 activity, were calculated. A computational model of peripheral 11-oxygenated biosynthesis was fitted to the serum data and used to calculate relative HSD11B2 expression levels for each patient and control. We performed serum and urinary multi-steroid profiling in 90 patients with CKD [65% male, median age 64 (IQR 52-70) years, median estimated glomerular filtration ratio (eGFR) 23 (IQR 13-39) ml/min] and 56 healthy controls [11% male, median age 34 (IQR 30 – 41) years, median eGFR 103 (IQR 90 – 119) ml/min]. HSD11B2 activity declined with reducing eGFR. Serum concentrations of cortisone, 11KA4, 11KT and 11β-hydroxytestosterone (11OHT) were all significantly lower in patients with CKD compared to controls ($P<0.01$ for each). There was a strong correlation between eGFR and HSD11B2-dependent steroids in serum [cortisone ($r=0.77$, $P<0.01$), 11KA4 ($r=0.48$, $P<0.01$), 11OHT ($r=0.35$, $P<0.01$) and 11KT ($r=0.58$, $P<0.01$)], and urine [cortisone ($r=0.59$, $P<0.01$), 11β-hydroxyandrosterone ($r=0.32$, $P<0.01$) and 11-oxoandrosterone ($r=0.39$, $P<0.01$)]. Significant associations between classic androgens and eGFR were not observed. Patients with CKD had an increased ratio of 11OHA4 /(11KA4 + 11KT + 11OHT), reflective of reduced HSD11B2 activation of 11-oxygenated androgens. This ratio declined significantly across each stage of CKD from III-V ($P<0.01$). Using a computational model based on enzyme kinetic parameters of 11β-hydroxysteroid dehydrogenase type 1, HSD11B2, 17β-hydroxysteroid dehydrogenase type 2 and aldoketoreductase 1C3, we accurately predicted HSD11B2 as the key enzyme responsible for reduced 11-oxygenated androgen activation in CKD, with predicted HSD11B2 expression correlated with eGFR. This is the first study to demonstrate impaired 11-oxygenated androgen biosynthesis in patients with CKD. It confirms a central role for renal HSD11B2 in the activation of 11OHA4 to the potent 11-oxygenated androgen 11KT.

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Abstract withdrawn

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Gonadal and sexual function in men living with HIV: a real-life single centre experience

Ilaria Bonaventura[1,1], Valeria Hasenmajer[1], Valentina Sada[1], Lorenzo Cerroni[1], Nicolò D'Addario[1], Gabriella D'Ettorre[2], Claudio Mastroianni[2], Carlotta Pozza[1] & Daniele Gianfrilli[1]
[1]Sapienza University of Rome, Experimental Medecine; [2]Sapienza University of Rome, Department of Public Health and Infectious Diseases

Background
Hypogonadism and sexual dysfunction, particularly erectile dysfunction (ED), are common in men living with HIV (MLWH), but the link between testosterone levels and sexual function remains unclear in this population. The aim of this study was to estimate the prevalence of hypogonadism and sexual dysfunction and to explore the relationship between HIV-related variables and gonadal and sexual function in MLWH.
Materials and Methods
Serum total testosterone (TT), sex hormone binding globulin (SHBG), luteinizing hormone (LH), follicle-stimulating hormone (FSH) and estradiol (E2) were assessed in sixty MLWH. Free testosterone was calculated (cFT) by using the Vermeulen equation. Sexual function was assessed through the International Index of Erectile Function-15 (IIEF-15). According to guidelines, diagnosis of biochemical hypogonadism was made when serum TT $\leq$ 12 nmol/l and/or cFT $<$ 0.22 nmol/l. Body mass index (BMI), waist circumference (WC) and HIV-related variables (duration of HIV infection, $CD4^+$ cells count, and antiretroviral therapy used, ART, such as Integrase Strand Transfer Inhibitor, INSTI, Non-Nucleoside Reverse Transcriptase Inhibitor, NNRTI, Nucleoside Reverse Transcriptase Inhibitor, NRTI and Protease Inhibitor, PI), were also evaluated.
Results
Out of 60 MLWH, 42 (70%) presented ED. Subgroup analysis was performed according to the presence or absence of hypogonadism, that was observed in 11 MLWH (18.3%), 8 of whom (72.7%) presented hypogonadotropic hypogonadism. Interestingly, no differences in the five domains of IIEF-15 were found between MLWH with hypogonadism and those with eugonadism, despite pathological scores in both groups. In addition, MLWH with hypogonadism compared to those with eugonadism had significantly increased BMI ($P=0.046$) and smoking habits prevalence ($P=0.002$) and lower E2 ($P=0.017$). Considering gonadal function in the whole cohort, TT was negatively related to BMI ($r=$-0.595, $P=0.001$) and WC ($r=$-0.656, $P=0.011$), and positively related to E2 ($r=0.457$, $P=0.006$) and SHBG ($r=0.325$, $P=0.033$). cFT was related to BMI ($r=$-0.519 $P=0.023$) and WC ($r=$-0.719, $P=0.019$). Considering ART, higher TT, SHBG and E2 were found in MLWH using PI (respectively, $P=0.018$, $P=0.015$ and $P=0.020$). Moreover, prevalence of ED was higher in MLWH using INSTI ($P=0.017$).
Conclusion
Sexual dysfunction is a highly prevalent multifactorial disorder in MLWH. Decreased serum testosterone levels, which are also related to increased visceral fat accumulation, are not the only driver of the onset of ED. HIV-related factors, such as ART, also appear to have an impact on gonadal and sexual function. Consequently, the clinical management of sexual health in MLWH requires a multidisciplinary approach, involving experts in infectious diseases and sexual medicine.

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Clinical, biological and socio-professional characteristics of patients harboring the 46,XX/47,XXY mosaic sex chromosome aneuploidy: the MOSAI-XX multicenter study

Nadia Zaegel[1,2], Ingrid Plotton[3], Morel Bouvattier Claire[1,4], Fanny Chasseloup[1,4], Jean-Christophe Maiza[5], Olivier Vanakker[6],

Peter Kamenicky[1,2], Sylvie Salenave[1,2], Tosca Lucie[7], Nathalie Veyt[8], Jacques Young[1,2] & Luigi Maione[1,2]
[1]Université Paris-Saclay, Inserm UMR-S 1185, Physiologie et Physiopathologie Endocriniennes, Assistance Publique-Hôpitaux de Paris, Le Kremlin Bicetre, France; [2]Service d'Endocrinologie et des Maladies de la Reproduction, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicetre, France; [3]Service de médecine et de la reproduction, Hospices Civils de Lyon, Université Claude Bernard Lyon1, U1208, Lyon, France; [4]Service d'Endocrinologie Pédiatrique, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicetre, France; [5]Service d'Endocrinologie-Maladies Métaboliques, Chu Saint Pierre, La Reunion, France; [6]Center for Medical Genetics Ghent University Hospital, GHENT, Belgium; [7]Assistance Publique-Hôpitaux de Paris, Hôpital Antoine Béclère, Service d'Histologie-Embryologie-Cytogénétique, Université Paris-Saclay, Clamart, France; [8]ASO Klinische Genetica Centrum Menselijke Erfelijkheid Leuven, Leuven, Belgium

Background
Sex chromosome mosaic aneuploidy 46,XX/47,XXy (mKS-XX) is a very rare syndrome, with only twenty-one cases previously reported. No patients' series with mKS-XX and no comparative studies between mKS-XX and the common homogeneous Klinefelter syndrome (KS) have so far been described.
Aims
To describe the clinical, biological and socio-professional characteristics of the first series of previously unpublished patients with mKS-XX. To find predictors discriminating patients with mKS-XX from those with KS.
Patients and Methods
MOSAI-XX is a retrospective study providing descriptive analyses of consecutive patients having mKS-XX diagnosed across different European tertiary referral centers. The clinical presentation, the prevalence of disorders of sex development/ovotesticular disorder (DSD/OT), anthropometric measures, hormone levels, gonadal characteristics and socio-professional statuses (schooling, precariousness scores and job positions) of mKS-XX have been compared to those from a cohort of 121 KS patients.
Results
Fifteen patients (fourteen adults) with mKS-XX have been identified and confirmed from 1986 to 2022 from four European tertiary referral centers. The mean ($\pm$SD) percentage of XX lineage in peripheral karyotypes was 57$\pm$27% (range 7-82%). The prevalence of DSD/OT was higher in mKS-XX than in KS patients (26.7% vs 1.1%, $P=0.0067$). 3/30 gonads from mKS-XX and 0/242 from KS patients had an ovarian component ($P=0.0012$). However, the number of gonads harboring ovarian tissue was lower in our series than in pooled previous case reports (17/36, $P=0.01$). The final height and the statural gain over midparental height were both lower in mKS-XX than in KS patients (173.6$\pm$14.3 vs 181.3$\pm$7.9 cm, $P=0.016$, and -3.8$\pm$6.8 vs +7.9$\pm$7.4 cm, $P=0.0003$, respectively). Testicular volumes did not differ between mKS-XX and KS (2.4$\pm$0.7 vs 3.0$\pm$1.8 mL), nor did concentrations of LH, FSH, total testosterone, estradiol and testicular peptides ($P=$ns for all comparisons). Individuals with mKS-XX performed better in schooling achievements and more frequently occupied high intellectual professions than KS ($P=0.017$ and $P=0.015$, respectively). Precariousness scores were lower in mKS-XX than in KS patients ($P=0.017$).
Conclusion
We describe the first European series of patients carrying a 46,XX/47,XXy mosaic KS. We found a lower DSD/OT and a higher KS-like phenotype prevalence than those previously known from case reports. Beyond DSD/OT, we found that anthropometric measures and socio-professional statuses were also able to discriminate mKS-XX from KS. Our results improve the current knowledge about the mKS-XX syndrome. In addition, our results may have an impact on the genetic counseling for pregnant women and couples confronted with offspring carrying this rare chromosomal formula.

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Regulation of PGR gene expression in immortalized human endometrial stromal cells

Alejandra Monserrat Retis Resendiz[1], Martha Paloma Domínguez Mora[1], yesenia Cid-Cruz[1], Moisés León-Juárez[2], Jessica Romero Reyes[1], Elizabeth García-Gómez[1], Ignacio Camacho-Arroyo[1] & Edgar Ricardo VÁZquez Martínez[1]
[1]Instituto Nacional de Perinatología "Isidro Espinosa de los Reyes"-Facultad de Química, UNAM., Unidad de Investigación en Reproducción Humana, Mexico City; [2]Instituto Nacional de Perinatología "Isidro Espinosa de los Reyes", Inmunobioquímica, Mexico City

Background
Decidualization, a crucial process for successful pregnancy establishment and maintenance, involves endometrial stromal cell differentiation. This process is orchestrated by estradiol (E2), progesterone, and other stimuli that increase intracellular cyclic adenosine monophosphate (cAMP) levels. The progesterone receptor (PR) plays a pivotal role in regulating decidualization, and alterations in its expression are linked to endometrial pathologies. However, the mechanisms governing PR gene (*PGR*) expression in endometrial stromal cells during decidualization are not fully understood. This study aimed to identify the mechanisms of *PGR* expression regulation in immortalized human endometrial stromal cells.
Methods
Immortalized human endometrial stromal cells (T-hESC, ATCC, CRL4003) were exposed to individual and combined treatments of E2, medroxyprogesterone (MPA), and cAMP. To understand the underlying action mechanisms of the decidualization stimulus components, we examined the effect of estrogen receptors and PR antagonists, as well as a Protein Kinase A (PKA) inhibitor. We evaluated the expression of *PGR* isoforms and decidualization-associated genes by RT-qPCR. ChIP-seq and 4C experiments were also performed to identify putative distal regulatory regions involved in *PGR* expression in T-hESC treated with E2, MPA, and cAMP (EMC).
Results
The expression of *PGR-AB* and *PGR-B* was induced after 24 hours of treatment with EMC compared to the vehicle. Interestingly, cAMP induced *PGR-AB* and *PGR-B* expression by activating the PKA signaling pathway, while MPA downregulated their expression through the PR. Furthermore, four distal regions interacting with the *PGR* promoter were identified, three characterized by the presence of H3K4me1 and an increase in the enrichment of H3K27ac when T-hESC were treated with EMC for 24 hours.
Conclusion
This study provides evidence that during *in vitro* decidualization with EMC, cAMP plays a crucial role in inducing the expression of *PGR-AB* and *PGR-B* through PKA signaling pathway. Moreover, the identification of distal regions interacting with the *PGR* promoter, enriched with H3K4me1 and H3K27ac, suggests the existence of complex networks of genetic regulation influencing *in vitro* decidualization in T-hESC cells.
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Congenital hypogonadotropic hypogonadism by PNPLA6 mutations: identification of a wide phenotypic spectrum and functional correlations with the NTE *in vitro* activity

Luigi Maione[1], Jerome Bouligand[2], Antoine Rousseau[3], Salome Prevost[4], Lydie Naule[5], Sylvie Salenave[1], Philippe Chanson[1], Ursula Kaiser[6] & Jacques young[7]
[1]Saclay University, Endocrinology and Reproductive Diseases, Le Kremlin-Bicêtre, France; [2]Saclay University, Genetics, Le Kremlin-Bicêtre, France; [3]Saclay University, Ophtalmology, Le Kremlin-Bicêtre, France; [4]Kremlin-Bicètre, Genetics, Le Kremlin-Bicêtre, France; [5]Paris, Sorbonne University, Paris, France; [6]Brigham and Women's Hospital, Boston, United States; [7]Saclay University, Endocrinology and Reproductive Diseases, Le Kremlin-Bicêtre, France

Background
PNPLA6 mutations are associated with complex autosomal recessive disorders including congenital hypogonadotropic hypogonadism (CHH): Gordon-Holmes syndrome, Boucher-Neuhauser syndrome and hereditary spastic paraplegia, which include ophthalmologic and neurologic disorders in addition to CHH. *PNPLA6* gene encodes the neuropathy target esterase (NTE), an endoplasmic reticulum-associated enzyme intervening in the metabolism of membrane phospholipids.

Aim
Analysis of prevalence of *PNPLA6* mutations within a large cohort of CHH patients. Clinical, biological, neuroendocrine and molecular characterization of six patients from three unrelated families, carrying five *PNPLA6* biallelic mutations.
Patients and Methods
Neuroendocrine profile: measurement of 4 hours-spontaneous LH pulsatility and response to bolus and repeated GnRH (by pump), neurological and ophthalmological examinations of affected patients. Assessment of the enzymatic activity on cell lysates expressing wild-type (WT) and mutant NTE.
Results
Biallelic *PNPLA6* mutations are very rare (<1% among 800 exomes in CHH patients). Two brothers harbored a homozygous, four patients a composite heterozygous mutation. Phenotypic spectrum was wide, ranging from severe neurological and ophthalmological manifestations (spastic paraplegia, cerebellar ataxia and chorioretinitis) to a very mild phenotype. Neuroendocrine profile showed apulsatile and unresponsive LH to bolus and repeated GnRH exposure. Molecular analyses showed a variable degree of loss of activity of NTE function according to various mutations. A phenotype-genotype correlation was observed, with a low impact NTE disruption seen in patients with the mildest phenotype.
Conclusion
PNPLA6 mutations are associated with a more diverse phenotype than that previously known. *PNPLA6* mutations cause a pituitary deficiency at the level of gonadotropes. Following our results, we recommend to include the sequencing of *PNPLA6* gene in all patients with CHH.

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Expression of the serotonin signaling pathway in a testicular adrenal rest tumor in a patient with 21-hydroxylase deficiency

Lola Menager[1], Aurelie Rives-Feraille[1,2], Laura Moutard[1], Nathalie Rives[1,2], Hervé Lefebvre[1,3] & Estelle Louiset[1]
[1]Univ Rouen Normandie, Inserm, NorDiC UMR 1239, Rouen, France; [2]Rouen University Hospital, Biology of Reproduction-Cecos Laboratory, Rouen, France; [3]Rouen University Hospital, Department of Endocrinology, Diabetes and Metabolic Diseases, Rouen, France

Testicular adrenal rest tumors (TART) are frequently detected in male patients with 21-hydroxylase (21-OH) deficiency. Increase in plasma ACTH levels, due to cortisol deficit, is responsible for TART growth. Indeed, glucocorticoid substitution reduces both plasma ACTH and TART development in the majority of patients. Nevertheless, some patients with TART are resistant to the glucocorticoid treatment, suggesting the existence of other factors stimulating TART growth. The aim of the study was to characterize the phenotype of TART cells in the testicular tissue of a treatment-resistant 38-year-old patient. It also aimed to investigate the expression of the serotonin (5-HT) signaling pathway in TART, similar to that described in adrenal hyperplasias of patients with 21-OH mutations (Le Mestre *et al*. JCEM 2019; 104:4967-80). Immunostainings showed the presence of ACTH receptor (MC2R), 3β-hydroxysteroid dehydrogenase (3β-HSD2), a steroidogenic enzyme involved in the synthesis of glucocorticoids and androgens, and 11β-hydroxylase, the key enzyme for cortisol production, in the majority of TART cells. In addition, some tumor cells were immunopositive for 17β-HSD type 5 (17β-HSD5, AKR1C3), the enzyme responsible for testosterone synthesis in adrenal glands, whereas they were immunonegative for 17β-HSD3, the testicular isoenzyme. The study revealed the expression of TPH1, the limitant enzyme in 5-HT synthesis, and 5-HT receptor types 4 and 6 in the tissue. These data confirm the adrenal phenotype of TART cells and demonstrate expression of several actors of the 5-HT signaling pathway in the patient's TART tissue. This work should be extended to a series of TART tissues. Moreover, *in vitro* functional studies conducted on TART cell cultures might evaluate a possible role of locally-produced 5-HT on tumor cell proliferation.

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Different adipose tissue depots: metabolic implications in polycystic ovary syndrome

Jelina Basnet[1,2], Samar Rezq[1], Alexandra M Huffman[1], Licy L yanes Cardozo[1] & Damian G Romero[1]
[1]University of Mississippi Medical Center, Jackson, United States; [2]University of Mississippi Medical Center, Pharmacology andToxicology, Jackson, United States

Background
Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in reproductive-age women. PCOS women often have hyperandrogenemia that is associated with adiposity and a worse metabolic profile. However, the depots-specific effect of different white adipose tissues (WAT) in mediating the systemic metabolic dysfunction is not fully understood in PCOS. Therefore, using a well-established mouse model of PCOS, we aim to test the hypothesis that excess androgen will induce systemic metabolic dysfunction and depot-specific WAT derangements.
Methods
Three-week old female mice (C57BL/6N) were implanted with Silastic tubes filled with DHT (8 mg, s.c.) or vehicle ($n=6$/grp) for 30 days. Weekly body weight (BW, gravimetry), body composition (EchoMRI), retroperitoneal fat (RPF) mass- visceral fat depot and inguinal-gluteal subcutaneous fat (SCF) mass (gravimetry) were assessed. Serum leptin, adiponectin, and non-esterified free fatty acid (NEFA) were measured with ELISA. RPF and SCF, the lipogenesis markers acetyl coA carboxylase (ACC) and fatty acid synthetase (FAS), the lipolytic markers adipose triglyceride lipase (ATGL) and hormone sensitive lipase (HSL) and adipogenesis marker peroxisome proliferator-activated receptor-γ (PPAR-γ) protein levels were assessed by Western blot.
Results
PCOS mice showed significant ($P<0.05$) increases in BW (1.15-fold), lean mass (1.14-fold), total fat mass (2-fold), RPF mass (2-fold), SCF mass (1.2-fold), leptin (1.2-fold), NEFA (1.3-fold) and lower insulin-sensitizing adipokine adiponectin levels (50%) compared to their vehicle. At the molecular level, in RPF, DHT downregulated ACC and FAS by 50% and 20% respectively. PCOS mice has lower lipolysis in the RPF represented by lower expression of lipases ATGL (50%) and HSL (40%). There was also decrease in the adipogenesis marker PPAR-γ (40%) in RPF in PCOS mice. On the other hand, in SCF ATGL (15%) and HSL (20%) was increased with no changes in FAS and ACC in PCOS mice compared to their vehicle.
Conclusion and significance
Our findings suggest systematic metabolic dysfunction is associated with the depot specific alteration or changes in the markers of adipogenesis and lipogenesis, where both were increased in RPF and decreased in SCF. The observed decrease in SCF could be protective and could help to ameliorate some of the metabolic changes associated with PCOS. Therefore, depot specific targeting may be a possible therapeutic approach for PCOS associated metabolic dysfunction.

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Prenatal testosterone exposure and offspring body composition at 7 years-of-age. odense child cohort

Camilla Palm[1,2,3], Dorte Glintborg[1,3], Anders Grøntved[4], Dorte Jensen[2], Freja Hansen[1], Jan Jørgensen[5], Henrik Christesen[3,6], Tina Jensen[7,8,9] & Marianne Andersen[1,3]
[1]Odense University Hospital, Endocrinology; [2]Odense University Hospital, Steno Diabetes Center Odense; [3]University of Southern Denmark, Clinical Research; [4]University of Southern Denmark, Sports Science and Clinical Biomechanics, Research Unit for Exercise Epideomiology; [5]Odense University Hospital, Gynecology and Obstetrics; [6]Odense University Hospital, Hans Christian Andersens Hospital for Children and Adolescents; [7]Odense University Hospital, Odense Child Cohort, Hans Christian Andersen Hospital for Children and Adolescents; [8]University of Southern Denmark, OPEN Patient Explorative Network (OPEN); [9]Odense University Hospital, Clinical Pharmacology, Pharmacy and Environmental Medicine

Background
Maternal free testosterone (FT) increases during 3rd trimester pregnancy and FT levels are higher in women with polycystic ovary syndrome (PCOS) compared to controls. Fetal exposure to maternal FT during 3rd trimester was associated with lower weight, length and shorter abdominal circumference at birth, in boys. Furthermore, lower birth weight has been related to higher abdominal fat mass in young children.

Aim
To examine associations between maternal 3rd trimester testosterone exposure and body composition in children born of women with and without PCOS using whole body dual X-ray absorptiometry (DXA), and to consider the importance of offspring sex.
Hypothesis
Higher prenatal testosterone exposure associates with more fat mass in young children and boys are more susceptible than girls.
Methods
The study is part of the prospective Odense Child Cohort comprising 1,486 mother-child dyads, with a PCOS diagnosis in 145 (9.8 %) women. *Exposure*: Maternal testosterone at gestational week 28; FT was calculated from total testosterone (TT), analyzed by mass spectrometry. *Outcome*: Body composition of 1,008 children (520 boys) at 7 years-of-age (7.0-7.6 years) measured by DXA (lean body, fat, gynoid- and android fat percentage, fat mass index and fat free mass index) and clinical examination (weight, height, body mass index (BMI), abdominal- and head circumferences). Multiple linear regression models were adjusted for maternal age, parity and birth weight.
Results
Maternal FT and TT were comparable in women carrying a boy or a girl. At age 7 years, boys were significantly higher (126.6 vs 125.5 cm, $P<0.001$) and abdominal circumference was longer (56.5 vs 55.6 cm, $P<0.001$) compared to girls. In boys, a doubling in FT and TT were associated with an increase in weight of 0.53 kg ($P=0.01$) and 0.47 kg ($P=0.05$), respectively and a doubling in FT was associated with an increase in BMI z-scores of 0.16 ($P=0.01$) and a 4.4 % increase in fat mass index ($P=0.03$). A maternal PCOS diagnosis tended to be associated with a lower gynoid fat percentage of 1.8 % ($P=0.07$) in girls.
Conclusion
Prenatal exposure to higher FT was linked to larger weight and fat mass index in boys at 7 years. Our data supported an increased susceptibility to prenatal testosterone exposure in boys compared to girls, which may increase future metabolic risk. Furthermore, gynoid fat percentage tended to be lower in girls of women with PCOS compared to controls.

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Mental health and illness uncertainty of individuals with polycystic ovarian syndrome: how is the quality of life affected?

Selda Çelik[1], Merve Murat[1], Gülden Anataca[2] & Hande Peynirci[2]
[1]University of Health Sciences; [2]Kanuni Sultan Süleyman Training and Research Hospital, Turkey

Introduction
Polycystic ovary syndrome (PCOS) stands out as one of the prevalent endocrine disorders affecting women in their reproductive years, impacting 8-13% of females as per World Health Organization (WHO) statistics. This condition has significant repercussions on a woman's sense of self, mental well-being, and overall life quality. While individuals with PCOS often grapple with anxiety and sadness throughout the diagnosis and treatment phases, external factors can influence these emotions. This uncertainty stems from a lack of comprehensive understanding about various aspects of the syndrome, such as its lifelong progression, diverse symptomatology, and overall morbidity. The concept of illness uncertainty, prevalent in both acute and chronic conditions, is characterized in literature as a cognitive stressor, a sense of loss of control, and a state of evolving perceptual doubt. This uncertainty is closely tied to an individual's challenges in adapting to the ongoing process of the disease.
Aim
The objective of this study is to assess the levels of mental health and illness uncertainty in women diagnosed with PCOS and to analyze how these factors influence their quality of life.
Method
This study is a descriptive cross-sectional examination conducted with a pilot sample of 127 women attending a public hospital in Istanbul, Turkey. Information was gathered through a Personal Information Form, along with the Depression Stress and Anxiety Scale, the Mishel Uncertainty in Illness Scale, and the World Health Organization Quality-of-Life Scale (WHOQOL-BREF).
Results
The individuals involved in the study had an average age of 30.9 ± 5.40 years, predominantly single (52.8%), and most had completed high school (62.2%), with incomes generally matching their expenses (44.1%). Regarding PCOS characteristics, the participants were diagnosed with PCOS at a mean age of 18.1 ± 2.17 years. Notably, all participants underwent hormone treatment, with only 29.9% adhering to their medication regimen, and a mere 1.6% receiving PCOS education for self-care. A majority of participants exhibited symptoms such as excess body hair (69.3%), acne (33.9%), irregular menstrual cycles (58.3%), and sexual problems (22.0). The participants recorded elevated scores on the Mishel Uncertainty in Illness Scale, the Depression Stress and Anxiety Scale, and the WHOQOL-BREF.
Conclusion
The findings indicate heightened levels of depression, stress, and anxiety and illness uncertainty among women with PCOS, and implementing targeted interventions has the potential to alleviate these symptoms and raise quality of life.

Keywords: Polycystic ovary, illness uncertainty, mental health, quality of life
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P363

A multinational study to explore the management of dermatological manifestations associated with polycystic ovary syndrome (PCOS) across europe

Kyranna Lafara[1], Gesthimani Mintziori[1], Dimitrios Goulis[1], Amynta Arshad[2], Sahrish Khan[3], Agatha Chu[4], Angharad James[5], Elmira Abdullayeva[6] & Team Dekode[7]
[1]Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Birmingham Medical School, University of Birmingham, Birmingham, United Kingdom; [3]Queen Elizabeth Hospital, Birmingham, United Kingdom; [4]Hull University teaching hospital NHS trust, Hull, United Kingdom; [5]South Tyneside and Sunderland NHS Foundation Trust, South Tyneside, United Kingdom; [6]PCOS and hirsutism clinic, yeditepe University hospital, Instabul, Turkey; [7]Institute of Applied Health Research, University of Birmingham, Bermingham, United Kingdom

Objective
To investigate the management of dermatological manifestations associated with PCOS and its management across Europe.
Methods
This multinational retrospective study was conducted from June 2023 to January 2024. All women over 18 years of age attending a first consultation for PCOS from 1st January 2020 to 30th December 2023 in the UK ($n=359$), Turkey ($n=239$), Greece ($n=92$) and Georgia ($n=10$) were included. Those without PCOS or undergoing follow-up were excluded. Data was collected during the first consultation, including sociodemographic variables, reasons for referral, dermatological manifestations, and treatment before and after consultation. Descriptive statistics were performed with SPSS 28.0.
Results
In total, 700 women were seen for the first PCOS consultation. The most common reasons for referral across all countries were irregular menses (65.7%), hirsutism (61.1%) and acne (38.9%). Irregular menses were the most common reason for referral in the UK (59.6%), Greece (82.6%) and Georgia (100.0%), whereas hirsutism was the most common reason for referral (70.3%) in Turkey. Overall, 74.6% of referrals were made due to women having dermatological concerns (UK: 60.7%, Turkey: 94.1%, Greece: 77.2% and Georgia: 100.0%). In total, 611 (87.3%) women were diagnosed with a form of dermatological manifestation of PCOS after the first consultation. All countries showed a similar trend in dermatological diagnoses made, with hirsutism being most common (UK: 92.5%, Turkey: 71.4%, Greece: 85.5% and Georgia: 100.0%) followed by acne (UK: 34.0%, Turkey: 69.6%, Greece: 78.3% and Georgia: 40.0%) and androgenic alopecia (UK: 16.3%, Turkey: 11.2%, Greece: 10.8% and Georgia: 10.0%). Before the first consultation, laser hair removal was the most popular treatment for hirsutism across all countries (33.4%), followed by the oral contraceptive pill (OCP) (22.4%) and shaving (13.9%). Laser treatment was most popular in Turkey (51.8%), Greece (39.8%) and Georgia (90.0%), whereas shaving was most popular in the UK (26.9%). Following assessment at first consultation, 446 (73.0%) women were commenced on pharmacological treatment for hirsutism. Across all countries, the most common drug prescribed was spironolactone (40.8%), followed by the OCP (35.4%) and metformin (32.1%). In the UK, metformin was the most prescribed drug (54.4%), whereas the OCP was the most prescribed drug in Greece (29.9%) and Georgia (100.0%). Spironolactone was most prescribed in Turkey (68.8%).
Conclusion
Dermatological concerns associated with PCOS comprise a large proportion of referrals to tertiary care. Developing a standardised approach to assess and manage dermatological concerns may minimise variation in care internationally and improve patient outcomes.

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The risk of obesity and metabolic complications in hyperandrogenic physically inactive young women with PCOS

Justyna Kuliczkowska-Płaksej[1], Aleksandra Jawiarczyk-Przybylowska[1], Lukasz Gojny[1], Aleksandra Zdrojowy-Wełna[1], Felicja Lwow[2] & Marek Bolanowski[1]
[1]Wrocław Medical University, Department of Endocrinology, Diabetes and Isotope Therapy, Wroclaw, Poland; [2]Wroclaw University of Health and Sport Sciences, Department of Physiotherapy, Wroclaw, Poland

Background
Polycystic ovary syndrome (PCOS) is a condition affecting up to 20% of reproductive-aged women. PCOS is associated with obesity and serious metabolic complications. There is a lack of research evaluating differences in metabolic complications between hyperandrogenic physically active and inactive individuals.
Objective
We used a cross-sectional study to compare the risk of obesity, metabolic syndrome, visceral adipose index, and insulin resistance between normoandrogenic, hyperandrogenic, and healthy women, as well as hyperandrogenic active and inactive women.
Participants and design
A total of 259 women aged 20–35, of which 148 had PCOS and 111 were healthy age-matched controls. Anthropometric parameters were calculated and hormonal and biochemical assays were performed in all patients. Physical activity (PA) level was assessed using the International Physical Activity Questionnaire and each participant was classed as inactive or active.
Results
We found an association between free androgen index and PA in hyperandrogenic PCOS women, but not in normoandrogenic or healthy women. Hyperandrogenic individuals presented higher odds ratios of obesity (7.3 times, $P < 0.001$), metabolic syndrome (9 times, $P < 0.001$), and insulin resistance (3.84 times, $P < 0.001$) than the normoandrogenic women. Furthermore, hyperandrogenic women who performed at least 7.5 MET $\times$ h $\times$ week^{-1} of physical activity had lower odds ratios of obesity (5.67 times; $P < 0.001$), MS (5.69 times; $P < 0.001$), and insulin resistance (2.99 times; $P < 0.005$) than inactive hyperandrogenic individuals.
Conclusion
Physical activity should be recommended as an important element for health improvement supporting pharmacotherapy, especially in hyperandrogenic PCOS women.

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Early changes in muscle strength and body composition under gender-affirming hormonal therapy in transgender people assigned female at birth

Seda Hanife Oguz[1], Banu Ertürk[2], Sinem Güneri[3], Alp Çetin[3] & Bulent Yildiz[1]
[1]Hacettepe University School of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism, Ankara, Turkey; [2]Hacettepe University School of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism, Ankara, Turkey; [3]Hacettepe University School of Medicine, Department of Physical Therapy and Rehabilitation, Ankara, Turkey

Background
The effects of gender-affirming hormonal therapy (GAHT) on body composition in transgender people assigned female at birth (AFAB) have been an area of interest. However, the impact of GAHT on muscle strength remains inadequately studied. We aimed to evaluate early alterations in muscle strength following GAHT in transgender people AFAB by isokinetic dynamometry, the gold standard for assessment of strength.
Subjects and Methods
A total of 20 transgender people AFAB were assessed at baseline, and after 3 months of testosterone injections. Fifteen participants were also assessed after 6 months. Muscle strength parameters including lower limb peak torque (PT), PT to body weight ratio (PT/BW) and average PT (AvPT) were measured using isokinetic dynamometry. Hand-grip strength (HGS) was also assessed by a dynamometer. Bioelectrical impedance analysis was used to assess body composition characteristics. Serum androgens, fasting glucose and insulin were measured at all three time points.
Results
The mean age and BMI ($\pm$SD) were 23.0$\pm$3.5 years and 25.1$\pm$5.7 kg/m^2 at baseline. Free androgen index was correlated with lean body mass ($r = 0.45$, $P = 0.04$), and fasting insulin was with truncal fat mass ($r = 0.65$, $P = 0.002$) before initiation of GAHT. BMI did not show a significant change after 3 and 6 months of GAHT. After three months, significant increases occurred in knee flexors' PT (56.6$\pm$18.7 N-m to 63.7$\pm$20.1 N-m, $P = 0.008$), PT/BW (82.5$\pm$24.2% to 92.8$\pm$27.3%, $P = 0.01$) and AvPT (52.1$\pm$17.0 N-m to 57.9$\pm$18.7 N-m, $P = 0.02$), as well as in lean body mass (49.8$\pm$9.0 kg to 54.6$\pm$8.9 kg, $P = 0.001$). There were no further alterations in these composition and strength parameters after 6 months. However, an increase in HGS was only significant after 6 months. Serum creatinine increased significantly with GAHT but remained within the normal range. Lean body mass and knee flexors' AvPT were positively correlated at all timepoints. Muscle strength did not show any correlation with biochemical parameters including serum androgens and insulin.
Conclusion
Our results suggest an early increase in lower limb muscle strength and lean body mass within the first three months of GAHT in transgender individuals AFAB which are preserved and accompanied by a significant increase in upper limb strength at 6 months. Muscle strength appears to be associated with lean body mass. Given these outcomes, early initiation of an exercise plan to further enhance muscle mass and mechanical function may be considered for individuals undergoing GAHT.

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"Brief intelligence test" questionnaire in klinefelter syndrome: may words improve diagnosis?

Davide Vimercati[1], Lorenzo Marinelli[2], Serena Cagnina[2], Tommaso Daffara[1], Andrea Bichiri[2], Cataldo Di Bisceglie[2], Giovanna Motta[2], Fabio Lanfranco[3] & Marco Zavattaro[1]
[1]Ospedale Maggiore di Novara, Novara, Italy; [2]Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Torino, Italy; [3]Humanitas Gradenigo, Torino, Italy

Background
The clinical burden of Klinefelter Syndrome (KS) is not limited to the impairment of gonadal function and an increased prevalence of cardio-metabolic, endocrinological and oncological diseases, but also involve several cognitional, behavioural and psychological issues. Because of the wide heterogeneity in clinical phenotype, the diagnosis of KS is still challenging, resulting in a significant number of patients to remain undiagnosed or to have a late diagnosis. Verbal deficits in reading/-spelling, delayed language development, impaired syntax, word retrieval and language production/perception are among the most characteristic functional features of KS (up to 70-80% of patients) determining a slight reduction in verbal Intelligence Quotient (IQ). The primary endpoint of our study was to focus on language skills in the area of reading, thus further evaluating whether specific questionnaires might represent a reliable tool for early diagnosis of KS.
Methods
An observational, cross-sectional, multicenter study was performed, consecutively enrolling adult KS patients and a control group of unaffected males, matched for age and years of study, referring to the outpatient clinics of the "S.C.U. Endocrinology, Diabetology and Metabolism - University of Turin" from 1st November 2018 until 1st September 2021 All patients performed the "Brief Intelligence Test" (TIB) test for assessing the overall, verbal and performance IQ. This validated questionnaire relies on the correlation between global intelligence and reading skills, leading to explore the areas of language and learning through the evaluation of errors in pronunciation and accentuation of 54 commonly used words read aloud.
Data on andrological anamnesis, physical examination and hormonal profile were also recorded.
Results
34 unaffected males and 34 KS patients, aged [median (IQR)] 46.5 (45.75 - 54.75) years and with an average length of studies of 15.0 (8.0 - 15.0) years, were enrolled. KS patients were more prone to make mistakes in accentuation ($p < 0.001$) but not in pronunciation ($p = 0.119$) than controls, leading to lower scores (but still within normal range) in overall, verbal end performance IQ ($p < 0.001$). None of the clinical and hormonal variables was found to correlate with the TIB and IQ scores.
Conclusions
TIB questionnaire proved to be a reliable tool in highlighting verbal deficits in KS patients (especially in reading) when compared to unaffected males. Thus, the use of TIB might represent a very useful, quick and effective tool for screening verbal disabilities in a wide number of people, potentially improving the possibility of early diagnosis of KS.

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P550

Comprehensive WES reanalysis of rare endocrine patients for the identification of novel disease-causing genes

Muhammad Yousaf[1], Mariateresa Zanobio[2], Francesca Allosso[1], Vincenzo Nigro[2] & Daniela Pasquali[1]
[1]University of Campania Luigi Vanvitelli, Department of Advanced Medical and Surgical Sciences, Naples, Italy; [2]University of Campania Luigi Vanvitelli, Department of Precision Medicine, Naples, Italy

Rare diseases affect more than 300 million people worldwide, often lead to chronic illness, disability, and premature death. The recent advancements in genetics through Next Generation Sequencing (NGS) have revolutionized research and diagnostics. NGS technologies allowed the identification of novel candidate disease-causing genes, significantly also in-depth modification of our understanding of genetic architecture of various rare endocrine diseases. However, despite these recent advancements, over 50% of cases typically remain unsolved. In these unsolved cases, periodical reanalysis has been proposed as a solution to enhance the diagnostic yield. Here, we report results from WES reanalysis of patients with endocrine pathological phenotype from Telethon Undiagnosed Disease Program (TUDP). Our study aimed to identify potential novel disease-causing genes by focusing on unsolved patients, whereas reanalysis of solved patients could reveal potential link of already known disease-causing genes in the endocrine disorders. TUDP cohort comprised of 4809 solved and 6278 unsolved patients. Initially, we selected 359 patients among the solved and 227 patients from unsolved ones, based on human phenotype ontology (HPO). Successively, we considered 39 solved and 26 unsolved patients which had the strongest endocrine phenotype for this pilot study. WES data reanalysis was performed employing bioinformatics in-house pipelines, whereas human genome version 19 (hg19) was used as the reference genome in all cases. For variant interpretation, established guidelines were used as VarSome germline classification. Moreover, we also interrogated variants and genetic disorders databases to validate the association of genes with the patient's phenotype. Furthermore, results from each analysis were compared with the most recent literature studies. Preliminary results obtained from solved patients led us to detect a *de novo AFF2* mutation (NM_002025:c.1444G>A; p.Gly482Arg in exon 10) in a patient diagnosed with cryptorchidism. Among the unsolved patients, a heterozygous compound *PKD1* variant (NM_001009944.3 :c.12436G>A; p.Val4146Ile and c.3496G>A; p.Gly1166Ser, respectively in exon 45 and 15) was observed in a patient with clinical presentation of Hypophosphatemic Rickets. To better understand the putative involvement of *PKD1* gene in endocrine disorders, we are searching for other patients carrying variants in the same gene interrogating MatchMaker Exchange platforms, which facilitates the matching of phenotype-genotype for candidate disease-causing genes connecting researchers and clinicians worldwide. Based on these results, we provide practical evidence to increase novel genetic diagnosis through WES reanalysis. Finally, this study emphasizes the power of reanalysis of WES data, particularly in a clinical context given the implications.

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Endocrine responses to kisspeptin in an unusual case of kallmann syndrome with unilateral anosmia

Jovanna Tsoutsouki[1], Alexander N Comninos[1,2], Maria Phylactou[1,2], Bijal Patel[1], Edouard Mills[1,2], Megan Young[1], Arthur Yeung[1], Kanyada Koysombat[1], Manish Modi[1], Deborah Papadopoulou[1,2], Sasha Howard[3], Waljit S Dhillo[1,2] & Ali Abbara[1,2]
[1]Section of Investigative Medicine, Department of Metabolism, Digestion and Reproduction, Imperial College School of Medicine, Imperial College London, London, United Kingdom; [2]Department of Diabetes and Endocrinology, Imperial College Healthcare NHS trust, London, United Kingdom; [3]Department of Paediatric Endocrinology, Queen Mary University of London, London, United Kingdom

Introduction
Kallmann syndrome (KS) is a rare condition characterised by congenital hypogonadotropic hypogonadism (CHH), usually due to defective migration of olfactory axons and GnRH-neurons. KS is typically associated with absent (anosmia) or reduced (microsmia) sense of smell. Unilaterally hypoplastic or absent olfactory bulbs on MRI are reported, although disturbance in smell is usually bilateral. Kisspeptin is a potent stimulator of hypothalamic GnRH-neurons, and endocrine responses to kisspeptin boluses are usually minimal in CHH. We present an unusual case of KS with unilateral anosmia and her responses to kisspeptin.
Case Presentation
An 18yr old woman presented to the endocrine clinic for management of KS. Her mother and sister were known to have KS (heterozygous for FGFR1-mutation) having previously presented with primary amenorrhea and anosmia. Her mother required ovulation induction to conceive. She had spontaneous albeit borderline late menarche aged 16yrs, but only five menstrual periods over the subsequent two years, followed by secondary amenorrhea. She didn't have any other medical history, psychological stress, undertake excessive exercise and took no regular medications. At presentation, her BMI was 22 kg/m^2 and she had normal secondary sexual characteristics. Unusually, she reported a normal sense of smell via the right nostril, but anosmia via the left nostril. Unilateral anosmia was confirmed with an UPSIT smell test (right nostril 32/40 (normosmia); left nostril 12/40 (anosmia)). MRI-brain revealed unilaterally absent left olfactory nerve, bulb, and sulcus. She had undetectable serum estradiol (<100 pmol/l), low LH (0.2 IU/l) and low FSH (0.4IU/L). Pelvic ultrasound demonstrated a thin endometrium (3mm), consistent with hypoestrogenism. Whole-exome sequencing confirmed a heterozygous FGFR1 variant. An intravenous GnRH-test (100 mg) induced an LH rise of 24.8IU/L indicating a functional pituitary gland. An intravenous bolus of kisspeptin-54 (9.8 nmol/kg) induced a subnormal early rise in LH (3.4IU/L), which is greater than typically seen in CHH. On separate occasions, intranasal (12.8nmol/kg) KP54 delivered only to the right nostril, led to a small rise in LH of 0.5IU/L, whereas KP54 delivered only to the left nostril did not induce any LH rise.
Discussion
This lady had spontaneous puberty and menarche indicating some residual GnRH-neuronal function, despite inheriting an FGFR1 variant. Further, she had a small early subnormal gonadotropin response to kisspeptin, rather than the absent response typically observed in complete KS. This, and in view of her unilateral anosmia, unilateral olfactory bulb on MRI, a unilateral albeit small response to intranasal kisspeptin-54, suggest that she has an unusual partial/unilateral form of KS.

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Hypoechoic testicular lesions in klinefelter syndrome show volumetric reduction in response to testosterone therapy

Davide Ferrari[1], Franz Sesti[1], Marta Tenuta[1], Francesco Carlomagno[1], Daniele Gianfrilli[1], Carlotta Pozza[1] & Andrea Isidori[1]
[1]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy

Introduction
Patients with Klinefelter Syndrome (KS) often display small, multiple, non-palpable, and typically benign testicular micro-nodules at ultrasonographic examination, representing Leydig cell hyperplasia or Leydig tumors. Increased LH levels raising from testicular damage might play a pivotal role by acting as growth factor for Leydig cells. To date, evidence on the efficacy of testosterone replacement therapy (TRT) on decreasing the micro-nodules volume are lacking.
Materials and Methods
We prospectively evaluated KS patients with classic karyotype (47, XXY) aged 15 to 50 years and naive to TRT. This evaluation included testicular ultrasound and hormone assessment. Mosaic karyotypes, previous pituitary surgery or radiotherapy or medications affecting the hypothalamus-pituitary-gonadal axis were excluded. Hypogonadal patients who received TRT were assessed after at least 6 months to evaluate the estimated volumetric change in the micro-nodules. The volume of hypoechoic lesions was calculated with the sphere formula ($1/6 * \pi * D^3$). For multiple lesions, the sum of the volumes of the two dominants lesions for each testicle was considered.
Results
Seventy patients (mean age 26.4±8.7 years) were included in the study, 35 of which (Group A) displayed at least one testicular micro-nodule, while the other 35 (Group B) did not show clear lesions. Group A patients were significantly older than those in Group B (P=.010) and showed higher LH levels (P=.001) and lower Testosterone/LH ratio (P=.005), though total Testosterone (tT) levels did not differ significantly (P=.328). Testicular microlithiasis was present in 18 patients, 12 (34%) from Group A and 6 (17%) from Group B (P=.086). The tT/LH ratio effectively predicted the presence of micro-nodules (B= -1.074, OR= 0.342, 95CI= 0.123 - 0.947, P=.039) whereas the increase in age (P=.265) and concomitant microlithiasis (P=.482) did not reflect in increased lesion risk. An interim longitudinal analysis was performed on 20 of the patients who started TRT(44% gel, 56% injective). After 16.7 (11.9-31.2) months, the micro-nodules displayed significant volumetric reduction (62.9 to 22.9 mm^3, P<.001) and were no longer detectable in 4 patients (20%). No difference was observed in volumetric change between TRT formulations (P=.897). Treatment duration did not correlate with the micro-nodules volumetric reduction (P=.512).
Conclusion
Our data demonstrate for the first time the efficacy of TRT in reducing the volume of testicular, non-palpable hypoechoic micro-nodules in patients with KS. These changes are likely secondary to the restoration of more physiological LH and tT/LH.

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Patient and public involvement in simulation via instant messaging – birmingham advance (SIMBA) training improves clinicians' confidence in managing reproductive endocrinology cases

Sangamithra Ravi[1], Tamzin Ogiliev[2], Maiar Elhariry[1], Pavithra Sakthivel[1], Abby Radcliffe[1], Rahul Sagu[1], Harshin Balakrishnan[3], Dengyi Zhou[4], Punith Kempegowda[5,6] & Simba and Comics team[5]
[1]College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; [2]Lancaster University Medical School, Lancaster, United Kingdom; [3]School of Medicine, Far Eastern Federal University, Vladivostok, Russian Federation; [4]London North West University Healthcare NHS Trust, Harrow, United Kingdom; [5]Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; [6]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

Introduction
Simulation via Instant Messaging – Birmingham Advance (SIMBA) is a virtual simulation-based medical training model that improves clinicians' confidence. However, it has lacked input from patients living with these conditions. Engaging patients and members of the public in the formulation and discussion of cases could guide clinicians to tailor management to meet the concerns and expectations of patients better.
Method
A two-day conference took place on 27 and 28 September 2023. Nine reproductive endocrinology cases, focussing on PCOS (two cases), Thyroid disease, Premature Ovarian Insufficiency, Menopause, Azoospermia, Opiate induced hypogonadism, Idiopathic hypogonadism and Kallman syndrome, were simulated over the two days via Whatsapp in real-time. Real patient cases, anonymised to maintain confidentiality, were used to formulate these scenarios. Members of the general public living with these conditions were recruited from several support groups to partake in a workshop-style discussion to provide their opinions on how representative the cases were and how the management of the condition could be improved. Following the simulated cases, the content was discussed by expert speakers, each a specialist in various aspects of reproductive endocrinology. This discussion was interactive so that participants could ask questions and clarify doubts. Pre- and post-SIMBA surveys were sent to participants to evaluate self-perceived improvement in confidence and ACGME Core Competencies, as well as perceptions surrounding SIMBA. Quantitative and qualitative analysis of these responses was undertaken using the Wilcoxon Signed Rank test and thematic analysis of the open-ended questions respectively.
Results
In total, 29 participants completed both the pre- and post-session surveys. Overall, participants' self-reported confidence of simulated cases significantly increased from 36.54% to 88.62% on Day 1 ($n=16$) and from 36.54% to 84.62% on Day 2 ($n=13$) post-session ($P<0.0001$). Self-reported improvements in ACGME Core Competencies were seen in most participants, with 100% ($n=29$) in knowledge of patient management, system-based practice and practice-based learning, and 96.55% ($n=28/29$) in patient care and professionalism. 100% ($n=29$) of participants rated the session as excellent or good and 93% ($n=27/29$) would attend future sessions. Thematic analysis of open-ended questions revealed clinicians' improvements in clinical knowledge and communication skills.
Conclusion
Patient involvement in SIMBA effectively improved clinicians' confidence in reproductive endocrinological scenarios. Implementing SIMBA in larger-scale studies will determine the long-term effectiveness of simulation-based learning in reproductive endocrinology.

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Revitalizing kidney health in polycystic ovary syndrome: a novel approach— targeting STAT3 signaling for restored mitochondrial function and reduced kidney injury

Samar Rezq[1], Jelina Basnet[1], Alexandra M Huffman[1], Joseph Flaherty[1], Ngoc H Hoang[1], Kristin Edwards[1], Licy L Yanes Cardozo[1] & Damian G Romero[1]
[1]University of Mississippi Medical center, Pharmacology and Toxicology, Jackson, United States

Background
Polycystic ovary syndrome (PCOS) is characterized by hyperandrogenism and polycystic ovaries. Renal injury is prevalent in PCOS, yet the molecular mechanisms are poorly understood. The JAK/STAT3 signaling pathway, activated by the inflammatory cytokine interleukin-6 (IL-6), negatively impacts renal mitochondrial function to induce oxidative stress and renal injury. Despite its chronic activation by excess androgen in extra-renal tissues in PCOS, its role in PCOS associated renal injury is unknown. We aimed to test the hypothesis that excess androgen activates the JAK/STAT3 pathway, leading to renal injury by inducing mitochondrial dysfunction in PCOS.
Methods
PCOS was induced in 3-week-old female mice by dihydrotestosterone Silastic tubes implantation (DHT, 8 mg, 12 weeks). Eight weeks later, the mice were given the JAK/STAT3 inhibitor Stattic (10 mg/kg, SC, 3x/week) or vehicle for 4 weeks. Kidney weight, serum IL-6 (Bioplex), glomerular filtration rate (GFR, transcutaneous fluorescence), and urinary albumin to creatinine ratio (UACR, clinical chemistry analyzer) were assessed. Renal JAK1, JAK2, active STAT3 [phosphorylated-STAT3 (Tyr705)], total STAT3, and mitochondrial markers (cytochrome C, succinate dehydrogenase A, and stress protein HSP60) were assessed by Western blot. IL-6 mRNA was quantified by RT-qPCR. Histopathological analysis was done in H&E-stained renal sections. Mitochondrial reactive oxygen species (mtROS, Amplex Red assay), complexes I and II-driven respiration, and complex IV activity (Oroboros Fluorespirometer) were measured in freshly-isolated kidney mitochondria. Oxidative stress measurement (DCF fluorescence) was performed in DHT (10nM)/Stattic (100nM) or vehicle-co-treated mouse proximal tubule (MCT) cells.
Results
DHT significantly increased kidney weight, UACR, and both systemic and renal IL-6 levels (1.4-3.2-fold) while decreasing GFR (1067.2 $\pm$ 59.9 vs 1335.6 $\pm$ 60.3 uL/min/100g body weight). PCOS mice have more active STAT3 signaling (higher JAK1, JAK2, and active STAT3). Renal mtROS was higher (2-fold) and complexes I, II, III, and IV respiration was lower (43-71%) in PCOS mice, along with lower cytochrome c (32%), and higher HSP60 (4-fold) levels. These changes were associated with worsen renal histological structure with congested glomeruli and luminal epithelial lining exfoliation. Stattic didn't affect kidney weight but normalized UACR and GFR while decreasing both glomerular and tubular injury. Stattic decreased renal HSP60 and mtROS generation while increasing complexes I, II, and IV derived respiration. Stattic co-treatment abolished DHT-mediated oxidative stress in MCT cells.
Conclusion and significance
Our findings suggest that STAT3 activation plays a significant role in renal outcomes in PCOS, and its targeting could be a novel therapeutic approach to ameliorate renal injury in PCOS.

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P555

Klinefelter syndrome is associated with early-onset metabolic defects that are not reversed by testosterone therapy

Karim Chouchane[1], Susanna Hofbauer[1], Ilaria Giordani[1], vionnet nathalie[1], Mohammed Barigou[1], Nelly Pitteloud[1], Michael Hauschild[2] & Georgios Papadakis[1]
[1]Lausanne University Hospital, Service of Endocrinology, Diabetes and Metabolism, Lausanne; [2]Children Hospital, Unit of pediatric endocrinology-diabetology, Lausanne, Switzerland

Background
Klinefelter syndrome (KFS) is the most common chromosomal aberration in men, characterized by an extra-X chromosome (47, XXY). Besides the well-known reproductive defects, KFS is characterized by a 4-fold increase in metabolic syndrome, cardiovascular morbidity and mortality. The exact cause of this constellation remains unclear.
Methods
Data from non-mosaic KFS adults and adolescents, evaluated in the endocrine unit of Lausanne University Hospital between 2015 et 2022, were analyzed. Only men without testosterone replacement therapy (TRT) at the moment of evaluation were included. Metabolic phenotyping consisted of a fasting blood test, an oral glucose tolerance test and body composition assessment using Dual X-ray absorptiometry. A longitudinal analysis was conducted in men with available metabolic data after at least 1 year of TRT intake.
Results
seventy-five men were included of whom 57 at diagnosis (TRT-naïve) and 18 after TRT wash-out. The cohort spanned across a large age range (31.4 $\pm$ 11.9 years). As expected, the majority of patients were hypogonadal, defined as clinical and biochemical [morning serum total testosterone (T) $<$ 10.4 nmol/l] signs of testosterone deficiency. Mean TT levels were moderately decreased (9.4 $\pm$ 6.1 nmol/l) as opposed to normal estradiol (E) levels (0.09 $\pm$ 0.03 nmol/l). Consequently, most participants had relative hyperestrogenism defined as a T/E

ratio < 100. Roughly half of participants were overweight (BMI > 25 kg/m^2), whereas two third of them were insulin resistant (HOMA-IR > 2.6) and had fat excess defined as a fat mass index (FMI) > 6 kg/m^2. Hypogonadal men had higher incidence of metabolic syndrome (26% vs 11%), glucose intolerance (33% vs 10%) and hypertension (11% vs 5%) as compared to those with normal TT levels. Linear regression revealed an inverse association of T with several metabolic traits including FMI (r=-0.48, P=0.002) and HOMA-IR (r=-0.33, P=0.03). Interestingly, T/E ratio exhibited even stronger associations (r=-0.66, P<0.0001 and r=-0.46, P=0.002 for FMI and HOMA-IR, respectively). Sustained TRT intake in 20 patients for a mean follow-up of 5 years led to a slight but significant increase in BMI (mean delta + 1.2 kg/m^2, P=0.02). FMI and HOMA-IR did not significantly improve during TRT.

Conclusions

KFS is characterized by high metabolic risk that is only partially reflected in BMI. Besides hypogonadism, other imbalances such as relative hyperestrogenism may contribute to the metabolic deterioration. The absence of improvement in surrogate metabolic markers by long-term TRT implies the need to evaluate additional therapies for KFS-associated metabolic risk.

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4 Cases of postmenopausal hyperandrogenism in glasgow

Ashley Leong[1], Mohammed Azharuddin[2], Chris Jones[2] & Hiba Abdelrahman[2]
[1]University of Glasgow, United Kingdom; [2]Inverclyde Royal Hospital, United Kingdom

Background

New onset postmenopausal hyperandrogenism (PMH) is rare and is a diagnostic and therapeutic challenge.

Clinical Case

AB, a 69-year woman, had 14-years of hirsutism and 1-year of male-pattern balding. Androgen profile was high: testosterone (T) 4.9nmol/L, androstenedione (A) 3.7nmol/L, 17OHP 2.3nmol/L. DHEAS and pre- and post-1 mg ONDST cortisol was normal. Adrenals and ovaries on CT were unremarkable, hence benign ovarian source assumed. She declined surgery, leuprolin and finasteride. Spironolactone was trialled but discontinued due to nephrotoxicity. Symptoms are currently controlled by topical minoxidil. CD, a 46-year woman, had 1-year of hirsutism, clitoromegaly, mood changes and bilateral labial hypertrophy. Androgen profile was high (T 2.0nmol/L; A 4.8nmol/L; 17OHP 6.9nmol/L); a normal SST excluded NCCAH. DHEAS was normal. TVUS showed normal ovaries; MRI showed unremarkable ovaries and adrenals. Benign ovarian source was assumed. Leuprolin caused T suppression (1.1nmol/L after 5 months), hence laparoscopic BSO was done; ovarian histology was normal with few cystic follicles. 2 months later, A reduced (3.2nmol/L) and symptoms improved. WX, a 58-year woman, had 4-years of hirsutism and male-pattern balding. Pre- and post-ONDST androgen profile was high (T 12.4nmol/L, A 5.4nmol/L, 17OHP 2.8nmol/L) with no suppression (T 11.3nmol/L, A 4.4nmol/L, 17OHP 2.7nmol/L). ACTH, pre- and post-ONDST cortisol, DHEAS, 24h-urinary steroids and CA125 were normal. CT showed unremarkable adrenals and ovaries. Benign ovarian source was assumed. Leuprolin improved biochemistry (T <0.5nmol/L, A 1.4nmol/L after 3 months) and symptoms. WX awaits bilateral oophorectomy. YZ, a 56-year woman, had 9-months of hirsutism, hair loss and mild clitoromegaly. Pre- and post-ONDST androgen profile was high (T 4.9nmol/L, A 3.7nmol/L, 17OHP 2.3nmol/L) with no suppression (T 4.0nmol/L, A 2.0nmol/L, 17OHP 2.1nmol/L). Prolactin, DHEAS and 24h urinary steroids were normal. No adrenal/ovarian tumour was found on CT; pelvic USS showed normal postmenopausal ovaries (volume right 4.6ml, left 2.7ml, n<6ml) and some small fibroids. Benign ovarian source was assumed. Leuprolin improved biochemistry and symptoms (T <0.5nmol/L after 3 months). Laparoscopic BSO was done; histology showed ovarian hyperthecosis. Androgens normalised after 8 months with symptom improvements (T 0.6nmol/L, A 2.7nmol/L).

Conclusion

We propose an algorithm to standardise initial workup of PMH and highlight that: 1) PMH has significant phenotypic variability; 2) DHEAS and pre- and post-1 mg ONDST androgen profile may differentiate ovarian/adrenal sources; 3) consider combined ovarian and adrenal imaging regardless of malignancy risk; and 4) localising source and excluding malignancy can inform management.

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P557

MiRNAs specific for PCOS phenotypes

Olivia Trummer[1], Jonas Hoeller[1], Sharmaine Reintar[1], Veronika Tandl[1], Ines Föbl[1], Valentin Borzan[1], Verena Theiler-Schwetz[1], Christian Trummer[1], Elisabeth Lerchbaum[1] & Barbara Obermayer-Pietsch[1]
[1]Medical University of Graz, Department of Internal Medicine, Graz, Austria

Background

Polycystic ovary syndrome (PCOS) is a common endocrine condition of unclear origin, characterized by hyperandrogenism (HA), oligo-/amenorrhoea (OM), and polycystic ovarian morphology (PCOM). According to the Rotterdam criteria, PCOS phenotypes A-D range from mild to severe and are defined as phenotype A (HA, OM and PCOM), phenotype B (HA, OM), phenotype C (HA, PCOM) and phenotype D (OM, PCOM). Recent discoveries indicate that microRNAs (miRNAs) play a role in the development of PCOS and may be potential biomarkers. Our main aim was to characterize miRNAs previously reported to be altered in PCOS, in women with different PCOS phenotypes.

Methods

We conducted a pilot study (n=51) with 11 women in each phenotype group and 8 control women. Candidate miRNAs were selected based on previously reported associations with PCOS. MiRNA isolation, complementary DNA (cDNA) synthesis and quantitative real-time PCR (qRT-PCR) were performed with assays from Qiagen. UniSp 2/4/5/6 were used as exogenous controls, and qRT-PCR data were normalized to the mean of miR-484 and snu6 as reference genes. After verifying the normal distribution and homogeneity of variances, a one-way-ANOVA or a non-parametric Kruskal-Wallis test was conducted, followed by Dunnet and Tukey's post-hoc tests. The diagnostic value for discriminating a PCOS phenotype from the other phenotypes was calculated by area under the curve (AUC) and by a receiver-operating-characteristic (ROC) analysis. TargetScanHuman8.0 was used to identify potential target genes of differentially expressed miRNAs.

Results

Systemic expression of miR-23a-3p was upregulated in phenotype B and discriminated PCOS phenotype B from the other phenotypes (AUC=0.837; 95% confidence interval (CI), 0.706-0.968; P=0.006). MiR-424-5p was downregulated in phenotype C and discriminated this phenotype from the others (AUC=0.801; 95%CI, 0.591-1.000; P=0.007). A subgroup analysis between hyperandrogenic PCOS phenotypes (phenotypes A, B, C, n=32) and PCOS women without hyperandrogenism (phenotype D, n=8) showed no group specific differences in their miRNA expression profiles. Functional annotation of differentially expressed miRNAs revealed binding sites in genes of pathways related to insulin resistance and carbohydrate metabolism, iron and lipid metabolism, inflammation, steroid and peptide hormones as well as fertility.

Conclusion

Understanding the differential hormonal and miRNA profiles across various PCOS phenotypes is important to improve the pathophysiologic understanding of PCOS. The miRNAs identified, miR-23a-3p and miR-424-5p, hold promise as potential biomarkers for differentiating between specific PCOS phenotypes. These findings contribute to a deeper understanding of PCOS heterogeneity, potentially improving diagnostic and treatment strategies for women with PCOS.

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Anti-Müllerian hormone as a predictor of ovarian function in patients undergoing radioiodine treatment for thyroid cancer

Barbora Havlinova[1,1], Ilona Součková[2] & Jiří Doležal[3]
[1]University Hospital Hradec Králové and Charles University, Faculty of Medicine in Hradec Králové, The 4th Department of Internal Medicine – Hematology, Hradec Králové, Czech Republic; [2]University Hospital Hradec Králové and Charles University, Faculty of Medicine in Hradec Králové, Department of Clinical Immunology and Allergology, Hradec Králové, Czech Republic; [3]University Hospital Hradec Králové, Department of Nuclear Medicine, Hradec Králové, Czech Republic

Background

Differentiated thyroid carcinoma is the most common endocrinological malignancy with an increasing incidence over the last 30 years. It is the fifth most common cancer among the young population (15–39 years), with women being more frequently affected. Surgical removal of the tumour is the standard treatment method. In indicated cases, total thyroidectomy with subsequent adjuvant radioiodine administration is performed, despite international trends towards less aggressive treatment. International studies have reported anti-Müllerian hormone

(AMH) as the best endocrine marker to assess physiological age-related oocyte loss for healthy women. The possible adverse effects of radioiodine (RAI) on ovarian function and female fertility for women are currently being investigated.
Methods
The aim of our ongoing prospective study is to determine serum AMH to estimate ovarian reserve for premenopausal women treated with RAI. Over the course of one year, 33 serum samples from women with thyroid cancer and 3 serum samples from healthy women were examined. The mean age of the whole group was 35.5 years. The mean RAI dose was 4 888 MBq. AMH levels were compared before and after radioiodine treatment (4–6 months after RAI, 8–12 months after RAI). The Enzyme-Linked ImmunoSorbent Assay (ELISA) microtiter plates were used to test blood samples.
Results
Mean of the AMH level was 5.4 ng/mL ($n=$ 33) prior to RAI. A significant decrease in AMH levels occurred 4–6 months after therapy (mean 1.8 ng/mL) and 22.2 % of patients experienced a decrease in AMH levels to 0 ng/mL from non-zero levels after treatment. A subsequent slight rise in AMH level was 8–12 months after RAI (mean 2.7 ng/mL). Equivalent radioiodine dose to the ovaries was calculated with a mean of 180 mGy in the treated group. Very low AMH values at the beginning of treatment and after radioiodine administration were significant in women aged around 50 years.
Conclusion
AMH has gained interest as a possible predictor of ovarian reserve in recent years. The effects of RAI on the change in AMH levels were more significantly observed in patients older than 35 years. Although findings from retrospective studies suggest a slight decrease in AMH levels after radioiodine treatment of DTC, a long-term decrease in pregnancy rates has not been demonstrated. However, more data from prospective studies are needed.

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Assesing the proficiency and alignment of ChatGPT 3.5 responses with guidelines in addressing frequently asked questions by transgender individuals

Selin Tekin[1], Banu Ertürk[1], Seda Hanife Oguz[1] & Bulent Yildiz[1]
[1]Hacettepe University School Of Medicine, Division of Endocrinology and Metabolism, Ankara, Turkey

Background
ChatGPT, an advanced language model, employs sophisticated deep learning techniques to generate human-like responses. It stands as one of the most extensive publicly accessible language models. Despite the longstanding application of Artificial Intelligence (AI) in diverse domains, its application in healthcare raises concerns about the reliability of information. It is equally important to assess whether the provided information is supported by dependable references and remains up-to-date.
Methods
A cross-sectional non-human subject study was conducted, posing 20 commonly asked questions to ChatGPT 3.5 related to gender dysphoria and transitioning. The questions were formulated in accordance with the recommendations provided in current guidelines and frequently asked questions posed by patients. Questions were categorized into five subgroups; (a) terms and definitions ($n=3$), (b) gender affirming hormonal therapy ($n=4$), (c) adverse outcomes and long-term care ($n=4$), (d) surgical procedures ($n=2$), and (e) other frequently asked questions ($n=7$). The responses from ChatGPT 3.5 were categorized into four groups based on adherence to the Endocrine Society Guideline for endocrine treatment of gender-dysphoric/gender incongruent persons and World Professional Association Standards of Care-8: 1-compatible, 2-compatible but insufficient, 3-partially incompatible, and 4- incompatible.
Results
Eleven of the responses from ChatGPT 3.5 were in accordance with current guidelines (%55), while the answers to the remaining nine questions were aligned but deemed insufficient (%45). The majority of questions with insufficient answers were associated with the treatment and side effects (75% of questions in subgroup-b and 75% of questions in subgroup-c). However, the responses provided by ChatGPT 3.5 to 3 questions (1/3 in subgroup-d, 2/3 in subgroup-e) contained more information than the guidelines, addressing queries on the specialized centers for surgery as well as questions about insurance coverage. Additionally, there were more detailed responses to questions related to increased facial hair density, a common inquiry among transgender men.
Conclusion
The first study in the literature evaluating the responses to the most frequently asked questions about gender dysphoria and transgender individuals using ChatGPT 3.5 suggests that the model can provide accurate information regarding the path and treatment process for individuals undergoing gender transition; even though some responses lack the necessary detail. Some responses to questions are more detailed than those provided in guidelines. Nevertheless, the source and accuracy of this information cannot be definitively confirmed. To enhance accessibility to accurate and comprehensive information, there is a call for scientific studies and guidelines tailored to the unique needs of individuals experiencing gender dysphoria.

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Dampened HPG axis activity and improved reproductive lifespan in dummerstorf superfertile mouse lines

Joachim Weitzel[1], Ludwig Carolin[1] & Michaelis Marten[1]
[1]Forschungsinstitut für Nutztierbiologie, Dummerstorf, Germany

Research in the field of reproductive biology is largely based on informative mouse models. Almost all of these mouse models (~99%) exhibit an unfavourable reproductive phenotype - these mouse models are subfertile or infertile in one or possibly both sexes. In contrast, the number of animal models that show an enhanced reproductive phenotype is extremely rare. Nevertheless, these mouse models could be very informative in identifying mechanisms and pathways associated with enhanced fertility. We analyse two Dummerstorf outbred mouse lines that have been selected for high fertility for 200 generations (fertility lines 1 and 2; FL1, FL2). In both mouse lines, the number of offspring per litter almost doubled (from 11.5 (ctrl) to 20.6 (FL1) and 21.4 (FL2)), without the offspring showing any signs of growth retardation compared to animals from a non-selected control line. We analysed the lifetime fecundity of all three lines and found significant differences. Control and FL1 females gave birth to up to 10 litters, whereas FL2 only gave birth to a maximum of six litters per female per lifetime. In a first set of experiments, we analysed the ovarian phenotype of FL1 females. We noticed a reduced concentration of FSH, both on serum hormone levels (-60%) as well as in pituitary gene transcription (-90%). In line with this decreased FSH levels also hypothalamic GnRH transcription was decreased by 70% compared to ctrl. Gene expression analysis in ovaries revealed that multiple genes associated with follicular development, such as Lhcgr, Esr1, Kit or Foxl2 are differentially expressed in FL1 mice. Holistic gene expression analysis in ovarian granulosa cells further identified a differential regulation of multiple genes involved in follicular atresia. These data suggest that the phenotype of FL1 is at least partly due to attenuated follicular atresia leading to increased follicular survival. More successful folliculogenesis is in turn associated with higher ovulation rates (from 13 (ctrl) to 24 (FL1) oocytes per cycle). There is evidence that the complex interplay of endocrine and molecular changes leading to enhanced follicular development in FL1 females is associated with good reproductive longevity and health. Several genes associated with reproductive lifespan, such as Per2, Kl, Tex14 and Rora, are differentially expressed in the ovaries and granulosa cells of FL1 mice. These data suggest that the unique ovarian phenotype of FL1 females selected for high fertility provides valuable approaches for the search for molecular mechanisms predisposing to increased fertility.

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In vitro analysis of FSHR internalization and signalling mediated by two different FSH preparations

Lara Baschieri[1,2], Clara Lazzaretti[1], Elisa Mascolo[1], Carmela Perri[1,2], Samantha Sperduti[1,3], Claudia Fusco[1], Manuela Simoni[1,3,4] & Livio Casarini[1,3]
[1]Unit of Endocrinology - University of Modena and Reggio Emilia, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy; [2]University of Modena and Reggio Emilia, International Ph.D. School in Clinical and Experimental Medicine (CEM), Modena, Italy; [3]University of Modena and Reggio Emilia, Center for Genomic Research, Modena, Italy; [4]Azienda Ospedaliero-Universitaria di Modena, Department of Medical Specialties, Modena, Italy

Follicle stimulating hormone (FSH) is produced by the anterior pituitary gland and is a key hormone in the reproductive system. FSH is a heterodimeric glycoprotein composed with two extensively glycosylated protein subunits (α and β) N-glycosylated in two positions (Asn^{52} and Asn^{78}in the FSHα subunit and Asn^{7} and Asn^{24} in the FSHβ subunit). Due to different glycosylation pattern, several FSH isoforms may differently act on the receptor (FSHR). We compared *in vitro* the trafficking mediated by two FSH commercial preparations, characterized by different glycosylation pattern, Gonal-f® (Merck KGaA) and Rekovelle® (Ferring Pharmaceuticals). HEK293 cells transiently overexpressing FSHR were treated by

increasing doses of FSH (nM-μM range) and with/without Dynamin inhibition (Dynasore). We evaluated cAMP production, interaction between FSHR and endosomal specific markers, and CRE-controlled reporter gene activation using luciferase and energy transfer-based methods. Statistics: Mann Whitney's U-test ($P<0.05$; $n=4$-5). We found no different interaction between FSHR and the marker of early endosome Rab5, in cells treated with Gonal-f® or Rekovelle®, regardless the presence of Dynasore ($P>0.05$; $n=5$). Dynamin inhibition was linked to increased Gonal-f®-, but not Rekovelle®-induced FSHR-Rab7 interaction, indicating preparation-specific routing to the degradation pathway ($P<0.05$; $n=5$). Gonal-F® induced more pronounced cAMP production at 1 μM concentration, while at 10 nM Rekovelle® induced a significantly higher cAMP production, regardless of Dynasore treatment ($P<0.05$; $n=4$). Finally, CRE reporter gene activation in absence of Dynasore is higher at 60 nM concentration of Gonal-F®, compared to Rekovelle® ($P<0.05$; $n=4$). To conclude, Gonal-f® and Rekovelle® mediate different FSHR internalization and signaling.

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Assessment of muscle mass and strength in women with PCOS following oral contraceptive therapy

Seren Aksun[1], Levend Karaçoban[2], Ilkay Idilman[3] & Bulent Yildiz[4]
[1]Hacettepe University, Internal Medicine, Ankara, Turkey; [2]Hacettepe University, Sports Medicine, Ankara, Turkey; [3]Hacettepe University, Radiology, Ankara, Turkey; [4]Hacettepe University, Internal Medicine, Division of Endocrinology, Ankara, Turkey

Background and Aim
Polycystic ovary syndrome (PCOS) is characterized by androgen excess and ovulatory dysfunction and appears to be associated with alterations in muscle mass and function. Combined oral contraceptives are commonly used for the long-term management of PCOS and their potential impact on muscle mass and strength remains unknown. This study aimed to assess whether oral contraceptive (OC) use along with general lifestyle advice would alter muscle mass and strength in women with PCOS.
Methods
Twenty women with PCOS (median age and BMI: 20.5 years and 26.1 kg/m^{2}respectively) and 20 age- and BMI-matched healthy controls were included. Following clinical, hormonal and biochemical assessments, body composition analyses were performed by magnetic resonance imaging (MRI) proton density fat fraction (PDFF%). Muscular strength parameters including lower limb extensor/-flexor torque, total work and average power (AvP) were obtained by isokinetic dynamometry, gold standard for assessment of muscle strength. Measurements were made for all participants at baseline and repeated after OC use in women with PCOS.
Results
Women with PCOS at baseline had higher levels oftotal testosterone, free androgen index (FAI), and homeostasis model assessment of insulin resistance (HOMA-IR) levels compared to healthy women ($P<0.001$, $P=0.001$, $P=0.004$ respectively). The PCOS group showed significantly higher average power (AvP) of knee extensors at 60°/sec compared to controls before initiation of OC therapy ($P=0.002$), with positive correlations noted between AvP and total testosterone and FAI levels in the whole study group ($r=0.45$, $P=0.004$, $r=0.318$, $P=0.045$ respectively). The median duration of OC therapy in the PCOS group was 121 days (IQR: 85-149). Testosterone levels and FAI showed significant decline following OC use ($P=0.02$, $P<0.001$ respectively). However, these alterations were not associated with any significant change in thigh muscle mass or lower limb strength.
Conclusion
The results of this study suggest that short-term OC use ameliorates androgen excess but does not alter muscle composition or strength in women with PCOS. Further research is needed in PCOS to understand potential effects of long-term management strategies on muscle mass and function.
Keywords: Polycystic ovary syndrome, oral contraceptive, adiposity, body composition, insulin resistance, muscle strength

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Investigation of circulating androgens' circadian variations: expanding the knowledge by monitoring phase II metabolites

Federico Ponzetto[1], Mirko Parasiliti Caprino[1], Lorenzo Campioni[1], Lorenzo Marinelli[1], Fabio Settanni[2], Antonello Nonnato[2], Giulio Mengozzi[1], Roberta Giordano[1] & Ezio Ghigo[1]
[1]University of Turin, Department of Medical Sciences, Turin; [2]City of Health and Science University Hospital, Clinical Biochemistry, Turin

Background
Many endogenous steroid hormones are reported to be subjected to distinct circadian rhythms, which are driven by central regulators, hormonal bioavailability and half-life. Recently, the measurement of androgens phase II metabolites has gained interest in the diagnosis and management of different endocrinological pathologies, such as polycystic ovarian syndrome (PCOS), female adrenal hyperandrogenism and hirsutism, prostate cancer, but their circadian patterns have not yet been characterized.
Methods
Serum samples were collected at six different time points across 24 hours (8:00, 10:00, 12:00; 16:00, 20:00, 8:00) from 19 healthy volunteer males. In-house UHPLC-MS/MS method was used for measuring in a single analysis circulating concentrations of 13 steroid hormones together with 13 androgens phase II metabolites (7 glucuronides and 6 sulphates). Cosinor analysis was performed to obtain diurnal models including mesor (rhythm adjusted median), zenith, and nadir concentrations, to measure rhythm's acrophase and amplitude as well as to test variations' statistical significance.
Results
The monitoring of target steroids' circadian rhythmicity highlighted that among endogenous hormones, all ACTH-related steroids showed significant fluctuations throughout the 24-hours period, with the highest concentrations measured in early morning samples then decreasing until afternoon collection. Concerning androgens, for testosterone a less pronounced but significant circadian rhythm was observed, while DHT did not show any variation during the day. A similar pattern was obtained by investigating phase II metabolites: the absence of diurnal fluctuations was noticed for both sulpho- and glucuro-conjugated androgens, with the latter owning a shifted zenith at 10 a.m.
Conclusions
The outcomes of this study highlighted that, in contrast with the majority of circulating steroid hormones, androgens phase II metabolites have satisfactory performance in terms of intra-day stability of circulating levels. For this reason, their introduction in clinical practice as biomarkers of pathological conditions to be monitored with longitudinal monitoring in the context of individualized precision medicine could be envisaged.

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Thyroid

P155

Low TPO-antibody titers appear to promote aggressive thyroid cancers tumorigenesis: analysis of a large multinational dataset

Rodis Paparodis[1,2,3], Evaggelos Karvounis[1,4], Aikaterini Kapezanou[4], Dimitra Bantouna[1], Sarantis Livadas[1,5], George Simeakis[1,6], Dimitrios Askitis[1,7], Ioannis Androulakis[1,8], Nicholas Angelopoulos[1,7], Dimitra Zianni[1,5], Ilias Perogamvros[9], Anastasios Boniakos[1,5], Andreas Rizoulis[10], Shanawaz Imam[11] & Juan Carlos Jaume[3]
[1]Hellenic Endocrine Network, Athens, Greece; [2]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Patras, Greece; [3]Loyola University Medical Center / Edward Hines Jr VA Hospital, Maywood, IL, United States; [4]Euroclinic Hospital, Center for Excellence in Edocrine Surgery, Athens, Greece; [5]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Athens, Greece; [6]401 General Military Hospital of Athens, Endocrine Deptartment Thyroid Cancer Outpatient's Clinic, Athens, Greece; [7]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Kavala, Greece; [8]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Chania, Greece; [9]University of Manchester, Manchester, United Kingdom; [10]Endocrinology, Diabetes and Metabolism Clinics, Private Practice, Larisa, Greece; [11]University of Toledo College of Medicine and Life Sciences, Center for Diabetes and Endocrine Research, Toledo, OH, United States

Introduction
In the thyroid gland, humoral immunity manifests with thyroid peroxidase (TPO) antibodies. In our studies, when TPO concentrations increased, thyroid cancers of follicular origin (TCFO) tended to develop less frequently.[1] Other studies, though, reported an opposite trend in less aggressive cancers. The present work was designed to characterize the differential role of TPO antibodies in aggressive forms of TCFO (AGG) as compared to non-aggressive (NAG) ones.
Methods
We performed a retrospective review of data from subjects who had thyroidectomy at 4 centers, in 2 countries [USA: 1 (2007-2013) and Greece: 3 (2021-2023)] on gender, age, surgical pathology and preoperative TPO antibody concentrations. Tumors producing distant metastases, spreading to multiple lymph nodes (LNs) ($\geq$ 10 or $\geq$ 6 with a positive malignant to benign ratio $\geq$75%), those requiring $\geq$ 2 courses of I-131 therapy or large structural local

recurrences were deemed AGG, while those not exhibiting these features were deemed NAG, and a control group was formed from subjects with benign histology (BEN). TPO were divided in very low (VL) (< 1 IU/ml), low (L) (1 - 10 IU/ml), intermediate (IN) (10 - 30 IU/ml), high (HI) (30-300 IU/ml) and very high (VH) (≥300 IU/ml). AGG thyroid cancer ratios were compared between these subgroups.

Results

TPO titers were available for 1,943/11,212 subjects; n = 948 BEN (48.8%). Overall mean age 46.7 ± 14.9 years, lower in TCFO (45.7 ± 14.6) compared to BEN (47.7 ± 15.1), and in AGG (40.2 ± 15.3) compared to non-AGG (46.2 ± 14.5), $P < 0.01$ for all comparisons. Overall n = 1477 (76.0%) were females; 736/1477 (49.8%) with TCFO as compared to 259/466 (55.6%) in males, $P = 0.02$. Out of 995 TCFO, n = 73 (7.3%) were AGG. These were found more frequently in the VL ($P = 0.018$) and less frequently in the H groups ($P = 0.016$).

Conclusion

Patients with very low TPO titers harbor aggressive (AGG) thyroid cancers of follicular origin (TCFO) more commonly, while those with high titers harbor these more rarely. These findings imply that immune response in the form of TPO antibodies modulates the risk to develop aggressive thyroid cancers. A strong autoimmune response appears protective with regard to the development of aggressive tumors even though abnormal.

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P156

Thyroid hormone transporter Mct8/Oatp1c1 deficient mice display impaired CNS capillary network formation

Boyka Markova[1], Androniki Alevyzaki[1], Philippa Spangenberg[2], Daniel Robert Engel[2], Steffen Mayerl[1] & Heike Heuer[1]
[1]University Duisburg-Essen, Endocrinology, Diabetes & Metabolism, Essen, Germany; [2]University Duisburg-Essen, Institute f. Experimental Immunology, Essen, Germany

The thyroid hormone (TH) transporters Mct8 (encoded by Slc16a2) and Oatp1c1 (encoded by Slco1c1) are critically involved in mediating TH passage across mouse brain barrier cells. Mct8/Oatp1c1 deficient mice (= DKO mice) exhibit a strongly reduced brain TH content and consequently, an impaired neuronal development and hypomyelination all of which are also seen in patients with MCT8 deficiency (Allan-Herndon-Dudley Syndrome, AHDS). Our recent studies of mouse mutants lacking both TH transporters specifically in blood-brain-barrier (BBB) endothelial cells (= Endo del mice) underscore the physiological relevance of Mct8/Oatp1c1 in facilitating TH access to the CNS. yet, these Endo del mice showed a much milder phenotype compared to DKO animals pointing to additional pathogenic CNS events in global Mct8/Oatp1c1 deficiency that still needs to be unraveled. We considered a hitherto unknown function of both TH transporters in brain angiogenesis and therefore examined brain capillary network formation in wildtype, single and double TH transporter knockout mice. For this, we performed immunoflurescence stainings of brain vibratome sections using the endothelial vascular marker CD31. Quantification of vessel parameters was conducted using the open-source software 'VesselExpress'. While vessel parameters at postnatal day P6 were similar in all experimental groups, quantification of cortical vessel length and branching at P12 revealed an almost 50% reduction in DKO mice. Single TH transporter mutant mice were not affected. Brain vessel rarefaction was also observed at P21 and P120 in DKO mice. Moreover, comparing the total vessel lengths of capillaries with different diameter revealed a significantly reduced total length only of DKO capillaries with a diameter less than 10 µm. Of note, while Oatp1c1 is ubiquitously found in all brain endothelial cells under physiological conditions, Mct8 is preferentially expressed by CNS endothelial cells of small capillaries suggesting that this subgroup of endothelial cells is particularly impacted by combined Mct8/Oatp1c1 deficiency. We further quantified the transcript levels of different capillary proteins in dissected brain areas of four months old animals and confirmed reduced CD31, Vegfa as well as glucose transporter Glut1 mRNA expression in DKO mice. Altogether, our observation of a reduced microcapillay network in DKO mice that potentially compromises local oxygen and/or nutrient supply may thus add novel insights into the pathogenic mechanisms underlying human MCT8 deficiency. (Study is financially supported by DFG and embedded in CRC/TR296-P01, P09, P19)

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P157

Plasmablastic lymphoma presenting as a rapidly increasing thyroid mass: a case report

Charikleia Paschalidi[1], Athanasios Fountas[1], Athina Markou[1], Charikleia Vlachou[2], Bazani Efthymia[2], Georgios Gorgolidis[2], Marina Sassi[3], Ioannis Nitsios[3], Ioanna Liokati[4], George Papastergiou[4] & Labrini Papanastasiou[1]
[1]General Hospital of Athens 'G Gennimatas', Department of Endocrinology, Athens, Greece; [2]General Hospital of Athens 'G Gennimatas', Department of Hematology, Athens, Greece; [3]General Hospital of Athens 'G Gennimatas', Department of Pathology, Athens, Greece; [4]General Hospital of Athens 'G Gennimatas', Department of Otolaryngology, Athens, Greece

Introduction

Primary thyroid lymphoma is a rare entity accounting for <5% of thyroid malignancies and <2% of extra-nodal lymphomas with diffuse large B-cell lymphoma (DLBCL) being the most common subtype. Plasmablastic lymphoma (PBL) is an uncommon and aggressive subtype of DLBCL mainly detected in patients with immunosuppression, especially related to HIV infection. Typically, PBL occurs in extra-nodal sites, usually the oral cavity and the gastrointestinal tract while primary thyroid PBL is extremely rare.

Objective

To report an extremely rare case of extra-nodal PBL presented as a rapidly increasing thyroid mass.

Case presentation

A 73-year-old male with a history of multinodular goiter and autoimmune thyroiditis, presented to the emergency department with a rapidly growing, painless, cervical mass and dyspnea. Computed tomography (CT) scan revealed an enlarged heterogenous thyroid gland (12 cm right lobe, 10 cm left lobe), causing trachea compression and displacement to the left side. Fine needle aspiration (FNA) cytology suggested an undifferentiated thyroid cancer and a core biopsy was performed to confirm the diagnosis. However, histological examination revealed the presence of a PBL with expression of Vimentin, LCA, CD79a, slgk, CMyC (in 35% of the tumor cells), while staining for TTF1 and TG was negative; cell proliferation index Ki-67 of 50% was found. Bone marrow biopsy showed no lymphoma cells infiltration, but whole body CT scan showed stage IV disease (multiple subcutaneous nodules, as well as abdominal and inguinal lymphadenopathy). Thyroid function was normal (TSH 1.71 µIU/ml, fT4 15.07 pmol/L, NR 9-19), while anti-TPO and anti-Tg were positive (>2000 IU/ml, NR <5.6 and 143.32 IU/ml, NR <4, respectively). Virology testing for HIV was negative. Treatment with systemic chemotherapy DA-EPOCH (dose adjustment etoposide, prednisolone, vincristine, cyclophosphamide and doxorubicin) was initiated with ≥30% decrease of the longest diameter of the thyroid masses after the completion of 3 cycles of chemotherapy. Compression of the trachea was significantly decreased and the patient does not experience any dyspnea.

Conclusion

To our knowledge, this is the third documented case of primary thyroid PBL. Due to its rarity, primary thyroid lymphoma can be challenging to diagnose and it should always be suspected in patients with a rapidly enlarging cervical mass. FNA is often insufficient for diagnosis and a core biopsy with histological confirmation is necessary to differentiate thyroid lymphoma from anaplastic thyroid cancer. Early and appropriate treatment can lead to significant patient's response and outcome improvement.

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P158

Subacute thyroiditis in the SARS-Cov-2 era: a multicenter prospective study

Roberta Sueri[1], Sara De Vincentis[2], Simona Loiacono[3], Eleonora Zanni[3], Maria Laura Monzani[2], Daniele Santi[2], Ilaria Muller[4], Francesco Di Marco[5], Erica Crivicich[5], Uberto Pagotto[6], Carolina Cecchetti[6], Lorenzo Tucci[6], Manuela Simoni[2] & Giulia Brigante[2]
[1]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [2]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy; [3]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [4]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; Department of Endocrinology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [5]School of Specialisation in

Endocrinology, University of Milan, Milan, Italy; [6]Alma Mater Studiorum - Bologna University, Medical and Surgical Sciences Department, Bologna, Italy; IRCCS Sant'Orsola-Malpighi Polyclinic, Endocrinology and Diabetes Care and Prevention Unit, Bologna, Italy

Introduction
Several cases of subacute thyroiditis (SAT) have been described in patients with SARS-CoV-2. However, no prospective data about follow-up in SARS-CoV-2-related SAT are known.
Aim
The characterization of clinical peculiarities and response to medical treatment of SAT cases, correlating to virus exposure, ascertained with antibody (Ab) dosage.
Methods
A prospective, 3-years, multicentre study was conducted, enrolling patients with SAT diagnosis based on anamnesis, physical examination, blood tests (TSH, freeT4, freeT3, thyroglobulin (Tg), TgAb, Ab to thyroperoxidase (TPOAb), TSH receptor-Ab, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), complete blood count and thyroid ultrasound (US). At baseline, a serum sample was taken to assess the presence of IgG against the SARS-CoV-2 spike protein or nucleocapside, distinguishing natural infection and vaccination. Patients were evaluated after 1, 3, 6, 12 months with anamnesis, physical examination, blood tests and US. The study was supported by the 'ESE COVID-19 Research Grant', from the European Society of Endocrinology.
Results
A total of 66 subjects were enrolled. Eight were excluded because of symptoms onset earlier than 60 days before diagnosis. At baseline, 54 subjects presented with pain, 36 (67%) for at least 15 days. Only 4 did not report previous/concomitant neck pain but they all presented with non-homogeneous thyroid echostructure, TgAb and TPOAb negativity, thyrotoxicosis, elevated ESR and/or CRP. In 52 subjects, serum SARS-COV-2 IgG measurement was performed, documenting that the 13.5% had infection before SAT diagnosis (Covid+). At baseline, 17 patients were taking nonsteroidal anti-inflammatory drugs (NSAIDs), 7 β-blockers, 14 steroids, 2 levothyroxine, and 3 methimazole. However, this bias equally affected the Covid+ and Covid- groups. Between them, at diagnosis, there were no statistically significant differences except for respiratory symptoms and fever, more represented in Covid+ ($P=0.039$ and 0.021), despite significantly lower ESR values ($P=0.021$). 41 subjects completed follow-up. Covid+ and Covid- did not differ for therapeutic approach to SAT (NSAIDs, β-blockers, steroid), all having an improvement in pain, inflammation parameters, US features. The 30% of subjects experienced transient hypothyroidism without difference in the percentage that restored thyroid function (100% in Covid+ and 81% in Covid-) or developed permanent hypothyroidism (0% in Covid+ and 8.3% in Covid-) at 12 months.
Conclusions
This is the first prospective study investigating any difference at diagnosis and at follow-up between classical and SARS-CoV-2–related SAT. Our data confirm that the diagnosis of SAT is often delayed and demonstrate that SARS-CoV-2 infection does not modify SAT onset, progression and outcome.

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P159

Transcriptomic characterization of single cells derived from immortalized human thyroid follicular epithelial cell lines

Leonie Wittner[1], Marie Schnapp[1], Tobias Busche[1,2] & Joachim Feldkamp[3]
[1]Bielefeld University, Medical School and University Medical Center East Westphalia-Lippe, Bielefeld, Germany; [2]Bielefeld University, Center for Biotechnology (CeBiTec), Bielefeld, Germany; [3]Bielefeld University, Medical School and University Medical Center East Westphalia-Lippe, Klinikum Bielefeld, Academic Department of General Internal Medicine, Endocrinology and Diabetes, Infectiology, Bielefeld, Germany

Immortalized human thyroid follicular epithelial cell lines represent a valuable tool for the investigation of thyroid physiology *in vitro*. While there is an extensive selection of human thyroid carcinoma cell lines, the number of healthy follicular epithelial cell lines is limited. The vast majority of studies on thyroid physiology is based on the human immortalized cell line Nthy-ori 3-1, leading to comprehensive characterization of this cell line. However, in 2021 Hopperstad *et al.* generated four novel immortalized cell line variants derived from normal human thyroid tissue (CI-huThyrEC clone 1-4). In order to verify, if results obtained from the different cell lines are comparable, we decided to characterize and to compare the transcriptomic profile of each cell line. For this, we chose a novel approach that focusses on RNA sequencing of particularly low cell numbers. We prepared RNA sequencing libraries from one cell, four cells and ten cells derived from the different cell lines, which then underwent Illumina Next Sequencing. Overall, we obtained high quality sequencing data with minor variability depending on the method of cell separation. Further, gene detection and mapping statistics are comparable. On average 10k – 12k genes were detected with 80 % – 90 % uniquely mapped reads independent of the input number of cells. Downstream principal component analysis (PCA) revealed that sequencing data generated from samples containing ten Nthy ori 3-1 cells cluster closer than data from lower cell numbers, pointing to a high transcriptional similarity and reproducibility at this cell number. The CI-huThyrEC clones 1-4 show a greater variability in the PCA plot indicating that the four cell line variants differ in their transcriptional profile. Comparing the transcriptomic profile of the cell lines it is noticeable that CI-huThyrEC show a significant upregulation of *NKX2-1* gene expression that encodes the thyroid transcription factor-1 (TTF-1). Having established RNA sequencing of ultra-low cell numbers enables us to transfer this method to further questions. Next, we aim to transcriptionally characterize single neoplastic cells derived from fine needle aspiration biopsies of high-risk thyroid nodules. This might lead to the identification of new potential oncogenes or tumor suppressor genes, which might serve as potential biomarkers in the context of thyroid cancer and tumor stage assessment.

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P160

New plasma biomarkers: XIAP and survivin in patients with medullary thyroid cancer (MTC)

Piotr Glinicki[1,2], Alicja Szatko[1,2], Agnieszka Żyłka[3], Joanna Długosińska[3], Magdalena Ostrowska[1], Małgorzata Gietka-Czernel[1], Maciej Ratajczak[1], Wojciech Zgliczyński[1] & Marek Dedecjus[3]
[1]Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland; [2]EndoLab Laboratory, Centre of Postgraduate Medical Education, Warsaw, Poland; [3]Department of Oncological Endocrinology and Nuclear Medicine, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Introduction
Medullary thyroid carcinoma (MTC) constitutes 3.5-5% of all thyroid cancers. Routine biochemical diagnostics include determination of calcitonin (CT), procalcitonin (PCT) and carcinoembryonic antigen (CEA). XIAP (X-linked inhibitor of apoptosis protein) and survivin belong to the family of proteins – inhibitors of apoptosis (IAP). Using tissue microarrays, the expression levels of XIAP and survivin were tested in patients with medullary thyroid cancer. The study showed different expression of these biomarkers in patients with MTC at different stages of the disease. The clinical evaluation of the determination of these two proteins in blood in patients with medullary thyroid cancer has not been evaluated.
Materials and Methods
Thirty-four patients with MTC were included in the study. Patients were divided into two groups. Patients with confirmed active MTC ($n=15$) and patients with confirmed MTC in the stable phase, without recurrence or metastasis ($n=19$). The control group consisted of 40 healthy subjects. Serum CT and PCT levels were determined by the CLIA immunoassay. The concentration of CEA was determined by IRMA immunoassays, and the concentration of XIAP and survivin were determined in plasma by ELISA immunoassay.
Results
Levels of the tested biomarkers were assessed in patients with MTC in the active form of the disease, in patients with stable MTC and in the control group. Statistically significant differences were found between the study groups. The study groups were compared with each other: **XIAP**: MTC (active form) vs. control group: $P=0.797$; **Survivin**: MTC (active form) vs. control group: $P=0.857$, **XIAP**: MTC (stable form) vs. control group: $P=0.793$, and **Survivin**: MTC (stable form) vs. control group: $P=0.844$. ROC curves were used to compare the biomarkers studied in the group of patients with MTC (active form) vs. the group of healthy subjects. AUC (95%CI): **XIAP** 0.477 (0.296;0.657; $P=0.866$), **Survivin** 0.483 (0.302;0.664; $P=0.951$); CT 0.940 (0.857;1.203; $P<0.001$); PCT 1.000 ($P<0.001$); CEA 0.855 (0.704;1.004; $P<0.001$).
Conclusion
Determination of concentrations of new biomarkers: XIAP and survivin in the diagnostics of MTC can complement biochemical diagnosis in this group of patients.

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P161

Differentiated thyroid cancer in pregnancy. A retrospective analysis of newly diagnosed patients

Maciej Bulwa[1], Konrad Samborski[1], Magdalena Kolton[1], Malgorzata Haras-Gil[1], Barbara Jarzab[1], Daria Handkiewicz-Junak[1] & Jolanta Krajewska[1]
[1]M. Sklodowska-Curie National Research Institute of Oncology Gliwice Branch, Nuclear Medicine and Endocrine Oncology Department, Gliwice, Poland

Introduction
The question of whether pregnancy has any impact on the prognosis of differentiated thyroid cancer diagnosed in pregnant women was addressed mainly in retrospective analyses, which showed no significant differences in overall and progression-free survival between women diagnosed during pregnancy in comparison to women whose thyroid cancer diagnosis was unrelated to pregnancy. Thus, following the recent guidelines, watchful waiting is the preferred option, and surgical intervention may be postponed to the postpartum period. Surgery may be considered in the second trimester if high-risk features are present or a significant tumor is observed.
Aim
The aim of this study is to analyze the dynamics of malignant thyroid nodules followed in pregnant women.
Methods
A retrospective analysis of a group of 75 women at a mean age of 30.9 ± 4.8 years with suspected thyroid nodules detected during pregnancy. All patients underwent fine-needle aspiration biopsy (FNAB). The FNAB result was classified according to the Bethesda System for Reporting Thyroid Pathology. The diagnosis was confirmed by two independent pathologists. Only patients with the Bethesda V category (suspicious for malignancy) or Bethesda VI category (malignancy) were considered. Patients were followed by neck sonography (US) every 2-3 months until surgery. The median follow-up from the diagnosis to surgery or the last follow-up was 10.0 months (range 1.0-39.0).
Results
Papillary thyroid cancer (Bethesda VI) was diagnosed in 53 patients, whereas in the remaining 22 patients, the FNAB result was suspicious for papillary thyroid carcinoma (Bethesda V). The mean nodule diameter at the first US evaluation was 12 ± 7.7 mm. Thirty-nine nodules were ≤ 10 mm in diameter. In 29 nodules, the tumor diameter ranged between 11 and 20mm. Only 7 nodules (9,3%) were stable during the whole follow-up in 65 (86.6%) patients. The nodule diameter increased in 9 (12%), while in one patient, the nodule dynamics could not be evaluated. Lymph node metastases were diagnosed at initial evaluation in 1 patient. Although in 55 patients (73.3%) thyroid nodules were diagnosed before 24 weeks of gestation, the majority of them chose watchful waiting. Only 2 women were operated on during pregnancy. Sixty-five (86.7%) underwent surgery after delivery. Histopathological data and outcomes will be presented during the congress.
Conclusions
Watchful waiting is a safe option for patients diagnosed with papillary thyroid carcinoma or suspicion of papillary thyroid carcinoma. However, careful monitoring should be considered to choose the most optimal time for surgery.

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P162

Falsely elevated thyroid function tests due to laboratory interference

Jan Drugda[1], Filip Gabalec[1] & Radomír Hyšpler[2]
[1]University Hospital Hradec Králové, 4th Department of Internal Medicine, Hradec Králové, Czech Republic; [2]University Hospital Hradec Králové, Department of Clinical Biochemistry and Diagnostics, Hradec Králové, Czech Republic

Introduction
Thyroid function tests (thyroid hormones and thyreotropin) are frequently used by physicians all over the world. The interpretation is usually quite simple and straight-forward, however sometimes there is a strange discrepancy between the laboratory findings and clinical presentation. There are several potential explanations to this discrepancy and interference in laboratory assay may be one of them.
Observation
We present a case of a 73-year-old woman without any significant comorbidities except of atrial fibrilation and arterial hypertension. She was presented to endocrinologist by her general practitioner because of elevated estradiol, free thyroxine and triiodothyronine coupled with elevated thyreotropin but she was lacking any signs or symptoms of thyreotoxicosis. Central hyperthyreoidism was mainly considered so we started thyrostatic treatment with thiamazol. Nevertheless the MRI and PET/CT was negative, other pituitary hormones were normal and thiamazol was totally ineffective. At this point we started to think about possible laboratory interference. We suspected presence of antibodies that block the antibody of the assay we used. That was confirmed by precipitation of the sample with polyethylene glycol after which the estradiol, tyroxine, triiodothyronine and thyreotropin normalized. According to the literature IgM rheumatoid factor is the most common cause of such interference so we evaluated it and it was indeed positive. We then immediately withdrawn thiamazol and after short follow up the patient was handed over back to her general practitioner.
Conclusion
Laboratory interference in thyroid function tests is fortunately very rare. However if there is a discrepancy between the laboratory findings and clinical presentation it is good to have it in mind. It is generally quite easy to exclude and it can help you to avoid misdiagnosis and pottentialy harmful unnecessary treatment.

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The effect of monoclonal antibodies alemtuzumab and ocrelizumab on the thyroid function of patients with multiple sclerosis

Paraskevi Kazakou[1], Aigli G Vakrakou[2], Dimitrios Tzanetakos[2,3], John S Tzartos[3], Maria Anagnostouli[2], Panos Stathopoulos[2], Alexandros Dermentzoglou[4], Georgia N Kassi[5], Constantinos Kilidireas[2] & Evangelia Zapanti[5]
[1]Endocrine Unit and Diabetes Centre, Department of Clinical Therapeutics, Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [2]Multiple Sclerosis & Demyelinating Diseases Unit, 1st Department of Neurology, Eginition Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [3]Second Department of Neurology, School of Medicine, National and Kapodistrian University of Athens, 'Attikon' University Hospital, Athens, Greece; [4]Department of Endocrinology, 'Korgialenio-Benakio', Red Cross General Hospital, Athens, Greece.; [5]Department of Endocrinology, Alexandra Hospital, Athens, Greece

Aim
Autoimmune thyroid disease (AITD) is the most common adverse effect in alemtuzumab (ALZ) treated relapsing–remitting (RR) multiple sclerosis (MS) patients. The objective of this prospective study was to analyze the occurrence, timing of onset, clinical course, and laboratory characteristics of AITD post-ALZ and subsequently the clinical outcome of AITD post-ALZ in patients who received ocrelizumab.
Patients and methods
We evaluated 36 RRMS patients treated with ALZ; of which 3 patients subsequently received ocrelizumab. Clinical and laboratory data were collected before ALZ initiation and thereafter quarterly on follow-up with a median of 55.5 months.
Results
Nineteen out of 32 patients (59.4%) with no prior history of thyroid dysfunction developed AITD with a mean onset of 19.7 ± 11 (SD) months after the first ALZ cycle. The incidence of AITD and during the first year of follow-up was 18.8%, and 50% after the second ALZ course. Ten patients developed Graves' disease (GD), one developed hypothyroidism with positive stimulating thyrotropin receptor antibodies (TRAb) and eight developed Hashimoto thyroiditis (HT), of which one developed hypothyroidism. The mean time to TRAb and anti-thyroglobulin (anti-Tg) and/or anti-thyroperoxidase (anti-TPO) antibody positivity onset from the first ALZ infusion was 24.8 ± 8.1 months and 18.1 ± 12.7 months, respectively. Seven of ten (70%) GD patients showed a fluctuating course of hyperthyroidism-hypothyroirdism. All GD patients commenced antithyroid drugs (ATDs); six continued on 'block and replace' treatment; one required radioactive iodine and one total thyroidectomy. Five patients developed mild Graves' ophthalmopathy. Remission was reported in four out of ten GD patients (40%); one spontaneously and three after ocrelizumab treatment with a mean time of 31.5 ± 11.7 months. No significant relationship of AITD with age at the time of ALZ treatment, sex, smoking status, previous DMTs, positive baseline anti-TPO/anti-Tg antibodies and family history of AITD was found. Only in patients who were treated with fingolimod as last treatment before ALZ a trend for an increased incidence of TRAb positivity was reported ($P = 0.07$). Two successful pregnancies were recorded: one with HT and hypothyroidism and the other with GD.
Conclusions
Our analysis showed earlier onset of ALZ-induced AITD in comparison to most other ALZ cohorts. We observed a higher rate of fluctuating GD, with earlier onset and lower remission rate than previously reported. The majority of patients required prolonged 'block and replace' therapy in the minimum dose of each

therapeutic agent or more definitive interventions. Treatment with ocrelizumab contributed in remission of GD.

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High local and systemic expression of pentraxin-3 in anaplastic thyroid cancer

Andreea Bojoga[1,2,3], Pepijn van Houten[2], Martin Jaeger[2], Katrin Rabold[2], Dumitru Ioachim[4], Birgitte Walgreen[5], Liesbeth van Emst[2], Corin Badiu[1,6] & Romana Teodora Netea-Maier[2]

[1]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [2]Radboud University Medical Center, Department of Internal Medicine, Division of Endocrinology, Nijmegen, Netherlands; [3]National Institute of Endocrinology, Bucharest, Romania; [4]National Institute of Endocrinology, Department of Pathology, Bucharest, Romania; [5]Radboud University Medical Center, Laboratorium Rheumatology, Nijmegen, Netherlands; [6]National Institute of Endocrinology, Department of Endocrinology IV, Bucharest, Romania

Introduction

Long pentraxin 3 (PTX3), a protein cells produce in response to several inflammatory stimuli, is essential in innate immunity, controlling inflammation, tissue remodeling, and cancer dynamics. PTX3 promotes the migration and invasion of cells in different tumor models. This study aims to (I) immunohistochemically assess the presence and distribution of PTX3 in tissue samples from non-medullary thyroid cancer (NMTC) and (II) (TC) to determine the differences of circulating PTX3 in patients with NMTC vs patients with benign goiters.

Methods

We prospectively included 55 patients (41 preoperatively, 14 with recurrent active disease) with various subtypes of NMTC: 42 with papillary, 3 with follicular, 4 with oncocytic, 4 with anaplastic (ATC), 2 with poorly differentiated (PDTC). The control group consisted of 32 patients with multinodular goiter. Patients with chronic systemic inflammatory diseases (such as rheumatologic diseases), other active neoplasms, active infections, or pregnancy were excluded. PTX3 plasma levels were analyzed using ELISA. Local PTX3 and CD68 expression were assessed by co-staining on paraffin-embedded tissue in a patient with ATC with a positive somatic v600E BRAF mutation and a patient with goiter.

Results

No significant differences in PTX3 plasma levels between the control group and non-medullary differentiated TC were found. PTX3 plasma level in patients with ATC was significantly higher compared to control, and compared to the rest of the TC subtypes, including the aggressive histological subtypes. The plasma level of PTX3 did not correlate with tumor load (defined as the sum of all tumoral foci). There were no significant differences between patients with recurrence and those included preoperatively. The intensity and quantitative expression of PTX3 were higher in ATC, both interstitial and cellular expression, compared to normal thyroid tissue or goiter where immunostaining for PTX3 was virtually absent, with sparse and faint staining. The IHC expression of CD68 was also diffusely increased in ATC compared to goiter, suggesting infiltration by tumor-associated macrophages (TAMs). Less than 10% of the cells were double-positive for PTX3 and CD68 suggesting another source of PTX3 than TAMs.

Discussions and Conclusions

Our findings highlight significantly elevated PTX3 levels in ATC, both in plasma and in tumor tissue, compared to other TC types and control subjects. The low number of double-positive TAMs suggests that PTX3 might likely be produced by tumoral cells, stromal cells, or other immune cells. Further investigation is needed to consolidate the significance of PTX3 in ATC and its effect on the tumor microenvironment.

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Clinical and histopathological factors associated with the prognosis of medullary thyroid cancer in a tertiary center

Mafalda Martins Ferreira[1], Tânia Carvalho[1], Joana Madeira[2], Sofia Lopes[1], Miguel Melo[1], Cristina Ribeiro[1], Joana Saraiva[1], Patrícia Oliveira[1] & Isabel Paiva[1]

[1]Centro Hospitalar e Universitário de Coimbra, Portugal, Endocrinology, Diabetes and Metabolism, Coimbra, Portugal; [2]Centro Hospitalar e Universitário de Coimbra, Portugal, Pathologic Anatomy, Coimbra, Portugal

Introduction

Medullary thyroid cancer (MTC) is a rare tumour. Mostly sporadic, 25% are associated with multiple endocrine neoplasia (MEN2A/B) or isolated familial MTC. Surgery is the only curative option: its response is defined as complete (no evidence of biochemical or structural disease), incomplete (only structural response) and persistence of structural disease. We aimed to analyse the clinical and pathological factors associated with the prognosis of MTC.

Materials and Methods

Retrospective analysis of clinical and pathology records from MTC cases in a tertiary centre from 2001-2023. Surgical response was assessed through cervical ultrasound and calcitonin 6 months postoperatively. Histopathological reports included tumour size, uni-/multifocality, margin distance, C-cell hyperplasia, coagulative necrosis, and linfovascular invasion. The remaining parenchyma was assessed for nodular hyperplasia or chronic lymphocytic infiltration.

Results

From 42 patients, 64% ($n=27$) were female. Mean age at diagnosis was 46.2 ± 2.8 years. Mean follow-up duration was 12 ± 1.1 years. 35.7% presented symptoms at diagnosis (mostly cervical swelling); two had diarrhoea (both with distant metastases). 19% ($n=8$) had a RET germline mutation, 5 of whom performed a prophylactic thyroidectomy. Surgery resulted in excellent response in 71.4% ($n=30$), biochemical incomplete response in 16.7% ($n=7$) and persistent structural disease in 11.9% ($n=5$). Among patients with excellent response, 16.6% ($n=5$) experienced recurrence, 3 were only biochemical. Male patients were more likely to have persistence of structural disease after surgery (35.7%), $P=0.003$. Multifocal MTC showed less complete response rates (46.2% vs 82.1% in unifocal MTC), $P=0.029$. Only 30% of patients with linfovascular invasion in the histopathology report exhibited a complete response to surgery ($P=0.003$). All patients with nodular hyperplasia showed complete response post-surgery, compared to those with chronic lymphocytic infiltration (75%) or thyroid parenchyma without these alterations (55.6%), $P=0.041$. Coagulative necrosis was present in 2 patients and was associated with persistence of structural disease ($P=0.012$). Tumours that touched the thyroid margin showed a poorer response to surgery ($P=0.021$). Higher recurrence was associated with RET germline mutation ($P=0.04$) and with T staging at diagnosis ($P=0.009$). Thirty-nine patients are alive: 61.5% ($n=24$) cured; 38.5% ($n=15$) with disease persistence. N staging at diagnosis associated strongly with disease persistence ($P<0.001$). 3 patients died, 2 due to MTC.

Conclusion

An incomplete response to surgery, whether biochemical or structural, was associated with male gender, multifocal MCT, linfovascular invasion and coagulative necrosis. Adjacent nodular hyperplasia associated with better response to surgery. Higher recurrence was associated with RET germline mutation and with T staging at diagnosis.

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P166

Graves' disease relapse after 30-year remission in a female patient due to SARS-CoV-2 infection- a case report

Dimitrios Askitis[1]

[1]Private Practice for Endocrinology, Alexandroupolis, Greece

Introduction

COVID-19 has been established as a multisystemic disease with the potential of affecting all the organs of the human organism including the thyroid gland which features ACE2 receptors for the cellular entry of SARS-CoV-2. Graves' disease comprises the most common cause of thyrotoxicosis, manifests in genetically predisposed individuals with an autoimmune background and may be triggered by a variety of environmental factors, including viral infections. A few cases of new-onset or relapsed Graves' disease related to SARS-CoV-2 infection have been reported globally. Herein, we present the case of an otherwise healthy patient who developed hyperthyroidism due to Graves' disease reactivation after 3 decades of remission following exposure to SARS-CoV-2.

Case report

A 65-year old female patient with a history of active Graves' disease over a period of 2 years and remission over the past 30 years presented for endocrinological evaluation due to newly detected hyperthyroidism. The patient had been tested positive for COVID-19 10 days ago with persistent fever over a period of 2 days and concomitant heart palpitations. The neck ultrasound revealed a pattern typical of autoimmune thyroiditis with diffuse heteroechogenicity and inhomogeneity accompanied by elevated blood flow bilaterally. The adjunctive laboratory evaluation showed a hyperthyroid state with elevated TRAb-titers and negative anti-Tg and anti-TPO autoantibodies. The patient was started on thyrostatic medication with methimazole 15 mg daily combined with propranolol 10 mg thrice daily. Biochemical and clinical euthyroidism was rapidly restored in 6 weeks and the methimazole dosis was progressively reduced till complete

cessation 8 months after diagnosis. Neck ultrasound at that point showed a remission of the autoimmune process with normalization of the blood flow, whereas the laboratory assessment showed negative TRAb. The patient remained euthyroid without related medication since.

Conclusion

The above case presentation comprises the first official report of Graves' disease relapse following COVID-19 in northern Greece, as well as the case of autoimmune hyperthyroidism with the second longest remission duration before relapse due to SARS-CoV-2 infection in the literature. Clinicians should be aware of thyroid-related complications due to SARS-Cov-2, especially in individuals with a known history of autoimmune thyroid diseases and conduct the appropriate diagnostic and therapeutic procedures in cases of suspected infection-triggered thyroid dysregulation.

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P167

Characterizing TSH-receptor antibody (TRAb) seropositive and TRAb seronegative patients with Graves hyperthyroidism - a cross-sectional study

Simon Mifsud[1], Zachary Gauci[1] & Sandro Vella[1]
[1]Mater Dei Hospital, L-Imsida, Malta

Background

The concept of autoantibody-negative Graves' disease (GD) is a subject of debate. Studies have revealed that autoantibody-negative GD does exist, albeit rare.1

Method

Over a 3-year period, a total of 108 hyperthyroid patients who exhibited diffuse or normal thyroid uptake on thyroid scintigraphy, were assessed in a cross-sectional study. The thyroid function tests, TSH-receptor antibody (TRAb) levels, anti-thyroid peroxidase (anti-TPO) antibody levels, and thyroid ultrasound scans of these subjects at initial diagnosis were reviewed. TRAb-seronegative GD was defined as the presence of hyperthyroidism with a negative TRAb and diffuse or normal thyroid uptake on thyroid scintigraphy. Continuous variables were compared using the Mann-Whitney U test, while categorical variables were compared using the Chi-Square test. Statistical significance was defined by a two-tailed p-value <0.05.

Results

The mean (SD) age of the study group was 58.59 (16.782) years with a female dominance of 66.67% ($n=72$). 83.3% ($n=90$) had overt hyperthyroidism whilst the remaining had subclinical hyperthyroidism. In the cohort with overt hyperthyroidism, 52.2% ($n=47$) had a positive TRAb status. In the cohort of patients with overt hyperthyroidism, thyroid-stimulating hormone (TSH) levels were significantly lower in TRAb-seropositive GD when compared to TRAb-seronegative GD (median TSH:0.008mIU/mL [IQR:0.008-0.011] vs median TSH:0.012mIU/mL [IQR:0.008-0.0285], respectively; $P=0.0013$). Furthermore, in the overt hyperthyroid cohort, free thyroxine (fT4) and free triiodothyronine (fT3) levels were significantly higher in TRAb-seropositive GD when compared to TRAb-seronegative GD (median fT4:34.1 pmol/L [IQR:25.1-46.85] vs median fT4:27.1 pmol/L [IQR:22.37-34.5], respectively; $P=0.026$ and median fT3:11.1 pmol/L [IQR:8.5-17.2] vs median fT3:8.1 pmol/L [IQR:6.6-10.8], respectively; $P=0.001$). Only 23.8% ($n=5$) of TRAb-seronegative GD had a positive anti-TPO antibody status when compared to TRAb-seropositive GD ($P=0.0019$). Age ($P=0.242$), gender ($P=0.102$), and presence of thyroid nodule/s ($P=0.152$) did not differ significantly between the overt TRAb-seropositive GD and TRAb-seronegative GD groups.

Conclusion

Our findings suggest that whilst TRAb-seropositive and TRAb-seronegative patients with Graves' overt hyperthyroidism have comparable findings concerning age, gender, and thyroid nodule distribution, TRAb-seronegative GD is associated with a less severe form of biochemical thyrotoxicosis. In addition, our results indicate that TRAb-seronegative GD tends to be associated with negative anti-TPO antibody status.

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P168

Thyrotoxicosis and thyrotoxic periodic paralysis in hong kong: a population-based cohort study

Gloria Hoi-yee Li[1], Ching-Man Tang[1], Ray Shing-Hin Li[1], Xiaoyu Wan[1], Kathryn Choon-Beng Tan[2], Elaine Yun-Ning Cheung[3] & Ching-Lung Cheung[4]
[1]The Hong Kong Polytechnic University, Department of Health Technology and Informatics, Hong Kong; [2]The University of Hong Kong, Department of Medicine, Pokfulam, Hong Kong; [3]The Chinese University of Hong Kong, Hong Kong Institute of Diabetes and Obesity, Shatin, Hong Kong; [4]The University of Hong Kong, Department of Pharmacology and Pharmacy, Pokfulam, Hong Kong

Background

Thyrotoxic periodic paralysis (TPP) is a rare complication of thyrotoxicosis, characterized by recurrent hypokalemia, episodic muscle weakness and paralysis. It is potentially fatal in serious attacks with occurrence of life-threatening cardiopulmonary complications. Currently, lack of large cohorts comprising individuals with TPP history restrict the conduct of relevant epidemiology study.

Methods

Clinical data from a population-wide electronic medical database in Hong Kong, namely the Clinical Data Analysis and Reporting System (CDARS), was retrieved for the study. The diagnostic coding and/or potassium test records in blood were used to randomly identify 100 potential cases of thyrotoxicosis [by International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM): 242.××] and TPP (by ICD-9-CM: 242.×× and 359.3, plus low potassium level) for validation, respectively. The positive predictive value (PPV) of the clinical data from CDARS for thyrotoxicosis and TPP were determined by reviewing clinical notes and examining relevant laboratory test records. A population-based registry of thyrotoxicosis and TPP in Hong Kong was subsequently established. With reference to the United Nations population, we computed the standardized incidence rate of both thyrotoxicosis and TPP in Hong Kong, with average annual percentage change (AAPC) for trend analysis.

Findings

The PPV of clinical data in CDARS for thyrotoxicosis and TPP were 86% [95% Confidence Interval (CI): 79.2%-92.8%] and 98% (95% CI: 95.3%-100%), respectively. With this high PPV, we established a populational-based cohort, comprising 83,185 and 971 adults with diagnosis of thyrotoxicosis and TPP respectively from 1 January 2002 to 31 December 2021. The proportion of thyrotoxicosis patients experiencing TPP was 1.17%. The age- and sex-standardized incidence rate of thyrotoxicosis increased from 50.031 to 76.516 per 100,000 person-years from 2002 to 2021, with AAPC of 4.6 (95% CI: 1.11-8.01). Such increasing trend was also observed in male and female. Since more male thyrotoxicosis patients had TPP with reference to female patients, the age-standardized incidence rate of TPP in both sexes were calculated. In 2002 and 2021, the incidence rate in male was 1.405 and 1.226 per 100,000 person-years respectively. Whereas the incidence rate in female was 0.097 and 0.131 per 100,000 person-years. No significant trend was observed in both sexes.

Interpretation

This is the first study validating the clinical data in electronic medical database for TPP. The high PPV of validation enabled us to establish the largest population-based cohort of individuals with TPP history to-date, facilitating future epidemiology studies of this rare complication.

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P169

Determination of the relationship between the development of persistent hypothyroidism after subacute thyroiditis and subtypes of human leukocyte antigen

Fatma Nur Korkmaz[1], Mustafa Sahin[1] & Klara Dalva[2]
[1]Ankara University, Faculty of Medicine, Department of Internal Medicine, Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara University, Faculty of Medicine, Department of Internal Medicine, Hematology, Tissue Typing Laboratory, Ankara, Turkey

Introduction

Subacute thyroiditis (SAT) can often resolve completely; however, it has been observed that in 11.6% of patients, permanent hypothyroidism (PHT) may develop the follow-up after diagnosis. Various studies have explored the relationship between thyroid volume at the time of diagnosis, post-treatment changes in thyroid volume, steroid therapy, and the development of PHT following SAT. While some studies suggest associations, there are also data indicating that no single factor can be determinative. The role of Human Leukocyte Antigens (HLA) in controlling the immune response, influencing the development of autoimmune diseases, and contributing to the development of chronic hypothyroidism is well-established.

Objective

In our study, we examined the impact of an individual's HLA characteristics on the development of hypothyroidism following SAT, considering other clinical factors as well.

Method
In this retrospective study, data were obtained from the hospital information management system for 51 patients diagnosed with SAT who were followed in the endocrinology outpatient clinic between June 2019 and October 2021, and whose HLA types were known. Diagnostic and follow-up data of the patients were reviewed, and 48 patients with data available for more than 180 days were included in the study. PHT was defined as the detection of thyroid-stimulating hormone levels above the reference range (4.2 μIU/ml) for six consecutive months. HLA-A, -B, -C, -DQB1, and -DRB1 genotyping was performed using the MiaFora Flex5 typing kit (Immucor, Peachtree Konars, GA) and the Illumina platform (Illumina, San Diego, CA) upon the extraction of DNA from blood sample. The results of the sequencing were analyzed using the MiaFora NGS software.
Results
In the 48 SAT patients, 33 patients without PHT (PHT (—)) and 15 patients with PHT (PHT (+)) were detected. In the PHT (+) group, the frequency of HLA-B*44:02 and –C*15:02 was observed to be higher compared to the PHT (—) group, while the frequency of HLA-B*35:02 and -DQB1*05:02 was found to be lower. Additionally, the SAT area on ultrasonographic examination was lower, and C-reactive protein levels (CRP), as well as the frequency of TPO positivity, were higher at the time of diagnosis in the PHT(+) patients.
Discussion
Patients exhibiting factors such as a reduced SAT area on ultrasonographic examination, elevated CRP levels, and TPO antibody positivity—factors potentially linked to the development of PHT following SAT—require heightened vigilance in monitoring. Further studies are necessary to identify high-risk HLA alleles.

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P170

Reference range and determinants of serum thyroglobulin in south-western greece

Georgios Markantes[1], Anastasia Armeni[1], Panagiotis Bountouris[1], Dionysios Chartoumpekis[2], Irene Mamali[1], Ioannis Kioutsioukis[3] & Marina Michalaki[1]
[1]University of Patras, Division of Endocrinology - Department of Internal Medicine, Patras, Greece; [2]University of Lausanne, Service of Endocrinology, Diabetology and Metabolism, Lausanne, Switzerland; [3]University of Patras, Department of Physics, Patras, Greece

Background
Thyroglobulin (Tg) is a protein exclusively synthesized by follicular thyroid cells. Serum Tg levels depend on thyroid volume, serum TSH levels, gender, age, smoking, and iodine intake. Consequently, serum Tg reference range may exhibit variations among different populations. It is crucial to establish population-specific reference ranges, especially when interpreting serum Tg values in the follow-up of patients with differentiated thyroid cancer who have undergone lobectomy or total thyroidectomy without radioiodine ablation.
Objectives
The aim of our study was to assess Tg levels in euthyroid individuals without autoimmunity in an iodine sufficient area, and to identify factors affecting Tg in our population.
Methods
Participants were attendants of our outpatient endocrinology clinic. Screening included a complete medical history and physical examination, thyroid function tests (TSH, T3, T4, Tg, thyroid autoantibodies), urinary iodine excretion assessment, and thyroid ultrasound with estimation of the total thyroid volume.
Results
We selected 115 euthyroid and iodine sufficient individuals (65 women and 50 men), without thyroid autoimmunity, with a mean age of 36.93 (range 17-72) years. None of them had abnormal sonographic findings, and none had known thyroid disease or was on medication interfering with thyroid function. Tg levels were non-normally distributed in our population. The mean Tg level was 14.55 ng/mL (range: 0.39-56.74 ng/mL) and the median value was 12.38 ng/mL (interquartile range: 10.82 ng/mL), with 95% of the data falling in the interval 1.8-31.5 ng/mL. Tg levels were higher in smokers vs non-smokers (Median / IQR: 17.73 / 12.01 ng/mL vs 11.85 / 9.41 ng/mL, $P=0.003$). Tg was positively correlated with T3 ($r=0.250$, $P=0.038$) and T4 ($r=0.235$, $P=0.012$) levels. In multiple linear regression, the best model for Tg prediction had three regressors (smoking, T4, and TSH) and explained 11.7% of Tg variability. Non-linear models were able to explain $>90\%$ of Tg variance, but most of the explained variance was due to random effects.
Conclusion
We propose a reference range of 1.8-31.5 ng/mL for Tg in a euthyroid, iodine sufficient Greek population. Tg is higher in smokers, and is weakly correlated with T3 and T4 levels, but not with thyroid volume. Tg levels in our cohort seem to depend on unknown factors, other than those traditionally described in the literature.

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P171

Diagnosis of medullary thyroid microcarcinoma by calcitonin measurement in fine-needle aspiration washout

Bogdan Radu Ditescu[1], Luca Diana-Simina[1], Stan Andrei[1], Caragheorgheopol Andra[2], Terzea Dana[3], Niculescu Dan Alexandru[1,4] & Poiană Cătălina[1,4]
[1]Department of Pituitary and Neuroendocrine Disorders, C. I. Parhon National Institute of Endocrinology, Bucharest, Romania; [2]Research Laboratory, C. I. Parhon National Institute of Endocrinology, Bucharest, Romania; [3]Pathology Department, C. I. Parhon National Institute of Endocrinology, Bucharest, Romania; [4]Department of Endocrinology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Introduction
Medullary thyroid carcinoma (MTC) is an uncommon thyroid malignancy arising from calcitonin-producing parafollicular cells. Micro-MTC is defined traditionally as MTC that measures ≤ 1 cm and represents a very rare entity. Ultrasound-guided fine-needle aspiration biopsy cytology (FNAB-C) sensitivity is about 63% for MTC and can be improved by measurement of calcitonin in the needle washout (FNA-CT). The value of FNA-CT in micro-MTC has not been studied. Our aim was to further investigate the value of FNA-CT as a diagnostic marker for micro-MTC.
Methods
We retrospectively analyzed all patients with thyroid micronodules and elevated serum calcitonin in whom FNAB-C and FNA-CT was performed during 2019-2023. Clinical, imaging, biochemistry and pathology parameters were retrospectively extracted.
Results
A total of 21 patients with elevated serum calcitonin and thyroid micronodules detected on ultrasound, underwent FNAB-C and FNA-CT. Furthermore, 12 patients underwent surgical treament whenever a cytological suspicion for malignancy existed. Validation of the technique for these cases was realized through the correlation between the cytologic diagnosis of thyroid FNAB and the postoperative histopathologic diagnosis. The specificity and sensitivity for MTC was 100% for both FNAB-C and FNA-CT at a cut-off value of 62.7 pg/ml.
Conclusion
Early clinical detection and preoperative confirmation of MTC still represent a diagnostic challenge in clinical practice and through this study we demonstrated that FNA-CT measurement is an effective method for micro-MTC diagnosis. We set our own laboratory cut-off for calcitonin at 62.7 pg/ml. Although FNA-CT is a important complementary diagnostic tool, it should only be integrated but not substitute FNAB-C to detect micro-MTC.

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P172

Safety of primary care-led surveillance for low-risk thyroid cancer patients

Gedoni Eni[1] & Mohamed Malik[1]
[1]Scunthorpe General Hospital, Scunthorpe, United Kingdom

Background
Post-treatment monitoring of thyroid cancer depends on risk stratification for future recurrence or possible extra-thyroidal metastasis. Current guidance suggests that patients with favourable prognostic factors and a low likelihood of recurrence can be effectively monitored in community settings. This study explores the safety of community-based surveillance for stable low-risk thyroid cancer patients discharged from specialised thyroid clinic.
Methodology
A retrospective review of 26 thyroid cancer patients discharged from the thyroid clinic, Scunthorpe General Hospital to primary care surveillance in the period from 2021 to 2023 was conducted. The study involved a comprehensive review of diagnosis, histology reports, blood and radiology results, and clinic correspondence extracted from electronic medical records.
Results
During the study period, 26 patients with thyroid cancer were discharged for long-term primary care (community) surveillance. 73% were female and median age was 61 years (IQR 48-70). Among the discharged patients, papillary carcinoma (18) was the predominant histological diagnosis and 34.6% were micro carcinomas. Definitive treatment among the study population comprised of surgery with radio-iodine ablation (61.5%) and surgery alone (38.5%). Median duration of thyroid clinic follow-up prior to discharge was 12 years (IQR 8-17). Written recommendations for post-discharge screening protocol were provided to the general practitioners for all 26 patients. Compliance with the screening

protocol was observed in 21 patients (81%); among these, only 5 patients underwent complete screening in accordance with the prescribed protocol (annual assessment of thyroid-stimulating hormone, thyroglobulin levels, and neck examination), while 16 patients had partial screening (less than annual, average interval of 18-24 months). There was no difference observed in screening uptake or frequency between age groups, gender, micro or macro carcinomas, and mode of primary treatment. Average TSH value was (1.46 mU/L $\pm$ 1.5); none had raised tumour markers (thyroglobulin) or positive finding to suggest recurrence.
Conclusion
Upon reviewing low-risk thyroid cancer patients discharged from Scunthorpe General Hospital's thyroid clinic, it becomes apparent that community-based surveillance, following an initial period of specialist clinic follow-up, is safe and appropriate. To enhance the effectiveness of this approach, we propose improvement of the patient recall system incorporating automated prompts within the shared electronic medical records and utilising posted or emailed letter reminders. Additionally, we recommend sustained support from specialist teams through periodic audits and expert advice.

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P173

Thyroid health in inflammatory bowel disease

Suleyman Sami Guzel[1], Ahmet Numan Demir[2], Tugce Eskazan[3], Ali Ibrahim Hatemi[3] & Mustafa Sait Gonen[2]
[1]Istanbul University-Cerrahpasa Cerrahpasa Faculty of Medicine, Department of Internal Medicine, Istanbul, Turkey; [2]Istanbul University-Cerrahpasa Cerrahpasa Faculty of Medicine, Department of Internal Medicine, Division of Endocrinology, Metabolism, and Diabetes, Istanbul, Turkey; [3]Istanbul University-Cerrahpasa Cerrahpasa Faculty of Medicine, Department of Internal Medicine, Division of Gastroenterology, Istanbul, Turkey

Aim
Changes in thyroid functions, parenchymal structure and increased frequency of thyroid diseases in inflammatory bowel diseases(IBD) have been described in various studies. In the literature, studies using the data scanning method, most of which belong to the past period, stand out. In this study, we wanted to investigate the relationship between IBD and thyroid diseases in a non-retrospective study. The aim of this study is to systematically check whether there is a relationship between Hashimoto's thyroiditis and IBD, which is especially common and whether the thyroid parenchymal structure of people with IBD is impaired, using the newly defined/started to be used VESINC scoring system. In this study which was conducted with subgroups receiving classical treatment and biological agent treatment for ulcerative colitis(UC) and Crohn's disease(CD), the thyroid health was examined.
Material and Method
Among the patients diagnosed with CD and UC who were followed up in our hospital's IBD outpatient clinic those who applied to the hospital between January-June 2023, met the study criteria and accepted to attend the study were included. A healthy control group similar to patient group in terms of age and gender was also included in the study. Thyroid stimulating hormone(TSH), free T_3(fT_3), free T_4(fT_4), anti thyroid peroxidase(anti-Tpo), anti thyroglobulin(anti-Tg) was measured and thyroid gland structure was evaluated using the VESINC system by thyroid USG in patients with a known diagnosis of UC/CD and healty control group. At the same time, sociodemographic characteristics, clinical/endoscopic parameters were recorded from the patients' files. Each group was also separated and compared according to the drug groups they used(conventional treatments, biological agents).
Results
A total of 260 individuals, including 203 patients and 57 healthy controls were evaluated cross-sectionally/prospectively. In the IBD arm, it was observed that the thyroid structure was impaired, the number of nodules increased and the gland volume increased compared to the healthy control group. Biological agents used in the treatment of IBD also have different effects on thyroid gland echogenicity;it was concluded that the rate of thyroid isoechogenicity was higher in patients receiving ustekinumab and infiliximab compared to other groups. TSH, fT_3, fT_4levels were similar between CD/UC and control groups regardless of treatments. Autoantibody levels were also found to be similar in all groups regardless of treatment.
Conclusion
Thyroid gland morphology changes in IBD. There are changes in gland volume, nodule number and heterogeneity compared to the healthy population. Since the study was cross-sectional, long-term prospective follow-up of these patients may reveal the high rate of thyroid dysfunction and autoantibody positivity that may be overlooked during the disease process. The positive effect of ustekinumab on thyroid morphology may be worth investigating as a potential therapeutic approach.

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P174

Changes of lipid profile in subclinical hyperthyroidism and following restoration of euthyroidism

Grzegorz Kaminski[1], Ewelina Szczepanek - Parulska[2], Michał Olejarz[3], Marek Ruchała[4] & Marek Saracyn[1]
[1]Military Institute of Medicine - National Research Institute, Endocrinology and Radioisotope Therapy, Warsaw, Poland; [2]Poznan University of Medical Sciences, Endocrinology, Metabolism and Internal Medicine, Poznan, Poland; [3]Poznan University of Medical Sciences, Endocrinology, Metabolism and Internal Medicine, Poznan; [4]Poznan University of Medical Sciences, Endocrinology, Metabolism and Internal Medicine, Poznan, Poland

Background
The impact of subclinical hyperthyroidism (sHT) on lipids concentration is still unclear. The aim of the study was to prospectively evaluate the changes in lipid profile in patients with sHT and following restoration of euthyroid state.
Patients and methods
The studied group consisted of 44 patients (37 females, 7 males), diagnosed with endogenous sHT in the course of either toxic multinodular goiter, diffused thyroid autonomy or autonomously functioning thyroid nodule. All patients were treated with radioiodine. We measured TSH, fT3, fT4, total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides (TG), and sex hormone binding globulin (SHBG) serum concentrations at admission, and at every check-up visit until the last visit, which was scheduled 6 months after the restoration of euthyroidism.
Results
The restoration of euthyroidism was associated with a statistically significant increase in LDL cholesterol from 114.3 to 121.9 mg/dl ($P=0.018$) and HDL cholesterol from 64.02 to 66.25 mg/dl ($P=0.041$). An increase in serum triglycerides from 95.2 to 102.6 mg/dl was also observed but it was not statistically significant ($P=0.273$). The total cholesterol serum concentration also increased after treatment (from 204.6 to 211.1 mg/dl), however the increase was statistically nonsignificant ($P=0.11$).
Conclusion
Treatment of sHT results in a statistically significant increase in LDL cholesterol and HDL cholesterol serum concentration. The rise in serum triglycerides and in total serum cholesterol did not reach statistical significance. Further studies assessing the impact of sHT treatment on lipid metabolism are still needed. It is still unclear how different treatment modalities and different causes of sHT impact lipid metabolism and whether the observed changes are clinically relevant in terms of cardiovascular risk.

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P367

ALK fusion genes in a large cohort of thyroid carcinomas

Barbora Bulanova[1], Vlasta Kuklikova[1], Karolina Mastnikova[1], Eliska Vaclavikova[1], Jitka Carkova[1], Petr Vlcek[2], Petr Lastuvka[2], Rami Katra[2], Petr Bavor[2], Daniela Kodetova[2], Martin Chovanec[3], Jana Drozenova[3], Jaromir Astl[4], Jiri Soukup[4], Josef Vcelak[1] & Bela Bendlova[1]
[1]Institute of Endocrinology, Prague, Czech Republic; [2]Motol University Hospital, Prague, Czech Republic; [3]University Hospital Kralovske Vinohrady, Prague, Czech Republic; [4]Military University Hospital, Prague, Czech Republic

Objectives
ALK fusion genes are a rare genetic alteration and have been described in various t types of thyroid carcinomas, particularly in papillary thyroid carcinomas (PTCs), poorly differentiated thyroid carcinomas (PDTCs) and anaplastic thyroid carcinomas (ATCs). The aim of this study was to identify *ALK* fusion genes in thyroid carcinoma samples, correlate them with clinical and histopathological features, and determine the prognostic significance of *ALK* fusion genes based on long-term follow-up of patients.
Methods
The cohort consisted of 1221 fresh frozen thyroid carcinomas, including 1051 PTCs, 11 PDTCs and 17 ATCs. The samples were sorted based on the mutation detected. Samples positive for *BRAF*, *HRAS*, *KRAS*, *NRAS* or *RET* mutations or *RET/NTRK* fusion genes were excluded from further analysis of the *ALK* fusion gene. Samples were analyzed for the presence of *ALK* fusion genes using the FusionPlex Comprehensive Thyroid and Lung panel (Invitae) by next-generation sequencing (MiSeq, Illumina).
Results
ALK fusion genes were detected in 13/1051 (1.2%) of PTCs. The mean age of patients at diagnosis was 23.7 $\pm$ 14.7 years, and 7/13 patients with *ALK* fusion-

positive PTC were of childhood or adolescent age (2-20 years). Three types of *ALK* fusions were found, including the following partner genes: *STRN, EML4* and *FMNL2*. *STRN/ALK* was identified in ten cases, *EML4/ALK* in two cases and *FMNL2/ALK* in one case. All *ALK* fusion-positive samples had no other mutation, and even none of the samples had a *TERT* or *TP53* mutation. The majority (10/13; 76.9%) of PTCs with a positive *ALK* fusion gene were of the follicular subtype. Lymph node metastases were found in 7/13 (53.8%) patients and distant metastases were found in 1/13 (7.7%) patients. Radioiodine treatment was indicated in 10/13 patients. In the first two years after surgery, 4/11 patients had a structural incomplete response to treatment due to local or distant metastases. In 3/4 patients, radioiodine treatment eliminated the metastases. In 1/4 patients, a reoperation was necessary. Current response to treatment in all 11 evaluable patients is excellent.

Conclusion

In summary, *ALK* fusion genes were identified only in PTCs and occurred in pediatric and adolescent patients rather than in adult patients. The most common type was the *STRN/ALK* fusion gene. The prognosis of patients with *ALK* fusion-positive PTC was favorable. Genetic molecular testing of *ALK* fusions is important for patient's diagnosis, prognosis and also for possible targeted therapy.

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P368

Long-term gene expression changes in the rat thyroid by neonatal irradiation - a possible mechanism related to thyroid carcinogenesis by childhood radiation

Nariaki Fujimoto[1], Mutsumi Matsuu-Matsuyama[2] & Masahiro Nakashima[2]

[1]Hiroshima University, Research Institute for Radiation Biology and Medicine, Hiroshima, Japan; [2]Nagasaki University, Atomic Bomb Disease Institute, Nagasaki, Japan

Introduction

Radiation exposure at young ages is a risk of thyroid cancer. Although early studies of the infants treated with X-rays already indicated an association, the risk became well-known by a rapid rise in childhood thyroid cancer cases after the Chernobyl nuclear plant accident. Human cases have been investigated extensively, but the underlying mechanisms have yet to be elucidated. Our previous investigation in rats found that neonatal X-irradiation induced long-term mRNA expression changes in the thyroid cancer-related marker genes, which may be a key to understanding childhood susceptibility to thyroid carcinogenesis. Then, in the present study, we performed a global gene expression analysis to identify the thyroid genes whose expressions were altered by neonatal irradiation in the rat model.

Materials and Methods

Male Wistar rats at 1 week old (neonates) and 8 weeks old (adults) were cervically X-irradiated at 0, 6, or 12 Gy. After 8 weeks, the thyroid was dissected and subjected to the gene expression analysis by the RNA-Seq (20 million reads, 100 bp pair-end analysis) to classify the genes regulated by radiation. The expression changes in the newly identified genes were confirmed by Q-RT-PCR. The expression changes were further examined in the thyroid tumors induced by feeding with an iodine-deficient diet in rats.

Results

1) The RNA-Seq analysis identified 114 up-regulated and 29 down-regulated thyroid genes in 8 weeks after irradiation. 2) A comparison between neonatal and adult irradiation found that 9 up-regulated and 5 down-regulated genes were specific to neonatal radiation exposure. 3) Among them, Cdkn1a and Vnn1 were identified as the up-regulated genes in the thyroid tumors.

Conclusions

We successfully identified a series of thyroid genes whose expression could be changed long-term after a single cervical irradiation during the neonatal period. Some of those genes, such as Cdkn1a and Vnn1, were also up-regulated in the thyroid tumors. These findings suggested that the alteration of gene expressions by neonatal radiation may contribute to the increased risk of thyroid cancer by childhood radiation exposure.

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P369

The association of gestational thyroid function and thyroid autoimmunity with offspring neurodevelopment: an individual participant meta-analysis

Joris Osinga[1, 2], Leonie Warringa[1, 2], Consortium on Thyroid and Pregnancy[3], Robin Peeters[1, 2] & Tim Korevaar[1, 2]

[1]Erasmus MC, Internal Medicine, Rotterdam, Netherlands; [2]Erasmus MC, Academic Center for Thyroid Diseases, Rotterdam, Netherlands; [3]Working group on offspring neurodevelopment (see https://www.consortiumthyroidpregnancy.org)

Objective

Adequate thyroid hormone availability is essential for foetal neurodevelopment. While overt maternal hypothyroidism is associated with lower offspring IQ, recent studies suggested an inverse U-shaped association, with suboptimal offspring neurodevelopment for both the lower and higher thyroid function range. Our aim is to investigate the association of gestational thyroid function with offspring IQ scores, assess if this association is different based on the gestational age at blood draw or TPOAb positivity.

Methods

We performed an individual participant data meta-analysis using data from prospective birth cohorts on gestational thyroid function and offspring IQ. Exclusion criteria were pre-existing thyroid disease, thyroid hormone altering medication usage, multiple gestation. IQ measurements <50 or >150 were winsorized. Neurodevelopmental tests were standardized to a mean of 100 and standard deviation of 15 to facilitate comparison among cohorts. We performed hierarchical linear mixed regression models accounting for repeated measurements, adjusting for potential confounders including maternal age, education, ethnicity, body mass index, smoking status, parity, gestational age at blood sampling and fetal sex. We used multilevel multiple imputation for missing covariate data and inverse probability weighting to account for attrition.

Results

The final study population comprised 14, 767 participants from 11 cohorts of whom 6, 064 had repeated IQ measurements (median age of measurement 6.1 years, interquartile range [IQR] 3.1-8.7 years). There was an inverted U-shaped association of FT4 concentrations with child IQ ($P=0.00048$). For both low and high FT4 this corresponded with a mean difference in IQ scores of -5.5 to -6.5 in the full range and -1.0 to -1.5 in the euthyroid range. A leave-one-out analyses to prevent a single cohort from driving the association yielded similar results. After stratification for gestational age at blood sampling (median 13.2 weeks, IQR 11.6-17.5), there was no association between FT4 and child IQ scores after 25 weeks of gestation, although data were limited in this period. There was no statistically significant association of TSH, TPOAb positivity, subclinical hypothyroidism, isolated hypothyroxinaemia, subclinical hyperthyroidism or overt hyperthyroidism with child IQ scores.

Conclusions

Both low and high maternal FT4 concentrations, but not TSH, in pregnancy are associated with lower child IQ scores. This is the first multicentre study to replicate these findings and add important data on time dependency and persistency of the effect until older offspring age. These results emphasize that caution should be exercised when supplementing thyroxine in pregnancy at the risk of overtreatment and possible detrimental effects on offspring neurodevelopment.

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P370

Clinical value of reverse triiodothyronine in the identification of euthyroid sick syndrome and prediction of mortality in critically ill patients

Shaoyong Xu[1, 2] & Jingjing Zeng[2]

[1]Xiangyang Central Hospital, Affiliated Hospital of Hubei University of Arts and Science, Department of Endocrinology, Xiangyang, China; [2]Xiangyang Central Hospital, Affiliated Hospital of Hubei University of Arts and Science, Center for Clinical Evidence-Based and Translational Medicine, Xiangyang, China

Background

Elevated reverse triiodothyronine (rT3) is a characteristic feature of euthyroid sick syndrome (ESS), which is associated with mortality in critical patients. However, the lack of reference values limits the use of rT3 for ESS diagnosis and the prognostic value of rT3 is unclear. This study aimed to determine the reference range of rT3 in the ESS identification and mortality prediction in critically ill patients.

Methods

This ongoing prospective cohort study was conducted from April 2022 at eight hospitals in China. Patients who had been hospitalized in intensive care unit for at least 24 hours without thyroid disorders were consecutively enrolled. Demographic characteristics, APACHE II, and thyroid function were evaluated on admission. Patients were followed up at the time of ICU discharge, hospital discharge, and 90 days after discharge. Study outcomes included ESS diagnosis (defined as decreased free triiodothyronine on admission without thyroid itself lesion), in-hospital death, and 90-day death. The 2.5th percentile ($P_{2.5}$) of rT3 in ESS patients

was calculated as early warning. The optimal cut-off points of rT3 for the ESS diagnosis and mortality prediction were determined using receiver operating characteristic (ROC) curve and time-dependent ROC curve, respectively.
Results
This preliminary analysis presented the results of data collected up to January 2024. A total of 959 critical patients were screened, of which 849 (mean age 64.63 years, 3.25% male) were eligible and 34 were lost to follow-up after discharge. Of those, 394 (46.41%) had ESS on admission, 79 (9.31%) died during hospitalization, and 250 (30.67%) experienced 90-days deaths. The $P_{2.5}$ of rT3 levels in ESS patients was 0.57 ng/mL. The optimal cut-off point of rT3 for diagnosing ESS was 1.06 ng/mL, with an area under the curve of 0.745, sensitivity of 73.32%, and specificity of 67.13%. The optimal cut-off points for predicting in-hospital and 90-days mortality were 1.92 and 1.62 ng/mL, respectively. The log-rank test showed that patients with high rT3 level had higher in-hospital and 90-days mortality than those with low rT3 ($P < 0.001$). Sensitivity analysis (excluding patients discharged from ICU to home) did not significantly change the results.
Conclusion
In critically ill patients, rT3 had clinical value in identifying ESS and predicting mortality, which would contribute to risk stratification and care. The different levels of rT3 may have different clinical implications: 0.57 ng/mL for ESS early warning, 1.06 ng/mL as the optimal cut-off point for ESS diagnosis, and 1.62 ng/mL for mortality risk stratification.

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P371

Papillary thyroid cancer and body mass index: the role of mitochondrial arginase-2 in tumor microenvironment

Rebecca Sparavelli[1], Francesca Signorini[1], Riccardo Giannini[1], Elio Marchetti[1], Ferruccio Santini[2], Alessio Basolo[2] & Clara Ugolini[1]
[1]University of Pisa, Department of Surgical, Medical and Molecular Pathology and Critical Care Medicine, Unit of Anatomic Pathology; [2]University of Pisa, Obesity and Lipodystrophy Center, Endocrinology Unit

Background
Papillary thyroid cancer (PTC) is a disease with an indolent course, excellent overall prognosis and long-term survival. However, some PTCs are associated with an increased risk of recurrent disease and aggressive behaviour. Many exogenous factors, as obesity, could be implicated in the pathogenesis of thyroid cancer but the biological mechanisms that may explain this connection have been only partially described. Potentially factors that combine overweight with this cancer should be searched for in the immune pathways and chronic inflammation onset. In this study, we evaluated the role of immune system in patients affected by PTC and stratified according to body mass index (BMI).
Methods
Based on BMI, samples were subdivided into four categories: underweight, normal weight, overweight, and obese. The analysis of the expression profiles of >700 immune-related genes was performed in 36 PTCs. Normal weight was considered as reference category. Furthermore, results of gene expression analysis -and thus the existence of an effective concordance between gene expression and protein synthesis- were confirmed by immunohistochemistry (IHC), calculating the H-score, a semiquantitative measure based on the combined assessment of staining intensity and the percentage of positive neoplastic cells.
Results
The immune microenvironment of PTC does not seem strongly influenced by BMI; however, we identify a statistically significant downregulation of *CASP3*, *FCGR2A*, *HMGB1*, *MAPK1*, *SPP1* and an upregulation of *ARG2*, *BCL2*, *NT5E*, *RORA* in the obese category. One of these genes, the mitochondrial arginase-2 (*ARG2*), was significant upregulated after application of Benjamini-yekutieli correction. A directly proportional and statistically significant correlation was observed between H-score and ARG2-mRNA, and between H-score and BMI, therefore the IHC results agree with those of the molecular analysis and show that the expression of ARG2 in the tumor microenvironment of PTC patients increases in relation to the increase in BMI, being significantly more intense in obese patients.
Conclusions
ARG2, which hydrolysed arginine into urea and ornithine, can influence the endogenous level of polyamines, proline, and NO (nitric oxide), key components for collagen system, tissue proliferation, immune system regulation and inflammatory response. In the last years, many studies have focused on the relationship between altered metabolism and the activity of immune system. Although, molecular mechanisms linking excessive adiposity with the development of cancer are complex and still not completely known. The investigation of molecular processes in tumor microenvironment may provide an opportunity to understand the role of immunometabolism in thyroid cancer.

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P372

Diagnosis and therapy of medullary thyroid cancer. A real-life, retrospective, multicentric, Hungarian study

Zsuzsánna Réti[1, 2], Judit Tőke[1], Réka Balla[3], Péter Reismann[1], Kristóf Attila Kovács[4], Zoltán Sápi[5], Miklós Bodor[6], Endre Nagy[6], Gábor Iványi[7], Zsuzsanna Valkusz[7], Emese Mezosi[8] & Miklós Tóth[1]
[1]Semmelweis University, Faculty of Medicine, Department of Internal Medicine and Oncology, Budapest, Hungary; [2]George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Faculty of Medicine, Department of Endocrinology, Târgu Mureș, Romania; [3]Semmelweis University, Faculty of Medicine, Students' Scientific Association, Budapest, Hungary; [4]Semmelweis University, Faculty of Medicine, Department of Pathology, Forensic and Insurance Medicine, Budapest, Hungary; [5]Semmelweis University, Faculty of Medicine, Department of Pathology and Experimental Cancer Research, Budapest, Hungary; [6]University of Debrecen, Division of Endocrinology, Department of Internal Medicine, Faculty of Medicine, Debrecen, Hungary; [7]Albert Szent-Györgyi Medical School, University of Szeged, Department of Medicine, Szeged, Hungary; [8]Medical School, University of Pécs, First Department of Medicine, Pécs, Hungary

Introduction
Medullary thyroid cancer (MTC) is a rare thyroid neoplasm arising from parafollicular C-cells secreting calcitonin. Although it possesses specific histological and biochemical markers, real-life diagnosis and management remain challenging.
Aim
A retrospective analysis of MTC patients from four Hungarian endocrine university centres over 23 years (2000-2023) was undertaken. Demographic data and biochemical markers, staging, germ-line RET mutation, intervention types, and monitoring through calcitonin-doubling time were analyzed.
Results
Data from 156 patients were collected from patient files. Bilateral disease was demonstrated in 26, 6% of patients, with 37, 5% having lymph node involvement at the time of diagnosis. Preoperative calcitonin was measured in 84, 2% of cases, and FNAB was performed in 72% of patients. Diagnosis of MTC based on preoperative cytology accounted for 67, 4% of cases. The use of preoperative diagnostics increased with time ($P<0$, 05). Nearly one-third of patients were diagnosed with advanced disease (stage IV). Total thyroidectomy and node dissection were performed in 53, 8%; this rate was higher following 2015 vs before ($P<0.05$). Progression of disease was recorded in 47, 8% of patients. Two, three and four neck dissections were performed in 43, 17 and 4 patients, respectively. In the first year after surgery, calcitonin measurements were available in 75% of patients. Forty-four patients (29.53%) were declared cured after the first surgery. Postoperative calcitonin doubling time less than two years was associated with significantly lower progression-free survival than calcitonin doubling time longer than two years ($P<0.05$). RET mutation analysis was performed in 73% of patients, and of these, 34, 2% were confirmed to have RET germ-line mutation, and the most frequent genetic alteration was on codon 634. In advanced disease, tyrosine kinase inhibitors were instituted in 35 cases. Disease progression and drug-induced adverse events were significantly more frequent with multikinase inhibitors as compared to that of selpercatinib ($P<0.05$).
Conclusion
Despite the progress and more widespread use in diagnostic procedures and recent advances in drug treatment options, there are still unmet needs in managing MTC. Preoperative calcitonin measurement is the best marker for diagnosis, although its routine use in screening is debated. FNAB alone is often not sufficient for exact preoperative diagnosis of MTC; completion with immunocytology or calcitonin measurement from the washout fluid could increase the sensitivity of preoperative biopsies. Surgery can be curative, mostly in local diseases. Advanced cases need an individualized approach. Recently, germ-line/somatic RET mutation analysis has become indispensable in choosing appropriate targeted medical treatment for MTC.

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P373

Women-specific reference ranges for serum TSH in Liguria: the impact of age and time of collection in a single-centre cross-sectional study

Massimo Giusti[1, 2] & Marilena Sidoti[1, 3]
[1]Endocrine Unit, Centro Clinico Diagnostico Priamar, Savona, Italy; [2]Dipartimento di Medicina Interna, Università di Genova, Genoa, Italy; [3]Endocrine Unit, Azienda Sanitaria Locale 2 Savonese, Savona, Italy

Background
TSH is the first-line test for thyroid function. Since the 1990s, 3rd-generation assays have been available on automated platforms, and the normal ranges

provided by manufacturers are generally used in diagnoses. In the age of gender medicine there is a need to refine normal TSH ranges. The aim of this study was to construct a normal TSH range in women living in our district.
Methods
From 2005 to 2020, 4544 records from women undergoing their first endocrinological examination were anonymously evaluated; 18% of records were excluded owing to lack of data (65%), age (<18 years; 18%), pregnancy (7%), non-Caucasian ethnicity (6%) and other reasons (4%). Age, BMI, TSH, TPOAb, pharmacological treatments and US findings were collected from 3724 records. 1638 were excluded owing to the presence of overt diseases, interfering treatments and TPOAb positivity. Thus, statistical analysis was performed on a sample of 2086 medical records. Data are reported as medians and 2.5-97.5 percentiles.
Results
Median TSH was 1.70 mIU/l (0.20-7.41 mIU/l). The median of TSH values collected from 2005 to 2020 ranged between 1.20 mIU/l (2005) and 1.99 mIU/l (2017), with significant differences between 2017 and 2005 ($P<0.01$), 2010 ($P=0.03$) and 2014 ($P=0.02$). On stratifying the sample into 3 age-groups (18-44 years, N=910; 45-64 years N=780; >65 years, N=393), TSH was 1.75 mIU/l (0.41-6.21 mIU/l), 1.66 mIU/l (0.20-6.93 mIU/l) and 1.52 mIU/l (0.07-7.78 mIU/l), respectively. In the whole sample, no correlation emerged between TSH levels and age or BMI. A significant ($P<0.0001$) decrease in the percentage of women considered to have sub-clinical hypothyroidism was observed when the upper limit of normal TSH was set at the age-related value of 97.5% (3.5%) instead of the TSH range reported in the assays (7.8%). By contrast, no difference in the percentage of women considered to have sub-clinical hyperthyroidism was noted when either the calculated age-related normal lower TSH limit (2.7%) or the manufacturers' normal lower TSH range (2.3%) was applied.
Conclusions
This is the first study in Liguria aimed at establishing new age- and gender-specific reference values for TSH. Based on a large number of women (about 2% of adult women living in the Savona district), this new age-related range could be more extensively employed in order to improve diagnoses and therapies. The main result of implementing age- and gender-related normal TSH levels between the 2.5 and 97.5 percentiles seems to be a reduction in the hasty diagnosis of sub-clinical hypothyroidism.

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P374

Adolescent with multiple benign skin lesions, cutaneous angiosarcoma and multiple thyroid nodules. what is the diagnosis?

Eirini Dikaiakou[1], Evgenia Magkou[2], Marina Servitzoglou[2], Marina Vakaki[3], Periklis Makrythanasis[4], Joanne Rachel Synodinou-Traeger[4], Nikolaos Marinakis[4], Myrsini Gkeli[5], John Skondras[6], Margarita Baka[2] & Elpis Vlachopapadopoulou[1]
[1]Children's Hospital 'P. & A. Kyriakou', Endocrinology Growth and Development, Athens, Greece; [2]Children's Hospital 'P. & A. Kyriakou', Oncology Department, Athens, Greece; [3]Children's Hospital 'P. & A. Kyriakou', Radiology Department, Athens, Greece; [4]Medical School, National and Kapodistrian University of Athens, St. Sophia's Children's Hospital, Laboratory of Medical Genetics, Athens, Greece; [5]General Hospital "Agios Savvas", Athens, Greece, Radiology Department, Athens, Greece; [6]Children's Hospital 'P. & A. Kyriakou', Department of B' Pediatric Surgery, Athens, Greece

Objective
To present the rare case of a patient with cutaneous angiosarcoma, multiple benign skin lesions together with multiple thyroid nodules and to discuss his genetic diagnosis.
Case Presentation
A $13^{2/12}$ years-old boy was referred to the Endocrinology department, following chemotherapy and radiotherapy. His medical history was uneventful until the age of 8 years. His mother reported Graves' disease and his maternal grandmother papillary carcinoma. Starting at the age of 8 years, he gradually developed multiple skin lesions: 1. Hemangioma on the right tibia, 2. Skin lesion on the left posterior chest wall characterized as Kaposi-form hemangioendothelioma that recurred after 1 year. 3. Infiltrating vascular skin neoplasm on the left posterior chest wall, with lymph node involvement, characterized as cutaneous angiosarcoma. The patient received chemotherapy together with radiotherapy. 4. New multiple benign skin lesions (skin fibromas, papillomatous lesions, lymphangioma) appeared during follow-up. The initial clinical assessment was remarkable for macrocephaly (head circumference 1 cm, >97th perc.) as long as obesity (BMI 31.8, >95th percentile), while his height (1.71m) was at the 95th percentile. He was pubertal with testicular size 12ml. Thyroid ultrasound revealed multiple nodules, including a prominent one on the right lobe with dmax:12.9mm, solid, strongly hypo-echogenic, with increased vascularization, wider than taller, without calcifications. Fine needle biopsy (FNB) revealed a hyperplastic nodule, BETHESDA II. Thyroid function was normal whereas anti-TPO, anti-TG were negative. From the age of 14 to the age of $16^{10/12}$ years, two additional FNBs were performed, because during regular follow up, the size of the nodule on the right lobe was increased (dmax: 24mm at the age of $16^{10/12}$ years old). They were both characterized as BETHESDA II. Thyroglobulin progressively increased to 143ng/ml. Genetic testing with WES revealed a variant in *PTEN*, NM_000314.8:c.389G>A, p.(Arg130GIn), which is characterized as pathogenic.
Conclusions
Pathogenic variants in *PTEN* are associated with Cowden syndrome (CS), Bannayan-Riley-Ruvalcaba syndrome (BRRS), *PTEN*-related Proteus syndrome (PS), and *PTEN*-related Proteus-like syndrome. They include a wide range of clinical manifestations, as well as increased risk of cancers mainly breast, thyroid, endometrial and renal. However, cutaneous angiosarcoma is not a typical manifestation of these syndromes. To our knowledge, this is the second case to be reported. Given the patient's increased risk of thyroid cancer, close follow-up with thyroid US is recommended. Any changes suggestive of malignancy should be appreciated and if results of FNB are suspicious, a total thyroidectomy should be performed.

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P375

Complications associated with the performance of thyroidectomies in a third-level hospital

Mónica Gómez-Gordo Hernanz[1], Gloria Collado González[1], Alberto García Piorno[1], Isabel Losada Gata[1], Marta Pérez Noguero[1], Ignacio Jiménez Hernando[1], Blanca Farache Suberviola[1], Amaya Morales Jaurrieta[1], Aurelio López Guerra[1] & Olga González Albarrán[1]
[1]Hospital General Universitario Gregorio Marañón, Endocrinology, Madrid, Spain

Introduction
major complications of thyroid surgery include; injury to the recurrent laryngeal nerve that can cause dysphonia and acute respiratory distress, postsurgical hematoma, infection and hypoparathyroidism, which can be transient or permanent.
Objective
to analyze the complications observed after performing thyroid surgery with different pre-surgical diagnoses in our center.
Methods
retrospective descriptive study of thyroidectomies performed during the years 2018 to 2021 by the General surgery, Otolaryngology, Thoracic surgery and Pediatric surgery services of the Gregorio Marañón Hospital in Madrid, Spain.
Results
A total of 624 patients were included, 69.6% of whom were women. The presurgical diagnoses were: multinodular goiter (36.1%), hyperparathyroidism (14.6%), nodule suspicious for malignancy (4.5%), thyroid cancer (24.8%), Graves-Basedow disease (7.1%) and others (5%). 47 patients (7.5%) underwent reoperation. Total thyroidectomy was performed in 56.4%, followed by right hemithyroidectomy in 19.2%, left hemithyroidectomy in 11.5%, parathyroidectomy in 2.4% and others in 1.4%. 80.3% of the surgeries were performed by General surgery, 5.6% by Otolaryngology, 2.4% by Thoracic Surgery, 3% by other services. Lymphadenectomy was performed in 18.3%. Of the patients who underwent surgery, 6 of them (1%) presented pre-surgical hypoparathyroidism. After surgery, 21.5% of patients had transient hypoparathyroidism, which was the most frequently observed complication and 5.8% had permanent hypoparathyroidism. In more than 60% of patients both recurrent laryngeal nerves were visualized and intraoperative neuromonitoring was performed. In 61%, intraoperative parathyroid hormone (PTH) drop was calculated in addition to pre- and postoperative PTH. In relation to recurrent paralysis, it was transient in 7% and permanent in 3.4%. 26 cases (4.2%) of postsurgical hematoma and 6 cases (1%) of infection were documented.
Conclusion
the most common postsurgical complication was transient hypoparathyroidism (21.5%) followed by transient recurrent paralysis (7%). Intraoperative determination of PTH is a predictive factor for the development of hypoparathyroidism. Neuromonitoring during surgery helps to preserve recurrent nerves. The development of postsurgical complications is greater in patients undergoing surgery for thyroid cancer, in total thyroidectomy and to a large extent depends on the experience of the center and the surgeons.

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PTEN variants in thyroid tumors of czech patients

Karolina Mastnikova[1], Barbora Bulanova[1], Vlasta Kuklikova[1], Eliska Vaclavikova[1], Jitka Carkova[1], Karolina Hrckulakova[1], Rami Katra[2], Petr Vlcek[3], Daniela Kodetova[4], Martin Chovanec[5], Jana Drozenova[6], Radoslav Matej[6], Jaromir Astl[7], Jiri Hlozek[7], Jiri Soukup[8], Josef Vcelak[1] & Bela Bendlova[1]

[1]Institute of Endocrinology, Department of Molecular Endocrinology, Prague, Czech Republic; [2]2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Ear, Nose, and Throat, Prague, Czech Republic; [3]2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Nuclear Medicine and Endocrinology, Prague, Czech Republic; [4]2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Pathology and Molecular Medicine, Prague, Czech Republic; [5]3rd Faculty of Medicine, Charles University and Hospital Kralovske Vinohrady, Department of Otorhinolaryngology, Prague, Czech Republic; [6]3rd Faculty of Medicine, Charles University and Hospital Kralovske Vinohrady, Department of Pathology, Prague, Czech Republic; [7]3rd Faculty of Medicine, Charles University and Military University Hospital, Departments of Otorhinolaryngology and Maxillofacial Surgery, Prague, Czech Republic; [8]3rd Faculty of Medicine, Charles University and Military University Hospital, Department of Pathology, Prague, Czech Republic

Objectives
Phosphatase and tension homolog (PTEN) is a part of signal pathways which are essential for cell proliferation, cell cycle progression, and apoptosis. Variants in the *PTEN* gene occur in different types of thyroid tumors with unclear diagnostic and prognostic impact. Most variants are somatic, but they can also be germline, which are associated with PTEN hamartoma tumor syndrome (PHTS). PHTS includes Cowden syndrome, which is characterized by hamartomas, and an increased risk of developing benign and malignant thyroid and other tumors. The aim of the study was to detect variants in the *PTEN* gene in a large cohort of patients with malignant as well as benign thyroid tumors.
Methods
The study consisted of 665 fresh frozen thyroid tumor samples from patients aged 3-91 years. Extracted DNA was used for next-generation sequencing of the *PTEN* gene (NM000314.8, exons 5-8). Variants in the *PTEN* gene were visualized in Integrative Genomics Viewer (Broad Institute) and evaluated by the VarSome platform (Saphetor SA). MLPA fragmentation analysis was performed to determine the presence of large-scale deletion or duplication in *PTEN*-positive samples. Data were evaluated by Coffalyser (MRC Holland).
Results
Pathogenic or likely pathogenic variants in the *PTEN* gene were detected in 11/411 (2.68 %) carcinomas (seven papillary thyroid carcinomas (PTCs), two anaplastic thyroid carcinomas, one follicular thyroid carcinoma, one oncocytic carcinoma), in 5/56 (8.93 %) low-risk neoplasms, and in 5/198 (2.53 %) benign nodules. The variants in the *PTEN* gene coexisted in three cases with variants in the *RAS* genes, in four cases with variants in the *TP53* and once with the *BRAF* V600E. MLPA revealed structural abnormalities in 5 *PTEN*-positive samples (1 PTC, 3 low-risk neoplasms, 1 benign nodule). Two patients with PTC had germline variant in the *PTEN* gene and had other symptoms of Cowden syndrome. Most patients with *PTEN*- positive carcinoma received one or two doses of radioiodine with different responses to treatment, only one patient with 90mm PTC died after 2× 7.4 GBq of radioiodine treatment with final stimulated thyroglobulin 24, 345 µg/L. In this PTC, *PTEN* c.801+1G>A and *TP53* R306* were identified.
Conclusion
In summary, *PTEN* variants were detected in 21/665 (3.16 %) thyroid tissues, higher appearance was in low-risk neoplasms (8.93 %). Due to the frequent occurrence of structural abnormalities in the *PTEN* gene, screening for copy number variants should be performed in *PTEN*-positive samples. *Supported by AZV NU21-01-00448 and MH CR RVO 00023761.*

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P377

Characterization of a series of 661 papillary throid microcarcinoma with excellent response to treatment

Elisabete Rodrigues[1, 2], Paulo Silva[2], Joao Magalhaes[2, 3], Mafalda Pinto[4, 5], Tiago Pimenta[2, 6], Manuel Sobrinho-Simões[2, 4, 5] & Paula Soares[2, 4, 5]

[1]Uls Sao Joao, Endocrinology; [2]Faculty of Medicine of the University of Porto - FMUP; [3]Uls Sao Joao, Pathology; [4]Instituto de Patologia e Imunologia Molecular da Universidade do Porto - Ipatimup; [5]3S -Institute for Research & Innovation in Health; [6]Uls Sao Joao, Endocrine Surgery

Introduction
The management of small size (≤ 1 cm) papillary thyroid carcinoma, also known as papillary thyroid microcarcinoma (PTMC) is a debated topic as it includes tumors with a wide range of biological characteristics and behavior.
Objectives
To describe prevalence, clinical and histological characteristics of PTMC with excellent response to treatment after a median follow up of 9.85±6.21 years.
Methods
We did a retrospective analysis of clinical and histopathological data of all patients operated on for thyroid cancer at our hospital between 1996 and 2013 with diagnosis of PTMC. Statistical analysis was done with SPSS 22.0 for MAC.
Results
During this period 1057 patients were diagnosed with PTMC. Of these 661 (577 females and 84 males with a mean age of 51.2±13.5 and 55.4±12.7 years, respectively) showed an excellent response to treatment. In 472 (72%) the diagnosis of PTMC was incidental and in 182 (27.8%) was non incidental. Incidental PTMC were significantly smaller than nonincidental (3.86±2.82 vs 7.43±2.36mm, $P<.001$). Initial surgery was lobectomy in 142 (21.5%), total thyroidectomy (TT) in 488 (73.8%), subtotal thyroidectomy in 5 (0.8%), totalization of thyroidectomy in 24 (3.6%) and TT+neck dissection in 2 (0.3%). Most cases were classical PTC and follicular variant of PTC (84% and 11%, respectively). In 547 (82.8%) cases no additional treatment was necessary after first surgery (group A), whereas in 114 (group B) another surgery and/or radioiodine was done. When comparing these groups we found significant differences between them in terms of age at diagnosis (71.7% were ≥45 years in group A vs 58.8% in B), incidental finding (77.8% in group A vs 45.6% in group B), multifocality (23.3% in group A vs 54.4% in B), vascular invasion (0.6% in group A vs 21.1% in B), extrathyroidal extension (2.8% in group A vs 26.3% in B), lymph node involvement (0% in group A vs 7.9% in B). During the follow-up tumor relapse occurred in 12 cases (1.8%), all locoregional, 8 initially treated with lobectomy and 4 with total thyroidectomy. The time to relapse was 5.08±5.56 (1-18) years.
Conclusion
PTMC is frequently found and the optimal treatment is still a matter of debate. Most of them had an excellent prognosis and no further treatment was needed after lobectomy or thyroidectomy. However some patients have clinical and histopathological poor prognostic factors as it is demonstrated in this series that justifies a longer follow-up.

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Ocular myasthenia gravis and sub clinical hyperthyroidism- a rare occurrence

Umer Qazi[1], Yusuf shaikhali[1] & Melina Kostoula[1]

[1]Watford General hospital, Endocrine and diabetes clinic, Watford, United Kingdom

Introduction
The coexistence of myasthenia gravis (MG) and autoimmune thyroid disease (AITD) is well recognised, with 5-10% of MG patients also having an AITD[1-2]. Among AITD, hyperthyroidism association with MG is the most common[3]. Conversely, MG has a relatively low incidence of around 0.2% in individuals with hyperthyroidism[2, 4]. This implies a potential immunological cross-reactivity between the neuromuscular junction and thyroid components in certain cases of MG and hyperthyroidism[3]. Nevertheless, the precise pathogenic link between these two autoimmune diseases remains uncertain. There are reports of ocular MG in conjunction with hyperthyroidism[5-8]. There are limited reports of ocular MG in association with sub-clinical hyperthyroidism[10].
Case summary
A 60-year-old man with a history of prostate cancer underwent various treatments. In April 2023, he presented with right ptosis for three months with no associated symptoms. Initial thyroid tests in June revealed sub-clinical hyperthyroidism, suggesting thyroid-associated orbitopathy. Despite starting carbimazole, his ocular motility worsened, and he developed double vision when looking to each side. Positive acetylcholine receptor antibodies led to an ocular myasthenia gravis diagnosis in August 2023. A pyridostigmine trial showed inconsistent improvement, so prednisolone was initiated in September. A CT thorax and neck ruled out significant abnormalities, and thyroid function tests returned to normal. Ongoing carbimazole treatment was recommended after an October endocrinology review.
Discussion
The exact cause of this is unclear; immunological cross-reactivity and a genetic link have been postulated. For instance, an increase in thyroid antibodies has been found in patients with ocular MG[5-6]. Human leukocyte antigen (HLA) specificity (B8, DR3 and BW46) has also been reported between MG and thyroid disease[6, 11]. More recently, the TNF- α-863 polymorphism and HLA DQ-3 have both been

linked with MG and Graves' disease[12]. However, our understanding of the underlying mechanism behind MG and hyperthyroidism's association remains limited. Both hyperthyroidism and MG can present with ocular manifestations[9]. Thus, the initial presentation in this case was thought to be thyroid-associated orbitopathy. The patient's symptoms initially worsened until ocular MG was diagnosed; this highlights the importance of early diagnosis as about half of patients who present with ocular myasthenia develop generalised weakness within 6 months[13]. Previous case reports have also demonstrated thyrotoxicosis delaying the diagnosis of MG[14]. The patient in this case initially presented with unilateral ptosis. Ptosis is uncommon in thyroid-associated orbitopathy and suggests coexistence of MG[9-10, 15]. He then developed orbicularis oculi weakness and a positive Cogan lid twitch sign which strongly indicated MG[10, 15].

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Autoimmune endocrinopathies in patients with relapsing and remitting multiple sclerosis

Sofia Chatzi[1], Vasiliki Georgakopoulou[1], Stavroula Paschou[2] & Georgios Boutzios[1]
[1]National and Kapodistrian University of Athens, Department of Pathophysiology, Medical School, Athens, Greece; [2]National and Kapodistrian University of Athens, Endocrine Unit and Diabetes Center, Department of Clinical Therapeutics, Alexandra Hospital, School of Medicine, Athens, Greece

Introduction
Patients with multiple sclerosis (MS) demonstrate, in a number of studies, increased risk of acquiring another autoimmune disease compared to general population. Autoimmune thyroid diseases, type 1 diabetes, psoriasis and inflammatory bowel disease are the most common reported. The aim of our study is to determine potential factors that affect the presence of autoimmune endocrinopathies in patient with relapsing and remitting MS.
Methods
We conducted a retrospective study in the outpatient clinic of autoimmune endocrinopathies of the Department of Pathophysiology at Laikon University Hospital. All patients were diagnosed with MS. We collected data from the medical record of patients with MS and autoimmune endocrinopathies. We compared the study group with control group consisting of patients with MS without endocrine autoimmunity. Patients with MS who have been treated with alemtuzumab were excluded from the study due to the association with hyperthyroidism.
Results
A total of 55 patients [29 MS patients with autoimmune endocrinopathy and 26 MS patients without, 46 (83.6%) females] were enrolled in the study. Hashimoto thyroiditis (HT) was the most common comorbidity, observed in 20 patients (68, 9%). Moreover, seven patients (24, 1%) had Graves' disease (GD) and two patients (6, 8%) diabetes mellitus type 1(DM1). Comparing the MS patients with autoimmune endocrinopathies and MS patients without, we observed a statistically significant difference in the mean value of age (50.62 ± 10.95 years vs 42, 88 ± 13.12 years, $P=0.021$) and the median value of years of disease duration [15 years (range 1-51) vs 9 years (range 1-23). $P=0.044$]. Performing binary logistic regression analysis neither age nor duration of the disease exhibited independent association with autoimmune endocrinopathy in MS patients. In addition, we did not detect any statistically significant difference between the MS patients with autoimmune endocrinopathy and MS patients without regarding gender, smoking, presence of cancer, presence of other autoimmunities and family history of autoimmunity.
Conclusion
In our study we showed a statistically significant difference in age and MS duration between patients with and without concomitant autoimmune endocrinopathies and HT was the most common disease presented.

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Interrelationships between thyroid function, autoimmunity, low-grade inflammation, lipid profile and insulin resistance in graves' disease

Celestino Neves[1], João Sérgio Neves[1], Luis Miguel Pereira[1], Oksana Sokhatska[2, 3], Joana Queirós[1] & José Luís Delgado[2, 3]
[1]São João University Hospital, Faculty of Medicine of University of Porto, Department of Endocrinology, Diabetes and Metabolism, Porto, Portugal; [2]Faculty of Medicine, University of Porto, Basic and Clinical Immunology Unit, Department of Pathology, Porto, Portugal; [3]Faculty of Medicine, University of Porto, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal

Aim
The aim of this study was to evaluate the association between thyroid function in Graves' disease (GD) with high-sensitivity C-reactive protein (hs-CRP), lipid profile, homocysteine, folate, vitamin B12 and insulin resistance.
Methods
We performed a cross-sectional of 104 patients with recently diagnosed GD. All participants were in the first cycle of treatment with methimazole. We collected demographic information, body mass indexes (BMI), laboratory data including thyroid function tests (TSH, FT3 and FT4), antithyroid antibodies levels (TRAb, anti-TPO and anti-thyroglobulin), lipid profile, hs-CRP, homocysteine, folate, vitamin B12 and insulin sensitivity indexes obtained from a 75 g OGTT. Statistical analysis was performed using the Mann-Whitney test, Spearman's correlation coefficients and logistic regression models adjusted for age and BMI. A two-tailed $P<0.05$ was considered statistically significant.
Results
Of the 104 subjects with GD, 94% were female. Forty-nine subjects were included in the hyperthyroid group and 55 in the euthyroid group. No differences were observed between groups regarding age and BMI. Patients with higher levels of TRAb (OR = 1.166; $P=0.004$), hs-CRP (OR = 3.064; $P=0.042$), Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) (OR = 1.613; $P=0.025$) or insulinogenic index (IGI) (OR = 2.933; $P=0.046$) had a higher risk of being hyperthyroid. In the overall population, TSH levels were positively correlated with folate ($r=0.240$; $P=0.021$), hepatic insulin sensitivity index (HISI) ($r=0.217$, $P=0.046$) and whole-body insulin sensitivity index (WBISI) ($r=0.356$, $P=0.001$). TSH levels were negatively correlated with TRAb ($r=-0.461$, $P<0.001$), HOMA-IR ($r=-0.218$, $P=0.045$) and IGI ($r=-0.313$, $P=0.004$). FT3 and FT4 levels were positively correlated with HOMA-IR ($r=0.284$, $P=0.008$ and $r=0.261$, $P=0.016$ respectively) and negatively correlated with HISI ($r=-0.283$; $P=0.009$ and $r=-0.261$, $P=0.016$ respectively) and WBISI ($r=-0.233$, $P=0.032$ and $r=-0.260$, $P=0.016$ respectively). Negative correlations were also found between FT3 levels and quantitative insulin sensitivity check index (QUICKI) ($r=-0.281$, $P=0.009$) and between FT4 levels and HDL-C ($r=-0.198$, $P=0.046$). In the hyperthyroid group, FT3 levels were positively correlated with levels of Lp(a) ($r=0.367$; $P=0.020$) and with HOMA-IR ($r=0.384$; $P=0.017$), and negatively correlated with QUICKI ($r=-0.379$; $P=0.019$) and HISI ($r=-0.384$; $P=0.017$). In the euthyroid group, TSH levels were positively correlated with WBISI values ($r=0.291$; $P=0.047$) and the levels of FT3 and vitamin B12 were negatively correlated ($r=-0.358$; $P=0.01$).
Conclusion
Our study shows a significant interrelationship between thyroid function, autoimmunity, insulin resistance, lipid profile, folate, vitamin B12 and low-grade inflammation in patients with GD.

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Serum CD5L as potential biomarker of thyroid hormone status during pregnancy

Sabrina Asaad[1], Thilo Chillon[1], Dorota Filipowicz[2], Britta Wilms[3], Frank Strenge[4, 5], Ewelina Szczepanek-Parulska[2], Minich Waldemar[1], Sebastian Meyhöfer[6, 7], Jens Marquardt[5], Jens Mittag[3], Henrik Oster[4], Marek Ruchala[2] & Lutz Schomburg[1]
[1]The Institute for Experimental Endocrinology, Charité-Universitätsmedizin; [2]Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences; [3]Institute for Endocrinology and Diabetes, Center of Brain Behavior & Metabolism, University of Lübeck; [4]Institute of Neurobiology, Center of Brain, Behavior and Metabolism, University of Lübeck; [5]Department of Medicine I, University of Lübeck; [6]Institute for Endocrinology & Diabetes, University of Lübeck; [7]German Center for Diabetes Research (DZD)

Introduction
The thyroid hormone (TH) status is routinely assessed by thyrotropin (TSH) and thyroxine (T4). Both biomarkers are mainly regulated by thyroid hormone receptor beta, whereas many peripheral organs employ the alpha receptor. Serum CD5L is a liver-derived protein under control of both TH receptor isoforms, but the data base is small [1]. An additional biomarker of TH status is needed in particular during pregnancy, where the routine biomarkers become dynamically disturbed [2]. Ideally, such a diagnostic parameter should display little circadian variation in order to be suitable for routine measurements [3].

Objective
This study aimed to determine possible covariates regulating serum CD5L and to test its potential suitability as additional TH biomarker during pregnancy.
Subjects and Methods
A sandwich ELISA for serum CD5L was established using newly raised antibodies. Circadian effects and the impact of liver disease on serum CD5L concentrations were assessed. Serum samples from pregnant women with well-characterized TH and trace element status were analyzed, and CD5L concentrations were correlated with other indicators of TH status including TSH, fT4, fT3, copper and selenium concentrations.
Results
The new quantitative assay for CD5L showed high accuracy. Serum CD5L was stable in dilution and refreezing experiments and did not show strong circadian variance or dependency on liver disease. In serum of pregnant women, CD5L correlated positively to fT3, but not to fT4 or TSH. Significant positive correlations of CD5L were observed with serum levels of the TH-responsive trace elements selenium and copper.
Conclusion
The data support the potential suitability of serum CD5L as an additional marker of TH status, with potential value for pregnancy and thyroid disease. This notion needs to be tested in sufficiently large clinical studies.
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Antithrombotic/anticoagulant drugs did not increased the riscк of bleeding during thyroid fna (nor its whithdrawal up to one month reduced iťs risk)

Catarina Roque[1], Cláudia Correia[1], Sandra Silva[1], Andreia Caldeira, Nurse[1], Ricardo Valadares, Nurse[1], Ana Paula Fernandes, Nurse[1], Filipa Barreiros, Nurse[1], Ana Osório[1], Sofia Oliveira[1] & Ricardo Fonseca[1]
[1]Hospital Prof Dr Fernando Fonseca

Introduction
Thyroid fine-needle aspiration cytology (TFNA) is a widely used diagnostic method that is generally safe. Aiming to reduce haemorrhage doctors frequently advise patients to withdrawal antithrombotic/anticoagulant (AT/AC) drugs before TFNA. There are no guidelines recommending so and the so called 'novel anticoagulants' have been poorly studied in this context. Some patients are likely being exposed to increased thrombotic risk unnecessarily. Evidence is little but increasing indicating no extra risk of haemorrhagic complications and possibly no need of antithrombotic/anticoagulant (AT/AC) drug withdrawal.
Objective
To compare the incidence of haemorrhage in patients with and without AT/AC drugs during FNA in our centre.
Method
Retrospective observational study of the FNAs performed between the 1st of may 2019 and the 31st of december 2021. Records of haemorrhage and drug treatment were made prospectively during FNA. All FNAs were performed by the same operator, using the same technique and needle gauge. In warfine treated patients FNA was performed if INR was 2-3.
Results
We evaluated 491 FNAs, patients average age was 61y.o. The general incidence of haemorrhage was 3.6%. Of the patients with this complication only 2 were taking AT/AC drugs (11%), one had stopped aspirin 3days, the other stopped dabigatran 1week and the rest was off any AT/AC drugs. The total of patients treated with AT/AC drugs was 78 (16%). In this group the incidence of haemorrhage was 2.5%, represents 2 patients both treated with antithrombotic drugs (one aspirin and the other clopidogrel). There were no haemorrhages with enoxaparin nor with any oral anticoagulant. There was no statistically significant difference (SSD) (p 0, 63) in the incidence of haemorrhages in the treated vs untreated group ($n=348$). There was no SSD (p 0, 30) in the incidence of haemorrhages in the treated group vs the group that stopped therapy 24h to 3days before the procedure ($n=16$). There was no SSD (p 0, 46) in the incidence of haemorrhages between the group that stopped therapy 24h to 3days before the procedure and the group that stopped therapy 4days to 1month before the procedure ($n=13$).
Conclusion
There was no significant association of haemorrhage with drug treatment. The incidence of complications was lower in the treated group. There were no complications in patients treated with anticoagulants, haemorrhage occurred in patients taking antithrombotic drugs only (the incidence was lower than in the untreated group). To withdrawal AT/AC drugs before the procedure did not provide a statistically significant decrease in haemorrhagic complications.
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Simultaneous presentation of thyrotoxicosis and diabetic ketoacidosis in two previously healthy men

Hani Meriem[1], Boucelma Fedwa[1], Allal Hanane[1], Imane el ghebir[1] & Ait Abderrahmane Samir[1]
[1]Algiers Province, Algeria

Graves' disease and type 1 DM (T1DM) both have an autoimmune aetiology. Also, Thyrotoxicosis (TT) has previously been described as a possible precipitant of diabetic ketoacidosis (DKA) in patients with T1DM. Due to the similarities in their clinical presentation, DKA can mask the diagnosis of TT and vice versa. We report two cases of the simultenous presentation of thyrotoxicosis and diabetic keto-acidosis in two previously healthy men. Case 1: A 27-year-old man with no history of any disease presented to the emergency department (ED) with unintentional weight loss of 15 kg in 1 month, excessive sweating, abdominal pain, anxiety and tremors of the extremities. On examination, the patient appeared anxious, dehydrated. Blood pression was 107/68 mmHg and heart rate at 98 beats/min. He had palpable goitre. Investigations revealed that HbA1c was 10.7%, blood glucose was 19 mmol/l with 3+ ketonuria and compensated mild acidosis. Thyroid function test revealed TSH (0.01 mIU/L), free T4 (35 pmol/L). Thyroid scintigraphy revealed a diffuse hypercaptating goiter. Both anti-GAD and anti-TSH receptor antibody were positives. The patient was managed with carefully administered intravenous fluids, intravenous insulin and electrolyte replacement. After resolution of DKA, the patient was transitioned to subcutaneously administered insulin and Carbimazole 20 mg was added. Case 2: A 24-year-old man with familial history hashimoto's disease presented to the emergency department (ED) with unintentional weight loss of 14 kg in 6 months, excessive sweating and palpitations. On examination, Blood pression was 121/64 mmHg and heart rate at 104 beats/min. He had palpable goitre. Investigations revealed that HbA1c was 14.9 %, blood glucose was 19 mmol/l with 2+ ketonuria and compensated mild acidosis. Thyroid function test revealed TSH (0.006 mIU/L), free T4 (57 pmol/L). Thyroid scintigraphy revealed a diffuse hypercaptating goiter. The patient was managed with carefully administered intravenous fluids, intravenous insulin and electrolyte replacement. After resolution of DKA, the patient was transitioned to subcutaneously administered insulin and Carbimazole 30 mg was added.
Discussion
Thyroid hormones affect glucose metabolism at the cellular level by causing insulin resistance, upregulating glucose production by glycolysis and gluconeogenesis pathways and increasing gut absorption of glucose. Thyroxine also decreases serum insulin levels by increasing renal excretion. The resulting state of insulinopenia and insulin resistance causes disinhibition of hormone-sensitive lipase. This leads to unchecked lipolysis and fatty acid oxidation with increased ketones production.
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Echocardiographic differences between the mild form of subclinical hypothyroidism and healthy subjects

Valentina Velkoska Nakova[1], Brankica Krstevska[2], Elizabeta Srbinovska Kostovska[3], Ljubica Georgievska Ismail[3], Cvetanka Volkanovska Ilijevska[4] & Tatjana Milenkovic[5]
[1]Faculty of Medical Sciences, Goce Delcev University, Stip, Republic of North Macedonia, Clinical Hospital, Internal medicine, Stip, Macedonia; [2]Internal Medicine Center 'Srce', Skopje, Macedonia; [3]Medical Faculty, Ss. Cyril and Methodius University in Skopje, RN Macedonia, University Clinic of Cardiology, Skopje, Macedonia; [4]Medical Faculty, Ss. Cyril and Methodius University in Skopje, RN Macedonia, Skopje, Macedonia; [5]Medical Faculty, Ss. Cyril and Methodius University in Skopje, RN Macedonia, University Clinic of Endocrinology, diabetes and metabolic disorders, Skopje, Macedonia

Background
Treatment of subclinical hypothyroidism (ScH) when TSH is between the upper reference value and 7mU/L, especially in patients younger than 65 years is controversial.
Objectives
To compare the risk factors for atherosclerosis and echocardiographic parameters in patients with ScH1 (4, $2 \leq TSH \leq 7$mU/L) to euthyroid subjects and patients with ScH2 (TSH $>$ 7mU/L).
Material and Methods
Prospectively 54 consecutive patients with newly diagnosed ScH (19 with TSH $\leq$ 7mU/L (ScH1) and 35 with TSH $>$ 7mU/L (ScH2)) started for the first time with levothyroxine therapy, and 30 healthy subjects were recruited from the outpatient department of the University Clinic of Endocrinology in Skopje, R. of N. Macedonia. Laboratory analyses and an echocardiography study were done at the first visit and after 5 months in a euthyroid stage in patients with ScH.
Results
The mean age and TSH value in ScH group were 43.1 ± 12.4y., and 8.71 ± 1, 9mU/L. Compared to healthy controls, patients with ScH1 had a higher mean triglycerides and non-HDL-C ratio (1.52 ± 0.9 vs 1.1 ± 0.6, and 4.3 ± 1.1 vs 3.79 ± 0.9, $P < 0.05$), lower E/A ratio (1.05 ± 0.25 vs 1.26 ± 0.36, $P < 0.05$), higher E/e' sep. ratio (8.56 ± 2.63 vs 6.04 ± 1.64, $P < 0.01$), higher myocardial performance index (MPI) (0.47 ± 0.09 vs 0.43 ± 0.07, $P < 0.05$), lower global longitudinal strain (GLS) (-19.34 $\pm$ 2.0 vs -20.9 $\pm$ 1.7%, $P < 0.05$), and lower S wave derived by tissue Doppler imaging (0.074 ± 0.01 vs 0.092 ± 0.01 m/s, $P < 0.01$). Compared to ScH2, patients with ScH1 have lower GLS but without statistical significance. Levothyroxine treatment (L-T4T) in patients with ScH1 contributed to higher EF (61.9 ± 5.2 vs 63.1 ± 4.6%, $P < 0.05$), lower E/e' sep. ratio (8.56 ± 2.63 vs 7.21 ± 2.23, $P < 0.05$), and lower MPI (0.47 ± 0.09 vs 0.43 ± 0.05%, $P < 0.05$), compared to values in ScH1 patients at baseline. The same parameters were improved in the ScH2 group after L-T4T.
Conclusions
In a small study, patients with ScH1 vs healthy individuals had subtle changes in certain parameters that indicate involvement of diastolic function of the left ventricle in ScH, and these parameters improved after L-T4T.

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hCG-TSHR cross-interaction: a rationale for in hyperemesis gravidarum?

Carmela Perri[1, 2], Clara Lazzaretti[2], Lara Baschieri[2, 3], Lorenzo Marchetti[2], Samantha Sperduti[2, 4], Claudia Fusco[2], Manuela Simoni[2, 4, 5], Giulia Brigante[2, 5] & Livio Casarini[2, 4]
[1]International Ph.D. School in Clinical and Experimental Medicine (CEM), Department of Biomedical, Metabolic and Neural Sciences; [2]Unit of Endocrinology-University of Modena and Reggio Emilia, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy; [3]International Ph.D. School in Clinical and Experimental Medicine (CEM), Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy; [4]Center for Genomic Research, University of Modena and Reggio Emilia, Modena, Italy; [5]Department of Medical Specialties, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy

About 50% of women have nausea and vomiting during pregnancy. In about 35% of women who have these symptoms, nausea and vomiting are clinically significant, worsening their living conditions and consisting in a case of gender gap. The severe form, hyperemesis gravidarum, ranges from 0.3 to 1.0% of cases and is characterized by persistent vomiting, gestational thyrotoxicosis, weight loss of more than 5%, ketonuria, hypokalemia and dehydration, although the pathophysiological mechanism is unknown. Some studies found that increasing human chorionic gonadotropin (hCG) levels overlap the fall of thyroid stimulating hormone (TSH) levels, the increase of thyroid hormone (T3 and T4) levels, and the appearance of hyperemesis gravidarum. Thus, it was hypothesized that hCG binds to TSH receptor (TSHR), perturbing thyroid functions and triggering hyperemesis gravidarum. The aim of this study is to characterize hCG-TSHR cross-interactions *in vitro*, finding a rationale to support the clinical hints. Mechanistic experiments evaluating TSHR-dependent cell signaling pathways were performed in COS7 cell line. Cells were transfected with TSHR-coding plasmid and treated with pM-nM hCG doses before Gs and Gq protein-mediated pathway analysis. Intracellular levels of cyclic adenosine monophosphate (cAMP) and calcium ions (Ca^{2+}) increase were measured by bioluminescence resonance energy transfer (BRET), while inositol monophosphate (IP1) was evaluated by homogeneous time resolved fluorescence (HTRF). Results were compared by Kruskall-Wallis test ($n = 5$; $P < 0.05$) and corrected by Dunn's post-hoc test. Results demonstrated that 50 nM hCG activates the TSHR/Gαq pathway, resulting in intracellular IP1 and Ca^{2+} increase, while no cAMP activation occurred. Results were compared to those obtained from transfected cells treated with the vehicle, in the absence of hCG, which did not result in any Ca^{2+}/IP1 increase. These data support the clinical relationship between hCG and thyroid functions in hyperemesis gravidarum.

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Pathogenic variants of CHEK2 gene in thyroid cancer (TC) patients with a personal and/or familial history of other malignancies

Dominika Kapusta[1], Bartosz Domagała[2], Norbert Kapczyński[1], Marek Kachnic[1], Anna Nogiec[3], Małgorzata Trofimiuk-Muldner[4] & Alicja Hubalewska-Dydejczyk[4]
[1]Jagiellonian University Medical College, Students' Scientific Group of Endocrinology at the Department of Endocrinology, Kraków, Poland; [2]University Hospital in Krakow, Department of Endocrinology, Endocrine Oncology, Nuclear Medicine and Internal Medicine, Kraków, Poland; [3]University Hospital in Krakow, Haematological Diagnostics and Genetcis Unit, Kraków, Poland; [4]Jagiellonian University Medical College, Chair and Department of Endocrinology, Kraków, Poland

CHEK2, located on chromosome 22q, is a tumor suppressor gene. Its' pathogenic variants are often associated with a tumor predisposition syndrome 4, with an increased risk of breast, prostate and colorectal cancers. There are some reports of an increased risk of papillary thyroid cancer (PTC) in carriers of the *CHEK2* pathogenic variants. Current guidelines, however, do not recommend general screening of TC patients. The study assessed the prevalence of pathogenic *CHEK2* variants in patients diagnosed with TC with a personal and/or familial history of other malignancies. The study was a retrospective analysis of a group of 163 patients (138 females and 25 males, mean age of 48.9 years) diagnosed with TC and with a positive personal and/or familial history of other mutation-related malignancies. *CHEK2* (exons 4, 5, 12) were analyzed by Sanger sequencing. If negative – deletions analysis was performed with MLPA. Pathogenic or likely pathogenic *CHEK2* variants were found in 25 patients (21 females and four males; 15, 3% of the study group). There was no significant difference in the mean age at diagnosis in patients positive and negative for *CHEK2* pathogenic variants (46 vs 49 years, respectively; $P = 0.39$). The average number of malignancies in the family members was higher in patients harboring *CHEK2* pathogenic variants; the difference was not statistically significant (1.88 vs 1.63; $P = 0.36$). There was no difference in the personal history (12% vs 29.7%, respectively) or family history (84% vs 83%, respectively) of other malignancies in *CHEK2*- positive and negative PT cancers. There was no significant difference between *CHEK2* positive and negative patients in number of breast, prostate and colon cancers combined in family members. Thyroid cancer was significantly more common in family members of patients with *CHEK2* pathogenic variants (9 cases vs 12 cases in *CHEK2* negative group, $P = 0.006$).
Conclusions
The frequency of *CHEK2* pathogenic variants in a preselected group of PT patients with a personal and/or familial history of other malignancies is similar to that previously reported in the unselected group of Polish patients with PTC. There is currently no convincing data justifying the selective screening for *CHEK2* in such a group. It seems reasonable to advise genetic testing for *CHEK2* pathogenic variants in TC patients with positive family history of thyroid cancer.

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Molecular characterization of circulating tumor cells (CTCs) in sporadic medullary thyroid carcinoma (spMTC) patients

George Simeakis[1], Elina Lagopodi[2], Katerina Saltiki[3], Cristina Romei[4], Raffaele Ciampi[4], Teresa Ramone[4], Pantelis Constantoulakis[5], Maria Alevizaki[3], Rossella Elisei[4], Athina Markoy[2] & Evi Lianidou[2]
[1]401 General Military Hospital of Athens, Endocrine Deptartment Thyroid Cancer Outpatient's Clinic, Athens, Greece; [2]National and Kapodistrian University of Athens, Analysis of Circulating Tumor Cells (ACTC) Lab - Deptartment of Chemistry, Athens, Greece; [3]National and Kapodistrian University of Athens, Athens, Greece; [4]University of Pisa, Deptartment of Clinical and Experimental Medicine, Pisa, Italy; [5]Genotypos S.A., Athens, Greece

Objectives
Distant metastases (DM) and/or biochemical persistent disease (BPD) in MTC, adversely affect disease prognosis. Calcitonin and CEA doubling-times (DTs) are

the main prognostic indicators for disease progression. Liquid biopsy based on CTCs enrichment and characterization seems to be an intriguing non-invasive tool providing information about tumor biology and molecular identity. The aim of this study was the molecular characterization of CTCs in spMTC patients with DM and/or BPD using epithelial, mesenchymal as well as MTC-specific markers.
Methods
Nine spMTC patients (DM:3, BPD:6) carrying somatic mutations in *RET* ($n=7$) and *HRAS* ($n=2$) were included. Peripheral blood (10mL-EDTA) was obtained every six months. Using identical blood draws for 31 PB-samples, CTCs enrichment was directly compared by EpCAM-based positive immunomagnetic selection (EpCam-IMS) and the size-based Parsortix microfluidics system (Angle PLC-UK). The EpCam-IMS was superior in terms of sensitivity since a significantly higher percentage of identical PB-samples was found positive at the gene expression level ($P<0.05$) while specificity was not affected. CTCs gene expression analysis was based on RT-qPCR for epithelial (*CK-8, CK-18, CK-19*), mesenchymal (*Vimentin-VIM*), MTC-specific (*Calcitonin-CALCA*) and chemo-kine-receptor markers (*CXCR4*). Calcitonin and CEA DTs were calculated, and disease status was determined according to the RECIST criteria.
Results
Calcitonin and CEA DTs were >2 years in all but one patient (mean:11.28 and 9.23 years, respectively). No structural disease progression (SDP) was documented except for one patient with *HRAS* mutation (pt-X). Interestingly, Calcitonin and CEA DTs of pt-X were 5.08 and 3.00 years, respectively, although there was an upward trend in CEA while serum Calcitonin levels were significantly elevated one month after SDP. Overexpression of *CALCA* was detected in one sample, related to pt-X, at a time-point set 60-days before marked serum calcitonin increase and 30-days before SDP was documented. *CXCR4* was strongly expressed in 3 samples related to pt-X; *CXCR4* expression was absent only at the final time-point of pt-X, when disease stabilization (biochemical and structural) was documented, after changing systemic treatment. Epithelial markers were not expressed in any of our samples while *VIM* was overexpressed in most of them ($n=20/31$ samples).
Conclusion
EpCAM-IMS seems to be a better method for CTCs isolation in MTC patients with DM and/or BPD. Expression of *VIM* in most of our patients advocates towards an epithelial to mesenchymal transition (EMT) process possibly occurring in progressive MTC. *CALCA* and *CXCR4* expression in CTCs, along with other epithelial and mesenchymal markers, should be studied in larger patients' series and for longer follow-up periods.

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P566

Modified systemic inflammation score for prediction of malignancy in indeterminate thyroid nodules- an effective tool in low-resource settings!

Shreyamsa Manjunath[1] & Praveen Kumar Devarbhavi[2]
[1]Maax Superspecialty Hospitals, Endocrine & Breast Surgery, Shivamogga, India; [2]Maax Superspecialty Hospitals, Endocrinology & Metabolism, Shivamogga, India

Background
About 20% of thyroid-nodules have indeterminate-cytology (IDC), classified as Bethesda categories-III/ IV. They carry varying risks of malignancy (6-18%, 10-40% respectively). Ideal test to determine the risk of malignancy in IDC is unclear. Molecular-profiling has shown promise, but availability & affordability is an issue. We aim to evaluate diagnostic value of modified systemic inflammation score(mSIS) to determine malignancy in IDC.
Methodology
Retrospective study of 79 patients with IDC thyroid-nodules at Maax Super-specialty Hospitals (Shivamogga, India), from January/2022-October/2023. Patients with thyroiditis, active-infections, hematologic, immuno-rheumatological, recurrent thyroid cancer or other co-morbidities excluded. Pre-operative hematology records were exmanined. Albumin(Alb) & lymphocyte-monocyte ratio(LMR) calculated and variables that may affect the development of malignancy studied.
Patients were divided into 3 groups:
mSIS-0: Alb >/= 4.0 g/ dL, LMR </= 3.4
mSIS-1: Alb <4.0 g/ dL OR LMR <3.4
mSIS-2: Alb <4.0 g/ dL, LMR <3.4
Relationship between mSIS and postoperative pathology, and the diagnostic value of mSIS was investigated.
Results
F:M=70:9. Mean age of patients was 35.8 (+/-9.076). The mean nodule size was 3.15 (+/-1.08)cm. 45 (57%) were Bethesda-III and 34 (43%) nodules were Bethesda-IV. Overall, of the 79 patients, 39 had benign nodules (BN), while 40 had malignant nodules(MN). Among MN, 25 were PTC, 5 FTC, 8 FVPTC & 2 were papillary microcarcinoma. There was no significant difference in baseline parameters in either groups. Mean LMR in BN group was 5.023 (+/-1.45), while that in MN group was 3.11 (+/-0.66). With a p-value=0.001, difference was significant. Mean albumin in BN group was 4.61 (+/-0.49) and MN group was 3.63 (+/-0.48). The difference was significant (p-value:0.001). Twenty nodules each in Bethesda-III(45%) and Bethesda-IV (59%) were malignant. 61% in mSIS-1, 92.8% in mSIS-2 were malignant. When risk-stratified for mSIS-1 and mSIS-2 groups, it showed a sensitivity-71.8%, specificity-97.5%, PPV-96.6%, NPV-79.6%.

		mSIS-0 ($n=30$)	mSIS-1 ($n=21$)	mSIS-2 ($n=28$)	p-value
Bethesda-III	Benign	19	5	1	0.001
	Malignant	1(5.2%)	6(54.5%)	13(93%)	
Bethesda-IV	Benign	10	3	1	0.012
	Malignant	0	7(70%)	13(93%)	

Conclusions
mSIS-1 & mSIS-2 groups carry high risk of malignancy. Though not a substitute, mSIS is a cost-effective & easy to perform test when molecular-profiling is not possible. It can help in selecting appropriate patients for surgical management

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P567

Genetic and environmental factors in autoimmune thyroid disease: exploring the associations with selenium levels and novel genetic loci in a latvian cohort

Sabine Upmale-Engela[1, 2], Ieva Kalere[3], Raitis Pečulis[4], Raimonds Rescenko[4], Helena Litvina[4], Tatjana Zake[5], Andrejs Skesters[6], Deniss Gogins[1], Vita Rovite[4] & Ilze Konrade[2, 5]
[1]Riga Stradins University, Faculty of Residency, Rīga, Latvia; [2]Riga East Clinical University Hospital, Department of Endocrinology, Rīga, Latvia; [3]Riga Stradins University, Daculty of Doctoral Studies, Rīga, Latvia; [4]Latvian Biomedical Research and Study centre, Rīga, Latvia; [5]Riga Stradins University, Department of Internal Diseases, Rīga, Latvia; [6]Riga Stradins University, Laboratory of Biochemistry, Rīga, Latvia

Background
The interplay of genetic, immune and environmental factors strongly contributes to the development of autoimmune thyroid disease (AITD) in the form of Graves' disease (GD) and Hashimoto thyroiditis (HT). One of the most studied exogenous factors in the pathogenesis of AITD is selenium, which in the form of selenoproteins strengthens the antioxidative defence system of thyroid cells against superoxide production. Furthermore, it modulates inflammatory cytokine release and autoantibody production.
Purpose
The aim of this study was to assess the association of genetic factors with selenium levels in an adult cohort with HT and GD, and healthy controls from Latvia.
Materials and Methods
A total of 2692 subjects were included in a cross-sectional study. They were divided into 3 groups:GD($n=148$), HT($n=102$), and a control group($n=2442$). Diagnosis of AITD was based on laboratory evaluation. In addition, serum selenium levels were measured and selenium intake score was assessed. The genotypes were determined using genome wide genotyping, imputation was carried out using TOPMed r2 imputation panel, and association analysis was performed with PLINK2.9.
Results
Out of 2692 participants 1684 were female (62.6%), 1008 – male (37.4%). Mean age was 54.3 years (SD 14.0) in the Control Group, 48.4 (SD 15.6) in GD, and 48.3 (SD 15.6) in HT patients. Mean selenium level was 84.4µg/L (SD 31.3), 69.3 µg/L (SD 17.1), and 83.4 µg/L (SD 27.0) in the respective groups. The overall cohort selenium level was below the reference levels(80-125 µg/L) for 62% of the participants (49% controls, 77% GD and 54% HT), with GD patients having significantly lower levels. Additionally, we found three loci associated with GD (LSAMP, HNRNPA3P5, NTN1) on chromosomes 3, 13, 17, respectively, and one locus associated with HT (VAT1L) on chromosome 16. Most of these lead SNPs of significantly associated characteristics have low population minor allele frequencies (<5%) and a fairly large effect (OR>3). Furthermore, one locus rs6567243 was associated with serum selenium >80 µg/L (LINC01544/RNF152/PIGN) on chromosome 18 [OR (95% CI) = 2.46 (1.76-3.43); $P<0.001$]. This SNP has a high minor allele frequency (54.8%) in a Non-Finnish European reference population.
Conclusion
The associations with the novel loci could be attributed to population-specific effects or unknown stratification in our cohort, and further assessment of these hits

are required to explain the relation of genetic traits with studied AITD and other phenotypes. This study was supported by the Latvian Council of Science(Grant No:lzp-2018/2-0059).

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P568

Long-term outcomes in children and young adults with graves' disease

Klara Gewert[1], Ruzan Udumyan[2], Gabriel Sjölin[3], Mikael Lantz[4], Helena Filipsson Nyström[5], Selwan Khamisi[6], Mats Holmberg[7], Jan Calissendorff[8], Bengt Hallengren[4], Göran Wallin[3] & Tereza Planck[4]
[1]Lund University, Department of Clinical Sciences, Lund, Sweden; [2]Örebro University, Clinical Epidemiology and Biostatistics, Department of Medical Sciences, Faculty of Medicine and Health, Örebro, Sweden; [3]Örebro University, Faculty of Medicine and Health, Örebro, Sweden; [4]Lund University, Department of Clinical Sciences, Lund, Sweden; [5]University of Gothenburg, Sahlgrenska Academy, Department of Medicine, Gothenburg, Sweden; [6]Uppsala University, Department of Medical Sciences, Uppsala, Sweden; [7]Karolinska Institutet, Department of Medicine, Huddinge, Stockholm, Sweden; [8]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden

Introduction
Graves' disease (GD) can negatively affect the quality of life. Research on GD in childhood, accounting for 1-5% of cases, has so far predominantly focused on treatment results. There is limited knowledge about association with other diseases and long-term psychosocial effects.
Aims
We aimed to compare disease burden and psychosocial outcomes between childhood/young adult GD patients and unexposed population controls.
Methods
This was a retrospective, matched cohort study using prospectively collected data from medical records and multiple Swedish registers. GD patients aged <21 years ($n=87$, of whom 55 were <18 years) were selected from an incidence study cohort including patients with newly diagnosed hyperthyroidism in 2003-2005 across 13 Swedish centres ($n=2916$). Each GD patient was matched through Statistics Sweden with ten population controls without GD ($n=29160$) based on age, sex, and county. The matched cohort was followed until December 31, 2019. Information on primary diagnoses, hospitalizations, education, sick leave, disability pension, and number of own children was collected. Results of a 10-year follow-up analysis are being presented here.
Results
Patients with GD exhibited a significantly higher incidence of 'endocrine, nutritional, and metabolic diseases' (ICD-10 E00-E90, excluding E05.0) with a hazard ratio (HR) of 19.7 ([10.7, 36.6], $P<0.001$) and 'diseases of the digestive system diseases' (ICD-10 K00-K95) with a HR of 7.39 ([1.7, 33.0], $P=0.009$) compared to matched population controls. Additionally, patients with GD had an increased risk of having two or more primary diagnoses besides GD (relative risk [RR]$=4.4$ [2.4, 7.8], $P<0.001$), more than three days of hospitalization (RR$=$ 5.5 [2.7, 10.9], $P<0.001$), over 60 consecutive days of sick leave (RR$=2.1$ [1.1, 3.9], $P=0.016$), and receiving disability pension (RR$=4.2$ [2.3, 7.8], $P<0.001$) compared to controls. Furthermore, patients with GD were more likely to only have completed compulsory education by the age of 30 (RR$=2.5$ [1.1, 5.8], $P=0.029$). No statistically significant differences were observed regarding other ICD categories or number of own children.
Conclusion
In conclusion, childhood/early adulthood GD leads to increased long-term morbidity, healthcare needs, and socioeconomic challenges, marked by more hospitalizations, sick leaves, disability pensions, and lower educational levels. These results highlight GD's status as a chronic condition, emphasizing the need for more research to reduce its long-term effects.

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P569

Thyroid core-needle biopsy. first experience in romania. 281 cases with only 1% non-diagnostic results

Emin Mammadov[1], Dana Terzea[2] & Mihai Ciprian Stoicea[1]
[1]Regina Maria Private Healthcare Network, Bucureţi, Romania; [2]Onco Team Diagnostic, Bucureţi, Romania

Background
There are two types of thyroid nodule biopsy: fine-needle aspiration (FNAB) and core-needle (CNB). Multiple studies mainly from Eastern Asia demonstrate safety and efficacy of CNB, however it is very rarely used in Europe.
Methods
Retrospective analysis of the first 281 CNBs performed in Romania, including 8 lymph nodes and 3 thyroid bed lesions. We used the Korean Thyroid Association reporting system (KTA-CNB) for histology reports.
Results
Of 281 CNBs, there were only 3 non-diagnostic results (1.1%), 21 category III results (7.5%) and 22 category IV results (7.8%). Categories IIIa and IVa were almost exclusively benign ($n=17$, of them 6 underwent surgery, 5 were confirmed benign, 1 NIFTP). Out of 7 patients with category IVc results, 6 underwent surgery, 4 of them had malignant results postoperatively. All category V ($n=5$) and VI ($n=18$) results were confirmed to be malignant on postoperative histology. Two of thyroid bed lesions were malignant, one benign (all confirmed on postoperative histology). One of 8 lymph nodes was malignant. There was one case of Hurthle cell carcinoma diagnosed preoperatively based on invasion observed at one of the passes, and one case of the lung adenocarcinoma metastasis diagnosed based on IHC. There were 2 cases of papillary microcarcinoma with confirmed extrathyroidal extension which lead to more curative surgical approach, and patients could avoid second surgery or radioiodine therapy. We performed on average 2.2 passes per lesion. There were no major complications, some minor adverse events were limited to bruising, perithyroidal hematoma and pain during or after procedure. Two patients had intrathyroidal hematoma.
Conclusion
The CNB is a safe and reliable diagnostic procedure for thyroid nodules, thyroid bed lesions and cervical lymph nodes. It offers very low chance of non-diagnostic results, lower chance of inconclusive results with a better stratification of risk between different subcategories (III a-d, IV a-c), among them the highest chance of malignancy was observed in category IVc in our study. CNB is a procedure which improves patient experience by reducing the number of procedures needed to make a clinical decision. It also offers possibility to use IHC and observe extrathyroidal extension.

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P570

Impact of the introduction of minimally invasive treatments of the thyroid (MITT) for benign thyroid nodules in an italian hospital: a cost-minimization analysis

Roberto Novizio[1], Martina Cicia[1] & Giampaolo Papi[2]
[1]Catholic University of the Sacred Heart, Rome, Italy; [2]Azienda Usl Modena, Italy

Background
Thyroid nodules prevalence is high in adult population, approaching 60% in women and older people. Most thyroid nodules are benign and asymptomatic. However, a not negligible part of them causes compressive symptoms and/or cosmetic concerns and need treatment. In the last decades, minimally invasive treatments of the thyroid (MITT) have been proposed in clinical practice as reliable cost-effective alternative to surgery in patients with symptomatic benign thyroid nodules (SBTNs).
Aim
Cost-minimization analysis comparing direct, indirect and intangible costs of radiofrequency (RFA) and laser thermal ablation (LTA) with traditional surgery in patients with SBTNs.
Methods
Data of patients treated by MITT for SBTNs from October 1st 2019 to September 30th 2022 in a single Italian Center were analyzed. Costs were compared to those of traditional surgery reported in the 2022 Associazione Medici Endocrinologi Guidelines on the Management of SBTNs.
Results
157 MITT of SBTNs were performed in 148 patients, 114 females and 34 males (mean age: 59 yrs). Before MITT, mean thyroid nodule volume was 19 ml; 1 year after MITT, volume reduction rate $>50\%$ and symptom relief were achieved in 89% and 93% of patients, respectively. No major complications occurred. Adding up pre-operative, operative and post-operative costs, total direct costs per single procedure are the following: 1361.43 € for LTA, using one optic fiber; 1761.43 € for LTA, using two optic fibers; 1968.53 € for RFA; 3338.39 € for hemithyroidectomy plus isthmectomy; 4034.99 € for total thyroidectomy. Surgery was impactful on direct-i.e., preoperative, operative and postoperative-costs, due to longer operating room occupation time and hospital stay. Overall, a total saving for the Italian National Health Service of 285, 377.15 € has been obtained treating the 148 patients by MITT instead of surgery. MITT was advantageous also for indirect costs-i.e., those related to "loss of productivity" caused by time off work-, for both the self-employed workers and the Government, the latter saving 53, 838.50 €. Intangible costs, related to patients' quality of life-e.g., residual surgical scar, convalescence, and life-long intake of L-Thyroxine replacement therapy-were all in favor of MITT.

Conclusion
This real-life cost-minimization analysis demonstrates that LTA and RFA are safe and cost-effective procedures for the treatment of SBTNs. In our 3 years experience, adding the savings of 285, 377.15 € for direct costs to those of 53.838, 50 € for indirect costs, in total 339, 215.65 € were saved. The saving concern patients, the National Health System and the Government.

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P571

Enhanced predictive validity of integrative models for refractory hyperthyroidism considering baseline and early therapy characteristics: a prospective cohort study

Xinpan Wang[1], Tiantian Li[1], Yue Li[1], Qiuyi Wang[1], Yun Cai[1], Zhixiao Wang[1], Yun Shi[1], Tao Yang[1] & Xuqin Zheng[1]
[1]The First Affiliated Hospital of Nanjing Medical University

Background
A subset of Graves' disease (GD) patients develops refractory hyperthyroidism, posing challenges in treatment decisions. The predictive value of baseline characteristics and early therapy indicators in identifying high risk individuals is an area worth exploration.
Methods
A prospective cohort study (2018-2022) involved 597 newly diagnosed adult GD patients undergoing methimazole (MMI) treatment. Baseline characteristics and 3-month therapy parameters were utilized to develop predictive models for refractory GD, considering antithyroid drug (ATD) dosage regimens.
Results
Among 346 patients analyzed, 49.7% developed ATD-refractory GD, marked by recurrence and sustained Thyrotropin Receptor Antibody (TRAb) positivity. Key baseline factors, including younger age, Graves' Ophthalmopathy (GO), larger goiter size, and higher initial free triiodothyronine (fT3), free thyroxine (fT4), and TRAb levels, were all significantly associated with an increased risk of refractory GD, forming the baseline predictive model (Model A). Subsequent analysis based on MMI cumulative dosage at 3 months resulted in two subgroups: a high cumulative dosage group (average $\geq$1 mg/d) and a medium-low cumulative dosage group (average $<$1 mg/d). Absolute values, percentage changes, and cumulative values of thyroid function and autoantibodies at 3 months were analyzed. Two combined predictive models, Model B (high cumulative dosage) and Model C (medium-low cumulative dosage), were developed based on stepwise regression and multivariate analysis, incorporating additional 3-month parameters beyond the baseline. In both groups, these combined models outperformed the baseline model in terms of discriminative ability (measured by *AUC*), concordance with actual outcomes (66.2% comprehensive improvement), and risk classification accuracy (especially for Class I and II patients with baseline predictive risk $<$71%). The reliability of the above models was confirmed through additional analysis using random forests. This study also explored ATD dosage regimens, revealing differences in refractory outcomes between predicted risk groups. However, adjusting MMI dosage after early risk assessment did not conclusively improve the prognosis of refractory GD.
Conclusion
Integrating baseline and early therapy characteristics enhances the predictive capability for refractory GD outcomes. The study provides valuable insights into refining risk assessment and guiding personalized treatment decisions for GD patients.

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P572

Regulatory T and B cells in autoimmune thyroiditis

Maria Kazakova[1], Ekaterina Troshina[2] & Ilya Dyakov[3]
[1]Endocrinology Research Center, Moscow; [2]Endocrinology Research Center, Moscow; [3]Mechnikov's research institute of vaccine and sera, Moscow

Introduction
Hashimoto's thyroiditis (HT) is multifactorial disease, caused by a complex interplay of genetic, hormonal, and environmental influences that provoke the development of inappropriate immune responses against thyroid on multiple levels and the initiation of a long-standing autoimmune reaction. Interaction between cellular and humoral immunity is base of HT's pathogenesis. Our research focuses on the functional activity and the quantity of T regulatory and B regulatory lymphocytes in blood from patients, who have features of HT. A more accurate understanding of role of regulatory cells in the immunotolerance disorders could be a base for the development of new prognostic markers and therapeutic strategies in the treatment of patients with HT.
Main part
We analyzed amount and functional activity subsets of regulatory T and B cells (CD3hiIL-10hi and CD19hiCD38hiCD24hi) in subjects's blood: patient with isolated hypothyroidism in the outcome of HT (n=23), carriers of antibodies to thyroid tissues (n= 18), patients with HT as a part of autoimmune polyglandular syndrome (APS) (n= 20), healthy donors (HD) (n=13). We found significant differences in the amount of regulatory cells (CD19hiCD38hiD24hi B reg) during *in vitro* incubation without additional activation in groups carriers of antibodies (1.75% vs 3.0%; P=0.0003) and in groups patients with HT as part of APS (1.5% vs 3.0% P=0.0002) as compared with HD. A decrease in the induction of regulatory B cells was found only in the group of patients with HT as part of APS (2.3%, P=0.04)
Conclusion
Our research has shown that carriers of autoantibodies and patients with HT as part of APS have reduced spontaneous activation of regulatory B cells *in vitro* and the latter has activation-induced induction of regulatory B cells in the comparison with HD. The quantity and induction of IL-10-producing T cells in the compared groups weren't significantly differ. The study is supported by the Russian Science Foundation, Grant No.22-15-00135

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P573

Focal thyroid incidentalomas in 18F-PSMA PET/CT – a retrospective analysis of incidence and clinical significance

Emilia Niedziela[1, 2], Łukasz Niedziela[1, 3], Iwona Palyga[1, 2], Janusz Kopczyński[4], Jarosław Jaskulski[1, 3], Janusz Braziewicz[5] & Aldona Kowalska[1, 2]
[1]Collegium Medicum, Jan Kochanowski University, Kielce; [2]Holy Cross Cancer Center, Department of Endocrinology, Kielce; [3]Holy Cross Cancer Center, Department of Urology, Kielce; [4]Holy Cross Cancer Center, Department of Pathology, Kielce; [5]Holy Cross Cancer Center, Department of Nuclear Medicine, Kielce

Introduction
^{18}F- Prostate-Specific Membrane Antigen Positron Emission Tomography/Computed Tomography (^{18}F-PSMA PET/CT) is currently used in the evaluation of prostate cancer. Due to increased expression of PSMA in the neovascular endothelial cells of malignant lesions other than prostate cancer, PSMA PET/CT has become of interest to researchers in the management of thyroid cancer. The goal of this study was to evaluate the incidence and clinical significance of PSMA thyroid incidentaloma (PTI) detected by ^{18}F-PSMA PET/CT scans.
Methodology
We retrospectively analyzed the clinical data of 23 patients with prostate cancer, who underwent endocrine follow-up for increased uptake in at least one focal thyroid lesion on ^{18}F-PSMA PET/CT performed between 2018 and 2023. The indications for ^{18}F-PSMA PET/CT were primary staging or diagnosis of biochemical recurrence after radical treatment of prostate cancer. We established our outcomes on the ^{18}F-PSMA PET/CT reports, indications for fine needle aspiration biopsy (FNAB) according to EU-TIRADS, and cytological results according to the Bethesda Thyroid Cytology Classification. Only patients with cytological verification of PTI were included into final analysis.
Results
Data of 22 patients with 23 PTI were analyzed. The median SUVmax of PTI on ^{18}F-PSMA PET/CT scans was 5.66 (range 2.3 - 48.39). In seven cases (31.8%), there were no indications for FNAB according to EU-TIRADS. Those patients were referred to FNAB only due to increased uptake in thyroid lesions on PSMA PET/CT. The results of FNAB were as follows: 19 (82.6%) benign; 2 (8.7%) atypia of undetermined significance; 1 (4.3%) follicular neoplasm; 1 (4.3%) malignant. The only malignant lesion was diagnosed as papillary thyroid cancer on cytology. The SUVmax of corresponding lesion on PSMA PET/CT was 3.6, and US revealed no indications for FNAB with EU-TIRADS 4 and size of the lesion of 8 mm. Due to the low stage of the tumor, this patient remains on active surveillance. Any other lesion that was subjected to further follow-up [median 5 months (0-42)] did not become clinically significant.
Conclusions
^{18}F-PSMA PET/CT seems not to be a useful modality for the differentiation of benign and malignant thyroid lesions. Standard methods of evaluating thyroid nodules are sufficient for further diagnosis of PTI, without the need to verify all lesions on FNAB. The only detected thyroid cancer in our study was a lesion with an indolent course. Further research on larger cohort is necessary to explore the role of PSMA PET/CT in management of thyroid nodules.

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P574

Thyrotoxicosis in metastatic choreocarcinoma

Vidya Nair[1], Rob Marwood[1] & Cecil Eboh[1]
[1]St Richards Hospital, Endocrinology and Diabetes, Chichester, United Kingdom

Introduction
Choriocarcinoma is a rare gynaecological cancer arising from the trophoblastic epithelium of the placenta. HCG induced thyrotoxicosis is a rare but recognised paraneoplastic phenomenon. The association of high BHCG levels and thyrotoxic state is thought to be secondary to similarities in the structure between HCG and pituitary hormones including TSH which share the same alpha unit and enables HCG to activate the TSH receptor at high levels. Kato et al in 2004 reported that the incidence of hyperthyroidism in choriocarcinoma is around 57%. Choriocarcinomas are highly susceptible to treatment with a cure rate of >90% even in metastatic gestational choriocarcinoma.
Case report
A 41-year-old female gravida5 para1, with a history of 4 previous first trimester miscarriages, positive IgM anticardiolipin antibody13 presented to A&E 4 months postnatal with chest pain, palpitations, breathlessness. Blood tests showed B-HCG level > 225, 000, d-dimer -1584, TSH < 0.03 and Free T4-29.1. She was started on carbimazole, propranolol for thyrotoxicosis. Thyroid antibodies were negative. Due to high BHCG values, transabdominal ultrasound was requested which showed no active pregnancy but an increased volume in left ovary. A CTPA with abdominal and pelvic views were negative for a PE but suspicious for pulmonary metastasis and a large left adnexal mass which was confirmed in MRI. The patient was diagnosed with choriocarcinoma, and B-HCG induced thyrotoxicosis and anti-thyroid medication was stopped and patient was commenced on chemotherapy. Her thyrotoxic symptoms were managed symptomatically with propranolol. Following treatment of the Choriocarcinoma, the thyrotoxicosis resolved with normalization of thyroid function tests. (table 1 below)

		post chemo
TSH(mu/L)	<0.03	0.52
Free T4(pmol/L)	29.1	11.9

Discussion
There have been studies in men with germ cell tumours producing HCG, women with choriocarcinoma, animals showing an association between high levels of HCG and hyperthyroidism. The primary treatment for this phenomenon is chemotherapy with symptomatic control for hyperthyroidism. It is important to note that initially the chemotherapy treatment may produce an initial surge in HCG levels, and it is important to monitor these patients for signs of thyroid storm, however, the thyroid function will usually normalise if the choriocarcinoma is susceptible to treatment.
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P575

Endoscopic ultrasound guided fine needle aspiration (EUS-FNA) with aspirate parathormone (PTH): a case report and review of the literature

Matteo Parolin[1], Antonino Caruso[2], Paola Sartorato[1], Pietro Fusaroli[3] & Ernesto Pasquale De Menis[1]
[1]Ospedale Ca' Foncello, Medicina Generale 2, Italy; [2]Ospedale Ca' Foncello, Gastroenterologia, Italy; [3]Ospedale S. Maria della Scalett, UOC di Gastroenterologia ed Endoscopia Digestiva, Bologna, Italy

Introduction
The prevalence of primary hyperparathyroidism is increasing owing to the more the routinely measurements of serum calcium. A single benign para-thyroid adenoma is the most frequent cause of sporadic PHPT. Primary hyperparathyroidism can also be due to ectopic mediastinal parathyroid adenoma in 11-25% of patients, more frequently involving inferior parathyroid translated in anterior mediastinum. In general to detect ectopic adenoma recent guidelines recommend the use of high resolution neck ultrasound, technetium-99 m-sestamibi subtraction scintigraphy, and contrast-enhanced four-dimensional (4D) computed tomography (CT). The use of endoscopic ultrasound (EUS) is reported in some case reports in literature and some cases in has been integrated with fine-needle aspiration and PTH sampling in the eluate.
Case report
A 68-year old female was admitted in our department for a spontaneous neck hematoma. She was overweight and had parossistic atrial fibrillation (she was not taking anticoagulative drugs), and dyslipidaemia. Laboratory exams revealed primary hyperparathyroidism with elevated total serum calcium 10, 9 mg/dl (8, 8-10, 1), decreased serum phosphorus 2, 1 mg/dl (2, 5-4, 5) and high parathormone 150 pg/mL (12-72). Neck ultrasound did not show images compatible with parathyroid, but a multinodular goitre. Computed tomography of neck revealed complex vascular anatomy of the thyroidal vascularization and a fusiform nodule between posterior side of right thyroid lobe and paraesophageal region, which was compatible with parathyroid gland (axial diameters were 18*12 mm). A double-tracheant scintigraphy revealed a 15 mm nodule in right posterolateral paraesophageal compatible with ectopic parathyroid. A echoendoscopy detected a dysomogeneus, hyperechoic and elonged lesion was noted, with iperenhancement using ultrasonographic contrast media (CEUS). FNAB was performed without complications. The cytological exam revealed minute and rare non-atypical epithelial aggregates, results at PTH + and TTF1 – at immunophenotypic investigations. PTH dosage on the washing liquid was > 2500 pg/ml, diagnostic of ectopic parathyroid.
Conclusions
In selected patients with primary hyperparathyroidism, second and third level diagnostic procedures as in this case could be useful to be sure of diagnosis, in particular if pluricomorbid and frail patients must receive parathyroidectomy with major surgery could include potential severe complications.
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P576

Radiofrequency ablation is an effective treatment for bethesda iii nodules without genetic alterations

Laura Fugazzola[1], Maurilio Deandrea[2], Stefano Borgato[1], Marco Dell'Acqua[1], Francesca Retta[2], Alberto Mormile[2], Chiara Carzaniga[1], Giacomo Gazzano[1], Gabriele Pogliaghi[1], Marina Muzza[1] & Luca Persani[1]
[1]Italian Auxological Institute San Luca Hospital, Endocrinology, Milano, Italy; [2]Mauriziano Umberto Hospital, Torino, Italy

Radiofrequency ablation (RFA) is effective in the treatment of thyroid nodules, leading to a 50-90% reduction with respect to baseline. Current guidelines indicate the need for a benign cytology prior to RFA, though, on the other side, this procedure is also successfully used for the treatment of papillary microcarcinomas. No specific indications are available for nodules with an indeterminate cytology (Bethesda III and IV). Aim of the present study was to evaluate the efficacy of RFA in Bethesda III nodules without genetic alterations as verified by means of a customized panel based on matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, and previously set up for the simultaneous identification of 13 known hotspot mutations and six recurrent fusion genes. We treated 33 patients (mean delivered energy 1069 ± 1201 Joules/ml of basal volume) with Bethesda III cytology, EU-TIRADS 3-4, and negative genetic panel. The mean basal nodular volume was 17.3 ± 10.7 ml. Considering the whole series, the mean volume reduction rate (VRR) was 36.8 ± 16.5% at 1 month, 59.9 ± 15.5% at 6 months and 62 ± 15.7% at 1-year follow-up. The sub-analysis done in patients with 1 and 2 years follow up data available, confirmed a progressive nodular volume decrease. At all-time points, the rate of reduction was statistically significant ($P < 0.0001$), without significant correlation between the VRR and the basal volume. Neither cytological changes nor complications were observed after the procedure. In conclusion, we show for the first time that one RFA session is extremely effective in the volume reduction of Bethesda III nodules whose very low risk of malignancy has been established on the bases of the lack of the most common oncogene variations. The procedure is applicable for indeterminate nodules of any size, treated with an appropriate energy per volume and the volume reduction is maintained at 1-2 years after treatment, but a longer follow up is needed to identify a further reduction or a possible progressive regrowth.
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P577

Using routine laboratory results to establish valid thyroid reference values

Finn Erik Aas[1], Oskar Kelp[1], Magnus Husøy[2], Per Medboe Thorsby[1] & Alexander Westbye[1]
[1]Hormone Laboratory, Dep. og Medical Biochemistry, Oslo University Hopital, Oslo, Norway; [2]Lillehammer Hospital, Lillehammer, Norway

Abstract P577
LRL: lower reference limit, URL: upper reference limit.

Analyte	LRL / URL (2.5 / 97.5 percentiles)	Direct method	Indirect methods								
		HUNT4	refineR			RefLim			Non-parametric		
			IH	HLc	HLu	IH	HLc	HLu	IH	HLc	HLu
TSH mIU/l	LRL	0.44	0.45	0.30	0.33	0.48	0.54	0.40	0.39	0.31	*0.01*
	URL	3.04	3.0	2.7	4.2	3.3	3.6	4.3	3.3	4.1	*5.6*
FT4 pmol/l	LRL	9.8	9.7	9.8	9.2	9.5	9.3	9.5	9.7	9.4	*9.1*
	URL	14	14.7	15.0	15.5	14.3	14.8	16.2	15.1	15.6	*21.0*
FT3 pmol/l	LRL	3.5	3.4	3.2	3.1	3.4	3.2	3.2	3.3	3.1	*2.9*
	URL	5.3	5.5	5.3	5.3	5.5	5.1	5.2	5.7	5.3	*10*
TT4 nmol/l	LRL	66	-	67	64	-	73	65	-	53	*53*
	URL	117	-	128	146	-	128	145	-	166	*172*
TT3 nmol/l	LRL	1.1	-	1.1	1.0	-	1.0	0.95	-	0.97	*0.81*
	URL	2.1	-	1.9	1.9	-	2.2	2.1	-	3.2	*3.2*

Background
Indirect methods is developed to estimate reference limits from patient data, i.e. data from a mix of sick and healthy people. The indirect methods use a large number of results. A prerequisite for the methods to work satisfactorily is that the proportion of patients is not too large (typically $<$ 20-30%).
Methods
We used direct and indirect methods for estimating reference limits for TSH, FT4, FT3, total T4 and total T3. All analysis were done with Abbot Alinity. We used was refineR and RefLim in addition to the simple non-parametric percentile method. All patients who have had thyroid parameters analyzed at the Hormone Laboratory in Oslo from December 2021 to June 2023 was included ($n=21\,539$).
Results
We analyzed the thyroid parameters by direct method form 140 healthy participants from the population based HUNT4 study in Norway. In the indirect method we first used our entire database (Hlu, n = 21 539). Then a selection were we excluded any sample form hospitals, or were TSH $<$ 0.1mIU/l and $>$ 10, or positive on anti-TPO or TRAb and only the first measurement of a patient were included (HLc, n = 3 366). To validate we included patient sample for the county of Innlandet, Norway, only analyzing samples received from GPs and only one sample from each patient (IH, n = 49 433).
Conclusion
In our Norwegian population it seems like the direct method using healthy individuals form a population based study, is not superior to using indirect methods form our own routine laboratory database.

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P578

12-month outcome with microwave ablation in benign thyroid nodules

Kelly Villa[1], Maite Rodrigo[1], Mattia Squarcia[1], Felicia A Hanzu[1], Aida Orois[1], Maria Claro[1], Karen Andrea Castillo Arias[1] & Mireia Mora[1]
[1]Hospital Clinic Barcelona, Barcelona, Barcelona, Spain

Most thyroid nodules are benign and majority do not require treatment, except for those large nodules that cause symptoms (compression, hormonal dysfunction and/or esthetic problems). Microwave ablation (MWA) is an attractive therapeutic option because it is minimally invasive, relatively inexpensive, capable of providing coagulative necrosis, and has a short treatment time. In the following, we present the experience of our hospital.
Objective
To evaluate the volumen (V) reduction (VRR: (initial V - final V)/(initial V $\times$ 100)) and the evolution of symptoms of thyroid nodules treated with AMO.
Material and methods
Prospective study of 20 patients (17 females, 3 males) with 22 benign, euthyroid thyroid nodules with mild to moderate compressive symptoms, treated with ultrasound-guided AMO, between 2021 and 2023, who were followed for 12 months (evaluated at month 1, 3, 6 and 12 after AMO). Success was defined as VVR greater than 50%.
Results
Twenty patients were evaluated, mean age 64 years, 22 nodules (13 solid and 9 mixed). The VRR during follow-up at 1, 3, 6 and 12 months was 12%, 55%, 56% and 69% respectively. Mean initial volume was 27 mL $\pm$ 19, and 10 mL $\pm$ 11.92 at 12 months. Ablation time was 657 sec $\pm$ 369 sec, power 30 W, mean energy used was 1219 $\pm$ 1194 (J/mL). Symptomatology remission was present in 18 patients. RRV $>$ 50% was observed at 1, 3, 6 and 12 months in 27%, 56%, 64% and 75% of the nodules, respectively.
Conclusions
Our study suggests that ultrasound-guided AMO is an effective and safe procedure for the treatment of thyroid nodules, with remission of symptoms at 12 months in 90% of patients and showing a successful volume reduction (VRR $>$ 50%) from the first control, reaching 75% at 12 months.

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P579

Is autoimmune thyroiditis in females with ehlers–danlos syndrome associated with lower bone density?

Babula Emilia[1, 2], Żuk-Łapan Aleksandra[1, 2], Poprawa Iga[1, 2], Podstawka Jakub[1, 2], Domański Jan[1, 2], Julia Latocha[1, 2], Zuzanna Szymańska[1, 2], Bernadetta Kaluza[1, 2] & Franek Edward[1, 2, 3]
[1]National Medical Institute of the Ministry of the Interior and Administration, Department of Internal Medicine, Endocrinology and Diabetology, Warsaw, Poland; [2]National Medical Institute of the Ministry of the Interior and Administration, Students Scientific Group of the Medical University of Warsaw at the Department of Internal Medicine, Endocrinology and Diabetology, Warsaw, Poland; [3]Mossakowski Medical Research Centre Polish Academy of Sciences, Warsaw, Poland, Department of Human Epigenetics, Warsaw, Poland

Background
Collagen, whose biosynthesis is regulated by thyroid hormones, is the most abundant connective tissue protein. Ehlers–Danlos syndrome alters collagen structure, which may affect bone mineral density (BMD). The purpose of this study was to assess the effect of autoimmune thyroiditis on BMD in females with Ehlers–Danlos syndrome.
Material and methods
The study involved a prospective assessment of 30 female patients, aged 20–53 years, with either hypermobile or classical Ehlers–Danlos syndrome. All patients underwent thyroid function tests, calcium and phosphorus metabolism tests, and BMD scans of the femoral neck and lumbar spine. Patients were divided into two groups: those with no autoimmune thyroiditis (group 1, n = 24) and those with autoimmune thyroiditis (group 2, n = 6).
Results
Study groups 1 and 2 showed no significant differences in terms of hypothyroidism ($n=4$ (16.7%) vs n = 2 (33.3%), $P=0.39$), thyroid-stimulating hormone (TSH) levels (2.06 $\pm$ 1.16 µIU/ml vs 2.35 $\pm$ 2.16 µIU/ml, $P=0.59$), free triiodothyronine levels (3.43 $\pm$ 0.64 pg/ml vs 3.19 $\pm$ 0.72 pg/ml, $P=0.42$), or free thyroxine levels (1.35 $\pm$ 0.25 ng/dl vs 1.34 $\pm$ 0.12 ng/dl, $P=0.44$), respectively. Moreover, no significant differences were noted in bone turnover markers, such as bone-specific alkaline phosphatase (9.89 $\pm$ 2.88 µg/L vs 8.1 $\pm$ 0.81 µg/L, $P=0.19$), beta-crossLaps (0.411 $\pm$ 0.19 ng/ml vs 0.3 $\pm$ 0.15 ng/ml, $P=0.2$), and osteocalcin (21.32 $\pm$ 7.82 ng/ml vs 17.62 $\pm$ 4.76 ng/ml, $P=0.34$), or in the BMD of the femoral neck (0.93 $\pm$ 0.12 vs 0.96 $\pm$ 0.15, $P=0.59$) or lumbar spine (0.95 $\pm$ 0.12 vs 0.94 $\pm$ 0.17, $P=0.98$). Furthermore, no significant correlation was observed between the levels of TSH, anti-thyroperoxidase autoantibodies, or anti-thyroglobulin antibodies on one hand and femoral neck BMD on the other (r_s 0.09, $P=0.61$; r_s 0.1, $P=0.59$; and r_s -0.03, $P=0.89$, respectively) or between any of those three markers and lumbar BMD (r_s 0.11, $P=0.56$; r_s 0.02, $P=0.93$; and r_s -0.03, $P=0.84$).
Conclusions
This study showed no relationship between autoimmune thyroiditis, bone turnover markers, and the BMD of either the femoral neck or the lumbar spine in women with Ehlers–Danlos syndrome.

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P580

Correlation between the expected risk of malignancy according to FNA and the actual percentage of malignancy found on pathological anatomy in thyroidectomies and hemithyroidectomies

Aurelio López Guerra[1], Isabel Losada Gata[1], Mónica Gómez-Gordo Hernanz[1], Gloria Collado González[1], Marta Pérez Noguero[1], Ignacio Jiménez Hernando[1], Blanca Farache Suberviola[1], Amaya Morales Jaurrieta[1], Laura Gonzalez Fernandez[1] & Alberto García Piorno[1]
[1]Gregorio Marañón General University Hospital, Madrid, Spain

Introduction
The Bethesda system gives each Fine Needle Aspiration (FNA) category a risk of malignancy (B1: 5-10%, B2: 0-3%, B3: 10-30%, B4: 25-40%, B5: 50-75%, B6: 97-99%). Based on this risk, therapeutic decisions are made that influence the patient's life. It is important to check whether the percentage of malignancy obtained in our daily clinical practice is similar to that expected according to this system.
Aim
To check whether the percentage of malignancy in the FNA performed in our hospital is similar to that expected according to the Bethesda system for each of its different categories.
Methods
The pathological anatomy service was asked for the list of thyroidectomies and hemithyroidectomies of thyroidectomies and hemithyroidectomies performed in the hospital from 2018 to 2021. The interventions that had FNA prior to surgery were analyzed, noting the Bethesda category of each one. The anatomopathological analysis of the surgical specimens was evaluated, differentiating between positive and negative for malignancy. Among those positive for malignancy, a subsequent adjustment was made, excluding those specimens that had been positive for malignancy because they presented a finding of incidental microcarcinoma (IM) in an area of the thyroid other than the one corresponding to the previous FNA.
Results
A total of 569 thyroid samples were received from thyroidectomies and hemithyroidectomies performed at the Hospital GregoRio Marañón. Preoperative FNA was performed in 450 procedures, distributed across Bethesda categories as follows: B1 (6.2%; n = 28), B2 (45.7%; n = 206), B3 (15.5%; n = 70), B4 (8.2%; n = 37), B5 (11.5%; n = 52), B6 (12.6%; n = 57). Of these, 164 were positive for malignancy. Malignancy percentages on pathologic anatomy within each FNA category were: B1 (28, 5%; $n = 8$), B2 (9.2%; n = 19), B3 (30%; n = 21), B4 (37.8%; n = 14), B5 (86.5%; $n = 45$), B6 (100%; n = 57). Excluding incidental microcarcinomas detected in the sample not corresponding to the evaluated nodule, the following percentages were obtained: B1 25%, B2 3.4%, B3 21.4, B4 35%, B5 84.6%, B6 100%.
Conclusions
The observed malignancy rate in our setting, after excluding non-concordant incidental microcarcinomas, aligns with Bethesda system expectations for categories B3, B4, and B6. The malignancy rate was notably higher in category B1 (25% vs 5-10%) and category B5 (84.61% vs 50-75%), with category B2 slightly exceeding the upper limit (3.4% vs 0-3%).

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P581

Thyroid function might decrease after adjuvant chemotherapy in postmenopausal women with early breast cancer

Djordje Marina[1], Kristian Buch-Larsen[2], Linn Gillberg[3], Mads Andersen[4], Michael Andersson[1], Åse Krogh Rasmussen[1] & Peter Schwarz[1]
[1]Rigshopitalet, Department of Endocrinology, Copenhagen, Denmark; [2]Rigshospitalet, Department of Endocrinology, København, Denmark; [3]University of Copenhagen Panum and Mærsk Tower, Department of Biomedical Sciences, København, Denmark; [4]Rigshospitalet, Department of Oncology, Centre for Cancer and Organ Diseases, København, Denmark

Objective
Adjuvant chemotherapy is often indicated in patients diagnosed with early breast cancer. Weight gain is one of the observed side effects of both chemotherapy and other cancer treatments, however, the mechanism is not well-described. In this study, we aimed to assess thyroid function before- and after the course of chemotherapy for early breast cancer.
Methods
This study is a 5-year prospective cohort study of patients diagnosed with early breast cancer. The main outcome was the thyroid function and body weight before and after completing chemotherapy. Secondary outcomes were the presence of thyroid autoantibodies and treatment radiation dosage. We included 72 patients. All patients received adjuvant chemotherapy, whereas 59 patients also received supraclavicular locoregional radiotherapy.
Results
At an average of 86 days after chemotherapy, we observed an increase in thyroid-stimulating hormone ($P = 0.03$) and a decrease in free-thyroxine ($P = 0.0006$), whereas no significant weight change. The prevalence of autoimmune thyroiditis was low, and we found no statistically significant difference in the thyroid function of women treated vs not treated with locoregional radiotherapy.
Conclusion
The present study suggests that thyroid function might be decreased in women with early breast cancer after adjuvant chemotherapy. The decrease in thyroid function was neither related to autoimmunity, low T3 syndrome, radiotherapy, nor high-dose corticosteroids, and an effect of adjuvant chemotherapy is suggested. It is still unknown whether the observed decrease in thyroid function is transient or permanent, and further studies with a longer follow-up of thyroid hormones are needed to observe the clinical significance of these changes.

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P582

Epidemiology of primary hypothyroidism in the republic of moldova

Stela Vudu[1]
[1]Nicolae Testemitanu State University of Medicine and Pharmacy, Endocrinology, Chịinău, Moldova

Disorders of the thyroid gland in the Republic of Moldova rank second among endocrine diseases (after diabetes mellitus), hypothyroidism being one of the most widespread diseases. In communities, the prevalence of overt hypothyroidism is from 0.1 to 2 percent, and that of subclinical hypothyroidism is up to 10 percent of adults (increasing even more in women, and with advanced age). Regarding the prevalence of hypothyroidism in the Republic of Moldova, it is necessary to mention the characteristics specific for the country: 1) a mild iodine deficiency; 2) the consequences of the nuclear explosion at the Chernobyl nuclear power station; 3) insufficient detection of primary hypothyroidism in the region. The above mentioned determined the need to study the prevalence of hypothyroidism in different districts of Moldova. The subjects were traced via the General Practitioners and Endocrinologists registers. The results of this cross sectional study conducted in 2021 revealed that, among endocrine diseases, thyroid gland disorders represent 30, 7 %, hypothyroidism (as a result of surgical treatment of thyroid cancer, toxic diffuse goiter, nodular goiter, and autoimmune thyroiditis) represents 9, 5 %, hypothyroidism due to Hashimoto thyroiditis constitutes 6, 1 %, and autoimmune thyroiditis – 11, 3 %. Among thyroid disorders, hypothyroidism (as a consequence of surgical treatment of thyroid cancer, toxic diffuse goiter, nodular goiter, and autoimmune thyroiditis) has a 31 % prevalence, and autoimmune hypothyroidism – 19, 9 %. Thus, in 2021, thyroid gland pathologies constituted about a third, *de facto* occupying the second place after diabetes mellitus, which prevails among endocrine diseases; autoimmune thyroiditis represented 11.3%; hypothyroidism – 9, 5 %, and autoimmune hypothyroidism – 6, 1 %. Among thyroid gland diseases, autoimmune thyroiditis and hypothyroidism constituted about a third each, and autoimmune hypothyroidism – a fifth. Comparing the data mentioned above with those obtained in 1997, the prevalence of thyroid gland disorders, autoimmune thyroiditis, and hypothyroidism of different ethiologies is increasing.
Conclusions
1. Thyroid gland disorders constitute one of the main endocrine diseases in the Republic of Moldova. 2. Autoimmune thyroiditis constitutes one third of the total number of diseases of the thyroid gland. 3. Hypothyroidism as a consequence of autoimmune thyroiditis, which affects almost all functions of the vital organs and systems of the body, was seen in 19.9 %. 4. The vector of thyroid gland diseases in the Republic of Moldova has an ascending character.

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Late-Breaking

P175

Novel homozygous pathogenic variant in the Vitamin-D binding protein in a patient with undetectable Vitamin D levels despite treatment with high doses of vitamin D

Eleni Terezaki[1,2], Mikael Oscarson[1,2] & Katarina Berinder[1,3]
[1]Karolinska University Hospital, Endocrinology; [2]Karolinska University Hospital, Centre for Inherited Metabolic Diseases; [3]Karolinska Institutet, Department of Molecular Medicine and Surgery

Vitamin-D binding protein (VDBP) is the main reservoir of circulating vitamin D and its metabolites in blood. VDBP deficiency leads to a benign phenotype of undetectable vitamin D in the blood without remarkable effects in the calcium and bone metabolism if dietary vitamin D is sufficient ((Safadi *et al* 1999, Banerjee *et al* 2021)). This paradoxical phenotype is probably explained by the free-hormone hypothesis, which suggest that only the unbound vitamin D fraction has biological effects. Besides the null mouse model, to date only three cases of patients with verified DBP deficiency have been described in the literature. Here we present a case of a 33-year-old man adopted from India, with undetectable vitamin D, despite intramuscular injection of 100.000 IE cholecalciferol every 6 weeks, normocalcemia, and reversible mild hyperparathyroidism. Besides two finger fractures at an early age, no other fractures occurred later in life. He has a progressing osteopenia, which can be at least partially attributed to treatment with supraphysiological doses of corticosteroids due to minimal change disease-nephrotic syndrome with preserved eGFR, severe food allergies, treatment of iatrogenic adrenal insufficiency and newly diagnosed Crohn's disease. Other factors that might have contributed to osteopenia were lactose intolerance with restricted dietary calcium intake and secondary hypogonadism with marginally reduced testosterone levels. Genetic analysis of the GC gene, encoding VDBP, revealed a homozygous pathogenic frame shift variant (c.1238del) in exon 11, which leads to a premature stop codon and probably a non-functional protein. In this 33-year-old male patient with apparently treatment resistant vitamin D deficiency we present a novel homozygous pathogenic variant in VDBP. This is line with three previously described cases with different mutations in VDBP all with undetectable levels of VDBP. Taken together, these cases highlight the importance to recognize this condition in patients with ';intractable'; vitamin D deficiency.

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P176

[18F]FET PET-MRI; A diagnostic tool to improve medical decision-making for small functioning pituitary adenomas in acromegaly patients

Romy van der Groef[1], Ilanah Pruis[2], Rutger Balvers[3], Julie Celine Refardt[1], Sophie Veldhuijzen van Zanten[2] & Sebastian Neggers[1]
[1]Erasmus University Medical Center, Internal Medicine Section Endocrinology, Rotterdam, Netherlands; [2]Erasmus University Medical Center, Radiology and Nuclear Medicine, Rotterdam, Netherlands; [3]Erasmus University Medical Center, Neurosurgery, Rotterdam, Netherlands

Background
Patients with acromegaly without detectable pituitary adenoma on conventional MRI are often excluded from adenomectomy due to inherent challenges of precise surgical planning, significantly limiting both their therapeutic options and chances of curation. Previous research showed that O-(2-[18F]fluoroethyl)-L-tyrosine ([18F]FET) PET-MRI is an accurate diagnostic tool to detect small functional pituitary adenomas (1). The present study aims to investigate the diagnostic yield of [18F]FET-PET-MRI in a cohort of acromegaly patients with suspected small adenomas.
Methods
Patients with acromegaly and a suspected primary or recurrent small functional pituitary adenoma underwent [18F]FET PET-MRI with administration of gadolinium, at 20 minutes post-injection. A PET-scan was defined as positive in case focal uptake of [18F]FET was detected as assessed by a nuclear radiologist. The accompanying MRI was evaluated separately by a single neuroradiologist. Outcomes were compared with clinical follow-up and sensitivity and positive predictive value (PPV) were calculated using post-operative pathology reports as reference.
Results
Fourteen acromegaly patients, 71.4% female, mean age 55 years (range 35-73 years) were included. Six patients (42.9%) had undergone transsphenoidal surgery prior to PET imaging. Positive [18F]FET uptake was seen in ten patients (71.4%), identifying five additional lesions missed by previous MRIs. During PET imaging, 8/14 patients used somastotatin analogues, and 2/14 cabergoline. The accompanying MRI showed a lesion in eight patients (57.1%), including one cystic lesion. Following positive PET, 1/10 patients received adjuvant radiotherapy and 4/10 underwent surgery. The other 5/10 are awaiting or have declined surgery. Histopathological examination confirmed that 4/4 resected tumours were adenomas staining positive for growth hormone, yielding an estimated sensitivity of 71.4% (95% CI 41.9 – 91.6%) and a PPV of 100% (95% CI 69.2-100%) for the detection of small GH-producing adenomas. Following transsphenoidal surgery, 2/4 patients achieved biochemical remission, the third patient was able to reduce the dose of medication and the last patient switched from pegvisomant to lanreotide. The patient who received adjuvant radiotherapy had no change in medication use.
Conclusion
[18F]FET PET-MRI increases the yield for detection of small GH-producing pituitary adenomas. [18F]FET PET-MRI emerges as a superior diagnostic tool to detect small functional pituitary adenomas and may enhance surgical planning and outcomes for acromegaly patients.
1. Pruis IJ, Verburg FA, Balvers RK, Harteveld AA, Feelders RA, Vernooij MW, Marion Smits M, Neggers SJCMM and Veldhuijzen van Zanten SEM. [18F]FET PET-MRI; a novel and accurate technique for detection of small functional pituitary tumours. J Nucl Med. 2024 (accepted)

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P177

Patient profile of asymptomatic primary hyperparathyroidism (APHPT) at tertiary care riga east clinical university hospital

Diana Sturite[1] & Ingvars Rasa[2]
[1]Rīga Stradiņs University, Faculty of Medicine, Rīga, Latvia; [2]Riga East Clinical University Hospital, Rīga, Latvia

Objective
Primary hyperparathyroidism is the third most common endocrine disorder, which often causes hypercalcemia in outpatient cases. This study aimed to evaluate the various demographic and clinical characteristics, biochemical data, as well as the prevalence of associated conditions, diagnostic accuracy of imaging modalities, and treatment outcomes in patients with APHPT.
Methods
We analyzed data collected from 168 individuals diagnosed with APHPT and treated at Riga East Clinical University Hospital from January 2021 to January 2024. This involved thoroughly examining their medical records, laboratory results, imaging scans, and surgical procedures. Statistical analysis was conducted using IBM SPSS 29.0.
Results
168 patients (mean age: 63.7 ± 11.8 years), 86.3% were females, 13.7% – males. The mean preoperative maximal calcium level was 2.9 ± 0.3 mmol/l, iPTH level – 247.6 ± 224.9 pg/mL, minimal phosphorus – 1.3 ± 6.7 mmol/l and 25-OH vitamin D level 28.3 ± 14.7 ng/mL. A positive correlation was observed between preoperative calcium levels and adenoma cross-sectional area (rs = 0.187, P = 0.029) and maximal dimension (rs = 0.215, P = 0.011). Ultrasonography verified parathyroid adenomas in 63.9% (107/168), SPECT/CT – 68.4% (52/76), 99mTc-sestamibi scan – 65.6% (61/93), 3D-CT - 70.6% (24/34), contrast-enhanced ultrasonography (CEUS) – 84% (21/25) and MRI in 40% (2/5) cases. 12.5% (n = 21) of patients had unlocated parathyroid adenoma. 22.0% (n = 37) of patients had kidney stones, 17.3% (n = 29) – gallstones, 34.5% (n = 58) – osteoporosis, 12.5% (n = 21) – osteoporotic fractures and 47.6% (n = 80) – osteopenia. 17.9% (n = 30) of patients received oral bisphosphonates, 4.0% (n = 7) intravenous bisphosphonates, 8.0% (n = 14) denosumab, and 1.1% (n = 2) had medication holidays. 80.4% (n = 135) of patients had thyroid nodules, 48.2% (n = 81) had nontoxic goitre, 24.4% (n = 31) had autoimmune thyroiditis, 41.7% (n = 70) had hypertension and 10.5% (n = 18) type 2 diabetes. 18.5% (n = 31) of patients were found to have a diagnosis of malignancy. 61.9% (n = 104) underwent parathyroidectomy. Histopathology and radiologic imaging of operated patients revealed a single parathyroid adenoma in 93.3% (n = 97), double parathyroid adenomas in 1.9% (n = 2), parathyroid hyperplasia in 2.9% (n = 3) and parathyroid carcinoma in 1.9% (n = 2) patients. The mean maximal postoperative calcium level (n = 103) was 2.4 ± 0.1 mmol/l, iPTH (n = 101) 63.5 ± 27.7 pg/mL, 25-OH vitamin D 41.5 ± 13.3 ng/mL and mean minimal phosphorus (n = 56) 1.1 ± 0.2 mmol/l. 3 patients developed hungry bone syndrome following parathyroidectomy.
Conclusion
Our findings highlight the complex nature of APHPT and emphasize the importance of recognizing complications and associated conditions to optimize outcomes for APHPT patients.

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P178

TNXB genotype and serum levels in individuals with and without congenital adrenal hyperplasia due to 21-hydroxylase deficiency

Marie Helene Schernthaner-Reiter[1], Nina Schmid[1], Oliver Koldyka[1], Boskovic Jelena[1], Gard Liliana-Imi[1], Bayerle-Eder Michaela[1] & Sabina Baumgartner-Parzer[1]
[1]Medical University of Vienna, Clinical Division of Endocrinology and Metabolism, Department of Internal Medicine III, Vienna, Austria

Introduction
In congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD), large *CyP21A2* deletions can also affect the adjacent tenascin-X (*TNXB*) gene. In patients with or without 21-OHD, pathogenic variants in the *TNXB* gene cause Ehlers-Danlos syndrome (EDS), a connective tissue dysplasia associated with cardiovascular complications. CAH in conjunction with *TNXB*-dependent EDS has been termed CAH-X. This study aims to characterize the genetic, biochemical and clinical characteristics of patients with CAH and monoallelic or biallelic *TNXB* deletions and compare them to patients with CAH and intact *TNXB* as well as to individuals without CAH.
Methods
CyP21A2 and *TNXB* genotypes were determined by Sanger sequencing and multiplex ligation-dependent probe amplification (MLPA). Sequence analysis was performed by Alamut. Serum TNX levels were measured by ELISA.
Results
Our cohort comprises 1315 individuals genetically analyzed due to suspicion of CAH. Of 100 patients with classic CAH, we have identified 12 (12%) with heterozygous deletions and 2 (2%) with duplications of *TNXB* exon 35. In patients with nonclassic CAH, *TNXB* exon 35 deletions were identified in 1 patient (1.4%). In individuals without 21-OHD, deletions of *TNXB* exon 35 were rarely detected (0.4%) whereas duplications were more frequent than in the other groups (4.4%). The clinical significance of *TNXB* duplications is currently not known. Sanger sequencing of *TNXB* exons 33-44 was performed in 23 samples. A total of 20 different genetic variants were detected, including 4 missense variants, 3 synonymous and 13 intronic variants; 17 were classified as benign or likely benign and 3 were classified as variants of uncertain significance (VUS). The highest serum TNX levels were detected in controls not affected by CAH, whereas patients with CAH-X (genetically characterized by deletion of *TNXB* exon 35) demonstrated TNX levels significantly lower than those of patients with CAH and intact copy number of *TNXB* exon 35 as well as controls.
Conclusion
The spectrum of genetic variation affecting *TNXB* in individuals with or without CAH includes large deletions, often in conjunction with large *CyP21A2* deletions, as well as duplications and single nucleotide variants. Further studies are necessary to characterize the clinical relevance of these genetic variants.

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Mortality in young women with turner syndrome is mainly due to aortic dissection - a 25-year follow-up in sweden

Sofia Thunström[1], Erik Thunström[1], Sabine Naessén[1], Kerstin Berntorp[1], Margareta Kitlinski[1], Bertil Ekman[1], Jeanette Wahlberg[1], Ingrid Bergström[1], Magnus Isaksson[1], Carmen Basic[1], Teresia Svanvik[1], Inger Bryman[1] & Kerstin Landin-Wilhelmsen[1,1,1]
[1]

Context
Turner syndrome (TS) is the most common sex chromosome aberration, affecting 1/2500 born girls. Reduced life expectancy has been reported.
Objective
The objective was to investigate the causes of mortality and identify the risk factors that contribute to death in women with TS.
Design and setting
A matched retrospective observational study of women with TS from the Turner centers in Sweden was conducted. Echocardiography was performed on average every 5th year according to the guidelines in TS.
Patients
A total of 472 women with TS, monosomy 57%, and 2357 controls, matched for birthyear and sex, mean age 28 (12) years, (range 16 - 78) years at inclusion were studied on a mean follow-up period of 17 years (range 1 - 26). Growth hormone had been given to 53%, ongoing estrogen was present in 85% and 13% of the women with TS had given birth to a child.
Outcome Measures
Survival analyses were performed with Cox proportional hazard models. Kaplan-Meier curves were generated. Cumulative incidence rates were evaluated by competing risks analysis, using cumulative incidence function.
Results
During a mean follow-up of 17 years, 35 (7.4%) women with TS and 70 (3.0%) controls died. Mean age at death was 54 (18) years in TS and 60 (15) years in controls. All-cause mortality was raised in TS, hazard ratio (HR) 2.90 (1.9-4.4), especially deaths related to cardiovascular diseases showed significantly higher HR: 9.11 (4.5-18.3). During the follow-up period, 20 women with TS experienced aortic dissection (4%) of whom eight died (40%). Death by aortic dissection occurred in two women (0.1%) among the controls. The main contributor to the increased mortality in young women with TS was aortic dissection with 5 deaths below the age of 45 while cardiovascular disease, other than aortic dissection, was not increased in young TS women. Death by cancer or external causes were not raised in TS. No women with TS died of breast cancer. Bicuspid aortic valves and enlarged aortic diameter were risk factors for death in TS. Karyotype, hypertension, previously given growth hormone or ongoing estrogen treatment were not associated with mortality in TS. None died during pregnancy.
Conclusions
The increased mortality observed in women with Turner syndrome in Sweden primarily resulted from cardiovascular disease, with aortic dissection being the single largest specific cause of death among the young. Life-long evaluation of the aortic size is recommended. Special care is needed before and during pregnancy.

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Immunohistochemistry in the differential diagnosis of atypical tumor and parathyroid carcinoma

Ekaterina Kim[1,1], Anastasiia Lavreniuk[1], Alina Elfimova[1], Anna Eremkina[1], Lilia Selivanova[1], Rustam Salimkhanov[1] & Natalia Mokrysheva[1]
[1]Endocrinology Research Centre, Moscow

Background
Atypical parathyroid tumor (APT) generally has a better prognosis compared to parathyroid carcinoma (PC). The differential diagnosis of APT and PC is crucial for further management. Diagnosis of both is based on morphological examination but sometimes can be challenging. In such cases immunohistochemistry (IHC) should be used.
Objective
To estimate the utility of IHC in the differential diagnosis of APT and PC.
Materials and Methods
We conducted a single-centre retrospective study of 44 patients with morphological diagnosis ";APT"; who underwent parathyroidectomy between 2018 and 2023. Method of sampling was continuous. The research complied with the principles of the Helsinki Declaration. IHC was performed in all cases: assessment of CD31/CD34 (to identify vascular invasion), parathyroid hormone (PTH) and parafibromin expression; Ki-67 evaluation. According to IHC results patients were divided into 2 groups: APT and PC followed by comparative analysis. This analysis included biochemical markers of Ca-P metabolism (Ca adj., P, PTH, eGFR CKD-EPI, ALP, osteocalcin, CT×); the frequency of ";classic"; PHPT complications and intraoperative signs of surrounding tissue invasion; size and volume of tumor according to US; morphological features of uncertain malignant potential. Comparison of two independent groups for quantitative data was performed using the Mann–Whitney test (U-test), the frequencies of binary variables using the two-tailed Fisher exact test. The Bonferroni correction was applied by correcting the significance threshold ($P = 0.002$).
Results
Based on the IHC results in 8/44 patients (18.2%) the diagnosis was reclassified as PC. In 7/8 (87.5%) vascular invasion was identified by CD31/CD34 expression (endothelial markers). In 1/8 (12.5%) additional sections revealed a foci of the tumor growth detected with PTH expression in the surrounding fatty tissue. PC and APT groups were comparable for high values of PHT, Ca adj. and 24-h urinary Ca excretion, the frequency of bone and kidney disorders. Moreover, there was no difference in morphological features of uncertain malignant potential. Statistically significant trend was defined only for the frequency of pathological mitosis (more typical in patients with PC). Ki-67% and parafibromin expression also did not differ between groups.
Conclusion
Evaluation of preoperative clinical and laboratory-instrumental data does not allow to differentiate APT and PC. If APT is morphologically suspected, IHC is strongly recommended to exclude PC.

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The relationship between glycated hemoglobin and glycemic variability in type 1 diabetics

Faten Mahjoub[1], Ines Bani[1], Nadia Ben Amor[1], Ramla Mizouri[1] & Jamoussi Henda[1]
[1]National Institute of Nutrition in Tunis, A, Tunisia

Introduction
Glycated hemoglobin has long been considered the gold standard for monitoring diabetic patients. however, the advent of CGM, revolutionized the monitoring of diabetics with the possibility of detecting glycemic variability in patients.
Method
This is a descriptive cross-sectional study conducted at the National Institute of Nutrition in Tunis. Adolescents with type 1 diabetes were recruited and they wore a CGM device for 7 days. A1C and clinical information were collected. We analyzed the CGM data for each patient and we calculated the coefficient of variability of glucose (CV), mean of glycemic excursions (MAGE) and the mean of daily differences (MODD).
Results
We included 81 patients with type 1 diabetes in our study, with an average age of 162 years old. A female predominance was noted (58%). The mean duration of diabetes was 6 4 years. A1C ranged from 5.7% to 14%, with a mean of 9.8 1.8%. The average of CV, MAGE and MODD was: 39.812%; 14145 mg/dl; and 8141 mg/dl respectively. Participants were stratified by high CV ($>36\%$; $n=48$) and low CV ($\leq 36\%$; $n=33$). A statistically significant difference was objectified in A1C levels between the groups In fact, patients in group low CV had higher A1C levels (10.3 1.7%) than those in group high CV (9.4 1.9%) with($P=0.042$). The high CV group spent more time in hypoglycemia compared with the group low CV (The average of Time Below Range (TBR) was 10.611% vs 1.52.5%) with $P=0.000$. The time spent in nocturnal hypoglycemia (calculated by CGM) was significantly higher in patients with high CV (15,712% vs 3.68.8%; $P=0,000$)
Conclusion
In our study, we found that A1C levels were higher in the low CV group, this underlines the fact that patients with target A1C levels may have high glycemic variability. The CV can better identify individuals at high risk of hypoglycemia compared with A1C alone. To conclude that glycemic variability metrics should be combined with A1C for better diabetes management in people with type 1 diabetes.

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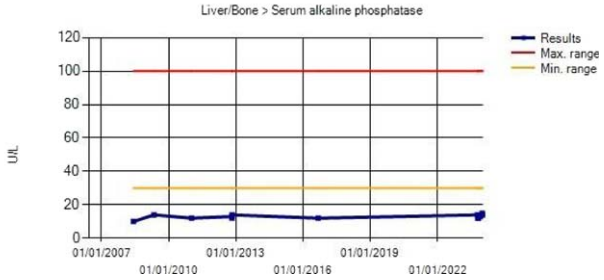
Sticks and stones could break my bones: a rare case of adult hypophosphatasia (HPP) at 24 weeks of pregnancy

Sargunann Naidu Krishnasamy Naido[1] & Tristan Richardson[1]
[1]Royal Bournemouth Hospital, Diabetes and Endocrinology, Bournemouth, United Kingdom

Hypophosphatasia (HPP) is a genetic condition affecting teeth and bones, identified by low levels of alkaline phosphatase (ALP) activity in the blood. This deficiency is caused by mutations in the ALPL gene, leading to an accumulation of substances that hinder bone mineralization. In adults, this can result in osteomalacia, frequent fractures, premature tooth loss, and arthralgia. We describe the case of a 38 year old Caucasian woman who was 24 weeks into her third pregnancy and was referred for a persistently low alkaline phosphatase enzyme (ALP). Her ALP has been low for over a decade (see graph), likely due to a genetic predisposition. She had a history of childhood fractures from low-impact trauma. She denies early loss of baby teeth. She reported myalgia during pregnancy with increased pain over the shoulder and pelvic girdles. Her first child, had metatarsal and metacarpal fractures from low- impact trauma and had lost dentition quite early in life. Her younger child, diagnosed with Tourette syndrome, had lost dentition and broken metatarsal and metacarpal bones from repetitive involuntary muscle twitching. Testing plasma copper level and serum selenium levels revealed normal results, however her plasma zinc levels were borderline and was replaced. A genetic testing revealed that she was a heterozygous for a likely pathogenic ALPL missense variant. Although the option for amniocentesis for prenatal diagnosis was discussed, it was decided against due to the advanced stage of pregnancy and the unlikelihood of changing pregnancy plans based on the results. This woman has been referred to the clinical geneticist for further evaluation. Currently, there is no approved treatment for adult HPP in the UK, but treatment is available, in the USA for pediatric cases using Asfotase alfa. This is a human recombinant tissue-nonspecific alkaline phosphatase that promotes mineralization of the skeleton. However, in spite of the limited treatment options, endocrinologists should have high suspicion of the clinical and biochemical features of adult HPP and refer them early to clinical geneticist for genetic counselling.

Serum alkaline phosphatase



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Clinical spectrum associated with variants in the ins gene in patients with suspected monogenic diabetes

Mariana Gomes Porras[1], Rosario Vallejo Mora[1], Maria Soledad Ruiz De Adana Navas[1] & Ángel Campos Barros[2,3]
[1]Regional Universitary Hospital of Málaga, Endocrinology and Nutrition, Málaga, Spain; [2]Institute of medical and molecular genetics (INGEMM), Health Research Institute of the La Paz University Hospital (IdiPAZ), Molecular Endocrinology, Málaga, Spain; [3]Institute of Medical and Molecular Genetics (INGEMM), Health Research Institute of the La Paz University Hospital (IdiPAZ), Molecular Endocrinology, Madrid, Spain

Background and aims
*INS*mutations can cause INS-MODy and have been described more frequently in cases of neonatal diabetes mellitus. The reported phenotypic expression of INS-MODy is quite variable.
Objective
To clinically, biochemically and molecularly characterize INS-MODy patients in two Spanish tertiary level hospitals during the period 2009-2023.
Methods
Cross-sectional study that included 121 pediatric patients with suspected monogenic diabetes analyzed by targeted NGS with a custom panel (MonDIABV1-4) including up to 482 genes involved in or associated with different types of dysglycemia. Variants were classified according to ACMG and prioritized using confidence and quality criteria, coverage (20x/pb $>95\%$), allele frequency ($<1\%$ gnomAD controls), impact and *in silico* prediction of pathogenicity (CADD V1.6, score >15).
Results
3/121 patients (2.5%), 2 males and 1 female, aged 154.58 years and with BMI 21.83.5 Kg/m2, presented with heterozygous *INS* deleterious variants. Segregation analysis revealed that the previously described (HGMD) pathogenic INS variants NM_000207.3:c.140G>A, p.(Gly47Asp) and NM_000207.3:c.163C>T, p.(Arg55Cys) were *de novo*. No allelic segregation study could be performed for the NM_000207.3:c.62 C>T; p.(Pro21Leu) (VUS), located in the preproinsulin signal peptide. All patients had a family history of DM, with diabetic debut at 122.6 years as simple hyperglycemia without cardinal clinic, negative pancreatic autoimmunity, preserved C-peptide at diagnosis and 2/3 after 4 years from diagnosis. Initial HbA1c was 6.40.5% (currently 6.72.1%) and their lipoproteic profile was normal. None developed acute or chronic complications after 42 years of follow-up. The patient with the INS p.(Pro21Leu) variant was overweight and his HOMA-IR (7.2) indicated insulin resistance, treated with metformin. The patient with the INS p.(Gly47Asp) variant presented poor metabolic control due to poor adherence to low-dose insulin therapy (0.32UI/Kg/day), his DM was initially classified as type 1b, delaying the molecular diagnosis for about 3 years. The patient with the INS p.(Arg55Cys) variant presented good metabolic control with hygienic-dietary measures.
Conclusion
The prevalence of INS-MODy is higher than reported in the literature. In our experience, phenotypic expression occurred in early childhood, varying from mild to severe hyperglycemia with insulinopenia up to insulin resistance in association with other predicted deleterious variants in candidate genes (MODy-X). Suspicion of INS-MODy should be raised in patients with early diabetic debut without pancreatic autoimmunity, even in the absence of a family history of DM. Therefore, the analysis of *INS* should be included in the molecular diagnostic routine of suspected monogenic diabetes.

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We used to be identical twins! a tale of MEN-1 and gigantism: the identical twin 1 foot taller than his brother

Caitlin McNeilage[1], Adhithya Sankar[1] & Tara Kearney[1]
[1]Salford Royal, Manchester, United Kingdom

A 24 year old male presented to his GP with rapid growth in height and joint pain and a physiotherapist suggested that he could have late stage gigantism. Upon presentation he had recently grown from 208 cm to 216 cm tall during a short number of months. His symptoms included fatigue, sweating, oily skin and deepening of his voice. Of note he had prognathism, frontal bossing, macroglossia, broadening of his nose and significant interdental spacing. His mother is 165 cm tall, his father is 172 cm tall. His paternal uncle is 188 cm tall and reportedly his paternal grandfather was over 183 cm tall. Interestingly he has an identical twin who is only 185 cm tall and wears shoes 6 sizes smaller than the patient. Childhood photos confirm that they are indeed identical twins and previously only close family could tell them apart. At the age of 16 he started to grow taller, and they now look remarkably different from each other in terms of both facial features and body size. Biochemical testing revealed an IGF-1 of 698ng/mL (98.7-289) with a growth hormone >40 on OGTT, confirming growth hormone hypersecretion and a diagnosis of gigantism. In addition, he was successfully treated for LH, FSH, TSH, ACTH deficiency with supplementary medication. Genetic testing was confirmatory for MEN-1. MRI pituitary scan identified a 4.7 cm giant pituitary macrodadenoma with bilateral cavernous sinus involvement. Visual field testing showed a significant left temporal field defect. He recently underwent transsphenoidal resection of the pituitary tumour. The histology showed a bone invasive densely-granulated somatotroph pituitary neuroendocrine tumour with Ki-67 $<1\%$. Post-operative recovery was complicated with meningitis and biochemistry on day 2 post-operation showed an IGF-1 of 586 with random GH of 15.8. However, further biochemical assessment will be required as an outpatient. This case highlights the importance of early identification and referral to specialist services. The patient reports distress that he visited his GP many times without a diagnosis or referral leading to irreversible physical changes. However, he is grateful that his family and any future offspring may be able to have genetic testing. This case raises several important discussion points including:

1. Why has one identical twin developed significant pathology whilst the other remains healthy?
2. How do we diagnose such a rare condition at an earlier stage to avoid preventable ongoing harm from excess GH secretion?

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Spectacular liver tests improvement during osilodrostat treatment in patient with cushing syndrome and impaired liver function

Mari Minasyan[1], Anna Bogusławska[2], Andrzej Fedak[3], Alicja Hubalewska-Dydejczyk[2] & Aleksandra Gilis-Januszewska[2]
[1], Endocrinology, Oncological Endocrinology, and Nuclear Medicine Department, University Hospital, Krakow; [2], Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [3], Department of Radiology, Jagiellonian University Medical College, Krakow, Poland

A case presents a 35 year old woman with a history of Cushing Disease (CD) diagnosed in 2014, who developed multiple complications of long lasting hypercortisolemia- obesity (BMI 55), poorly controlled diabetes mellitus (DM), heart failure, hypertension, hypercholesterolemia, mental disturbances and significant hepatic impairment. She underwent a non-radical pituitary adenoma removal in 2014 with subsequent radiotherapy in 2018. Choice of pharmacological treatment was challenged by patient's great non-compliance and severe metabolic complications of CD. Due to significant elevation of liver function tests (LFT) she could not start either ketoconazole treatment or one of the clinical study drug. Pasireotid was contraindicated because of poorly controlled diabetes mellitus. Shortly she was treated with metyrapone, however due to side effects she refused therapy continuation. In December 2021 she consented to osilodrostat treatment. Pre-treatment laboratory evaluation showed sustained LFT elevation- alanine transaminase (ALT) $4\times$ULN, aspartate transaminase (AST) $1.7\times$ULN, gamma glutamyl transpeptidase (GGTP) $4\times$ULN, dyslipidemia (triglycerides 4 mmol/l, total cholesterol 7.4 mmol/l), non-controlled diabetes mellitus (glycohemoglobin-HBA1c%- 10.80 %), high free urine cortisol ($1.7\times$ULN), elevated morning cortisol (32.2 mg/dl). In abdominal MRI liver steatosis with no other abnormalities was described. Since December 2021 patient started osilodrostat treatment with initial daily dose of 2 mg, followed by dose escalation in February 2022 to 4 mg daily. After 4 months of treatment we observed normalizing of serum morning cortisol (13.1 mg/dl), urine free cortisol (55.9 mg/day) and low late night salivary cortisol (0.091 mg/dl). ALT and AST started to lower down 1 year after treatment initiation, normalizing totally within 18 months since treatment. HBA1c% was going down gradually with significant drop after 12 months of treatment (7.2%) and normalisation after 24 months (6.2%). Prominent triglicerydes drop was observed 6 months since osilodrostat start and it normalised after 24 months. During treatment patient lost 3% of her baseline weight, thus the metabolic parameters improvement seems to be not related with weight changes. Liver evaluation on elastography 1 year since therapy start, showed liver steatosis and liver stifness value of 7.91 kPA. Osilodrostat is a steroidogenesis inhibitor which can be safely used in patients with Cushing Disease complicated with liver function impairment. Our case showed normalisation of LFTs during treatment with osilodrostat. Further multicenter studies are needed to investigate the link between hypercortisolemia, liver function and steroidogenesis inhibitors.

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Integrated analysis of fecal metagenomics and serum metabolomics reveals the role of gut microbiome-associated metabolites in detecting gestational diabetes mellitus

Chen Zhang[1], Shuo Ma[1] & Guoqiu Wu[1]
[1]Zhongda Hospital, Medical School of Southeast University, Center of Clinical Laboratory Medicine, Nanjing, China

Background
The gestational diabetes mellitus (GDM) is a metabolic disorder characterized by glucose intolerance in pregnant women without pre-existing diabetes, typically diagnosed in mid to late pregnancy. The global prevalence of GDM is on the rise, posing significant diagnostic and economic burdens on society and affecting the health of two generations, potentially impacting population quality. Early diagnosis or understanding of the pathophysiology of this disease in early pregnancy may effectively reduce its incidence. Emerging evidence indicates that the gut microbiome can modulate metabolic homeostasis, thereby influencing the development of GDM. However, it remains uncertain whether and how the gut microbiota and its blood-related metabolites change in GDM.
Methods
We collected serum samples from 698 pregnant women, including 190 in mid-pregnancy and 508 in early pregnancy, as well as partial fecal samples. Utilizing a combination of untargeted serum metabolomic analysis using liquid chromatography-mass spectrometry and fecal metagenomic sequencing, we identified significant changes in gut microbiome-associated metabolite abundance in GDM patients and matched controls. Subsequently, we developed diagnostic and early prediction models for GDM based on different modeling methods, which were evaluated in independent validation and other study cohorts.
Results
Our study revealed significant changes in 1024 serum metabolites in GDM patients, with 275 metabolites closely related to the gut microbiota. Among them, five metabolites showed significant differences in the early pregnancy stages of GDM development. Through repeated testing using untargeted metabolomics, these five metabolites could effectively distinguish GDM patients from normal individuals and even identify patients at risk of developing GDM. Constructing different diagnostic and predictive models based on these five metabolites yielded the highest AUC of 0.95 in the testing cohort and AUCs of 0.91 (sensitivity of 81.5%, specificity of 85.2%) and 0.88 (sensitivity of 79.5%, specificity of 82.4%) in the validation cohorts. Furthermore, the model demonstrated significant advantages in sensitivity, specificity, and accuracy in other studies.
Conclusion
The microbiota and serum metabolites of GDM patients significantly differ from those of matched controls, and the reprogramming of the gut microbiome in GDM patients is related to changes in the serum metabolome. The use of effective serum metabolite models can advance the prediction of GDM to early stages, thereby reducing the adverse consequences of GDM.

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Radiological diagnosis of atypical femoral fractures using qualitative and quantitative criteria: a retrospective cohort analysis across two centres over 10 years

Aongus O'Brolchain[1], Zander Englebrecht[2], Richard Steer[2], Alfred Phillips[2], Chen-i Lin[2] & Ian Hughes[2]

[1]Griffith University, Gold Coast Campus, Southport, Australia; [2]Gold Coast University Hospital, Southport, Australia

Objective(s)
Atypical femoral fractures (AFFs) are an important complication of treatment with anti-resorptive treatment, which remains the cornerstone of osteoporosis treatment. Recognition of this rare clinical entity is exceedingly important, as ongoing treatment with anti-resorptives is contraindicated. The American Bone and Mineral Research (ASBMR) have devised diagnostic criteria which are qualitative and subjective. Recent attempts have been made to create more quantitative and objective guidance for clinicians, but diagnosis remains challenging. This study aimed to assess the global performance, sensitivity and specificity, and interobserver agreement/variability of both the ASBMR and the recently devised Sydney AFF Score (SAS) criteria (a score of ≥ 2, 1 point for each of the following: lateral cortical width (LCW) >5 mm, femoral neck width (LCW) <37 mm, age <80).
Design
Retrospective observational study involving inpatients at two teaching hospitals in Queensland, Australia. Adult patients aged 18 years or older presenting with low-energy mechanism, subtrochanteric fractures between January 2012 and February 2022.
Primary outcomes measure(s)
Sensitivity, specificity and performance of each of the ASBMR and SAS criteria. Patients were divided into two groups for comparison: AFFs and 'typical' femoral fractures (TFFs). Measurement of interobserver variability/agreement using ASBMR criteria and the SAS using Kappa Fleiss statistic (FK). Accuracy of radiological reports by retrospective review
Results
A total of 869 femoral shaft fractures were screened. 46 AFFs were identified following expert panel review by 2/3 majority. A comparator group of 40 were selected from the remaining 149 TFFs. The sensitivity and specificity of the ASBMR criteria were: predominantly transverse orientation (TO) (91.4% [range 85.42 – 95.24%], 89.1% [81-94.6%]), minimal comminution (MC) (99.2% [range 97.7-100%], 63.9% [51.4-72.9%]) and periostial reaction (PR) (89.4% [84.1 – 97.6%], 96.4% [91.8% - 100%]). The Sydney AFF Score had comparable performance in this cohort compared to the index and validation cohorts (AUC 0.73). The ASBMR criteria showed good interobserver agreement (FK TO 0.72, MC 0.64, PR 0.76, $P=<0.001$). The agreement with the anthropometric indices using the SAS were (FK LCW 0.25, FNW 0.66, $P=0.002$, <0.001) Of the AFFs, just 13.2% of radiology reports referenced atypical or drug-related fracture.
Conclusion
Qualitative criteria outperform the most accurate quantitative indices. Incorporating fracture angle into the the SAS may yield superior diagnostic value and remove. This study demonstrates that AFFs are under-recognised by reporting radiologists.

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Relationship of lipoprotein-a levels with the metabolic profile, bone status and kidney function in patients with type 1 diabetes

Efstratios Kardalas[1], Dimitra Mpaikousi[1], Aikaterini Mpeka[1], Vasiliki Antonopoulou[1], Panagiotis Mouchtouris[1] & Marinella Tzanela[1]
[1]Evangelismos General Hospital, Department of Endocrinology 'D. IKKOS', Diabetes Center European and National Center of Excellence for Rare Endocrine Diseases

Background/aim
Lipoprotein a (Lpa) is a major atherogenic factor associated with increased cardiovascular risk among patients with type 1 diabetes (t1D). This study investigated the possible relationship of Lpa levels to the metabolic profile, bone status and kidney function of patients with T1D.
Materials and methods
122 adult patients with T1D (70 males and 52 females), were studied in an observational cross-sectional study. Demographic, clinical and laboratory data regarding glycemic regulation (HbA1c, Time in range 70-180 mg/dl [TIR])), lipid status (Tchol; Total cholesterol; HLD, LDL, triglycerides, Lpa) bone metabolism (BMD [bone mass density] and T-Score in FN [femoral neck] and LS [lumbar spine]) and renal function (eGFR [estimated glomelural filration rate] were recorded. Patients were divided in 2 groups based on their Lpa levels (low <30 mg/dl and high ≥ 30 mg/dl.) and on their HbA1c status (good, $<7\%$; bad $\geq 7\%$).
Results
Mean age and body mass index of the patients were 44.2 years and 26.6 kg/m^2 respectively. Mean HbA1c and Lp(a) values were 7.5% and 37 mg/dl respectively. Men exhibited notably higher HbA1c, Tchol, LDL and Lpa values (HbA1c: 7.67 vs 7.3%, $P=0.011$; Tchol: 221 vs 204 mg/dl, $P=0.06$; LDL: 112 vs 86 mg/dl, $P=0.043$; and Lpa:48 vs 24 mg/dl, $P=0.031$ respectively). Interestingly, patients with higher Lp(a) values had deteriorated metabolic profile (HbA1c: 7.7% vs 7.2%, $P=0.002$) and worse glycemic regulation (TIR: 64 vs 77%, $P=0.011$) than those with lower Lpa values. Furthermore, eGFR values were remarkably lower among the high Lpa group patients versus the low Lpa group ones (55 vs 62 mL/min/1.73m^2, $P=0.03$). Finally, patient with T1D and increased Lpa values exhibited decreased BMD and T-Score in the FN (BMD: 0.711 vs 0.784, $P=0.034$; T-Score: -1.1 vs -0.9, $P=0.04$) and the LS (BMD: 0.884 vs 0.901, $P=0.012$; T-Score: -0.95 vs -0.7, $P=0.033$) compared to those with increased Lpa values. Interestingly, patients with good metabolic control were found to have significantly lower Lp(a) levels than those with worse metabolic control (49 vs 28 mg/dl, $P=0.041$).
Conclusions
The results of our study indicate that Lpa could potentially be a major risk factor for worse metabolic, bone and renal profile among patients with T1D. Conversely, deteriorated glycemic regulation in patients with T1D is linked to markedly higher Lp(a) levels.

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Advanced liver fibrosis is associated with the presence of type 2 diabetes rather than body mass index

Meliha Melin Uygur[1], Caglayan Keklikkiran[2], Süreyya Özgür Uygur[3], Hatice KaradurmuŞ[4], Mohammed Abdulrahman Alzandan[4] & Emine Bade Topal[4]
[1]School of Medicine, Recep Tayyip Erdogan University, Department of Endocrinology and Metabolism Disease, Rize, Turkey, [2]School of Medicine, Recep Tayyip Erdogan University, Department of Gastroenterology Disease, Rize, Turkey, [3]Faculty of Civil Engineering, yıldız Technical University, Department of Geomatic Engineering, Istanbul, Turkey, [4]School of Medicine, Recep Tayyip Erdogan University, Rize, Turkey

Objective
Higher obesity rates are related with increased non-alcoholic fatty liver disease (NAFLD) prevalence which may progress further to non-alcoholic steatohepatitis (NASH) and cirrhosis. The utility of Fibroscan was shown in stratifying risk for significant liver disease. The aim of the study was to evaluate the relation between body mass index (BMI) and liver stiffness measurements (LSM) in overweight and obese patients.
Methods
We conducted the study in 369 (145 men, 224 women) patients aged between 18-75 years old and body mass index over 25 kg/m^{2}from department of endocrinology and metabolism disease and gastroenterology, School of Medicine, Recep Tayyip Erdogan University. We performed a fibroscan assessment and collected biochemical, demographic, and clinical data. Patients were categorized as group I with mild/moderate fibrosis (MF) (F0- F2) and group II with advanced fibrosis (AF) (F3-F4).
Results
Overall, 42.8% of patients had liver fibrosis. Among these, 56 patients had AF whereas 102 patients had MF. Mean BMI was 36.467.77 in group 1 vs 34.596.27 in group 2 (*P*:0.04). Type 2 diabetes was seen in 54.7% of patients in group 1 vs 70.2% of patients in group 2 (*P*:0.03). In binary logistic regression analysis, there was a negative association between BMI and LSM (OR: 0.409, 95% CI 0.202-0.827) whereas a positive association was found with presence of type 2 diabetes (OR: 2.495, 95% CI 1.203-5.176), (*P*:0.006).
Conclusion
The study showed that presence of type 2 diabetes is a strong predictor of advanced liver fibrosis, and physicians should suspect diagnosis even in lower BMI values particularly in patients with diabetes.
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Severe osteoporosis in a patient with APECED: atypical presentation

Anastasiia Lavreniuk[1], Ekaterina Kim[1], Rustam Salimkhanov[1], Anna Eremkina[1], Olga Spasskaya[1] & Natalia Mokrysheva[1]
[1]Endocrinology Research Centre

Hypoparathyroidism (HPT) is the most common autoimmune endocrine involvement of APECED syndrome (autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy, 79-96% cases). HPT is associated with reduced bone remodeling, abnormalities in microarchitecture and bone strength, thus low-energy fractures occur despite normal or even high bone mineral density (BMD). Other APECED components (hypogonadism, malabsorption, growth hormone deficiency etc.), may also affect bone metabolism.

Case Report

A 48-year-old male patient N. was admitted with periodic seizures, decreased libido and mood lability. HPT was diagnosed at the age of 7 years, when seizures and episodes of loss of consciousness appeared. Initially he received Ca and cholecalciferol, at 15 years old alfacalcidol was added to therapy. Further, the patient did not particularly monitor Ca and P levels. In adolescence N. was diagnosed with Fahr's syndrome (CT signs of basal ganglia calcification, cranial hyperostosis), later – bilateral cataracts. Hypogonadotropic hypogonadism was diagnosed in childhood. He received courses of gonadotropins until the age of 18 years. The secondary sex characteristics appeared at the age of 25 years. In adulthood, androgen therapy was periodically prescribed. At admission he irregularly received alfacalcidol 2.0 mg, Ca carbonate 2000 mg and cholecalciferol. Laboratory tests revealed hypocalcemia – 1.9 mmol/l (2.15–2.55), hyperphosphatemia – 2.15 mmol/l (0.74–1.52), hypocalciuria – 1.52 mmol/d (2.5–8). Therapy was corrected (alfacalcidol 2.5 mg, Ca carbonate 2500 mg) with normocalcemia achievement – 2.2 mmol/l, however mild hyperphosphatemia persisted – 1.63 mmol/l. BMD at the lumbar spine, femoral neck and distal third of the radius by DXA were within the expected range for age but the patient had a height loss of 5 cm. X-ray revealed multiple vertebral compression fractures (Th7, Th10, L2-3, L5). HPT and hypogonadotropic hypogonadism allowed us to suspect APECED. We excluded adrenal insufficiency, hypothyroidism and autoimmune gastritis but diagnosed esophageal candidiasis for the first time. Genetic analysis showed homozygous mutation in the *AIRE* gene. Because of hypogonadotropic hypogonadism, mixed testosterone esters were added. Considering the combination of severe osteoporosis with HPT, teriparatide became the drug of choice. This also allowed us to reduce the dose of alfacalcidol, Ca supplements while maintaining target Ca and P values. X-ray 6 months after did not reveal vertebral fractures progression.

Conclusions

Achievement of HPT compensation in APECED patients is challenging due to polypragmasia and malabsorption. Autoimmune hypogonadism, including hypogonadotropic, is found in 14-60% cases and affects bone metabolism. Prescribing teriparatide presumably has benefits in HPT patients with osteoporosis.

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P191

Activating somatic ESR1 mutation in an aggressive prolactinoma

Ticiana Silva[1], Jacobo Buelvas Mebarak[2], John C. Magnotto[2], George A. Stamatiades[2], Yanan Kuang[3], Cloud Paweletz[3], Edward R. Laws[4], Rona Stephanie Carroll[2], Rinath Jeselsohn[3], Dipika Mohan[5], Antonio Marcondes Lerario[6], Minh-Tam Truong[7], Wenya Linda Bi[4], David A. Reardon[3], David M. Meredith[8], Ursula Kaiser[2] & Ana Paula Abreu[1]
[1]Brigham and Women's Hospital and Harvard Medical School, Department of Internal Medicine, Division of Endocrinology, Diabetes and Hypertension, Boston, United States, [2]Brigham and Women's Hospital and Harvard Medical School, Department of Internal Medicine, Division of Endocrinology, Diabetes and Hypertension, Boston, United States, [3]Dana-Farber Cancer Institute, Department of Medical Oncology, Boston, United States, [4]Brigham and Women's Hospital and Harvard Medical School, Department of Neurosurgery, Boston, United States, [5]Washington University School of Medicine, Department of Medicine, St. Louis, United States, [6]University of Michigan, Department of Internal Medicine, Division of Metabolism, Endocrinology and Diabetes, Ann Arbor, United States, [7]Boston University Chobanian & Avedisian School of Medicine, Department of Radiation Oncology, Boston, United States, [8]Brigham and Women's Hospital and Harvard Medical School, Department of Pathology, Boston, United States

Introduction

Prolactinomas are benign tumors usually well controlled with dopamine agonists; few progress on medical therapy through unclear molecular mechanisms. Although the *SF3B1* mutation has been recently associated with aggressive prolactinomas, in most cases, no genetic mutations have been reported. We aimed to identify somatic genetic alterations associated with prolactinomas using a gene panel.

Method and Results

Oncopanel, a massively parallel sequencing panel, was performed to identify somatic genomic variants and copy number variation (CNV) in a cohort of 20 patients with prolactinomas (age, mean ± SD 38.6 ± 14.49 years; 12 women). 40% of our patients who underwent surgery were resistant to dopamine agonists. None of our patients had metastatic disease. We identified a somatic *ESR1* (encoding estrogen receptor alpha) mutation (p.y537S) in a post-menopausal woman with a recurrent prolactinoma in DNA obtained from her fourth surgery. No *SF3B1* variants or other pathogenic variants were identified in this cohort. The median CNV events was 46 events (IQR: 1-80) with 64% gene amplification and 36% gene losses. The prolactinoma harboring the $ESR1_{Y537S}$ had 233 CNV events consistent with a highly disrupted genome and much higher than the remaining of our cohort samples. We then sought to investigate if there was circulating cell-free DNA. We were able to identify $ESR1_{Y537S}$ in peripheral blood using droplet digital PCR, indicating high tumor shredding, which is not commonly seen in pituitary adenomas and raises the question of the benign nature of this tumor. $ESR1_{Y537S}$ is a hotspot mutation in metastatic breast cancer. $ESR1_{Y537S}$ confers resistance to classic hormonal treatment in breast cancer by activating the receptor independent of ligand binding. This results in high cell proliferation and confers an advantage over cells expressing wild-type estrogen receptors. Elacestrant, a second-line ER degrader, increases overall progression-free survival in patients with resistant breast cancer and $ESR1_{Y537S}$. Given the lack of response to multimodality therapies, elacestrant was initiated after completion of the third cycle of radiotherapy in this patient with aggressive prolactinoma harboring $ESR1_{Y537S}$. The combination of radiotherapy with this personalized treatment was able to control tumor growth and significantly reduce prolactin levels after years without adequate control.

Conclusion

ESR1 regulates lactotroph differentiation and proliferation. Our data supported a role for $ESR1_{Y537S}$ in the unusually aggressive behavior of this patient's prolactinoma in the postmenopausal setting. Molecular profiling revealing the $ESR1_{Y537S}$ mutation allowed us to use targeted therapy to promote control of a previously resistant prolactinoma.

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P192

Effectiveness of myo-inositol in treating infertility in patients with polycystic ovary syndrome

Kamilla Mamadjanova[1], Shakhnoz Mamadjanova[2] & Zulaykho Shamansurova[1,3]
[1]Central Asian University Medical School, Endocrinology, Tashkent, Uzbekistan, [2]Andijan State Medical Institute, Obstetrician and Gynecology, Andijan, Uzbekistan, [3]Institute of Biophysics and Biochemistry at the NUUz, Metabolomics, Tashkent, Uzbekistan

Polycystic ovary syndrome (PCOS) is a highly prevalent and representing the most common endocrine-metabolic disorder in reproductive-aged women. PCOS ishighly correlated with insulin resistance and hyperandrogenism. Myo-inositol (MI) supplementation in women with PCOS has been evaluated over the last years. Many hormonal and reproductive impairments associated with this disorder seem relieved by the supplement.

Material and Methods

The meta-analysis was done using the systematic search performed in MEDLINE, EMBASE, PubMed and Research Gate from the inception until October 20th, 2021. Randomized controlled trials (RCTs) included women diagnosed with PCOS and groups having inositols, metformin and placebo.

Results

Twenty-six RCTs were identified, including data of 1691 patients (806 myoinositol, 311 with placebo, and 509 metformin groups). In patients treated with inositols, the risk of having a regular menstrual cycle was found by 1.79 higher than in the case of placebo. Moreover, the inositols showed noninferiority compared to metformin in this outcome. In the case of BMI (MD = -0.45; CI: -0.89; -0.02), free testosterone (MD = -0,41, CI: -0.69; 0.13), total testosterone (MD = -20.39, CI: -40.12; -0.66), androstenedione (MD = -0.69, CI: -1,16; -0.22) , glucose (MD = -3.14; CI: -5.75; -0.54) levels and AUC insulin (MD = -2081.05, CI: -2745.32; -1416.78) inositol treatment induced greater decrease compared to placebo. Inositol increased sexhormone-binding globulin significantly compared to placebo (MD = 32.06, CI:1.27; 62.85). The primary outcome was normalization of menstrual cycle whereas secondary outcomes were body mass index (BMI), parameters of carbohydrate metabolism and clinical and laboratory hyperandrogenism. Results are reported as risk ratios or mean differences (MDs) with 95%

confidence intervals (CIs). This increased production of androgens is increased by the surplus of LH and by hyperinsulinism. In PCOS, treatment with metformin (MET) ameliorated insulin sensitivity and decreased the androgens levels. Studies shown that MI leads to a decrease in LH and androgen levels, as well as a decrease in insulin resistance. Thus, MI is believed to be able to re-establish ovulatory menstrual cycles (especially in obese women with PCOS).
Conclusion
Polycystic ovarian syndrome is a highly inherited complex polygenic, multifactorial disorder. Insulin resistance increases the production of androgens by the theca cells. Elevated androgen levels play a significant role in menstrual cycle disrturbance and anovulation. These factors then become obstacles in occurrence of pregnancy. Myo-inositol (MI) increases insulin sensitivity, decreases hyperandrogenism and improves the menstrual cycle.

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P193

A patient with an adrenal adenoma and pituitary and intracranial meningiomas due to an ARMC5 mutation

Kasiani Papadimitriou[1], Anastasios Tsitsimpis[1], Melpomenì Moustaki[1], Maria Rigana[1], Nikolaos Kalogeris[1], Konstantinos Barkas[2], Konstantinos Nastos[3], Constantine Stratakis[4] & Andromahi Vryonidou[1]
[1]Korgialenio Benakio, Red Cross Hospital, Endocrinology, Diabetes, and Metabolism Department, Athens, Greece, [2]General Hospital 'Agios Panteleimon', Neurosurgery Clinic, Nikaia - Athens, Greece, [3]General Hospital 'Attikon', Third Surgical Clinic, Chaidari - Athens, Greece, [4]Foundation for Research & Technology, Institute of Molecular Biology & Biotechnology, Heraklion, Greece

Introduction
Armadillo-containing repeat protein 5 gene (ARMC5) is a tumor suppressor gene expressed in different human tissues. Inactivating germline and somatic mutations of the gene are involved in the pathogenesis of primary bilateral macronodular adrenocortical hyperplasia (PBMAH). These mutations are mainly met in the familial form of PBMAH and are associated with a more severe Cushing Syndrome, meningiomas and T-cell immune response defects. However, the role of ARMC5 mutations in the pathogenesis of unilateral adrenal cortical adenomas is yet poorly investigated.
Case presentation
A 61 -year- old female was referred to our outpatient clinic due to a left adrenal incidentaloma and an 18F-FDG PET/CT with pituitary and left adrenal uptake. For the last year, she presented progressively worsening fatigue, weakness, headaches, depression and deregulation of arterial blood pressure under her regular treatment. Further diagnostic work up with adrenal CT revealed an inhomogeneous left adrenal lesion, 5,3 X 4,5 cm, with low wash out (absolute 27,8%, relative 20,4%) and pituitary MRI showed pituitary and intracranial lesions suggestive of meningiomas. Hormonal assessment revealed complete pituitary hormone sufficiency and ACTH independent cortisol hypersecretion. Initially the patient underwent a left adrenalectomy with subsequent remission of hypercortisolism, and afterwards on resection of the pituitary tumor. Pathology report was compatible with adrenal adenoma and meningioma, respectively. Genetic screening revealed a rare germline ARMC5 mutation [c.2192C>G (p.Pro731Arg, P731R), heterozygosity]. Post-surgically, the patient is under hormone replacement therapy with hydrocortisone and levothyroxine, and is regularly followed up at our outpatient clinic. Family screening is pending.
Discussion
This a rare case of a patient with ARMC5 mutation presenting with Cushing Syndrome, due to unilateral adrenal adenoma, and pituitary and intracranial meningiomas. Though the relationship between ARMC5 mutations and PBMAH has been established, ARMC5 mutations are considered very rare in unilateral adrenal adenomas. On the other hand, patients with meningiomas presented higher prevalence of adrenal nodules in a recent study. Further research is needed to elucidate the association between meningiomas, adrenal adenomas and ARMC5 mutations.

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P194

Metastatic pulmonary neuroendocrine carcinoma associated with AVP deficiency and panhypopituitarism due to a hypothalamic metastasis

Tiberiu Manole[1], Camille Baudry[1], Isabela Banu[1], Adela Voican[1] & Olivier Dupuy[1]
[1]Paris Saint Joseph Hospital, Endocrinology - Diabetology, Paris, France

Introduction
Arginine vasopressin (AVP) disorder, formerly known as diabetes insipidus (DI), is a disease that results in either decreased release and/or secretion of antidiuretic hormone (AVP deficiency or central DI) or a reduced response to it (AVP resistance or nephrogenic DI). Carcinoid tumors are rare malignant neuroendocrine epithelial tumor, 25% occurring in the lungs, making them the second most common site. Atypical carcinoids and the development of metastases are associated with a poor prognosis.
Objectives and Methods
To present a case report of a 59-year-old female with AVP deficiency and panhypopituitarism caused by a metastatic neuroendocrine tumour, with cerebral and bone metastases.
Case presentation
In 2022 the patient presented with a mild polyuro-polydipsic syndrome (4 L/day of water intake and urinary output) and chronic fatigue for which she did a chest CT, revealing a 19 mm right inferior pulmonary lobe mass. Tumor biopsy showed an atypical neuroendocrine carcinoma, with a Ki-67 index of 40% and a positivity for chromogranin A, while the somatostatin receptors were negative. The FDG and DOTATOC scans showed secondary lesions in the mediastinal and inguinal lymph nodes, brain and sternum. The primary lesion was resected and she received chemotherapy and radiotherapy. One year later, she returned to the Emergency Department with increasing polyuro-polydipsic syndrome, with hypernatremia up to 147nmol/l and an episode of a seizure. The MRI showed a progression of the cerebral lesions, as well as a hypothalamic lesion of 9/6 mm compressing the pituitary stalk and she was referred to our clinic.
Results
The water intake and urinary excretion were up to 7 L/day, while the serum osmolality was normal (288 mOsm/kg) and urinary osmolality was at the normal inferior limit (81 mOsm/kg, normal range 50-1400). The blood tests showed panhypopituitarism and a mild hyperprolactinemia. Hydrocortisone, levothyroxine and desmopressin substitution treatments were started. The neurosurgical consultation concluded that the hypothalamic lesion was unresectable. Treatment consisted of systemic chemotherapy resumption and localized radiotherapy for the cerebral metastases. Furthermore, endocrine follow-up is required for hormonal treatment adjustment.
Conclusion
AVP deficiency and metastatic pulmonary neuroendocrine carcinoma are two of the rarest endocrine disorders which can greatly affect patients' quality of life, the latter having a 5-year relative survival rate of 55%. Therefore, prompt diagnosis and treatment are mandatory, as well as close surveillance.

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P195

Age-stratified reference ranges for directly measured serum free testosterone in healthy men

Joeri Walravens[1], Gido Snaterse[1], Nick Narinx[2], Leen Antonio[2], Tim Reyns[3], Tom Fiers[3], Jean-Marc Kaufman[1] & Bruno Lapauw[1]
[1]Ghent University Hospital, Department of Endocrinology, Gent, Belgium, [2]Leuven University Hospital, Laboratory of Clinical and Experimental Endocrinology, Leuven, Belgium, [3]Ghent University Hospital, Department of Clinical Chemistry, Gent, Belgium

Introduction
Determination of serum (calculated) free testosterone (FT) in clinical practice has been suggested by several clinical guidelines for the diagnosis of male hypogonadism in men with borderline total T concentrations and in situations with altered sex hormone-binding globulin, as it correlates better with androgen exposure than total T. The gold-standard for the determination of FT levels is considered to be directly measured free testosterone (mFT) using equilibrium dialysis followed by mass spectromety (ED LC-MS/MS). However, no widely accepted reference ranges are available for this clinical parameter. We established mFT reference ranges for healthy men aged 18 to 69 years.
Objective
To establish reference ranges for measured FT in serum of healthy adult men.
Methods
Reference ranges were determined following Clinical & Laboratory Standards Institute guideline C28-A3c per age decade. Serum samples were analyzed from healthy men participating in the SIBLOS/SIBEX and EMAS studies, both population-based cohort studies. Exclusion criteria were medications or conditions that affect sex steroid metabolism or a BMI larger than 35 kg/m2. mFT levels were measured in 867 men using ED LC-MS/MS as previously reported (1). Subsequently, 95% reference ranges were determined using the non-parametric method.

Results

We present 95% mFT age-stratified reference ranges. These reference ranges show an expected, decreasing trend of mFT with aging. Lower limits and median mFT decrease at a remarkably stable rate of, on average, 12% per decade up into the 6th decade of life. However, in the upper limit, a marked decrease of 25% occurs after 39 years, followed by smaller decreases of 6% per decade in older age categories.

Age category (years)	Median mFT (ng/dl)	95% mFT reference range (ng/dl)
25-29 (n=148)	10.3	5.6 - 17.1
30-39 (n=252)	9.7	4.9 - 18.1
40-49 (n=207)	8.0	4.3 - 13.5
50-59 (n=146)	7.0	3.8 - 12.6
60-69 (n=114)	5.9	3.3 - 11.9

Conclusion

We have determined mFT reference ranges in healthy men aged 25 to 69. These reference ranges are a first step to improving the framework for further development and integration of free testosterone measurements and calculations in clinical practice.

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P196

Assessing medication adherence and unravelling the reasons for non-adherence among patients with diabetes mellitus

Mukhammadbektosh Khaydarov[1], Timurkhon Tillakhujaev[2], Malika Oblokulova[2], Asadbek Sultonov[2], Zulaykho Shamansurova[2,3] & Zamira Khalimova[4]
[1]Central Asian University - CAU, Toshkent, [2]Central Asian University, Endocrinology, Tashkent, Uzbekistan, [3]Institute Biophysics and Biochemistry at the NUUz, Metabolomics, Tashkent, Uzbekistan, [4]Republican Specialised Scientific Practical Medical Centre of Endocrinology, Endocrinology, Tashkent, Uzbekistan

Introduction

Chronic diseases pose an escalating health burden worldwide, affecting individuals across all age groups and socioeconomic backgrounds. The number of people living with diabetes has nearly quadrupled over the past four decades. The aim of our study was estimation of the level of medication (meds) adherence among DM type 2 patients whose admitted into Republican Specialised Scientific Practical Medical Centre of Endocrinology in Uzbekistan.

Material and methods

Pilot testing were conducted in 120 patients with DM in age between 18 – 75 years old. Type 1 DM – 7%. All people after their agreement and sign consent form, were questioned by using Morisky Medication Adherence Scale (MMAS) after approval from the local Scientific and Ethical Committees. All data was collected using Google template and undergo to statistics.

Results

Data analysis showed that 71% of observed patients were on retirement, 3% living alone, other lives with their family, female patients consisted big part of the group (65%). DM duration >10 years in 65%, between 2 to 10 years in 34%, less than 2 years in 1%. Despite the most of the people followed to healthy habits, 12% among them were smokers and 4.7% were alcohol users, 59% of them have HTN, 40% have CVD, 30% arthritis, 2% no any additional diseases. Only 6% of them achieved good glycemic control, 11% acceptable according to HbA1c level and other were in poor glycemic control. Reason for incompliance to taking prescribed medications were forgetting to take in 28.5%, in 50% careless, in 51% skipped the time to take of medication, 29% stop when fill worse, 46% experienced misunderstanding instruction, 24% stop due to side effects, 38% can change dosage without doctors. Interestingly, 48% of them intentionally stop taking meds, 5% do not take because not understand, 5% afraid to use meds, 8% just forget about Meds, 3% stop after feeling better, 2% due to delivery issues, 6% stop without reasons, 3% stop taking med because of long duration.

Conclusion

Leading cases of not reaching the good glycemic control among people with DM is adherence to prescribed medications due to their careless, misunderstanding, skip the time, stop when feeling worse or better, forgetting, or without any reason. It is necessary educate patients to more tight self-control of adherence to achieve better glycemia in patients with DM.

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P197

Improving the inpatient assessment and management of people with diabetes and frailty by the involvement of the diabetes in reach team

Eka Melson[1,2], Kashish Gera[1], Garima Gupta[1], Hnin Lwin[1], Anu Thomas[1], Mohamed Fazil[1], Kevin Thottungal[1], Vishnusankar Umasankar[1], HayMar Tun[1], Meri Davitadze[3], Alison Gallagher[1] & Kath Higgins[1,2]
[1]University Hospitals of Leicester, [2]University of Leicester, United Kingdom, [3]University of Birmingham, United Kingdom

Introduction

Our previous study has shown low rates of inpatient deintensification and high rates of adverse outcomes in people with diabetes and frailty[1]. The diabetes in reach (DiR) team consists of diabetologists working together with diabetes specialist nurses, proactively supporting non-specialists in the inpatient management of diabetes. This could be done either virtually or by face-to-face review in the medical ward. This study assessed the role of the DiR team in improving care for inpatients with diabetes and frailty.

Methods

We included all people with diabetes and clinical frailty score ≥ 6 discharged from our medical unit in the year of 2022. Data including demographics, medications and comorbidities were collected. Inpatient management and outcomes collected include involvement of the DiR team, deintensification rate, inpatient hypoglycaemia (defined by any episode of capillary blood glucose of <4 mmol/l), inpatient mortality and one-month readmission rates. Logistic regressions were conduction to assess for the association between the involvement of DiR with deintensification and other outcomes using StataSE v17.0.

Results

Six hundred and sixty-five people with diabetes and frailty were included in our analysis. 51.9% (n=345/665) were female with a median age of 79 years (71-86). 19% (n=119/625) were deintensified during admission. DiR teams were involved in the care of 26.8% (n=178/665) of the patients. People with inpatient hypoglycaemia were more likely to be reviewed by the DiR team compared to those without hypoglycaemia [aOR: 5.7 (95% CI: 3.7-8.6), $P<0.001$]. In patients who were deintensified, deintensification was done by the parent team in 38.7% (n=46/119) and 61.3% (n=73/119) by the DiR team. Irrespective of hypoglycaemia, being reviewed by the DiR team was associated with increased odds of deintensification compared to those that were not reviewed by the DiR team [aOR: 4.2 (95% CI: 2.6-6.8), $P<0.001$]. No associations were seen between being reviewed by DiR with inpatient mortality and readmission rate.

Conclusion

The majority of inpatient deintensification in people with diabetes and frailty was initiated by the DiR team, compared to the parent team. DiR could play an effective and important role in improving the inpatient deintensification rate in people with diabetes and frailty.

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P198

Comparing analytical and glucometric parameters in patients with type 1 diabetes

Pilar Pérez-Reyes[1], Pablo Vera-González[1], Ángel Rebollo-Román[1], Delia Marginean[1] & Verónica Torres-Herrera[2]
[1]Hospital Universitario Reina Sofia, Córdoba, Spain, [2]Facultad Medicina Cordoba, Córdoba, Spain

Aims

We aimed to evaluate the relationship between glycosylated hemoglobin (HbA1c), time-in-range (TIR), Glucose Management Index (GMI) and coefficient of variation (CV) in a cohort of adult patients with type 1 diabetes (T1DM) and flash glucose monitoring (FGM).

Material and methods

Cross-sectional study of patients with T1DM who FGM from Córdoba, Spain. Demographic and analytical data were collected. Glucose metrics and engagement statistics (adjusted for previous 90-day averages) were obtained from LibreView, coinciding temporally with the analytical determination of HbA1c. We defined ‘;stable diabetes‘; in our cohort as CV $<$ 36%, GMI $<$ 7% and TIR $>$ 70%. Statistical analysis was made with SPPS vs 25.

Results

169 patients (55% women, 45% men; mean age of 39.74 11.80 years) were enrolled in the study. The mean duration of diabetes was 19.94 10.63 years. Mean BMI was 26.194.46 kg/m^2. Regarding glycemic data, we found that 53.29% of

patients presented HbA1c below 7%, 55.82% GMI below 7%, 37.42% CV below 36% and 38.03% TIR above 70%. In the correlation analysis we observed a statistically significant positive relationship between HbA1c and GMI (rho = 0.793; $P<0.001$) and between HbA1c and CV (rho = 0.209; $P=0.007$). We also found a significant and negative relationship between HbA1c and TIR (rho = -0.735; $P<0.001$). Therefore, we found that when we measure glucose metrics for the last 90 days, there is a statistically significant linear and direct relationship between laboratory parameters (HbA1c) and glucometric parameters (GMI and CV), and a linear and inverse relationship between HbA1c and TIR.

Conclusion

In our cohort, we found that there's a congruent correlation between laboratory parameters of glycemic control and glucose metrics from FGM, since lower HbA1c levels were associated with stable diabetes according to glucometric data from FGM.

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P199

Endocrine toxicity is an independent predictor of survival in lung cancer patients treated with immune checkpoint inhibitors

Sofia Ntouraki[1], Emmanouil Panagiotou[1], Ioannis A. Vathiotis[1], Maria Effrosyni Livanou[1], Athanasios Trimis[1], Andriani Charpidou[1], Konstantinos Syrigos[1] & Melpomeni Peppa[1,2]

[1]Third Department of Medicine, Sotiria General Hospital for Chest Diseases, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, [2]Second Propaedeutic Department of Internal Medicine, Research Institute and Diabetes Center, Attikon University Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Lung cancer (LC) is a serious health problem worldwide. Survival outcomes have improved over time, due to the widespread adoption of therapeutic agents, including immune checkpoint inhibitors (ICIs). Endocrine immune-related adverse events (irAEs) are common in LC patients treated with ICIs. A retrospective study of LC patients was performed in a tertiary center for cases seen between January 2014 and October 2023. In total, 983 LC patients were included in the study, with a median age of 67 years. 670 patients (68.1%) received treatment with a PD-1 inhibitor, 221 patients (22.5%) with a PD-L1 inhibitor and 92 patients (9.4%) a combined therapy with a PD-1 and a CTLA-4 inhibitor. Endocrine irAEs presented at a median time of 4.1 months and included hypothyroidism (15.6%), hyperthyroidism (4.3%), adrenal insufficiency, (0.4%), hypophysitis, (0.4%), and diabetes mellitus, (0.2%). The median time to onset of thyroid disease showed a statistically significant difference ($P=0.004$), between hypothyroidism (4.87 months, 95% CI: 4.07 - 5.63 months), and hyperthyroidism (2.62 months, 95% CI: 2.10-3.77 months). The incidence of endocrine irAEs was similar between different classes of ICIs. Most (97.6%) endocrine irAEs were mild (grade 1-2) and did not require treatment interruption. In multivariate analysis, the presence of endocrine irAEs was associated with the presence of endocrine comorbidities at diagnosis, the absence of liver metastases, as well as the development of dermatologic irAEs or other irAEs. Median overall survival (OS) was higher in LC patients who experienced an endocrine irAE (31.6 months) compared to those who did not (10.8 months). The survival difference remained statistically significant in the 3-month (HR: 0.42) and 6-month landmark analysis (HR: 0.51). The OS advantage in patients with endocrine irAEs was observed in both NSCLC (HR: 0.36) and SCLC patients (HR: 0.27). Median progression-free survival was also higher (10.7 vs 3.8 months). Additional research is needed to validate the role of endocrine irAEs as an independent predictor of survival outcomes in LC patients.

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P200

The association between levels of Follicle stimulating hormone and Glomerular filtration rate in peri- and postmenopausal women

Elena Armeni[1], Nektaria Papanikola[1], Ifigeneia Avgousti[1], George Mavraganis[2], Aikaterini Stefanaki[1], Stavroula A. Paschou[1], Areti Augoulea[1], Iliana Karagkouni[1], Kimon Stamatelopoulos[2] & Irene Lambrinoudaki[1]

[1]National and Kapodistrian University of Athens, 2nd Department of Obstetrics and Gynecology, Aretaieio Hospital, Athens, Greece, [2]National and Kapodistrian University of Athens, Department of Clinical Therapeutics, Athens, Greece

Objective

Kidney function is known to be interrelated with the aging process. On the other hand, a number of studies support a link between the menopausal transition and kidney function, either directly or indirectly, secondary to the effect of the alternating hormone environment or the effect of the accumulated cardiovascular risk factors, respectively. We aimed to evaluate the cross-sectional association between kidney function and sex hormones at the time of the menopausal transition and beyond, in a sample of peri- and postmenopausal women.

Methods

We evaluated retrospectively the data of 217 women, recruited from the 2nd Department of Obstetrics and Gynaecology, Menopause Clinic, Athens, Greece. For the purpose of this study we reviewed electronic patient files, with normal to moderate kidney function (eGFR $>$ 60 mL/min/1.72m^2) corresponding to consultations in the clinic. Women were stratified according to their reproductive status as perimenopausal, so 12 months prior up to 12 months after the final menstrual period (FMP), early postmenopausal (1-5 years after the FMP) and late postmenopausal (>5 years after the FMP). Biochemical data were recorded including sex hormone levels. Kidney function was evaluated using the equation for CKD-EPI 2021.

Results

Women of this sample were aged 53.297.6 years, and were slightly overweight with a body mass index (BMI) of 26.364.12 kg/m^2. The baseline eGFR-EPI value was 94.27.67. Correlation analysis showed that eGFR-EPI values are related to stimulated hormone (FSH, r = -0.198, $P=0.005$) but not with total or free circulating estrogen, testosterone levels, or sex hormone binding globulin (SHBG). The eGFR-EPI values also correlated with menopausal age ($r=-0.177$, $P=0.003$). We evaluated eGFR-EPI values per reproductive status, kidney function decreased linearly with advancing reproductive status, estimated as values of eGFR-EPI (mL/min/1.73m^2): perimenopausal women ($n=81$), 97.813.5 vs early postmenopausal women ($n=74$), 92.115.7 vs late postmenopausal women ($n=100$), 91.712.9 (p for linear trend 0.005). Linear regression analysis showed that values of eGFR were associated with FSH (b-coefficient = -0.150, $P=0.010$) and age (b-coefficient = -0.270, $P<0.001$) with R2 of 9.5%. The model was adjusted for current smoking, homeostasis model assessment of insulin resistance, mean arterial pressure, waist to hip ratio, triglycerides, free estrogen index.

Conclusion

The results of this study highlight an association between the peri- and postmenopausal fluctuation of FSH and the kidney function in women. Further longitudinal studies are required to confirm our findings.

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P386

Molecular genetics of unresolved mody (Mody-X)

Mariana Gomes Porras[1], María Soledad Ruiz de Adana Navas[1], María Fontalba Romero[1], Ana Lago Sampedro[1], Cristina Maldonado Araque[1] & Ángel Campos Barros[2]

[1]Regional University Hospital of Málaga, Endocrinology and Nutrition, Málaga, Spain, [2]Institute of medical and molecular genetics (INGEMM), Health Research Institute of the La Paz University Hospital (IdiPAZ), Madrid, Spain

Introduction and Objectives

Although Next Generation Sequencing (NGS) technologies have significantly improved the molecular diagnosis of MODy, there is still a high percentage of cases in which the clinical suspicion remains without confirmatory molecular diagnosis. The main objective was to identify new candidate genes for MODy, by means of targeted NGS of a cohort of adult patients with clinically suspected MODy, in whom variants in the 14 known MODy genes implicated in its etiology were previously excluded.

Subjects and methods

Descriptive study that included 51 adult patients with diabetic debut before the age of 35 years, negative pancreatic autoimmunity, no clinical or analytical data of insulin resistance, negative ultrasensitive C-reactive protein, BMI $<$ 25, and first-degree family history of DM. Genomic DNA samples were sequenced using a proprietary targeted NGS panel to analyze 482 genes associated with dysglycemia (MonDiabV4 panel). Filtering, classification and prioritization of variants was performed with help of VarSeqV2.5 and Alamut Visual Plus V1.9 programs, using confidence and quality criteria, (depth $>$100x; % bp 20x $>$95%), allele frequency $<$1% (gnomAD V2.1.1 controls), impact ('missense', 'nonsense', 'frameshift') and *in silico* prediction of pathogenicity (CADD V1.4, score $>$20).

Results
100% presented heterozygous predicted deleterious variants in more than one gene, with a mean of 3.81.4 variants/case (range 2-6), 11 not previously described. 95.5% were missense, 2.2% frameshift or nonsense, and all were classified as variants of uncertain significance (VUS), using ACMG criteria. They were identified mostly in genes involved in the regulation of insulin secretion, in order of frequency: *CACNA1D, CACNA1B, CACNA1G, CACNA1H, CACNA2D2* and *CACNA2D4* (23.8%), all encoding subunits of voltage-dependent calcium channels expressed in pancreatic β-cells; in *SLC2A2, SLC22A3, SLC27A2, SLC6A1* and *SLC6A13* (14. 3%), encoding transporters of type 2 glucose, organic cations, long-chain fatty acids, and GABA, respectively; or in *VPS13C* (10.7%), *WFS1*(5.9%), *ADCy5* (4.7%), *ADCyAP1* (3.6%) and *ANK1* (1.2%). Deleterious variants were also identified in genes associated with the following pathophysiological mechanisms: reduced β-cell survival (*SIRT1, SERPINB4, THADA*), impaired insulin biosynthesis (*PLCXD3*), insulin exocytosis (*ETV5*), insulin signaling (*ADAMTS9, KLF14, TBC1D4, BMP3*), and pancreatic islet development and differentiation (*RFX6, NOTCH2, GATA6, FOXA2*).
Conclusion
NGS reveals a wide array of new candidate genes for MODy and suggests in most cases, a multifactorial genetic component that differs from DM2 by its earlier clinical presentation and absence of metabolic syndrome and inflammation.

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P387

Gemigliptin attenuates TGF-β-induced renal fibrosis by inhibiting the TGF-β/Smad3 signaling pathway through the upregulation of FGF21 expression

Gwonsoo Jung[1]
[1]Daegu-Gyeongbuk Medical Innovation Foundation, New Drug Development Center, Daegu, Korea, Rep. of South

Aim
Fibroblast growth factor 21, a well-known regulator of metabolic disorders, exhibits the potential to prevent renal fibrosis by negatively regulating the transforming growth factor β (TGF-β)/Smad3 signaling pathway. Gemigliptin and dipeptidyl peptidase-4 inhibitors are frequently utilized in the management of patients with type 2 diabetes. However, the protective effects of gemigliptin on renal fibrosis, particularly concerning its potential to upregulate the expression of fibroblast growth factor 21 (FGF21), remains incompletely understood. The purpose of this study was to investigate the gemigliptin's renoprotective effects against TGF-β-induced renal fibrosis by enhancing the expression of fibroblast growth factor 21 in the cultured human proximal tubular epithelial cell line, HK-2.
Methods
HK-2 cells were maintained with keratinocyte-free medium according to the supplier's recommendations, and exposed to the indicated doses of TGF-β, FGF21, and gemigliptin for 24 h. To elucidate the effect of FGF21, knockdown experiments were conducted by transfecting HK-2 cells with small interfering RNA targeting the fibroblast growth factor 21 for 24 h.
Results
Treatment of FGF21 effectively prevented TGF-β-induced renal fibrosis by attenuating TGF-β/Smad3 signaling pathway. Similarly, Gemigliptin showed protective effects against TGF-β-induced renal fibrosis by mitigating TGF-β/Smad3 signaling, which is achieved through the upregulation of FGF21 expression. However, the protective effects of gemigliptin were blocked when FGF21 expression was knockdowned in TGF-β-treated HK-2 Cells.
Conclusion
These results indicate that gemegliptin has the potential to confer protective effects against TGF-β-induced renal fibrosis by elavating FGF21 expression levels in the cultured human proximal tubular epithelial cells.

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P388

Is thyroid function associated with polycystic ovary syndrome? a bidirectional mendelian randomization study

Qinnan Zhang[1], Kai Wang[1] & Bingbing Zha[1]
[1]Shanghai Fifth People's Hospital, Fudan University, Department of Endocrinology, shanghai

Objective
Some observational studies have suggested the association between thyroid function and polycystic ovary syndrome (PCOS). However, it remains to be determined whether these associations are causal or not. The aim of this study was to investigate the underlying causal association between different thyroid function status and PCOS.
Methods
Bidirectional Mendelian randomization (MR) analysis was conducted to explore the impact of different thyroid function statuses on PCOS. The study included 10,074 individuals with PCOS and 103,164 controls for the primary analysis, with validation analysis repeated in the FinnGen R9 and EstBB PCOS cohorts. Female-specific thyroid function GWAS data were obtained from European population, including Hyperthyroidism (22,383 cases and 54,288 controls) and Hypothyroidism (27,383 cases and 54,288 controls) from the UK Biobank, and TSH (54,288 cases and 72,167 controls) and FT4 (49,269 cases and 72,167 controls) within the reference range from the ThyroidOmics Consortium. Inverse variance weighting (IVW) was chosen as the principal method, and sensitivity analysis was conducted to test for the presence of horizontal pleiotropy or heterogeneity.
Results
The IVW analysis indicated nominal significance between normal TSH levels and PCOS after adjusted for age and BMI [OR(95%CI) = 0.78(0.62,0.97), $P=0.029$], suggesting that maintaining normal TSH levels might act as a protective factor against the pathogenesis of PCOS. Besides, in order to increase the statistical power, we pooled PCOS GWAS above together by meta-analysis and found PCOS contributed to the occurrence of hyperthyroidism [OR(95%CI) = 1.37(0.73,2.57), $P=0.012$]. However, no causal relationship was found after Bonferroni correction (P-value < 0.0031).
Conclusion
Although the MR analysis didn't indicate genetic causal association between thyroid function and PCOS after Bonferroni correction. Further efforts are needed to interpret the potential causal relationship between thyroid function and PCOS in different age and BMI subgroup.

Keywords: Thyroid Function; Polycystic Ovary Syndrome; Mendelian randomization; Causal association.

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P389

Effect of endothelial no synthase gene polymorphism on the course of diabetic nephropathy in patients with type 2 diabetes mellitus

Andriy Nesen[1], Vira Zlatkina[2] & Polina Semenovykh[3]
[1]State Institution 'L.T. Malaya Institute of Therapy of the National Academy of Medical Sciences of Ukraine', Kharkiv, Ukraine, [2]V. N. Karazin Kharkiv National University, Kharkiv, Ukraine, [3]State Institution 'L.T. Malaya Institute of Therapy of the National Academy of Medical Sciences of Ukraine'

The aim of the study was to identify a possible association of the G894T (rs 1799983) polymorphism of the endothelial nitric oxide synthase (eNOS) gene with indicators of renal function and glucose metabolism in patients with type 2 diabetes mellitus (DM) with nephropathy.
Materials and methods
In the course of the study, 126 patients with diabetic nephropathy (DN) were examined. The control group consisted of 20 healthy individuals. After the initial examination, depending on the polymorphic variant rs 1799983 of the eNOS gene, patients with type 2 diabetes were divided into two groups: Group I - patients with DM - carriers of the G/G genotype of the G894T (rs 1799983) polymorphism of the eNOS gene ($n=80$); Group II - patients with DM - carriers of the G/T and T/T genotypes of the G894T (rs 1799983) polymorphism of the eNOS gene ($n=46$). Genotyping of the rs 1799983 polymorphism of the eNOS gene was performed using the Taq-Man® Fast Universal PCR Master Mix and TaqMan® SNP Assay.
Results and discussion
Our studies have shown that in patients with DN, the distribution of genotypes of the G894T polymorphism of the eNOS gene corresponds to the Hardy-Weinberg equilibrium in all studied groups and does not differ significantly from European populations. In the group of patients with DM with DN, the total frequency of G/T and T/T genotypes of the G894T polymorphism of the eNOS gene is 3 times higher than in the control group, which proves the undoubted influence of the T allele on the development of DN in this cohort of patients. Patients with DN - carriers of the mutant T allele (genotypes G/T and T/T) have significantly higher blood glucose and HOMA index ($P<0.05$) than homozygotes (genotype G/G). In patients with DN - carriers of the G/G genotype, the studied polymorphisms have better glomerular filtration rate and lower albuminuria compared to carriers of the G/T and T/T genotypes, $P<0.05$.
Conclusions
Establishing the association of eNOS gene polymorphism with the disease and further assessment of individual genetic risk is important for the development of a differentiated approach to the prevention and treatment of diabetic nephropathy in

patients with type 2 diabetes depending on the hereditary predisposition of a particular patient.

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Progression of joint and psychological complications in acromegaly and their association with treatments and disease control

Biagio Cangiano[1,2,3], Caterina Premoli[2], Davide Soranna[1], Giovanni Vitale[†,2], Silvia Grottoli[4], Valeria Cambria[4], Pietro Maffei[5], Francesca Dassie[5], Salvatore Cannavò[6], Marta Ragonese[6], Antonella Zambon[7], Luca Persani[1,2], Letizia Fatti[1] & Massimo Scacchi[3,8]
[1]Istituto Auxologico Italiano IRCCS, Milan, Italy, Division of Endocrine and Metabolic Diseases, Milan, Italy, [2]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy, [3]Istituto Auxologico Italiano IRCCS, Division of General Medicine, Ospedale S. Giuseppe, Verbania, Italy, [4]University of Turin, Department of Medical Sciences, Turin, Italy, [5]University of Padua, Padua, Italy, [6]University Hospital of Messina, Endocrine Unit, Messina, Italy, [7]University of Milano-Bicocca, Division of Biostatistics, Epidemiology and Public Health, Department of Statistics and Quantitative Methods, Milan, Italy, [8]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy

Background
Articular and psychological complications of acromegaly are known to impair patients' quality of life (QoL). The aims of this study are: (1) to look for clinical predictors for the progression of the articular and psychological complications, (2) to evaluate the progression of these complications in relation to the activity of the acromegalic disease, and (3) to evaluate how these complications interact to impair the QoL.
Material and Methods
97 patients with acromegaly were enrolled in this multicentric observational prospective study, excluding those harboring inflammatory rheumatic diseases. At the beginning of the study and after 42 months, patients' history, hormonal and physical exams were recorded, and specific questionnaires studying articular and psychological discomfort (WOMAC, AIMS, VAS), as well as a scale for QoL (AcroQoL), were administered to each patient.
Results
The log-gamma model to look for clinical predictors of psychological or articular disease progression, showed a significant correlation of female gender and a worsening of joint symptoms, as measured by VAS ($P=0{,}0139$), WOMAC pain ($P=0{,}0415$) e AIMS symptoms ($P=0{,}0448$) scales; similarly, previous radiation therapy was associated with a significant worsening of symptoms to AIMS questionnaire ($P=0{,}0084$). When evaluating the progression of both complications in relation to chronic acromegaly treatments, patients treated with dopamine agonists (DA) showed worsening of the AIMS depression scale over time ($P=0.01$). By studying the progression of scores in relation to disease activity, we found a paradoxical effect with worsening of arthropathy symptoms in patients gaining hormonal control and improvement in patients with disease recurrence. Depression scores improved, as expected, upon the achievement of disease remission. Finally, arthropathy and depression were confirmed to be independent factors impairing QoL in acromegaly. However, arthropathy showed a greater impact than depression on the worsening of patients' well-being ($P=0{,}0084$ vs $P=0{,}0500$).
Conclusion
Female sex was shown not only to be a factor associated with worse joint scores, but also a predictor of worsening joint symptoms over time, along with prior radiotherapy. If depression score decreases as expected once remission is achieved, the paradoxical worsening of arthropathy scores suggests a mixed effect of IGF1 on joint symptoms. DA seem to be associated with worsening of depression score over time, even if this effect must be confirmed in controlled trials. Arthropathy shows a greater but independent effect than depression on QoL.

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P391

Surgical outcomes in primary hyperparathyroidism: addressing factors predicting persistent or recurrent hyperparathyroidism

Yesmine Merhbene[1], Rihab Laamouri[1], Sabrine Mekni[1], Sawsen Essayeh[1], Karima Khiari[1], Nadia Mchirgui[1], Imen Rojbi[1] & Bennacef Ibtissem[1]
[1]Hospital Charles Nicolle, Tunis, Tunisia

Background
Primary hyperparathyroidism is a common endocrine disorder characterized by hypercalcemia, resulting from excessive secretion of parathyroid hormone. Parathyroidectomy, is considered as the definitive treatment for this condition, leading in most cases to remission and resolution of hypercalcemia. However, some patients experience surgical failure. Persistent hyperparathyroidism is defined as persistence of hypercalcemia after parathyroidectomy or recurrence of hypercalcemia within the first 6 months, whereas recurrent hyperparathyroidism is identified when hypercalcemia recurs after a normocalcemic period lasting more than 6 months.
Aim
This study aims to assess the efficacy of surgery as a definitive treatment for hyperparathyroidism by determining the prevalence of persistent and recurrent hyperparathyroidism as well as predisposing factors.
Methods
A retrospective cohort study spanning from 1976 to 2020 at Charles Nicolles Hospital. Two distinct groups were compared: one comprised of patients who achieved remission post-parathyroidectomy, while the other consisted of individuals experiencing persistent or recurrent hyperparathyroidism. Patient demographics, pre-operative biochemical profiles, were collected. Follow-up data included post-operative biochemical assessments. Descriptive statistics were employed to outline the demographic and clinical characteristics of the study, while statistical analyses aimed to identify factors linked to persistent or recurrent hyperparahyroidism.
Results
Eighty patients were included in our study. A sex ratio of 0.21 was observed. The overall success rate of surgery in treating hyperparathyroidism was substantial: 82.5% of the patients achived remission. Notably, no discernible differences were observed in age, or preoperative levels of calcium, phosphate, and PTH levels between the two groups. Big adenoma sizes were more prone to recurrence; (average size 30 mm in the recurrent group versus 24.7 mm). Patients with hyperplasia or carcinoma exhibited a higher likelihood of recurrence compared to those who had adenomas ($P=0.017$). Conversely, the persistent group demonstrated significantly elevated post-operative PTH levels ($P=0.046$). Moreover, postoperative hypocalcemia emerged as a predictive factor for achieving remission ($P=0.04$).
Conclusion
Our study reveals that surgery is a definitive and effective treatment for hyperparathyroidism. Nevertheless, surgical failure is not an uncommon occurrence, highlighting the need for continued vigilance in managing patients operated for primary hyperparathyroidism. Adenoma's size measurements and anatomopathology results are critical in identifying patients at higher risk of persistent or recurrent hyperparathyroidism. This study provides valuable insights for clinicians to refine their approach in managing those patients ultimately improving long-term prognosis.

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P392

Evaluation of 8-oxo-2'-deoxyguanosine as a surrogate marker of NF-κB/NLRP3 axis activation in experimental diabetes mellitus

Usatiuc Lia[1]
[1]Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

NLRP3 (NOD-like receptor family pyrin domain containing 3) inflammasome-induced IL-1β production plays an important role in the pathogenesis of type 1 and type 2 diabetes mellitus (DM). Oxidative stress and inflammation interact with each other in the pathogenesis of DM. Oxidative DNA bases modified by reactive oxygen species (ROS), such as 8-OXO-2'-deoxyguanosine (8-oxoG) are repaired by 8-oxoguanine DNA glycosylase1 (OGG1). It has been previously reported that OGG1-DNA interactions facilitate NF-κB binding to DNA targets. The aim of our study was to investigate the association between serum levels of 8-oxoG, NF-κB and NLRP3 in a rat model of Streptozotocin-induced DM. We also evaluated the effect of NLRP3 activation on insulin resistance by correlating it to the triglyceride to glucose index (TyG).
Material and Methods
Sixty Wistar-Bratislava white male rats were randomly divided into three groups: negative control were injected with citrate buffer, Streptozotocin (SZT) group that received 55 mg/100 g body weight (b.w.) SZT by intraperitoneal administration and SZTMetformin (SZTM) (100 mg Metformin/100g b.w.). For ten days the animals received by gavage water in control and SZT groups, respectively Metformin in the SZTM group. The serum levels of 8-oxoG and NF-κB, IL-1β, IL-18 and Gasdermin levels were determined. Additionally, we monitored the fasting glucose levels for each day during the experiment and we calculated TyG index using the formula TyG = ln [Fasting triglyceride (mg/dl) × fasting glucose (mg/dl)]/2.

Results
8-oxoG, NF-κB, IL1B, IL-18 and Gasdemin D were significantly increased in the STZ group compared to the control group ($P<0.01$). In the SZT group we noticed a statistically significant positive correlation between 8-oxoG, NF-κB, IL-18, IL-1B and Gasdermin. Metformin significantly reduced IL-1B levels and in the SZTM group we found no correlation between 8-oxoG and IL-1B. TyG index presented higher levels in the SZT group and was positively correlated to IL-1B, IL-18 and Gasdermin.
Conclusion
8-oxoG can be used as an indicator of NF-κB/NRLP3 axis activation. Increased levels of TyG index are correlated to NLRP3 activation, indicating its role in the associated insulin resistance development.
Keywords: NLRP3 inflammasome, NF-κB, 8-oxo-2'-deoxyguanosine, Diabetes Mellitus, TyG index
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P393

Beware of the imposter! A case report of pseudopseudohypoparathyroidism in Trinidad and Tobago

Ijaz Ogeer[1], Kevin Singh[1], Saajida Hosein[1], Joel Teelucksingh[1] & Neal Bhagwandass[2]
[1]San Fernando General Hospital, Internal Medicine, San Fernando, Trinidad and Tobago, [2]University of the West Indies, Medicine, St. Augustine, Trinidad and Tobago

Background
Hypoparathyroidism is a rare endocrine disorder that is rarely seen in clinical practice. Resistance to parathyroid hormone (PTH) gives rise to specific developmental and biochemical abnormalities allowing for a diagnosis of pseudohypoparathyroidism (PHP) [1]. Uniquely the skeletal defects seen in pseudohypoparathyroidism can occur in the absence of its associated biochemical sequelae, a condition referred to as pseudopseudohypoparathyroism (PPHP). The following case highlights this disorder.
Case
A 60-year-old female presented with generalized seizures. Past history noted diabetes and a cerebrovascular accident. Medications included metformin and once daily insulin. Examination revealed a short stature with height of 153 cm and an increased body mass index of 28.6 kg/m^2 There was brachydactyly of the 4th and 5th metacarpals bilaterally without involvement of the metatarsals. Neurological exam was negative for cognitive impairment. Routine blood investigations yielded normal complete blood count, renal and thyroid function with a markedly elevated low-density lipoprotein cholesterol of 219 mg/dl (reference range < 100). Her calcium, phosphorus and PTH were within range. Radiographs were negative for arthropathy. Antiepileptic therapy, a statin and antiplatelet agents were initiated. Discharge plan included lifestyle modifications and outpatient clinic follow up.
Conclusion
Patients with PPHP have mutations on the paternally inherited allele and have the PHP phenotype alone without hormonal resistance or the severe obesity.[2] Adult short stature is common to both PPH and PPHP due to early closure of the epiphyses of the long bones.[2] Increasing the likelihood of metabolic syndrome and diabetes mellitus. Clinical acumen is required to ascertain the physical findings of PPHP as patients often present with unrelated symptoms or diseases. Upon detection of these signs PTH and calcium measurements must be done so as to not miss the sinister differential of PHP.
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LC/MS untargeted lipidomics analysis in women with morbid obesity and type 2 diabetes mellitus: a comprehensive study

Laia Bertran[1], Carmen Aguilar[1], Teresa Auguet[1] & Cristóbal Richart[1]
[1]Universitat Rovira i Virgili

Background and Objectives
Since previously, we performed an untargeted metabolomics analysis in a cohort of morbidly obese (MO) women, in which we observed a different lipid metabolite pattern between metabolically healthy MO (MHMO) individuals and those with associated type 2 diabetes mellitus (T2DM). To validate these findings, now we have performed a complementary study of lipidomics.
Materials and Methods
We assessed a liquid chromatography coupled to a mass spectrometer untargeted lipidomic analysis on serum samples from 209 women, 73 normal-weight (NW) women (control group) and 136 MO women. From those, 65 MHMO and 71 with associated T2DM.
Results
Significantly elevated levels of ceramides, sphingomyelins, diacyl and triacylglycerols, fatty acids, and phosphoethanolamines were observed in MO vs NW. Conversely, significantly decreased levels of acylcarnitines, bile acids, lyso-phosphatidylcholines, phosphatidylcholines (PC), phosphatidylinositols, and phosphoethanolamine PE (O-38:4) were noted. Furthermore, comparing MO women with T2DM vs MHMO, a distinct lipid profile emerged, featuring increased levels of metabolites: deoxycholic acid, diacylglycerol DG (36:2), triacylglycerols, phosphatidylcholines, phosphoethanolamines, phosphatidylinositols, and lyso-phosphatidylinositol LPI (16:0).
Conclusions
Analysing both comparatives, we observed decreased levels of deoxycholic acid, PC (34:3), and PE (O-38:4) in MO women vs NW. Conversely, we found elevated levels of these lipids in MO women with T2DM vs MHMO. These profiles of metabolites could be explored for the research as potential factors of metabolic risk of T2DM in MO women.
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Effect of Mediterranean diet on quality of life and disease burden in patients with Hashimoto's thyroiditis

Manal Abushady[1], Nahla Adly[1], Sarah Ibrahim[1] & Sherihan Aboelyazed[1]
[1]Ain Shams University, Internal Medicine, Endocrinology Department, Cairo, Egypt

Background
Hashimoto's thyroiditis is one of the leading causes of hypothyroidism worldwide. Currently the only available treatment is Levothyroxine. Even though symptoms improve with treatment, many patients continue to suffer from a lower quality of life and inability to lose weight. The role of nutritional therapy in managing patients with Hashimoto's disease has been of interest lately.
Aim
The aim of our study was to assess the effects of Mediterranean diet on quality of life in Hashimoto's thyroiditis patients using ThyPRO questionnaire, as well as thyroid autoantibodies and thyroid profile parameters.
Methods
We performed a dietary interventional study on 40 female patients previously diagnosed with Hashimoto's disease over 3 months. The study participants were divided into two groups, Group 1 ($n=17$) were hypothyroid patients on Levothyroxine, while Group 2 ($n=23$) were euthyroid patients and not on levothyroxine. Both groups were started on a modified Mediterranean dietary plan with reduction of goitrogenic foods. Baseline evaluation of anti-thyroid peroxidase antibodies, anti-thyroglobulin antibodies, thyroid profile parameters, body mass index, total cholesterol, triglycerides, HDL, LDL, ESR, and ThyPRO questionnaire (for assessment of disease specific health-related quality of life) was done and reassessed at the end of the study.
Results
In both groups a statistically significant reduction was seen in levels of anti-thyroid peroxidase antibodies, anti-thyroglobulin antibodies, BMI, LDL, total cholesterol and triglycerides ($P<0.01$). Statistically significant improvement in all items of the ThyPRO scale were observed in both groups ($P<0.05$), except for eye symptoms, which were statistically non-significant in both groups. Regarding free T3 and free T4, statistically significant increases in their levels were seen in both groups, however in group 1 the observed changes were statistically more significant. Changes in free T3 and free T4 were (41.2%, $P<0.01$) and (54.32, $P<0.05$) respectively. We also observed statistically highly significant reductions in levels of thyroid stimulating hormone in group 1 (-39.09%, $P<0.01$), however, the changes in group 2 were statistically non-significant.
Conclusion
The disease burden of Hashimoto's disease is not only related to hormone levels, but could also be related to an underlying inflammatory state. A modified Mediterranean diet could have beneficial effects on symptoms burden, quality of life, lipid state, as well as autoantibodies levels and hence can be used as an adjuvant to levothyroxine treatment.
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Growth hormone-releasing hormone (GHRH) antagonists enhance radiosensitivity in non-small cell lung cancer cells

Iacopo Gesmundo[1], Francesca Pedrolli[1], Francesca Romana Giglioli[2], Alessia Bertoldo[4], Vanesa Gregorc[3], Anna Sapino[1,3], Luisella Righi[4], Renzhi Cai[5,6], Wei Sha[6], Mauro Giulio Papotti[7], Ezio Ghigo[1], Andrew V. Schally[5,6,8], Umberto Ricardi[9] & Riccarda Granata[1]
[1]Department of Medical Sciences, University of Turin, Turin, Italy, [2]Medical Physics Unit, A.O.U. Città della Salute e della Scienza, Turin, Italy, [3]Candiolo Cancer Institute, Fondazione del Piemonte per l'Oncologia (FPO)-IRCCS, Candiolo, Italy, [4]Department of Oncology, Pathology Unit, University of Turin, San Luigi Gonzaga Hospital, Orbassano, Italy, [5]Endocrine, Polypeptide, and Cancer Institute, Veterans Affairs Medical Center, Miami, FL, United States, [6]South Florida VA Foundation for Research and Education, Veterans Affairs Medical Center, Miami, FL, United States, [7]Department of Oncology, Pathology Unit, University of Turin, Turin, Italy, [8]Department of Medicine, Divisions of Medical Oncology and Endocrinology, and Department of Pathology, Miller School of Medicine, University of Miami, Miami, FL; Sylvester Comprehensive Cancer Center, Miller School of Medicine, University of Miami, Miami, FL, United States, [9]Department of Oncology, Radiation Oncology, University of Turin, Turin, Italy

Growth hormone-releasing hormone (GHRH), apart from stimulating GH secretion in the pituitary, exerts many peripheral functions, including stimulation of cell proliferation and survival. In fact, GHRH and GHRH receptors (GHRH-Rs) are expressed in different cancer cell types, where they promote proliferation and survival. Conversely, GHRH antagonists exert antineoplastic activities in several tumors, including lung cancer, one of the leading causes of death by cancer worldwide. Currently, radiotherapy is an important treatment in non-small cell lung cancer (NSCLC) patients, even if lack of tumor control, both locally and/or distantly, is quite common. Although different studies have demonstrated the ability of GHRH antagonists to potentiate the anticancer effect of chemotherapy, the role of these peptides in combination with radiotherapy remains unexplored. Thus, we explored the antitumor role of GHRH antagonists of MIA class, MIA-602 and MIA-690 in combination with radiotherapy, in human A549 and H522 NSCLC cells and primary lung adenocarcinoma cells. Our results revealed that MIA-602 and MIA-690, besides exerting inhibitory effects as single agents, potentiated the cytotoxic and antiproliferative effects of ionizing radiations (IR) in NSCLC and adenocarcinoma cells exposed to single doses of IR (2, 5 or 10 Gy). Furthermore, MIA-690 reduced the expression of GHRH-Rs and insulin-like growth factor (IGF)-I in A549 cells treated with 5 Gy IR. MIA-690 also potentiated the radiotherapy-induced inhibition of colony formation and expression of cell cycle promoters, while upregulating cell cycle inhibitors such as p21 and p27. The proapoptotic function of IR was enhanced by MIA-690, along with modulation of apoptosis effectors and elevation of p53 tumor suppressor protein. Mechanistically, MIA-690 also counteracted the response of A549 cells to IR by inhibiting proliferative, inflammatory, and oxidative pathways, such as PI3K/Akt, STAT3, NF-κB and COX2. Finally, MIA-690 hindered the IR-induced epithelial-mesenchymal transition (EMT) by upregulating mRNA for E-cadherin, while reducing vimentin, metalloproteinase (MMP)-2 and -9 and vascular endothelial growth factor (VEGF). Overall, these findings suggest potential application for GHRH antagonists in combination with radiotherapy for the treatment of NSCLC.

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Reversible and late-onset adrenal insufficiency in survivors of COVID19: results from a 24-month longitudinal study

Saroj Sahoo[1,2], Jayakrishnan Menon[1], Nidhi Tripathy[1], Monalisa Nayak[3] & Subhash Yadav[1]
[1]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Endocrinology, Lucknow, India, [2]Mid and South Essex NHS Trust, United Kingdom, Division of Endocrinology, [3]King's College Hospital, London, United Kingdom

Objective
The SARS-CoV-2 requires angiotensin-converting enzyme 2 (ACE2) receptor and transmembrane serine protease 2 (TMPRSS2) for gaining entry inside the cells (1). In humans, ACE2 and TMPRSS2 mRNAs are expressed in several endocrine glands, including the hypothalamus, pituitary, and adrenal cortex (2). Thus, it is possible that patients with COVID19 may have hypothalamic-pituitary-adrenal (HPA) axis dysfunction both during acute COVID19 and/or following recovery from COVID19. We studied the temporal course of hypothalamic-pituitary-adrenal (HPA) dysfunction in patients with corona-virus disease (COVID19).
Methods
After excluding patients receiving glucocorticoids or opiates prior to sampling, and pre-existing pituitary or adrenal disease, 302 patients (median age 54 years [interquartile range 42–64], 76% males, 97 had severe/critical illness) were recruited. HPA axis was evaluated by morning cortisol and adrenocorticotrophic hormone (ACTH) at admission ($n=231$) withing first 48 hours of admission. Adrenal insufficiency (AI) during acute illness was defined using a morning cortisol <83 nmol/l. AI at 12-months follow-up was defined using a peak cortisol <406 nmol/l in the ACTH-stimulation test (APST) ($n=90$). Those with AI at 12-months were further assessed by the APST 6-monthly for recovery of hypoadrenalism.
Results
The median morning cortisol and ACTH during COVID19 were 295 (IQR 136–461) nmol/l and 3.9 (0.8–6.9) pmol/l, respectively. AI was present in 33 (14%) patients; ACTH was elevated in three, and low or inappropriately normal in the rest 30 patients. At 12-months, AI was seen in 13% (12/90) patients and hypothalamic-pituitary in origin in all; five (42%) of them had not met the diagnostic criteria for AI during COVID19. AI diagnosed at admission persisted at 12-months in seven patients and recovered in seven; the remaining 19 patients were lost to follow-up. The presence of AI at 12-months was independent of severity, and steroid use during COVID19. A morning cortisol <138 nmol/l during COVID19 predicted presence of AI at 12-months. All patients showed recovery of HPA axis in the ensuing 12-months.
Conclusion
Central AI was common during acute COVID19 and at 12-months of follow-up. AI can be late-onset, developing after recovery from COVID19 and was transient in nature.

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GIP receptor is expressed by human cumulus granulosa cells

Mafalda V. Moreira[1,2,3], Duarte Pignatelli[3,4,5], Raquel Bernardino[1,2], Emídio Vale Fernandes[1,2,6] & Mariana P Monteiro[1,2]
[1]Unit for Multidisciplinary Research in Biomedicine, School of Medicine and Biomedical Sciences (ICBAS), University of Porto, Endocrine and Metabolic Research, Porto, Portugal, [2]Laboratory for Integrative and Translational Research in Population Health (ITR), University of Porto, Porto, Portugal, [3]i3S-Institute for Research and Innovation in Health, University of Porto, Porto, Portugal, [4]Faculty of Medicine of the University of Porto, Endocrinology, Porto, Portugal, [5]Cancer Signaling & Metabolism Group, IPATIMUP- Institute of Molecular Pathology and Immunology of the University of Porto, Porto, Portugal, [6]Centro Materno-Infantil do Norte Dr. Albino Aroso (CMIN), Centro Hospitalar Universitário do Porto (CHUPorto), Gynaecology, Porto, Portugal

Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies in women of reproductive age and, accounts for 80% of the causes of anovulatory infertility. Despite PCOS being often associated with obesity and insulin-resistance, these are not invariably present. As PCOS aetiology and underlying mechanisms remain unclear, clinical management is limited to target symptoms. Recent evidence suggested the potential of GLP-1 receptor agonists therapies in ameliorating PCOS endocrine and reproductive manifestations, in parallel to inducing weight loss and improving dysglycemia. Moreover, a dual GLP-1/GIP co-agonist drug with even more promising results was just rendered available. Notably, no previous study has been conducted to identify incretin receptors in the human ovary. Herein we aimed to investigate the presence of gastric inhibitory polypeptide (GIP) and glucagon-like-peptide-1 (GLP-1) receptors in human granulosa cells to understand the role of incretin hormones in ovarian physiology and to assess the potential use of incretin-based drugs for the treatment of PCOS-related infertility. For the first time, we were able to identify the presence of GIP receptor transcripts in cumulus cells from patients with and without PCOS undergoing fertility treatments. Additionally, the presence of the GIP receptor was also found on non-luteinized granulosa cells (HGrC1) and granulosa tumour cells (COV434). On the other hand, we were unable to detect the GLP-1 receptor in granulosa cells. Further studies are needed to evaluate whether there are differences in the expression levels of GIP receptors in granulosa cells from overweight/non-overweigh women with PCOS and overweight/non-overweight normo-ovulatory women. Overall, our preliminary findings suggest that GIP may have a significant role in modulating female reproductive function which may provide future targets for pharmacological intervention in reproductive disorders.

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Persistent parathyroid hormone elevation post-parathyroidectomy with biological remission: prevalence and predictive factors

Yesmine Merhbene[1], Rihab Laamouri[1], Essayeh Sawsen[1], Sabrine Mekni[1], Karima Khiari[1], Nadia Mchirgui[1], Imen Rojbi[1] & Bennacef Ibtissem[1]
[1]Hospital Charles Nicolle, endocrinology department, Tunis, Tunisia

Background
Primary hyperparathyroidism, is defined by hypercalcemia associated with an elevated or inappropriately normal parathyroid hormone(PTH) levels stemming from hyperfunctioning parathyroid glands. It's a prevalent endocrine disorder. Parathyroidectomy, the surgical excision of affected glands, stands as the definitive treatment, typically resulting in remission and normalization of calcium levels. However, persistent elevation of serum PTH post-parathyroidectomy presents a clinical hurdle, possibly indicating incomplete resolution of the condition or other contributing factors.
Aim
This study aims to ascertain the prevalence of persistent elevated PTH levels among patients achieving remission post-parathyroidectomy and to delineate predisposing factors associated with this persistence.
Methods
Conducted as a retrospective cohort study spanning from 1976 to 2020 at Charles Nicolles Hospital. The research compared two groups: one consisting of patients with persistent elevation of serum PTH levels post-parathyroidectomy, and the other without such elevation, both achieving biological remission. Data sourced from medical records included demographic data, preoperative biochemical profiles, surgical details, and postoperative outcomes. Descriptive statistics were employed to outline the demographic and clinical characteristics of the study cohort, while statistical analyses, including chi-square tests and logistic regression, aimed to identify factors linked to persistent elevation of serum PTH levels.
Results
We included 42 patients with a sex ratio of 0.23. Parathyroid adenoma was the predominant pathology in 76.2% of cases, followed by diffuse hyperplasia in 14.3%, with one case of parathyroid carcinoma detected. Despite achieving normocalcemia postoperatively, 45.2% of patients exhibited persistent elevation of PTH. Notably, no discernible differences were observed in age, creatinine clearance, histological patterns, adenoma size, or preoperative levels of calcium, phosphate, and alkaline phosphatase between patients with persistent PTH elevation and those without. However, serum vitamin D levels were marginally lower in the persistent PTH group. Patients with persistent PTH elevation experienced significantly higher rates of bone complications ($P=0.000$). Additionally, a significant association was noted between higher preoperative PTH levels and persistent hyperparathyroidism ($P=0.005$).
Conclusion
Our study reveals a noteworthy prevalence of persistent elevation in serum parathyroid hormone levels following parathyroidectomy, despite achieving remission. Our findings emphasize the need for continued vigilance in managing primary hyperparathyroidism. Identification of factors associated with persistent PTH elevation, such as higher preoperative PTH levels, underscores the importance of personalized treatment approaches. Further research is warranted to unravel the underlying complications and optimize clinical strategies for managing persistent PTH elevation post-remission.

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Diabetes prevalence and impact on stroke outcomes: an analytical study

Houda Ben Soltane[1], Yosra Hasni[2], Mariem Khrouf[1], Ons Haddaji[1], Safa Mehri[1] & Zied Mezgar[1]
[1]farhat hached university hospital, emergency departement, sousse, Tunisia, [2]farhat hached university hospital, endocrinology departement, sousse, Tunisia

Introduction
Rising stroke rates call for a closer look at risk factors such as hypertension, diabetes and obesity. The established association of diabetes mellitus with stroke risk and potential post-stroke complications underscores the need for thorough analysis to effectively mitigate these challenges.
Objective
This review aims to determine the prevalence of diabetes in acute stroke patients and investigate its association with post-stroke outcomes, encompassing both ischemic and haemorrhagic strokes.
Methods
A prospective study spanning 14 months (07.01.22 to 17.10.23) was conducted at the FH - Sousse emergency department. It included individuals aged 18 years and above presenting with abrupt or rapidly progressive focal neurological deficits, or transient ischemic attacks (TIAs) lasting less than one hour, after excluding other potential diagnoses. Both diabetic and non-diabetic patients were included in our study population.
Results
Our study included 150 patients, with a mean age of 66.02 /- 12.59. a male predominance was observed with a sex ratio of 1.54. 85.3% of our patients had associated comorbidities, notably hypertension and diabetes (55.3% and 47.3% of cases respectively). Almost half of our population (40.7%) had a history of a vascular accident, with an ulterior cerebral stroke in 51.9% of the cases and TIA in 9.6%. upon admission, all of our patients benefited from a cerebral CT scan. 44.8% of our patients had a normal CT scan while an angiography was required in 10.6% of the cases. An ischemic stroke was found in 73.4% of our patients, while 16.7% were diagnosed with haemorrhagic stroke and 10% with TIA. The most affected territory was that of the MCA in 57.9% of the cases. 22.7% of our patients were deemed having a severe presentation through clinical and imagery data observation, of whom 6.3% needed IMV, with a total mortality rate of 3.6%. Comparing diabetic and none diabetic patients, the former had significantly more comorbidities ($P<10^{-3}$) in univariate analysis: hypertension (OR = 2.6 IC [1.34-5.109], $P=0.04$) and dyslipidaemia (OR = 4.075, IC [2.029-8.183]; $P<10^{-3}$), with only dyslipidaemia being retained in multivariate analysis (OR = 5.014 IC [2.261-11.118]; $P<10^{-3}$). Diabetics also had a significantly more elevated risk of ischemic stroke in multivariate analysis (OR = 4.607 IC [1.845-11.502]; $P<10^{-3}$), but had no impact on mortality ($P=0.111$).
Conclusion
The study examines diabetes prevalence and its impact on stroke outcomes. It highlights the common occurrence of hypertension and diabetes among stroke patients, emphasizing the need to address these risk factors.

Keywords: diabetes mellitus, stroke, outcome.
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Pituitary dysfunction following mild traumatic brain injury in female athletes: neuropsychological and psychological functioning

Lára Ósk Eggertsdóttir Claessen[1], María Jónsdóttir[2], Hafrún Kristjánsdóttir[3], Sigrún Lund[4], Ingunn Unnsteinsdóttir Kristensen[2] & Helga Sigurjónsdóttir[5]
[1]Landspitali the National University Hospital of Iceland, Emergency Medicine, Reykjavík, Iceland, [2]Reykjavík University, Department of Psychology, Reykjavík, Iceland, [3]Reykjavík University, Department of Sport Science, Reykjavík, Iceland, [4]The University of Iceland, School of Engineering and Natural Sciences, Reykjavík, Iceland, [5]Landspitali the National University Hospital of Iceland, Department of Medicine, Reykjavík, Iceland

Background
Pituitary dysfunction (PD), neuropsychological and psychological symptoms, have been reported following mild traumatic brain injury (mTBI). These symptoms may be due to the brain injury itself or PD as hypopituitarism (HP) can have neuropsychological and psychological effects. To the best of our knowledge, this study is the first to report neuropsychological and psychological outcomes in female athletes with PD following sport-related mTBI.
Subjects
Female athletes aged 18 to 45 years currently active in or retired from soccer, team handball, basketball, ice hockey, and martial arts who answered an online questionnaire regarding mTBI history and mental health were included ($n=508$). Of the 308 women who reported one or more mTBI, 166 (53.8%) accepted further participation in an interview where neuropsychological tests were performed. All 166 women were subsequently invited to participate in a medical interview. Of those 151 accepted (90.9%) and 131 (86.7%) of them participated in pituitary hormone screening blood tests (SBT).
Methods
The online questionnaire included a post-concussion symptom scale, and mental health scales evaluating symptoms of anxiety, depression, stress, and quality of life. The neuropsychological tests performed included the Sustained Attention to Response Task (SART) as well as tests measuring executive functioning, visual search, motor and processing speed, divided attention, working memory, and intellectual abilities. The SBT were taken at 0800 hours and included S-IGF1 (age dependant reference range), S-cortisol (values <350 nmol/l were considered abnormal), S-prolactin (reference range 4.79 – 23.3 µg/l), S-TSH (reference range 0.270 – 4.20 mIU/l), S-fT4 (reference range 12 – 22 pmol/l), S-FSH, S-oestrogen, and S-progesterone measurements. If SBT were repeatedly O-RV, detailed endocrinological tests were performed for each axis as indicated.

Results
Following a detailed endocrinological evaluation, 16 women were diagnosed with PD (HP $n=6$, hyperprolactinemia $n=10$) following mTBI. Women with PD had a significantly higher mean SART error score than women with normal pituitary function (PF) (16.7 and 12.8 respectively; $P=0.04$). No other significant differences in neuropsychological outcome were found between the two groups. Moreover, there was no significant difference with regards to mTBI symptoms, anxiety, depression, stress, QOL or insomnia between women with PD and those with normal PF.
Conclusion
Sustained attention or inhibitory performance may be affected in women with PD following mTBI as they had a higher mean SART error score than women with normal PF. No other significant difference in neuropsychological or psychological outcome was demonstrated.

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Gonadis national registry on gonadal status in pituitary and adrenal disorders: prevalence and characterization of testicular morpho-structural and reproductive alterations in male patients with congenital adrenal hyperplasia

Davide Menafra[1], Davide Ferrari[2], Giulia Rastrelli[3], Cristina de Angelis[1], Marianna Minnetti[2], Chiara Simeoli[1], Linda Vignozzi[3], Giovanni Corona[4], Andrea Isidori[2] & Rosario Pivonello[1]
[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia ed Andrologia, Unità di Andrologia e Medicina della Riproduzione, Sessualità e Affermazione di Genere (Fertisexcares), Naples, Italy, [2]Università La Sapienza di Roma, Diparimento di Medicina Sperimentale, Rome, Italy, [3]Università di Firenze, Dipartimento di Scienze Sperimentali Cliniche e Biomediche 'Mario Serio', Florence, Italy, [4]AUSL di Bologna, U.O. di Endocrinologia e Malattie del Ricambio Ospedale Maggiore Bellaria, Bologna, Italy

Congenital adrenal hyperplasia (CAH) is a disorder due to mutations of genes coding for adrenal steroidogenesis enzymes, commonly caused by 21α-hydroxylase enzyme deficiency. Severe impairment of 21α-hydroxylase synthesis results in the classic form of CAH (c-CAH) characterized by cortisol and aldosterone deficiency (salt wasting form - SW), or partial enzyme deficiency characterized by cortisol deficiency (simple virilizing form - SV); mild impairment of 21α-hydroxylase synthesis results in the non-classic form of CAH (nc-CAH) potentially characterized by cortisol deficiency. Moreover, CAH is characterized by androgen excess which may promote secondary hypogonadism; furthermore, male patients suffering from CAH may present other andrological disorders including testis hypotrophy, testicular adrenal rest tumours (TARTs) and impaired spermatogenesis. The aim of the current study was to evaluate testis function in males with CAH due to 21α-hydroxylase deficiency. Data were retrieved from GONADIS, a national registry on gonadal status and reproductive and psycho-sexual function in patients affected by pituitary and adrenal disorders. Twenty one male patients aged 18-64 years suffering from CAH on chronic replacement therapy with glucocorticoids were evaluated, including 12/21 patients (57.2%) with c-CAH, 9/21 patients (42.8%) with nc-CAH. Prevalence of testis hypotrophy as well as semen parameters were assessed in the overall cohort of CAH patients and in a subanalysis a comparison between c-CAH vs nc-CAH was performed. The control of disease was defined as serum androstenedione levels within/above the normal range. In the overall cohort of CAH patients, 13/18 (72.2%) reached disease control. Unilateral/bilateral testis hypotrophy was detected in 11/20 (55%) and TARTs in 11/19 (57.9%) of patients; concerning seminal parameters, oligozoospermia was detected in 3/19 (15.8%), azoospermia in 6/19 (31.6%), asthenozoospermia in 4/13 (30.7%), teratozoospermia in 3/13 (23%) and oligo-astheno-teratozoospermia in 3/13 (23%) of patients. In a subanalysis on c-CAH vs nc-CAH patients, significantly lower ACTH ($P=0.04$) and higher testosterone ($P=0.01$) levels were detected in the c-CAH, compared to nc-CAH group; a significantly higher prevalence of TARTs ($P=0.03$), lower total sperm count ($P=0.002$) and sperm concentration ($P=0.04$), and higher prevalence of azoospermia ($P=0.01$), were detected in the c-CAH compared to nc-CAH group. This study demonstrated an overall high prevalence of pathological testis and semen parameters in male patients with CAH. Moreover, a significantly worse semen quality was highlighted in patients with c-CAH, which were also characterized by a significantly higher prevalence of azoospermia and TARTs, therefore suggesting that alterations in semen parameters might be predominantly due to testis damage induced by TARTs.

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LIMK1 variants are associated with divergent endocrinological phenotypes aligning with divergently altered exocytosis dynamics.

Irena Muffels[1], Theodore Carter[2], Holger Rehmann[3], Bas Vastert[4], Annemarie Verrijn Stuart[5], Andreas Blank[6], Aurore Garde[7], Bert Van Der Zwaag[8], Iris De Lange[8], Jaques Giltay[8], Koen Van Gassen[8], Klaas Koop[1], Cedric Asensio[2] & Peter Van Hasselt[1]
[1]Wilhelmina Children's Hospital, University Medical Center Utrecht, Metabolic Diseases, [2]College of Natural Sciences and Mathematics, Department of Biological Sciences, Denver, United States, [3]Flensburg University of Applied Sciences, Department of Energy and Biotechnology, Flennsburg, Germany, [4]Wilhelmina Children's Hospital, University Medical Center Utrecht, Center for Translational Immunology (CTI), Utrecht, Netherlands, [5]Wilhelmina Children's Hospital, University Medical Center Utrecht, Pediatric Endocrinology, Utrecht, Netherlands, [6]Wilhelmina Children's Hospital, University Medical Center Utrecht, Department of Pediatric Cardiology, [7]Centre de Génétique et Centre de référence maladies rares, Fédération Hospitalo-Universitaire Médecine Translationnelle et Anomalies du Développement (FHU TRANSLAD), Hôpital d'Enfants, Centre Hospitalier Universitaire de Dijon, Dijon, France, [8]Wilhelmina Children's Hospital, University Medical Center Utrecht, Department of Medical Genetics, Utrecht, Netherlands

Background
LIM kinase 1 (LIMK1) plays a pivotal role in dynamic actin remodeling through phosphorylation of cofilin. In turn, the dynamic remodeling of the actin cytoskeleton is involved in exocytosis, thereby contributing to tuned secretion of hormones and neurotransmitters, although the exact role of actin in these processes is still debated.
Results
We report two individuals with de novo variants in LIMK1 with dissimilar clinical phenotypes: one individual exhibited epileptic encephalopathy and developmental delay, the other showed common variable immune deficiency, glucose dysregulation, and episodic sinus tachycardia. Given the intragenic localization of these variants, one impacting the highly conserved kinase domain, the other variant located in the auto-inhibitory LIM domain, we suspected that the phenotypic features could be explained by opposite effects of the *LIMK1* variants on LIMK1-mediated exocytosis dynamics. Indeed, we found significantly decreased actin polymerization in individual 1, contrasting with increased LIMK1 availability, cofilin phosphorylation, and actin polymerization in fibroblasts of individual 2. As compared to wildtype, significantly slower and decreased insulin exocytosis was observed in insulin-secreting cell lines expressing the *LIMK1* variant of individual 1 (harboring the catalytically dead variant), which contrasted with rapid and uncontrolled insulin exocytosis in case of a lack of auto-inhibition for individual 2.
Conclusion
This first report of two individuals with *LIMK1* variants harboring divergent effects on cofilin phosphorylation and actin polymerization, reveals novel and important roles for LIMK1 in tuned exocytosis. These distinct exocytosis defects may underlie the epileptic encephalopathy and glucose dysregulation observed in these individuals.

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Weaning patients off long-term low dose prednisolone: an international survey of current endocrine practice

Katharine Lazarus[1,2], Pei Eng[1,3], Kavita Narula[1,2], Sirazum Choudhury[1,2,4], Niamh Martin[1,2], Florian Wernig[1,2], Debbie Papadopoulou[1,2], Tricia Tan[1,2,4], Yasir Elhassan[5,6], Anna Mitchell[7], Helen Simpson[8], Jessica Davis[9], Roisin Evans[9], Kate Single[9] & Karim Meeran[1,2]
[1]Imperial College London, Hammersmith Campus, London, United Kingdom, [2]Imperial College Healthcare NHS Trust, Endocrinology and Diabetes, United Kingdom, [3]NUHS, Endocrinology, Singapore, Singapore, [4], Department of Clinical Biochemistry, London, United Kingdom, [5]Queen Elizabeth Hospital Birmingham, Department of Endocrinology, Birmingham, United Kingdom, [6]University of Birmingham, Birmingham, United Kingdom, [7]Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom, [8]University College Hospital, Department of Diabetes and Endocrinology, London, United Kingdom, [9]Society for Endocrinology and Bioscientifica, Stoke Gifford, United Kingdom

Background
Prolonged glucocorticoid (GC) use is associated with significant morbidity and mortality, including the development of glucocorticoid-induced adrenal insufficiency (GI-AI). There is currently no consensus regarding testing or weaning of GCs prescribed for non-endocrine conditions.

Aim
To assess the long-term GC weaning practice by endocrinologists in the UK and Southeast Asia.
Methods
An anonymous survey was disseminated to the clinical membership of the Society for Endocrinology (SfE) in May and June 2023, and the ASEAN Federation of Endocrine Societies (AFES) and the Endocrine and Metabolic Society of Singapore (EMSS) in November 2023 and February 2024.
Results
Respondents were asked about their management practice of a patient who no longer requires long-term prednisolone 5 mg daily for asthma, and has an early morning cortisol 98nmol/l. A total of 239 members (SfE 163; AFES/EMSS 76) responded. A Short Synacthen Test (SST) was the choice of 42.2% (SfE 54.0%; AFES/EMSS 30.3%) of respondents, whilst 35.4% (SfE 33.1%; AFES/EMSS 51.1%) wean further before cortisol assessment, and 9.5% (SfE 11.0%; AFES/EMSS 9.2 %) accept this morning cortisol as confirmatory of adrenal insufficiency. A switch from prednisolone to hydrocortisone prior to SST is the practice of 2.3% (SfE 3%; AFES/EMSS 1.3%) of all respondents. GC weaning was the practice of 78.2% (SfE 77.2%; AFES/EMSS 80.3%) of respondents; 27.7% (SfE 29.6%; AFES/EMSS 23.7%) wean down prednisolone, whilst 50.4% (SfE 47.3%; AFES/EMSS 56.6%) switch to hydrocortisone before weaning. Still, 12.6% continue GC replacement without further assessment; 8.0% with hydrocortisone and 4.6% continue 5 mg prednisolone. Most respondents (71.7%: SfE 62.1%; AFES/EMSS 92.1%) did not have a local steroid weaning protocol. Over half (54.8%: SfE 52.4%; AFES/EMSS 47.4%) continue follow-up until prednisolone is weaned off; 39.3% would follow-up three-monthly and 46.2% six-monthly. The commonest perceived causes for weaning failure were relapse of the underlying GC-treated condition (54.7%) and GC withdrawal symptoms (20.1%). Subsequently-confirmed hypothalamic-pituitary-adrenal axis suppression on prednisolone led to a clinical decision by 19.2% of respondents not to pursue further steroid weaning. A lack of evidence-based studies was highlighted as a major challenge (36.8% of respondents). Other challenges included limited follow-up capacity (5.2%), access to Synacthen (5.2%), access to prednisolone 1 mg tablets (2.7%), and difficulty engaging non-endocrinologists to support weaning (6.5%).
Discussion
There remains huge variation in the management of long-term GC weaning. There remains a need to develop an evidence-based approach for safe and effective GC weaning and hypothalamic-pituitary-adrenal axis assessment.
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Unexpected diagnosis of a mixed corticomedullary tumor of the adrenal gland in a hypertensive patient with unexplained weight loss

Agnieszka Kuzior[1], Inmaculada Molinero-Marcos[2], Borja Santana-Ojeda[2], Carlos Rios-Gomez[2], Ricardo Jose de Leon-Durango[2], Alba Hernandez-Santana[3], Claudia Arnas-Leon[1,2], Carmen Acosta-Calero[4], Asunción Acosta-Merida[5] & Francisco Javier Martinez Martin[1,2]
[1]Clinica San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain, [2]University Hospital of Gran Canaria Dr. Negrín, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain, [3]Parc Taulí University Hospital, Endocrinology & Nutrition, Sabadell, Spain, [4]University Hospital of Gran Canaria Dr. Negrín, Cardiology, Las Palmas de Gran Canaria, Spain, [5]University Hospital of Gran Canaria Dr. Negrín, General and Digestive Surgery, Las Palmas de Gran Canaria, Spain

Introduction and Objective
Pheochromocytomas are usually monocomponent tumors, but very rarely there are also composite pheochromocytomas, with another medullary component (benign or malignant) derived from the neural crest present. Even more rarely there are mixed corticomedullary tumors, with pheochromocytoma plus a cortical adrenal tumor, eventually causing primary aldosteronism or hypercortisolim. Our objective in this communication is to illustrate an infrequent variety of pheochromocytoma, its clinical implications and prognosis, based on a clinical case.
Design & Method
Review of the patient's clinical record and the relevant literature.
Results
A 63-year-old male, previously diagnosed of obesity, type 2 diabetes mellitus, dyslipidemia and essential hypertension was admitted in Cardiology for ACS without ST-segment elevation; angiography revealed no coronary lesions. Four years later the patient was admitted in Internal Medicine for unexplained weight loss (about 20 kg). Blood pressure was well controlled with enalapril, amlodipine, hydrochlorothiazide and bisoprolol; LDL-cholesterol and HbA1C were also adequately controlled. Abdominal CT showed a solid, hyperdense, heterogeneous, indeterminate 4 cm mass in the right adrenal and a 1.7 cm hypodense mass labeled as adenoma in the left one. Biochemical testing for hypercortisolism and primary aldosteronism was negative. Plasma metanephrine/normetanephrine were 1045/546 pg/mL, and a MIBG scan/SPECT-CT showed a single abnormal uptake labeled as pheochromocytoma. After standard preoperative preparation, a robotic right adrenalectomy was performed: recovery was uneventful, and the patient is presently normotensive and asymptomatic with normal plasmatic metanephrines and catecholamines. The final pathology report described a single 40 × 34 × 30 mm mass, labeled as mixed corticomedullay tumor, with 75% pheochromocytoma and 25% cortical adrenal components, without extracapsular extension. There were no signs of malignancy in the cortical component, and the pheochromocytoma component scored 2/20 in the PASS risk scale and 2/10 in the GAPP risk scale (low risk for metastasis in both). Genetic testing is pending. Unfortunately there are no specific risk score scales available for adrenal mixed corticomedullary tumors, but the cortical component should not add to the low risk of malignancy of the medullary component.
Conclusion
Adrenal mixed corticomedullary tumors are extremely rare, owing to the presence of two distinct components of different embryonic lineage; less than 30 cases have been described. Besides hypertension the patients may present hypercortisolism, primary hyperaldosteronism or nonspecific symptoms like weight loss. Awareness of this entity is needed to avoid perioperative hypertensive crises or missing diagnosis such as Cushing's syndrome or primary hyperaldosteronism in addition to pheochromocytoma.
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The phenomenon of macro-TSH in a patient on oncoimmunotherapy: a clinical case report

Laura Ebanoidze[1], Ekaterina Pigarova[1], Larisa Dzeranova[1], Larisa Nikankina[1], Galina Kolesnikova[1] & Nadezhda Platonova[1]
[1]Endocrinology research centre, st. Dmitry Ulyanov, 11, Moscow

Introduction
The occurrence of autoimmune adverse events is a frequent complication of oncoimmunotherapy with antibody drugs to PD-1.
Clinical Case
At the age of 33, the patient was diagnosed with melanoma, which was surgically removed. After 3 years, there was a progression with the appearance of liver metastases which were embolized with further initiation of oncoimmunotherapy with nivolumab. As a complication of this treatment the patient developed autoimmune thyroiditis with primary hypothyroidism, and levothyroxine therapy was initiated with gradual dose escalation over several months up to 300 mg per day (2.6 mg per kg of body weight), but without normalization of the thyroid profile: thyroid stimulating hormone (TSH) – 24.68 mU/l (0.35 - 4.94), free T3 – 2.98 pmol/l (2.63-5.9), free T4 – 9.18 pmol/l (10-19). No factors that could potentially alter the bioavailability of levothyroxine were detected. Subsequently, liothyronine was added to levothyroxine therapy and gradually increased from dose of 25 mg in the morning to dose of 25 mg in the morning and 50 mg in the afternoon, which led to normalization of TSH levels while maintaining free thyroxine is in the low normal range. There were no clinical signs of hyperthyroidism in the patient. During the examination at our Centre an inadequate TSH levels were suspected for the given dose of thyroid hormones taken. To address this issue a blood serum test for TSH was performed initially and after precipitation with polyethylene glycol (it allows to remove a high-molecular fraction of immunoreactive TSH from the blood, presumably due to the binding of part of TSH molecules with anti-TSH IgG, by analogy with macroprolactin). The results of the analysis confirmed macro-TSH phenomenon: TSH – 12.8 mU/l (0.25-3.5), bioactive TSH – 2.8 mU/l (0.25-3.5), free T4 – 13.24 mmol/l (9-19), free T3 – 3.04 (2.6-5.7). Thyroid hormone therapy was adjusted as follows: liothyronine was canceled, the dose of levothyroxine was reduced to 225 mg per day.
Conclusion
The phenomenon of macro-TSH may be one of the manifestations of autoimmune complications of oncoimmunotherapy with immune endpoint inhibitors, complicating the interpretation of laboratory tests
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P407

Schmidt's syndrome: think about it in males too: A case report

Hasna Ouirar[1], Ikrame Qasdi[1], Caimae zouna[1], Karimi Meryem[1], Hajar Azagouagh[1], Kaoutar Elmoatamid[1], Fatima Toulali[1], Ghizlane Sabbar[1], Kaoutar Rifai[1], Iraqi Hinde[1] & Mohamed Elhassan Gharbi[1]
[1]Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco

Introduction
Autoimmune polyendocrine syndrome type 2 is a rare autosomal dominant life-threatening syndrome. It is defined by the presence of Addison's disease in combination with at least one of the known autoimmune diseases: thyroid autoimmune disease, type 1 diabetes, and hypogonadism. The coexistence of Addison's disease and autoimmune thyroid disease has been known as Schmidt's syndrome. We are detailing the case of a patient who exhibited this syndrome abruptly without a family history.
Case
A 44 years-old male patient with non-known medical history, presented to the emergency department feeling lethargic, with multiple episodes of vomiting and giddiness. On examination patient had cold clammy extremity with signs of dehydration. Hyperpigmentation of face and gums was noted. PR -128/min, hypotensive blood pressure of approximately 75/55 mmHg, hypoglycemia at 0.4g/l, and a microvoltage with a peaked T-wave on the EKG. Laboratory blood tests showed an hyperkalemia of 7.2 mmol/l, hyponatremia of 122 mmol/l and a low cortisol level indicating an Addisonian crisis. Associated with a high TSH level at 83 mui/l and anti TPO was positive suggesting autoimmune thyroiditis. The patient was treated for adrenal insufficiency first followed by thyroid insufficiency. Noteworthy clinical and biological improvement observed.
Discussion
Schmidt's syndrome is a rare disease and difficult to diagnose because the presentation depends on which gland is initially involved. It is more common in middle-aged females and is treatable if diagnosed early. It can be treated with respective substitution therapy. Early detection of the disease and appropriate management may reduce morbidity and mortality significantly in the patients with autoimmune poly glandular syndrome. Therefore, this case report can contribute to the medical literature on Schmidt's syndrome, which can help in early diagnosis and improve patient outcomes.

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P408

The impact of the acromegalic arthropathy on daily functioning in patients with acromegaly

Megan Heague[1], Sophie Hebden[1], Julie Lynch[2], Nawaz Z Safdar[2], David McLaren[2,3], Alberto Stefano Tresoldi[4,5,6], Kirstie Lithgow[4,5,6], Sandrine Urwyler[4,5,6], Chetna Varsani[7,8], Shahzad Akbar[9], Katie McLoughlin[10], Katarzyna Adeniji[10], Tara Kearney[10], Thozhukat Sathyapalan[9], Claire Higham[11], William Drake[7], Niki Karavitaki[4,5,6], Nikolaos Kyriakakis[2] & Robert D Murray[2,3]
[1]University of Leeds, School of Medicine, Leeds, United Kingdom, [2]Leeds Teaching Hospitals NHS Trust, Department of Endocrinology, Leeds, United Kingdom, [3]University of Leeds, Leeds Institute of Cardiovascular and Metabolic Medicine (LICAMM), Leeds, United Kingdom, [4]University of Birmingham, Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, Birmingham, United Kingdom, [5]Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, United Kingdom, [6]University Hospitals Birmingham NHS Foundation Trust, Department of Endocrinology, Queen Elizabeth Hospital, Birmingham, United Kingdom, [7]Barts Health NHS Trust, Department of Endocrinology, St Bartholomew's Hospital, London, United Kingdom, [8]Barts Health NHS Trust, Department of Endocrinology, St Bartholomew's Hospital, London, United Kingdom, [9]Hull University Teaching Hospitals NHS Trust, Department of Academic Diabetes and Endocrinology, Hull, United Kingdom, [10]Salford Royal NHS Foundation Trust, Department of Endocrinology, Salford, United Kingdom, [11]The Christie NHS Foundation Trust, Department of Endocrinology, Manchester, United Kingdom

Background
Despite biochemical control of GH and IGF-I levels patients with acromegaly continue to have marked impairment of their well-being. The acromegalic arthropathy has been identified as a significant contributor to the impaired well-being of these individuals. Few data are available to determine the impact of the arthropathy on function.
Methods
Patients with a diagnosis of acromegaly under follow-up in six tertiary pituitary centres were invited to complete a questionnaire relating to joint pain and distribution; and impact on function and QoL. We present data from (1) 'Disabilities of the Arm, Shoulder and Hand (DASH); (2) Oswestry Disability Index (ODI) to assess the impact of back pain; (3) Knee injury and Osteoarthritis Outcome Score (KOOS); (4) Foot Function Index (FFI); and (5) Health Assessment Questionnaire Disability Index (HAQ-DI). Scores range from 0 (no disability) to 100 (most severe disability) for the DASH, ODI and FFI; in contrast scores for the KOOS subscales are reversed with a score of 100 representing no disability. HAQ-DI values 0 to 1 are considered to represent mild to moderate difficulty, 1 to 2 moderate to severe disability, and 2 to 3 severe to very severe disability.
Results
411 patients completed the questionnaires, median age 60 (range 18-88) yrs, 56.1% female and mean age at diagnosis 43 (range 12-83) yrs, with duration of disease 13 (IQR 5.9-20.9) years. The median DASH score was 10.8 (IQR 0.8–32.8) and for the ODI 12 (IQR 0–32). Values for the KOOS subscales were KOOS-pain (80.6, IQR 58.3–100.0); KOOS-symptoms 80.0 (IQR 57.1–96.4); KOOS-ADL 87.5 (58.8–100.0); KOOS-sport function 75.0 (IQR 35–100.0); and KOOS-QoL 68.8 (IQR 43.8–100.0). The median FFI was 0.0 (IQR 0–32.4). The median HAQ-DI score was 0.25 (IQR 0.0-1.13), however 43 patients had a HAQ-DI score >2 consistent with severe disability and 75 a score of 1-2 in keeping with moderate to severe disability. 253 had inactive and 155 active disease. No difference in any questionnaire score was observed between patients with active and inactive disease. No correlation between any of the questionnaire scores and duration of acromegaly was observed.
Conclusions
Patients with a history of acromegaly demonstrate functional impairment which is greatest in areas which correlate with the most frequently affected joints (such as the knee joint). Moderate to severe disability is present in approximately 25% of individuals.

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P409

Increased cardiovascular risk in sheehan syndrome patients on optimal hormonal replacement therapy- a case-control study

Bashir ahmad Laway[1], Mohd Salem Baba[1] & Dr. Abid Rasool[1,1]
[1]sher-i-kasmir institute of medical sciences, Endocrinology, Koshur, India

Objective
Patients with Sheehan syndrome (SS) are predisposed to coronary artery disease (CAD) due to risk factors like abdominal obesity, dyslipidemia and chronic inflammation. In addition to estimate CAD risk enhancers like high sensitive C reactive protein (hsCRP), apolipoprotein B (ApoB) and lipoprotein A [Lp(a)], this study applies Framingham risk score (FRS) and coronary artery calcium (CAC) score to compute a 10-year probability of cardiovascular (CV) events in SS patients.
Design
Case–control study Sixty-three SS patients, on a stable hormonal replacement treatment except for growth hormone and 65 age, body mass index and parity-matched controls.
Measurements
Measurement of serum hsCRP, ApoB and Lp(a) and estimation of CAC with 16-row multislice computed tomography scanner.
Results
The concentrations of hsCRP, ApoB and Lp(a) were significantly higher in SS patients than in controls ($P<.01$). After calculating FRS, 95.2% of SS patients were classified as low risk, 4.8% as intermediate risk and all controls were classified as low risk for probable CV events. CAC was detected in 50.7% SS patients and 7.6% controls ($P=.006$). According to the CAC score, 26.9% SS patients were classified as at risk (CAC $>$ 10) for incident CV events as against 1.6% controls. The mean Multi- Ethnic Study of Atherosclerosis (MESA) score was significantly higher in patients with SS than controls. CAC corelated significantly with fasting blood glucose ($r=.316$), ApoB ($r=.549$), LP(a) ($r=.310$) and FRS ($r=.294$).
Conclusion
Significant number of asymptomatic SS patients have high coronary artery calcium score and are classified at risk for CAD.

Keywords agatston score, coronary artery calcium, Framingham score, panhypopituitarism, Sheehan syndrome

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P410

Cardiovascular evaluation of the patients with sleep apnea syndrome and acromegaly: A prospective study on the effects of continuous positive airway pressure (CPAP) therapy

Aysa Hacioglu[1], Zuleyha Karaca[1], Hatice Dogan Kesim[1], Sevda Ismailogullari[2], Muhammed Emre Urhan[1], Asli Sezgin Caglar[1], Nihat Kalay[3], Ugur Karabiyik[3], Serpil Taheri[4], Kursad Unluhizarci[1] & Fahrettin Kelestemur[5]
[1]Erciyes University School of Medicine, Department of Endocrinology, Kayseri, Turkey, [2]Erciyes University School of Medicine, Department of Neurology, Kayseri, Turkey, [3]Erciyes University School of Medicine, Department of Cardiology, Kayseri, Turkey, [4]Erciyes University School of Medicine, Department of Medical Biology, Kayseri, Turkey, [5]Yeditepe University School of Medicine, Department of Endocrinology, Istanbul, Turkey

Background
Patients diagnosed with acromegaly have an increased prevalence of sleep apnea syndrome(SAS). The data are scarce regarding the effects of continuous positive airway pressure(CPAP) use on cardiovascular parameters in these patients. We aimed to prospectively evaluate the cardiovascular effects of CPAP in patients with SAS and acromegaly.
Methods
Adult patients with newly diagnosed acromegaly were performed metabolic (body mass index (BMI), glucose, lipid values) and cardiovascular evaluation studies (24-hour ambulatory blood pressure monitoring, 24-hour ambulatory electrocardiography, carotid intima media thickness(CIMT), echocardiography), and polysomnography at the time of diagnosis. Serum levels of HIF-1 alpha was measured. Quality of life was evaluated by AcroQoL questionnaire. Control group was matched in terms of age, gender and BMIs. Patients were randomly assigned to 'CPAP-using' and 'no-CPAP' groups, and prospectively evaluated one year after remission.
Results
Forty-nine patients(29 female), mean age 42.3010.65 years, and 13 controls were included. Serum LDL, total cholesterol, and HIF-1 alpha levels were lower in the patient group ($P=0.029$, $P=0.006$, and $P=0.021$, respectively). Apnea-hypopnea index (AHI) was higher ($P=0.004$), and the results of cardiovascular evaluation studies were similar except for higher left ventricular posterior wall thickness at end-diastole among the patients ($P=0.006$). Average heart rate during polysomnography was higher in the patients ($P=0.023$). The patients were grouped on the basis of AHI scores (Group-1:AHI <5, Group-2:AHI ≥ 5 and <15, Group-3:AHI ≥ 15). The mean age was significantly higher in Group-3 patients when compared to groups 1 and 2. AcroQoL was lower in Group-3. Glucose values, BMIs, echocardiographic parameters, CIMT, mean blood pressures(MAP), and heart rates, HIF-1 alpha levels were similar across the groups at baseline. 'CPAP-using' ($n=8$) and 'no-CPAP' ($n=8$) groups who achieved acromegaly remission were compared at first year. BMIs remained similar in both groups, but fat mass increased in non-users ($P=0.018$). AHI scores improved only among CPAP users ($P=0.043$). Left ventricular systolic(LVSD) and diastolic diameters(LVDD) were significantly lower in CPAP-users than non-users after one year. Minimum heart rate showed decrease only among CPAP-users ($P=0.042$). CIMTs, MAPs, serum HIF-1 alpha levels, and AcroQoL scores were similar at first year across the groups. HIF-1 alpha levels were positively correlated with LVSD and LVDD at baseline ($P=0.008$, $r_s=0.476$, $P=0.005$ $r_s=0.499$). AcroQoL score was negatively associated with AHI, and positively with average O2 saturations ($P=0.012$, $r_s=-0.381$, $P=<0.001$ $r_s=0.611$).
Conclusion
Use of CPAP in patients with OSAS and acromegaly after remission may lead to better outcomes in terms of cardiac structure and heart rate, but not QoL.

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P411

Prevalence of hepatosteatosis in young women with polycystic ovary syndrome (PCOS)

Zaira Benetti[1], Simona Buti[1], Elisabetta Sciarroni[1], Luisa Pignata[1], Emilio Fiore[1], Antonio Salvati[2], Elena Benelli[1], Brunella Bagattini[1] & Massimo Tonacchera[1]
[1]University of Pisa, Department of Endocrinology, Pisa, Italy, [2]University of Pisa, Department of Hepatology, Pisa, Italy

Polycystic ovary syndrome (PCOS) is the most common endocrine disease in women of reproductive age, often characterized by obesity and insulin-resistance. NAFLD (Non-Alcoholic Fatty Liver Disease) is a metabolic disorder characterized by the accumulation of fat in the liver, in absence of alcohol consumption and other possible causes of hepatosteatosis. The association between hepatosteatosis and at least one cardio-metabolic risk factor is defined as MASLD (Metabolic Dysfunction-Associated Steatotic Liver Disease). A high prevalence of NAFLD in PCOS has been observed in several studies. The purpose of this study was to evaluate the prevalence of NAFLD, MASLD and hepatic fibrosis in patients affected by PCOS. In this prospective study 38 consecutive PCOS patients (mean age 23 years, IQR 6) were recruited at the Department of Endocrinology of Pisa. The diagnosis of PCOS was made following the International PCOS Network Guidelines. The diagnosis of NAFLD was based on laboratory assessment of liver function and liver imaging studies, by the use of ultrasound and transient elastography (TE) or Fibroscan, that estimates hepatosteatosis and fibrosis by measuring the Controlled Attenuation Parameter (CAP) and the Liver Stiffness Measure (LSM). Patients were divided in different groups according to their BMI (19% normal weight, 18 overweight and 63% obese) and to the presence of insulin-resistance (36.8% of the women). 31 out of 38 patients (81.6%) had hepatosteatosis at ultrasound; the majority of women (42.1%) exhibiting mild steatosis. The CAP revealed the presence of hepatosteatosis in the 47.2% of patients. The measurement of LSM showed that 72.3% of women had values >5 kPA, indicative of reduced liver elasticity. The 90.3% of the patients were diagnosed by MASLD, primarily due to the overweight. There weren't significant differences in liver stiffness values between insulin-resistant (IR) and non-insulin-resistant (NIR) patients. The BMI was higher in patients with hepatosteatosis and progressively increases according to the severity of the steatosis. A correlation between hyperandrogenism and hepatosteatosis in PCOS we observed: the values of FAI (Free Androgen Index) were significantly higher in patients with steatosis, especially if moderate/severe, and SHBG (Sex Hormone Binding Globulin) levels were significantly lower. The association between hepatosteatosis and SHBG remained significant indepen-dently of insulin-resistance. Furthermore, the levels of 17-OH-progesterone were significantly lower in patients with more sever liver damage. In conclusion, patients with PCOS show an increased prevalence of NAFLD, primarily due to the presence of obesity, insulin-resistance and hyperandrogenism.

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P583

Twelve years of experience using teriparatide for severe hypopar-athyroidism in an APS-1 patient: a case report

Tatiana Kokorina[1], Liudmila Rozhinskaya[1] & Zhanna Belaya[1]
[1]Endocrinology Research Centre, Neuroendocrinology and bone disease, Moscow, Russian Federation

Background
Managing hypoparathyroidism in patients with autoimmune polyendocrine syndrome type 1 (APS-1) poses significant therapeutic challenges. The presence of gastrointestinal candidiasis and associated malabsorption complicates treatment and may lead to refractory hypocalcemia. The use of high doses of calcium and active vitamin D metabolites to regulate serum calcium levels frequently results in hypercalciuria, which may cause long-term complications. Consequently, replacement therapy with biologically active fragments of parathyroid hormone (PTH) such as teriparatide and rhPTH (1-84) has been suggested.
Case Report
Patient A. was diagnosed with APS-1 at the age of 10 when she presented with acute adrenal insufficiency and hypocalcemia. Notably, she suffered from cutaneous candidiasis since age 4. Genetic testing identified an R257X mutation in the AIRE gene. Achieving normocalcemia was exceptionally challenging, even with high doses of alfacalcidol (up to 20 μg/day). The patient frequently experienced hypocalcemic seizures, needing repeated calcium IV administrations. By age 24, she had already developed secondary complications such as cataracts and cerebral calcification (Fahr's syndrome). At this point, patient A. began treatment with rhPTH 1-34 (teriparatide). Two daily injections of 20 μg (40 μg/d) were necessary to achieve normocalcemia. However, episodes of hypocalcemia still occurred occasionally. To lessen these calcium level fluctuations, she was transitioned to a continuous subcutaneous rhPTH 1-34 infusion via a pump. Three years following this adjustment, the patient opted to cease pump therapy in favor of conventional treatment with two to three daily injections of teriparatide (40-60 μg/day). At present, at the age of 35, the patient's condition is well-managed with three daily injections of teriparatide (60 μg/day), alfacalcidol (4 μg/day), and calcium (3g/day). Additionally, she receives 20 mg of hydrocortisone for primary adrenal insufficiency and fluconazole for candidiasis. The patient experienced infrequent hypocalcemia episodes (once a year), likely due to low treatment adherence and reductions in teriparatide and vitamin D dosages contrary to medical advice.
Conclusion
Twelve-year continuous teriparatide treatment has successfully maintained normocalcemia without inducing hypercalciuria and significantly reduced

alfacalcidol dose from 20 µg/d to 4 µg/d in the patient with severe hypoparathyroidism. No adverse effects of continuous long-term teriparatide therapy were noted.

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P584

Long-term bone health in women with a premenopausal risk-reducing salpingo-oophorectomy (RRSO) compared with women who underwent

Maarten Beekman[1], Lara Terra[1], Anniek Stuursma[2], Bernadette Heemskerk-Gerritsen[3], Marc van Beurden[1], Lena van Doorn[3], Eleonora van Dorst[4], Joanne de Hullu[5], Stijn Mom[6], Jeanine Roeters van Lennep[3], Katja Gaarenstroom[7], Tiny Korse[1], Bart de Keizer[4], Cristina Mitea[8], Riemer Slart[2], Snoeren Miranda[5], Marcel Stokkel[1], Hein Verberne[6], Christi van Asperen[7], Margreet Ausems[4], Lieke Berger[2], Truuske de Bock[2], Collee Margriet[3], Klaartje van Engelen[6], Lizet van der Kolk[1], Marijke Wevers[5], Encarna Gomez Garcia[8], Maartje Hooning[3], Angela Maas[5], Marian Mourits[2], Flora van Leeuwen[1] & Carola Zillikens[3]
[1]Netherlands Cancer Institute: Antoni van Leeuwenhoek, [2]University Medical Center Groningen, [3]Erasmus Medical Center Rotterdam, [4]University Medical Center Utrecht, [5]Radboud University Medical Center Nijmegen, [6]Amsterdam University Medical Center, [7]Leiden University Medical Center, [8]Maastricht University Medical Center

Introduction
To prevent ovarian cancer, *BRCA1/2* germline pathogenic variant carriers are recommended to undergo premenopausal risk-reducing salpingo-oophorectomy (RRSO). Premenopausal RRSO leads to immediate surgical menopause, which has been associated with an acute phase of rapid bone loss. However, data on long-term effects is scarce and inconclusive. Therefore, we investigated the long-term impact of premenopausal RRSO on bone mineral density (BMD).
Methods
We conducted a cross-sectional study nested in a nationwide cohort of women at high familial risk of ovarian cancer to assess long-term effects of a premenopausal RRSO compared with a postmenopausal RRSO on BMD. We included 500 women who underwent premenopausal RRSO ($\leq$45 years) with 240 women who underwent postmenopausal RRSO ($\geq$54 years). Participants underwent a Dual Energy X-ray absorptiometry (DXA) scan of the lumbar spine (LS) and femoral neck (FN) to asses BMD. Age differences between the pre- and postmenopausal RRSO groups were accounted for using Z-scores and subgroup analyses restricted to women aged 60-70 at study visit.
Results
Median age at study visit was 58.8 years in the premenopausal RRSO group and 69.0 years in the postmenopausal RRSO group ($P<0.001$), median time since RRSO was 16.1 years (IQR 15.3-21.3). Multivariable regression analyses showed that the Z-scores of both the LS and FN were significantly lower for the premenopausal RRSO group compared with the postmenopausal RRSO group (LS Z-score: 0.5 vs 1.2, $P<0.001$; FN Z-score: 0.1 vs 0.6, $P<0.001$). Furthermore, the relative risk (RR) of having a Z-score $\leq$-1.0 was higher in the premenopausal RRSO group compared with the postmenopausal RRSO group (LS RR: 2.35, 95% CI, 1.26-4.40; FN RR: 1.84, 95% CI, 1.08-3.13). Subgroup analyses in women aged 60-70 at study visit ($n=320$) showed that women in the premenopausal RRSO group had a higher prevalence of low BMD (T-score $\leq$-1.0) compared with the postmenopausal RRSO group (LS 52.0% vs 47.8%; FN 59.5% vs 56.9%; LS or FN 73.0% vs 66.4%), however, in multivariable regression analyses this difference was not statistically significant (LS $P=0.58$; FN $P=0.45$; LS or FN $P=0.35$).
Conclusion
Premenopausal RRSO appears to be associated with reduced BMD Z-scores more than 16 years after RRSO, however, in a subgroup of women of similar age we found no increased risk of low BMD based on T-score $<$-1.0.

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P585

Vitamin D and quality of life in patients with hashimoto thyroiditis

Zvezdana Jemuovic[1], Marina Nikolic Djurovic[1], Sandra Pekic Djurdjevic[1], Dragana Miljic[1], Marko Stojanovic[1], Ana Petakov[1], Ljiljana Dimitrijevic Jevremovic[2], Ivana Cekic[1], Ivan Jevtic[1] & Milan Petakov[1]
[1]Clinic for Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Center, Serbia, [2]General Hospital Krusevac, Krusevac, Serbia

Introduction
Hashimoto thyroiditis (HT), chronic autoimmune disease, is related with impaired quality of life (QoL) regardless of euthyroid state. Some studies showed decreased levels of vitamin D in patients with HT which implies there is a relationship between vitamin D deficiency and HT. It remains unclear whether decreased levels of vitamin D are result of autoimmune process or are part of its cause.
Aim
To investigate effect of vitamin D levels on QoL in patients with HT on levothyroxine therapy (LT4).
Methods
Cross-sectional, case control study with 42 HT patients (mean age 47.1413.25) on long levothyroxine replacement and 22 euthyroid healthy controls, matched for age, sex and educational level, were included. HT patients were divided into 2 groups, 25 patients with normal vitamin D levels (nVD) and 22 patients with vitamin D deficiency (dVD). Measurement of TSH, FT4, anti-TPO, anti-Tg, Vitamin D was done. Evaluation of QoL was evaluated by QoL questionnaire - SF36. Fisher's ANOVA analysis was used to compare means between (sub)groups.
Results
HT patients had higher TSH levels in both groups (nVD vs dVD) vs control (3.702.88 vs 2.621.76 vs 1.851.18mIU/l, $P=0.021$) and higher anti-TPO (nVD: 2638.783065.84 vs 2458.832335.37 vs 64.50170.82mIU/l, $P=0.001$). Vitamin D levels were lower in both HT groups (nVD vs dVD) vs control (31.246.96 vs 16.835.12 vs 38,4015.92ng/ml, $P=0.000$). Patients in both nVD and dVD groups reported worse general health – Scale 4 compared vs control (68.2416.59 vs 58.4118.44 vs 73.3615.05, $P=0.014$), physical health – Dimension A (60.2718.46 vs 70.4018.53 vs 73.7317.08, $P=0.042$), mental health – Dimension B (59.2320.47 vs 67.1617.50 vs 73.8617.03, $P=0.036$) and Total SF35 score (60.8620.66 vs 69.7217.54 vs 74.8616.84, $P=0.044$).
Conclusion
Patients with HT and vitamin D deficiency had statistically significant worse quality of life compared to healthy control. Future studies with larger cohorts and in longer observation periods are needed to clarify role of vitamin D in quality of life in patients with Hashimoto thyroiditis.

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P586

Clinical presentation of sporadic and familial medullary thyroid carcinoma: is there a real difference?

Valeria Tascini[1], Alessandro Prete[1], Cristina Romei[1], Antonio Matrone[1], Carla Gambale[1], Valeria Bottici[1], Laura Agate[1], Eleonora Molinaro[1] & Rossella Elisei[1]
[1]Pisa, Endocrinology Unit, Pisa, Italy

Introduction
Medullary thyroid carcinoma (MTC) is a rare neoplasm that occurs sporadically in 75% (sMTC) and hereditarily in 25% (fMTC) of cases caused by germinal mutations of the *RET* gene as an autosomal dominant trait. fMTC occurs in the setting of three syndromes: fMTC alone without any other clinical manifestations; and multiple endocrine neoplasia type 2A (MEN2A) and 2B (MEN2B) syndromes. In fMTC, cases are distinguished into index cases (1st clinically detected case) and gene carriers (identified through *RET* screening). According to this screening, gene carriers have usually a more indolent clinical behavior than index cases. The aim of our study is to compare the clinical presentation of patients affected by sMTC with index cases of fMTC.
Methods
We conducted a retrospective observational study of 674 sMTC and 115 fMTC index case patients referred to the Endocrinology Department of University Hospital of Pisa from 1993 to 2023.
Results
Patients with fMTC were younger compared with patients with sMTC (median age 44 vs 55, $P<0.001$), with no difference in gender (males 39% vs 44%, $P=0.3$). The primary tumors of fMTC did not differ in size compared with sMTC (median 1.2 vs 1.4 cm, $P=0.3$). The prevalence of minimal extrathyroidal extension was higher in fMTC compared to sMTC (37.3% vs 19.1%, $P<0.001$). The prevalence of tumor with T stage $>$ 2 was significantly higher in fMTC compared with sMTC (21.6% vs 13%, $P=0.03$). Lymph node metastases were more frequent in patients with fMTC (59% vs 43%, $P=0.002$), predominantly in the central compartment (59% vs 39%, $P=0.005$). However, we did not observe any difference in prevalence of distant metastases (fMTC 11.8% vs sMTC 8.9%, $P=0.37$) and stage IV disease (fMTC 27.5% vs sMTC 28.9%, $P=0.82$) between the two groups.
Conclusions
The clinical presentation of patients with fMTC appears slightly worse than sMTC, although this difference seems not to be clinically significant considering the similar prevalence of distant metastases and stage IV disease. However, the clinical presentation is approximately 10 years earlier in fMTC compared to sMTC.

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P587

Primary hyperparathyroidism: the relationship between serum calcium levels and renal function before and after curative surgery

Aija Fridvalde[1,2] & Kristine Geldnere[3,4]
[4]Rīga Stradiņš University, Riga, Latvia, [2]Riga East Clinical University Hospital, Riga, Latvia, [3]University of Latvia, Riga, Latvia, [4]Pauls Stradins Clinical University Hospital, Riga, Latvia

Introduction
The aim of this study was to examine the relationship between serum calcium levels and renal function before and after curative parathyroidectomy (PTX) in patients with primary hyperparathyroidism (PHPT).
Objective and methods
A retrospective evaluation of 48 patient cases, corresponding ICD-10 code E21.0, was carried out, including demographic data and such biochemical markers as serum calcium, creatinine and estimated glomerular filtration rate (eGFR) levels, calculated using MDRD equation.
Results
From 48 participants included in the study 83,3% were female, while 16,7% were male patients. The mean age was that of 61,5 (min 29, max 81, SD 11,8); 14,6% of the patients were below the age of 50. At the time of diagnosis, 52,1% of the patients presented with mild hypercalcemia, 37,5%- moderate, while 6,3%- severe hypercalcemia, but the least- 4,2%- were normocalcemic. The mean calcium levels were those of 2,93 mmol/l (min 2,43, max 3,85, SD 0,31). Altogether 23,1% of the patients had reduced renal function, corresponding to recommended criteria for surgery, already at the time of diagnosis- 10,3% had eGFR that of stage 3a, 12,8%- stage 3b. Further data analysis, using Pearson correlation, revealed association between serum calcium levels and both creatinine and eGFR levels in firstly diagnosed patients – a moderate positive correlation between serum calcium and creatinine levels (r(37)=.597, $P<0,01$) and moderate negative correlation between calcium levels and eGFR (r(37)= -.559, $P<0,01$). Looking at dynamic changes, there was also found a moderate positive correlation between calcium levels in newly diagnosed patients and postoperative creatinine levels, measured at least 6 months up to one year after curative surgery (r(28)=.525, $P<0,01$). In addition, paired T test results showed statistically significant difference (t(25)= -3,6, $P<0,01$) when comparing creatinine levels as measured during the first (M=79,4, SD=28,4) and last (M= 87,2, SD= 32,4) patient assessment, i.e., before and at least six months after the surgery.
Conclusions
This study shows an association between serum calcium levels and such renal function biomarkers as creatinine and/or eGFR, both at the time of diagnosis and after curative surgery, suggesting higher serum calcium as a predictive factor for chronic kidney disease in patients with PHPT even after surgical intervention. While results of this study suggest that PTX didn't halt the deterioration of renal function in PHPT patients, taking in account the small sample size, we would recommend further long-term large-scale controlled studies in order to evaluate surgical effects on renal function.

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P588

Psychiatric comorbidities in chronic hypoparathyroidism – a german single-center analysis in 133 patients

Carmina Teresa Fuss[1], Franca Hermes[1], Karen Gronemeyer[1], Ann-Cathrin Koschker[1], Stefan Unterecker[2], Jürgen Deckert[2] & Stefanie Hahner[1]
[1]University Hospital Würzburg, Department of Medicine I, Division of Endocrinology and Diabetology, Würzburg, Germany, [2]University Hospital Würzburg, Department of Psychiatry, Psychosomatics and Psychotherapy, Würzburg, Germany

Introduction
Reduction of quality of life in patients with chronic hypoparathyroidism (HPT) has been reported by several studies. Additionally, self-report data point to a higher prevalence of anxiety disorders in HPT compared to patients after thyroidectomy.
Objectives
To characterize psychiatric diseases in a systematically reviewed cohort of patients with chronic HPT.
Methods
We systematically assessed psychiatric comorbidities in a well-characterized cohort of patients with chronic HPT ($n=133$) using standardized questionnaires (depression: Patient Health Questionnaire (PHQ9), Beck Depression Inventory (BDI2), anxiety: State-Trait Anxiety Inventory (STAI)) and further performed a diagnostic interview using the Mini-DIPS ($n=103$).
Results
Out of the 103 interviewed patients, 69% were female (mean age 5811 years). 92% presented with postoperative HPT. The STAI provides a screening tool to assess both state (X1) and trait (X2) anxiety separately. Scores range from 20-80 with higher scores being positively correlated with higher levels of anxiety. In the STAI X1 18% of patients scored between 40 and 50 and 18% of patients had a score above 50 (mean 4113). Regarding trait anxiety (STAI X2) 21% of patients had values between 40 and 50, whereas 20% scored above 50 points (mean 4012). In contrast, most patients with chronic HPT did not show markedly elevated scores in PHQ9 (81% with scores below 9), as well as BDI2 (71.4% with scores below 13). No significant correlations could be observed between serum calcium, serum phosphate, parathyroid hormone, TSH, 25-OH-Vitamin D levels, disease duration or age and scores of STAI X1, X2 and PHQ9, whereas STAI-X1 and –X2, PHQ9 and BDI-2-scores significantly correlated with HPT symptom severity (all $P<0.001$, Person's r X1: 0.389, X2: 0.321, PHQ9: 0.411, BDI2: 0.478). In the diagnostic interviews, anxiety disorder was found in 42% of patients (agoraphobia $n=18$, specific phobia $n=17$, panic syndrome $n=11$, generalized anxiety disorder $n=12$, social phobia $n=6$).
Conclusion
The performance of systematic screening as well as diagnostic interview for psychiatric disorders in HPT showed a high prevalence of anxiety disorders despite established treatment of HPT. However, the pathophysiology still remains unclear.

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P589

The prevalence, distribution and use of analgesics for arthropathy in patients with acromegaly

Megan Heague[1], Sophie Hebden[1], Julie Lynch[2], Nawaz Z Safdar[2], David McLaren[2,3], Alberto Stefano Tresoldi[4,5,6], Sandrine Urwyler[4,5,6], Kirstie Lithgow[4,5,6], Chetna Varsani[7], Shahzad Akbar[8], Katie McLoughlin[9], Katarzyna Adeniji[9], Tara Kearney[9], Thozhukat Sathyapalan[8], Claire Higham[10], William Drake[7], Niki Karavitaki[4,5,6], Robert D Murray[2,3] & Nikolaos Kyriakakis[2]
[1]University of Leeds, School of Medicine, Leeds, United Kingdom, [2]Leeds Teaching Hospitals NHS Trust, Department of Endocrinology, Leeds, United Kingdom, [3]University of Leeds, Leeds Institute of Cardiovascular and Metabolic Medicine (LICAMM), Leeds, United Kingdom, [4]University of Birmingham, Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, Birmingham, United Kingdom, [5]Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, United Kingdom, [6]University Hospitals Birmingham NHS Foundation Trust, Department of Endocrinology, Queen Elizabeth Hospital, Birmingham, United Kingdom, [7]Barts Health NHS Trust, Department of Endocrinology, St Bartholomew's Hospital, London, United Kingdom, [8]Hull University Teaching Hospitals NHS Trust, Department of Academic Diabetes and Endocrinology, Hull, United Kingdom, [9]Salford Royal NHS Foundation Trust, Department of Endocrinology, Salford, United Kingdom, [10]The Christie NHS Foundation Trust, Department of Endocrinology, Manchester, United Kingdom

Background
Despite biochemical control of GH and IGF-I levels patients with acromegaly continue to have marked impairment of their well-being. The acromegalic arthropathy has been identified as a significant contributor to the impaired well-being of these individuals. We aimed to establish the true prevalence of arthropathy, distribution of joint involvement and use of analgesics for arthropathy in a large series of patients with acromegaly.
Methods
Patients with a diagnosis of acromegaly under follow-up in six tertiary pituitary centres were invited to complete a questionnaire relating to joint pain and distribution; management of their joint problems when present; and impact on function and QoL. We present data from the 'joint pain human figure' describing involved joints; 'joint pain scale'; and 'medication usage' questionnaires.
Results
411 patients completed the questionnaires, median age 60 (range 18-88) yrs, 56.1% female and mean age at diagnosis 43 (range 12-83) yrs. 338 (82.2%) patients reported joint, back or neck pain of >6 weeks duration within the preceding 3 months. The median number of joint sites affected was 4 (range 0-14), and median number of joints affected 5 (range 0–25). The most frequently involved individual joint was the knee ($n=225$; 57.1%), lower back (196; $n=49.7\%$), hip ($n=160$; 40.6%) and shoulder ($n=159$; 40.4%). The most painful joint was reported to occur most frequently within the large joints ($n=218$), compared with the axial skeleton ($n=133$) and small joints ($n=73$). Similar to the involved joints, the single 'most painful' individual joint was reported as the knee ($n=86$; 21.8%), lower back ($n=86$; 21.8%) or hip ($n=55$; 14.0%). On a scale of 0-10, severity of pain occurring during the preceding week was rated at a median of 4 (range 0-10). 52 patients had no pain (13.1%; score 0), 114 mild pain

(28.6%; score 1-3), 178 moderate pain (44.7%; score 4-7) and 54 severe pain (13.6%; score 8-10). 247 (61.4%) patients documented taking regular analgesics for joint pain. 173 used paracetamol, 110 oral non-steroidal anti-inflammatory drugs (NSAIDS), 64 topical NSAIDS, 65 codeine and 47 potent opioids or atypical analgesics (i.e amitriptyline, pregabalin). A single analgesic was used by 110 individuals; and two or more agents by 137. Most individuals taking two or more analgesics took a combination of paracetamol with an oral / topical NSAID.
Conclusion
Patients with a diagnosis of acromegaly have a significant arthropathy burden, frequently involving multiple joints and necessitating use of regular analgesics and anti-inflammatory agents.

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P590

Graves' orbitopathy: 40 years after diagnosis of graves' disease

Ons Maaoui[1], Sawsen Essayeh[1], Sabrine Mekni[1], Rihab Laamouri[1], Nadia Mchirgui[1], Karima Khiari[1], Imen Rojbi[1] & Ibtissem Ben Nacef[1]
[1]Charles Nicolle Hospital, Endocrinology

Introduction
Graves' orbitopathy (GO) is an autoimmune inflammation of the orbital tissues and it's the most frequent extrathyroidal complication of Graves' disease (GD). It typically develops concomitantly with GD, but, it can also precede it or occurs secondarily. We report the case of a patient who presented with GO 40 years after the diagnosis of GD.
Case report
A 74-year-old patient with history of arterial hypertension, type 2 diabetes, total thyroidectomy 40 years ago for GD, was hospitalized in our department for severe GO. The ophthalmological examination of the right eye showed visual acuity of 3/10 with conjunctival hyperemia, and the left eye showed exophthalmos with eyelid innoclusion, conjunctival hyperemia, limited ocular motricity, inferior corneal opacity and superficial punctate keratitis. An orbital MRI was performed, showing a dysthyroid orbitopathy with inflammatory thickening and fatty infiltration of the oculomotor muscles, responsible for bilateral grade 3 exophthalmos and no signs of optic neuritis. The patient was put on general measures and intravenous corticosteroid therapy. The clinical outcome was favorable with regression of inflammation's signs and improvement of visual acuity.
Conclusion
This case underlines the variable and often unpredictable nature of GO, and highlights the importance of vigilance for late-onset complications of GD and the need for ongoing monitoring even in patients with long-standing disease management.

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P591

Safety of continous subcutaneous insulin infusion therapy in adults with type 1 diabetes during hospitalization

Eduardo Torrecillas del Castillo[1], Ignacio Jiménez Varo[1], Mercedes Peinado Ruiz[1], Pablo Rodríguez de Vera[1], Isabel Serrano Olmedo[1] & María Asunción Martínez Brocca[1]
[1]hospital universitario virgen macarena, Sevilla, Spain

Aim
The use of continuous subcutaneous insulin infusion (CSII) systems in type 1 diabetic patients (DM1) is progressively increasing, leading to an increase in cases in which its maintenance during hospitalization is considered. The objective of the study is to analyze the safety of glycemic control with CSII therapy during hospitalization in DM1 adults.
Material and Methods
Retrospective observational study on a cohort of DM1 people hospitalized the last five years who maintained CSII therapy, at the Virgen Macarena University Hospital (Sevilla). We evaluated the differences in glycemic control between the hospitalization period, the month before and the month after hospitalization using the variables: "HbA1C" and percentages of glucometric ranges of the patient's "ambulatory glucose profile" (AGP). To avoid information bias, we performed a subanalysis according to type of CSII therapy and glycemic monitoring method.
Results
24 patients were analyzed: 62.5% women, average age 48.8 years. HbA1C 7.33%. Days of admission hospitalizated without CSII 11.68%. Most frequent reason for disconnection: surgery (7) and need for IV insulin infusion (3). Classification according to type of CSII and glucometry source: 640 + capillary controls (20.8%), 640 + integrated system (16.7%), 640 + flash glucose monitoring (45.8%), 670 (9.3 %) and 780 (8.3%). The overall analysis did not show serious complications associated with CSII treatment (severe hypoglycemia, diabetic ketoacidosis, severe isolated hyperglycemia). When subanalyzing the glucometric data in the subset of patients with interstitial glucose monitoring systems ($n=12$), limiting by the days of admission and the month before and the month after it, no significant differences were recorded in the AGP variables: <54 mg/dl: 1.29%, standard deviation (SD) 2.18 (during admission); 0.57%, SD 0.94 (previous); 1.04, SD 1.05 (later). $P=0.193$. 55-69 mg/dl: 3.44%, SD 3.75 (during admission); 2.02%, SD 2.56 (previous); 3.42%, SD 2.85 (later). $P=0.1$ 70-180 mg/dl: 55.94%, SD 16.35 (during admission); 57.90%, SD 20.34 (previous); 55.78%, SD 20.89 (later). $P=0.87$. 181-250 mg/dl: 32.79%, SD 13.40 (during admission); 30.09%, SD 15.07 (previous); 29.78%, SD 14.86 (later). $P=0.779$. >251 mg/dl: 6.53%, SD 8.44 (during admission); 9.41%, SD 9.94 (previous); 9.98%, SD 12.39 (later). $P=0.387$.
Conclusion
With adequate protocolization and supervision, maintaining CSII therapy during hospitalization is safe and allows glycemic control similar to the previous one.

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P592

Technological upgrade improves glycemic control and sleep quality in adults with type 1 diabetes

eleonora ciocca[1], federica carigi[1], francesco conti[1], chiara giuliani[1] & jonida haxhi[1]
[1]Sapienza University of Rome, Roma, Italy

Introduction
Type 1 diabetes results from autoimmune destruction of pancreatic beta cells and requires lifetime insulin treatment. Poor glycemic control may worsen sleep quality in people with diabetes and poor sleep quality may worsen glycemic control by increasing insulin resistance, which could further lead to an overall worsening of the quality of life in diabetes. Technology use in diabetes improves glycemic control and in pediatric populations, it has been shown to improve quality of life and sleep in patients and their caregivers.
Materials and methods
We investigated the changes in sleep quality (Pittsburgh Sleep Quality Index questionnaire) and wellbeing (WHO 5 item questionnaire) in 19 adult people with diabetes (age 4714 years, 79% women) who transitioned from a less advanced to a more advanced technology. Eleven patients transitioned form multiple daily injections (MDI) to automated insulin delivery (AID), three from sensor augmented pump (SAP) to AID and five from MDI to SAP.
Results
PSQI score improved significantly 3 months after the technological upgrade compared to baseline (5.22.8 vs 6.63.7, $P=0.04$), along with a significant improvement in time in range (TIR 73%11% vs 54%20%, $P=0.00064$), time above range (TAR250 6%6% vs 15%11%, $P=0.009$; TAR180-250 18%8% vs 30%15%, $P=0.001$) and HbA1c (7.1%1.1% vs 7.9%1.3%, $P=0.004$). No significant differences were observed in the wellbeing score, time below range (already low at baseline) body weight, blood pressure, renal function or lipid profile.
Conclusions
Technological upgrade results in better glycemic control (lower TAR and higher TIR) and better self-reported sleep quality in adults with T1D.

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P593

Calcaneal quantitative ultrasound as a screening tool in patients with acromegaly

Andrea Casabella[1], Claudia Campana[2], Federica Nista[2], Angelo Milioto[2], Diego Ferone[2], Sabrina Paolino[1,3] & Federico Gatto[4]
[1]IRCCS Ospedale Policlinico San Martino, Genova, Italy, [2]University of Genova, Endocrinology Unit, Department of Internal Medicine and Medical Specialties, School of Medical and Pharmaceutical Sciences, Genova, Italy, [3]University of Genova, Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine and Specialties, Genova, Italy, [4]IRCCS Ospedale Policlinico San Martino, Endocrinology Unit, Genova, Italy

Introduction
Patients with acromegaly have an increased fracture risk, particularly vertebral fractures. Growth hormone (GH) excess, and the related increase of IGF-1 levels, have been shown to impair bone microarchitecture more than bone density. Therefore, the assessment of trabecular bone score (TBS) has been recommended beside standard dual-energy X-ray absorptiometry (DXA). The calcaneal quantitative ultrasound (QUS) is less expensive and more accessible compared to DXA, and has been studied in multiple setting as a screening tool for bone status. The aim of this study was to investigate the ability of calcaneal QUS to screen for bone impairment in patients with acromegaly.
Material and Methods
Bone Mineral Density (BMD, g/cm^2), lumbar spine T-score (L1-L4), total hip, femoral neck as well as relative skeletal muscle mass index (RSMI) in whole body composition were calculated using a DXA scan [Lunar full-Prodigy (GE Lunar, Madison, WI, USA). Trabecular bone score (TBS) [TBS Insight Medipas Group v 3.0] was derived for each spine DXA examination. Calcaneal QUS (Osteosys BeeTLe, Caresmed) was analyzed and the relative T-score calculated. Fracture Risk Assessment Tool (FRAX), both conventional and modified by TBS, was calculated for each patient. Patient clinical data, including disease control and bone turnover markers, were collected.
Results
Thirty-two patients with acromegaly (44% females), with mean age 5911 years, were included in the study. Median age-adjusted IGF-1 $\times$ upper limit of normality ($\times$ULN) was 0.84 (IQR 0.36-1.32), with the majority of patients (68.8%) having a controlled disease (IGF-1 $\leq$ 1$\times$ULN). QUS T-score showed a strong positive correlation with DXA T-scores at all sites (rho 0.608-0.795, $P<0.001$), and a moderate correlation with TBS (rho 0.356, $P=0.04$). The ROC curve analysis showed that the QUS T-score was able to predict the presence of osteopenia with high sensibility (AUC$=0.810$, $P<0.02$). Consistently, a negative correlation was observed between QUS T-score and the FRAX computed for both major osteoporotic fractures and hip fractures (rho$=$ - 0.664 and -0.662, respectively, $P<$ 0.001). Similarly, QUS T-score showed a negative correlation with the FRAX modified by TBS (rho$=$ -0.686 and -0.700, respectively, $P<$ 0.001). Interestingly, QUS T-score showed a positive correlation with RSMI (rho 0.421, $P=0.016$).
Conclusion
Calcaneal QUS could be a useful tool to screen patients with acromegaly for the presence of osteopenia and fracture risk, selecting patients for DXA evaluation. Moreover, low QUS T-score is also associated with an impairment of bone microarchitecture and the presence of sarcopenia.

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P594

The prevalence of joint replacement surgery in patients with acromegaly

Sophie Hebden[1], Megan Heague[1], Julie Lynch[2], Nawaz Z Safdar[2], David McLaren[2,3], Alberto Stefano Tresoldi[4,5,6], Kirstie Lithgow[4,5,6], Sandrine Urwyler[4,5,6], Chetna Varsani[7], Shahzad Akbar[8], Katie McLoughlin[9], Katarzyna Adeniji[9], Tara Kearney[9], Thozhukat Sathyapalan[8], Claire Higham[10], William Drake[7], Niki Karavitaki[4,5,6], Robert D Murray[2,3] & Nikolaos Kyriakakis[2]
[1]University of Leeds, School of Medicine, Leeds, United Kingdom, [2]Leeds Teaching Hospitals NHS Trust, Department of Endocrinology, Leeds, United Kingdom, [3]University of Leeds, Leeds Institute of Cardiovascular and Metabolic Medicine (LICAMM), Leeds, United Kingdom, [4]University of Birmingham, Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, Birmingham, United Kingdom, [5]Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, United Kingdom, [6]University Hospitals Birmingham NHS Foundation Trust, Department of Endocrinology, Queen Elizabeth Hospital, Birmingham, United Kingdom, [7]Barts Health NHS Trust, Department of Endocrinology, St Bartholomew's Hospital, London, United Kingdom, [8]Hull University Teaching Hospitals NHS Trust, Department of Academic Diabetes and Endocrinology, Hull, United Kingdom, [9]Salford Royal NHS Foundation Trust, Department of Endocrinology, Salford, United Kingdom, [10]The Christie NHS Foundation Trust, Department of Endocrinology, Manchester, United Kingdom

Background
Patients with acromegaly experience early onset arthropathy characterised by initial joint space widening due to cartilage hyperplasia, with later degenerative changes characterised by joint space narrowing, sclerosis and osteophyte formation. To date no specific treatment is available for the arthropathy these patients experience, with management being limited to analgesics, anti-inflammatory agents, physiotherapy, joint injections, and potentially joint replacement surgery in the latter stages. We evaluated the prevalence of joint replacement surgery in a large population of patients with acromegaly.
Methods
Patients with a diagnosis of acromegaly under follow-up in six tertiary pituitary centres were invited to complete a questionnaire relating to joint pain and distribution; and impact on function and QoL. As part of the 'Medication Use' questionnaire, patients were asked to complete data relating joint replacement surgery.
Results
411 patients completed the questionnaires, median age 60 (range 18-88) yrs, 56.1% female and mean age at diagnosis 43 (range 12-83) yrs, with duration of disease 13 (IQR 5.9-20.9) years. Of the cohort 70 (17.4%) patients had undergone joint replacement, equating to a total of 130 episodes of joint replacement surgery. The median number of joints replaced was 2 (range 1–6). The most frequent joints replaced were the hip in 49 patients (70 joint replacements), knee in 30 (42 joint replacements), and shoulder in 9 (15 joint replacements). The median age at the time of joint replacement surgery was 59.0 (IQR 51.8-70.0) years. The median age in those with joint replacement at the time of questionnaire completion was 65.9 (IQR 56.4-73.0) years and 58 (IQR 47.9-68) years in those without joint replacement. Patients with joint replacements had a greater number of painful joints than those without joint replacements (5, IQR 3-7 Vs 3, IQR 1-6; $P=0.002$). There was no difference in the proportion of patients with active acromegaly between those who had and had not had joint replacement (38.8% Vs. 35.7%; $P=0.73$), however duration of disease was longer (17.0, IQR 8.2-24.3 Vs. 13.0, IQR 5.9-20.9; $P=0.024$) years. In addition to replacement joints, 70 patients had undergone other surgical joint interventions to the knees ($n=22$), spine ($n=16$), wrist ($n=12$), hallux ($n=9$), shoulder ($n=6$), elbow ($n=6$), ankle/foot ($n=4$) and hip ($n=3$).
Conclusions
Patients with a history of acromegaly have a significant risk of requiring joint surgery or replacement with correlates with higher number of joints affected, age and duration of disease.

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Comparison of hydrocortisone and prednisolone in managing adrenal insufficiency– HYPER-AID study interim results from a tertiary care centre

Masato Ahsan[1,2], Amy Morrison[1,2], Natasha Fowkes[1,2], Shailesh Gohil[1,2], Miles J Levy[1,2], Karim Meeran[3] & Narendra Reddy[1,2]
[1]Leicester Royal Infirmary, Leicester, United Kingdom, [2]University of Leicester, United Kingdom, [3]Imperial College London, United Kingdom

Background
Adrenal insufficiency (AI) requires life-long glucocorticoid substitution therapy (1), and bears significant risks of infection, cardiovascular (CV) & metabolic disease burden. Historically Hydrocortisone (HC) has been the mainstay of treatment. Prednisolone is a once-daily alternative due to a longer half-life (up to 3.2 hrs). Currently, there is no discernible evidence supporting the superiority of either medication (2).
Objective
To explore the impact of HC and Prednisolone on bone health, cardiovascular risk, glycaemia, and overall well-being among AI patients.
Methods
The retrospective observational study was carried out in University Hospitals of Leicester as per the established protocol for 'Hydrocortisone versus Prednisolone for the Treatment of Adrenal Insufficiency Disease' (HYPER-AID Study), IRAS ID: 234243. AI patients receiving stable HC replacement for at least 4 months were enrolled. Baseline anthropometric data, CV risk, and metabolic biochemistry data were collected prior to swapping of HC to once-daily low-dose Prednisolone ($<$5 mg/day), with a follow-up visit scheduled after a minimum period of four months.
Results
Out of 25 patients initially enrolled, 17 completed the study. 10/17 were male, mean age: 60.7 yrs, mean weight: 82.89 15.6 kg, mean duration of follow-up: 13 months. HC dosage varied from 20 to 30 mg/day, which was replaced with 3 to 5 mg of Prednisolone. There was no significant change in BMI (28.47 to 28.24 kg/m2), mean waist circumference, from 101.7 cm to 100.2 cm and HbA1C from 5.98% to 5.94%. No significant alterations were noted in blood pressure, heart rate, full blood count, bone profile, lipid profiles, serum electrolytes, renal function, liver functions and hormonal profiles. No adrenal crisis episodes, fractures or side effects were reported whilst on Prednisolone and all 17 patients wished to continue on Prednisolone due to ease-of-use and general wellbeing reasons.
Conclusion
Prednisolone as a replacement therapy in AI patients appears to be a safe alternative to HC, given no significant changes noted in bone, metabolic and anthropometric markers following the swap. Patient preference for Prednisolone over HC is noted due to ease-of-use of once-daily administration. The interim analysis indicates non-

inferiority of Prednisolone compared to HC. However, additional research involving larger cohorts is necessary to validate these results.

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Unravelling mitotane resistance in adrenocortical carcinoma: exploring alterations in lipid metabolism

Mariam Hassany[1,2], Kate Warde[2,3], Sarah Feely[2], Giulia Cantini[1], Arianna Propato[1], Luca Galtarossa[1], Michaela Luconi[1] & Michael Dennedy[2]

[1]University of Florence, Department of Experimental and Clinical Biomedical Sciences 'Mario Serio', Florence, Italy, [2]University of Galway, Discipline of Pharmacology and Therapeutics, Galway, Ireland, [3]Huntsman Cancer Institute, Salt Lake City, United States

Management of ACC is difficult. Diagnosis usually occurs at an advanced disease stage. Resection of localised disease offers a potential cure, but recurrence is common (75-85% of cases). For the treatment of unresectable/metastatic disease, mitotane is the only approved drug, alongside M-EDP chemotherapy. Mitotane has a narrow therapeutic window and is poorly tolerated. Additionally, ACC is a heterogenous disease regarding phenotype, genotype, disease progression and resistance to mitotane/chemotherapy. Better pre-clinical disease models are necessary to reflect ACC heterogeneity and offer insight into the mechanisms of treatment resistance. Investigating two ACC cell lines, mitotane sensitive H295R and mitotane-resistant MUC-1 demonstrated differing lipid droplet content whereby H295R cells predominantly store cholesteryl esters, while MUC-1 cells stored predominantly triacylglycerol, with an overall similar lipid droplet number in each cell line. Lipid storage may reflect the metabolic needs of each ACC cell line, thus we considered the metabolic and steroidogenic profiles of both cell lines. Seahorse XFe (Agilent) analysis demonstrated that MUC-1 cells rely significantly more on mitochondrial oxidative phosphorylation (OXPHOS) when compared to H295R: in MUC-1, OXPHOS contribution to the cell energy metabolism was 29,62 %, while in H295R 20,97 % ($P<0.01$). MUC-1 cells demonstrate significantly lower levels of androstenedione and cortisol when compared to H295R cells ($P<0.0001$). Additionally, MUC-1 cells express significantly lower levels of the steroidogenic enzyme, StaR, compared to H295R cells ($P<0.0001$) with no appreciable expression of CYP11B1 or CYP11B2 in MUC-1 cells, reflecting a difference in mitochondrial function between both cell lines. Overall, these results complement our previous findings in relation to TAG storage in MUC-1 cells and suggest that these cells use fatty acids derived from TAG lipolysis to fuel mitochondrial respiration through β-oxidation. Recent evidence shows that aggressive cancer cells can rely both on glycolysis and OXPHOS, and that the replenishment of the tricarboxylic acid cycle (TCA) intermediates can support many aspects tumor progression, including drug resistance. Therefore, we propose further investigation to better understand and overcome treatment-resistance in ACC.

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Unexpectedly high levels of 25-hydroxycholecalciferol in a patient with waldenström macroglobulinemia

Claudia Arnas-Leon[1,2], Agnieszka Kuzior[2], Alba Hernandez-Lazaro[3], Ricardo Jose de Leon-Durango[1], Carlos Rios-Gomez[1], Borja Santana-Ojeda[1], Inmaculada Molinero-Marcos[1], Jennifer Maria Perez-Rivero[4], Cintia Rodriguez-Hernandez[5] & Francisco Javier Martinez Martin[1,2]

[1]University Hospital of Gran Canaria Dr. Negrín, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain, [2]Clinica San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain, [3]Parc Taulí University Hospital, Endocrinology & Nutrition, Sabadell, Spain, [4]Centro Salud Escaleritas, Family & Community Medicine, Las Palmas de Gran Canaria, Spain, [5]Health center Arucas, Family & Community Medicine, Arucas, Spain

Introduction and Objectives

Vitamin D deficiency is highly prevalent. Both physicians and the population are increasingly aware of this fact, and the demand for determinations of vitamin D has escalated. The vitamin D status of the patients is most commonly assessed by the measurement of 25-hydroxycholecalciferol using an automated immunoassay. However, immunoassays are prone to interferences by circulating immunoglobulins such as rheumatoid factor, or more rarely by paraproteins in patients with multiple myeloma or monoclonal gammopathy. We hereby present the novel case of a patient with Waldenström macroglobulinemia who presented artifactually high levels of 25-hydroxycholecalciferol in successive routine clinical measurements, in order to raise awareness of this potentially dangerous laboratory error.

Methods

Review of the patient's clinical records and of the relevant literature

Results

A 66-year-old had been diagnosed with Waldenström macroglobulinemia in 2013 and was treated with rituximab. He was referred to our Endocrinology Clinic in October 2023 because in all five routine measurements of 25-hydroxycholecalciferol performed by immunoassay since April 2021 up to October 2023 the result was >154.2 ng/mL (normal range 30.0 - 84.2 ng/mL) over the maximum measurable range and potentially toxic. The patient denied taking any supplement of vitamin D or multivitamins, had little solar exposure and did not consume cod liver. The measurements of calcium (over 20 determinations in a10-year follow-up), phosphate and intact PTH were repeatedly normal. The patient had no history of renal lithiasis, but an abdominal CT scan from 2018 showed cholelithiasis, which had caused no symptoms. There were no symptoms of hypercalcemia or vitamin D toxicity, consistently with the normocalcemia of the subject. The proteinogram showed a monoclonal paraprotein (IgM kappa light chain), 16.4 g/l. Rheumatoid factor was negative. We suspected paraprotein interference in the 25-hydroxycholecalciferol immunoassay and in November 2023 ordered a liquid chromatography- tandem mass spectrography (LC-MS/MS, reference method) yielding a result of 23.0 ng/mL of 25-hydroxycholecalciferol (low-normal) while our routine immunoassay again returned >154.2 ng/mL from the same venous sample.

Conclusion

The reference method confirmed an artifactual elevation of 25-hydroxycholecalciferol and discarded toxic levels, with the Waldenström paraprotein as the most likely culprit. While there are a few reports of similar interferences in patients with multiple myeloma or monoclonal gammopathy, or high levels of rheumatoid factor, this is a novel result in Waldenström macroglobulinemia. Physicians, especially endocrinologists, should be aware of this fact In order to avoid unnecessary diagnostic and therapeutic procedures.

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P598

Changing landscape of comorbidities in acromegaly: a single-center experience

Polat Ercan[1], Büşra Fırlatan[1], Suleyman Nahit Sendur[2], Seda Hanife Oguz[2], Selcuk Dagdelen[2] & Tomris Erbas[2]

[1]Hacettepe University School of Medicine, Department of Internal Medicine, Ankara, Turkey, [2]Hacettepe University School of Medicine, Division of Endocrinology and Metabolism, Ankara, Turkey

Purpose

Acromegalic patients carry a high burden of cardiovascular, metabolic, and neoplastic diseases, but there are limited studies focusing on morphological and functional changes in the kidneys.

Methods

The data of acromegalic patients followed over a 43-year period at our center were examined for the development of chronic kidney disease (CKD), renal cysts, and urological cancers.

Results

A total of 394 patients (202M/192F, mean age at diagnosis: 41.112.3 years, median duration of disease: 17-years) were included in the study. The median GH and IGF-1 levels at diagnosis were 12.1 ng/mL and 891.6 ng/mL, respectively. The majority (77.1%) of the patients had a pituitary macroadenoma, with a median diameter of 15 mm (range: 2-51 mm). At least one renal cyst was observed in 41% of the patients (size: 2-90 mm), with 47.4% located bilaterally. In the multiple regression model (MRM) analyzing the development of renal cysts, advanced age (OR:1.04, $P<0.001$), nephrolithiasis (OR:2.45, $P=0.018$), liver cyst (OR: 2.65, $P=0.008$), and multiple neoplasia (OR:1.91, $P=0.045$) were defined as independent risk factors. A 1 mEq/l increase in serum potassium level at diagnosis correlated with a 57.1% lower risk of renal cyst development (OR:0.429, $P=0.028$). CKD and nephrolithiasis were detected in 16.1% and 15.1% of the patients, respectively. Advanced age (OR:1.052, $P=0.005$), male gender (OR:3.575, $P<0.001$), and hypertension (OR:2.786, $P=0.007$) were determined as independent risk factors for CKD. In patients with and without CKD or renal cysts, levels of GH and IGF-1 at baseline, during follow-up, and at the last visit were comparable. Among the 65 (16.5%) acromegalic patients followed with a cancer diagnosis, urological cancers were detected in 8 cases (7M/1F). Following thyroid cancer urological cancers were the second most common in our series, including 3 renal cell carcinomas (RCC), 2 ureteral cancers, 2 bladder cancers, and 1 renal PEComa. The median age of patients with

urological cancers was 68 (42-77) years, and the duration of acromegaly was 22.5 (10-37) years. In all three cases with RCC, there were also second primaries including papillary thyroid cancer, pancreatic cancer, and rectal cancer.
Conclusion
Our findings suggest that renal cysts are more prevalent in acromegalic patients compared to the general population, possibly indicating tubular dysfunction and morphological changes in the kidneys associated with chronic exposure to high levels of GH and IGF-1. The occurrence of urological cancers as the second most frequent type of cancer highlights the need for surveillance of acromegalic patients in this regard.

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P599

Differentiation of intra-tumoral necrosis between clusters 1 and 2 pheochromocytoma

Lise Ronger[1], Rachel Desailloud[1], Saint Fabien[2], Renard Cedric[3] & Abdallah Al-Salameh[1]
[1]Chu Amiens-Picardie, Endocrinology, Amiens, France, [2]Chu Amiens-Picardie, Urology, Amiens, France, [3]Chu Amiens-Picardie, Radiology, Amiens, France

Introduction
Pheochromocytoma is a catecholamine-secreting neuroendocrine tumor arising from the chromaffin cells of the adrenal medulla. It is rare and considered benign, but can be life-threatening in the event of catecholaminergic discharge. Tumors differ in genotype, mechanism of tumorigenesis and type of secretion. On imaging, it is often characterized by central intra-tumor necrosis; there is very little data in the literature on the genesis and pathophysiological role of the latter. As a result, necrosis is never measured at the time of diagnosis. In this study, we therefore wanted to investigate potential correlations between the extent of intra-tumor necrosis and the various hormonal secretions in pheochromocytomas.
Methods
We retrospectively identified all major patients operated on at Amiens University Hospital between 2005 and 2022 for adrenal pheochromocytoma confirmed by pathological examination and for whom diagnostic imaging (CT or MRI) and hormone assays were found in the database. The volume of intra-tumor necrosis was measured manually by a specialist radiologist at Amiens University Hospital.
Results
The analysis of this study is based on a total of 49 patients included between 2005 and 2022, 25 of whom were allocated to the group with necrosis and 24 to the group without necrosis after radiological assessment of intra-tumour necrosis. The mean age at the time of adrenalectomy was 53.4 15.2 years. MRI was preferred for the study of intra-tumour necrosis when it had been performed (9 patients). After multivariate analysis, there was a significant difference between the two subgroups in terms of tumour volume, female sex and intensity of urinary metanephrine secretion.
Conclusion
At present, our study appears to the only one to examine the clinico-biological impact of intra-tumoral necrosis in pheochromocytomas. Significant factors have emerged which may guide clinical practice, particularly with regard to the role of MRI in the choice of diagnostic imaging.

Key-words: Pheochromocytoma, intra-tumour necrosis, metanephrines, clusters 1 and 2.

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P600

Changes in lipid profile in patients with type 2 diabetes labeled as metformin-intolerant rechallenged with extended release metformin

Alba Hernandez-Lazaro[1], Ricardo de Leon-Durango[2], Borja Santana-Ojeda[2], Inmaculada Molinero-Marcos[2], Agnieszka Kuzior[3], Claudia Arnas-Leon[2,3], Jennifer Maria Perez-Rivero[4], Esperanza Perdomo-Herrera[5], Alba Lucia Tocino-Hernandez[6] & Francisco Javier Martinez Martin[2,3]
[1]Parc Tauli University Hospital, Endocrinology & Nutrition, Sabadell, Spain, [2]University Hospital of Gran Canaria Dr. Negrín, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain, [3]Clinica San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain, [4]Centro Salud Escaleritas, Family & Community Medicine, Las Palmas de Gran Canaria, Spain, [5]Centro de Salud de Playa Blanca, Family & Community Medicine, Playa Blanca, Spain, [6]Centro de Salud Los Gladiolos, Family & Community Medicine, Santa Cruz de Tenerife, Spain

Introduction and Objectives
Since 2005, the NICE guidelines on T2DM recommend extended-release metformin (XRM) in patients with gastrointestinal disturbances induced by conventional metformin, as the tolerance of XRM is clearly superior, improving patient compliance, satisfaction and outcomes. In Spain XRM is recently available, but only in a fixed combination with sitagliptin. As yet, data on the efficacy, tolerability and impact on lipid profile of this combination are not available. We undertook to study if treatment with XRM/sitagliptin can improve the lipid profile in patients with T2DM previously labeled as metformin-intolerant and treated with a DPP4 inhibitor (DPP4i)
Patients and Methods
Consecutive patients with T2DM, HbA1c >7% and GFR (CKD-EPI) >45 mL/min/1.73m^2 labelled as metformin-intolerant due to gastrointestinal symptoms, and treated with a DPP4i (with or without additional antidiabetic medication) were switched to the 50 mg sitagliptin plus 1000 mg XRM combination, taking 1 pill daily in the first month and afterwards 2 pills if the tolerance was good. Additional antidiabetic medication, if any, was unchanged; however, the patients received lifestyle advice, and antihypertensive and cholesterol-lowering medications were adjusted according to current ESC-ESH-EAS recommendations. Tolerability data were obtained by questionnaire in the follow-up visit. Data are given as meansd. The calculations were done by intention-to-treat. Comparisons were made by the paired t-test. All Included patients granted informed consent.
Results
Changes in lipid profile were studied in 70 patients (45 women, age 548 years, with 7.83.0 years since the diagnosis of T2DM), of which 51 (73%) tolerated 2 tablets of XRM/sitagliptin (1000/50 mg); 8 (11%) tolerated 1 tablet and 11 (16%) did not tolerate any. The reductions in fasting plasma glucose were 36 mg/dl with 1 pill and 44 mg/dl with 2 pills, and in HbA1c were 0.6% with 1 pill and 0.9% with 2 pills (all $P<0.01$). After 3-4 months of treatment, total cholesterol was reduced from 21733 to 19731 mg/dl ($P<0.001$); triglycerides from 19048 to 15846 mg/dl ($P<0.01$); LDL-cholesterol from 13029 to 10826 mg/dl ($P<0.001$), and HDL-cholesterol rose from 50 15 to 57 16 mg/dl ($P<0.01$).
Conclusion
A large majority of the patients with T2DM labelled as metformin-intolerant did tolerate XRM/sitagliptin, and their lipid profile significantly improved. The study intervention only added XRM as an antidiabetic drug, but in many of the patients there were additional interventions in lifestyle, antihypertensive and cholesterol-lowering drugs. Therefore, the changes in the lipid profile must be considered as multifactorial.

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P601

Different clinical presentations of cases with 11-beta-hydroxylase (11β-OHD) deficiency

Ons Maaoui[1], Sabrine Mekni[1], Rihab Laamouri[1], Sawsen Essayeh[1], Nadia Mchirgui[1], Karima Khiari[1], Imen Rojbi[1] & Ibtissem Ben Nacef[1]
[1]Charles Nicolle Hospital, Endocrinology, Tunisia

Introduction
Congenital adrenal hyperplasia (CAH) due to 11-beta-hydroxylase (11β-OHD) deficiency is, in order of frequency, the second most common form after 21 hydroxylase deficiency. We report the cases of patients with 11β-OHD followed in our department.
Patient 1
The patient was referred to our department at the age of 13. The history of the disease dates back to the age of 3, when the child presented pubic and axillary hair and a large penis. Examination revealed a 5-cm penis and empty bursae. The child also presented with hypertension and hypokalemia. Pelvic ultrasound revealed female internal genitalia and the karyotype was 46XX. The genetic study confirmed the diagnosis. The child was raised as a boy. At the age of puberty, he underwent two surgical procedures, one for bilateral breast hypertrophy and the second to correct a communication between the vagina and urethra. Genetic investigation revealed two healthy homozygous sisters and one heterozygous sister for the p.G379V mutation of CYP11B1.
Patient 2
Patient aged 16 years (karyotype 46, XY) was diagnosed with 11β-OHD at the age of 2. The patient had a staturoponderal and pubertal advance at the onset. His clinical presentation was characterized by resistant and unstable hypertension. He was hospitalized thrice for hypertensive emergencies. Due to his hypertension, he developed dilated hypokinetic cardiomyopathy, grade 3 hypertensive retinopathy, and hypertensive nephropathy.
Patient 3
The patient was referred to our department at the age of 16 years. She came from a consanguineous marriage, followed for an 11 B-OHD since the age of 17 months with a 46-XX karyotype. The diagnosis was established during the exploration of sexual ambiguity with genitography showing a 20 mm long vaginal cavity ending in the vertical portion of the urethra which was of the male type with major

hypospadia. Pelvic ultrasound revealed female internal genitalia. The patient underwent clitoral anastomosis resection and vaginoplasty. At the age of 5, hypertension was diagnosed and at the age of 14, she developed hirsutism with elevated testosterone level of 3.66 ng/ml despite treatment with hydrocortisone. Moderate adrenal hyperplasia was diagnosed on CT scan, leading to left adrenalectomy. Histological findings confirmed diffuse nodular hyperplasia. The postoperative testosterone control was 1.16 ng/ml.
Conclusion
We presented patients diagnosed with classic 11β-OHD with different clinical presentations. This particular disorder is relatively understudied. Our results highlight the need for further research to improve our understanding of the relationship between specific genetic features, clinical presentation and long-term course of this disorder.

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P602

A rare case of concurrent pituitary adenoma with granulomata

Yashaswini Choudhary[1], Adhithya Sankar[1], Federico Roncaroli[1,1] & Waseem Majeed[2]
[1]Salford Royal, United Kingdom, [2]Salford Royal, Salford, United Kingdom

Case presentation
A 60-year-old gentleman presented with altered vison. Past medical history included ulcerative colitis, henoch-schonlein purpura (HSP) and Graves' disease. Family history included a brother that underwent surgery for a pituitary macroadenoma. Pituitary MRI identified a 27 × 16 × 20 mm macroadenoma with chiasmal compression. Perimetry demonstrated bitemporal hemianopia. Clinical assessment showed no stigmata of endocrinopathy. Pituitary function tests were normal apart from hypogonadotrophic hypogonadism and testosterone replacement was initiated. The patient underwent trans-sphenoidal surgery. Post-operative pituitary MRI showed near total resection with minimal residuum and the patient remains well with stable pituitary function. Surprisingly, histology revealed a densely granulated (silent) corticotroph pituitary neuroendocrine tumour containing giant cell non-necrotising granulomas. Additional stains for associated infective organisms were negative. Histological samples did not contain normal pituitary tissue and therefore a diagnosis of granulomatous hypophysitis (GRH) could not be confirmed. Investigations for vasculitis, connective tissue diseases, sarcoidosis and IgG4 disease were negative and a whole-body CT ruled out systemic inflammation. Dual pathology within a pituitary is extremely rare and has only been reported in a few case reports and series. Interestingly, typical clinical and radiological features associated with hypophysitis were absent in this patient. In this patient, a background of inflammatory and autoimmune disorders raised the possibility of a systemic inflammatory disorder. Indeed, GRH in patients with Crohn's disease has previously been described. Interestingly, Force *et al*., report that hypophysitis remission was achieved with anti-TNF-α therapy, suggesting a shared underlying pathophysiological mechanism (1). However, ulcerative colitis is typically diagnosed in the absence of granuloma, therefore a shared inflammatory mechanism may be less likely in our case. It is also postulated that GRH may be triggered by autoantibodies against non-secretory pituitary proteins, leading to local immunological mechanisms within pituitary adenomas may drive granulomata formation, independent of systemic signals (2). This rare presentation of dual pathologies highlights the difficult nature of diagnosis and investigation of pituitary lesions. Attention is needed to identify such cases as separate treatments may be required. In this patient, we hypothesise that secondary granuloma may have developed in relation to local intra-adenoma mechanisms, with an alternative hypothesis of systemic inflammation related to inflammatory bowel disease

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P603

Corticosterone induces adiposity and insulin resistance in a dose dependent manner in a murine model of adrenal insufficiency

Mhairi Paul[1], Boglarka Nagy[1], Natalie Z.M. Homer[1], Robert Semple[1], Roland Stimson[1] & Mark Nixon[1]
[1]Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, United Kingdom

Adrenal insufficiency, characterised by inadequate cortisol production, significantly impacts quality of life and overall health. Current treatment primarily involves hydrocortisone replacement. However, dosing challenges and risk of adverse cardiovascular complications persist with this therapy. Consequently, there is a pressing need for safer glucocorticoid replacement options to mitigate the cardiometabolic toxicity, while effectively managing adrenal insufficiency. Preliminary evidence suggests another endogenous glucocorticoid, corticosterone, does not induce the same metabolic effects in adipose tissue as cortisol, and so may be a viable option as a safer, alternative replacement therapy. While animal models of glucocorticoid excess suggest high-dose corticosterone induces cardiometabolic dysregulation, its effect at lower doses, especially in adrenal insufficiency, remains unclear. Therefore, the aim of this study was to investigate the dose-dependent effects of corticosterone in a mouse model of adrenal insufficiency. Adult male C57Bl/6J mice (8 weeks old) were adrenalectomised and administered corticosterone in drinking water (25, 50, or 100 μg/mL) or vehicle (1% v/v ethanol) for 4 weeks ($n=7$-10 per group). Energy expenditure was assessed by indirect calorimetry using the Promethion Core (Sable Systems) after 3 weeks. Body composition was measured by TD-NMR (Bruker MiniSpec) between 3-4 weeks of treatment. At week 4, insulin sensitivity was assessed by an insulin tolerance test. Mice were fasted for 6 hours (0800-1400) before insulin bolus (0.75U/kg; IP) and quantification of glucose levels over 2h. Fasting blood was used to quantify insulin levels (ELISA, Millipore). Mice were culled by decapitation, and blood and tissues harvested for downstream analysis. Circulating and tissue corticosterone levels were quantified by liquid chromatography- tandem mass spectrometry. While corticosterone did not induce changes in body weight, body composition was significantly altered, with corticosterone increasing fat-mass and decreasing lean-mass in a dose-dependent manner. This increase in adiposity occurred independently of changes in energy expenditure, food intake, or physical activity. Corticosterone impaired insulin tolerance in a dose-dependent manner, in parallel with reducing the glucose disposal rate (K_{ITT}). Moreover, corticosterone dose-dependently increased fasting insulin levels, and increased the HOMA-IR index of insulin resistance. Circulating and adipose corticosterone levels were only significantly increased with the highest dose (100μg/ml vs Vehicle). However, Pearson correlation analysis identified significant correlation between adipose corticosterone and indices of metabolic regulation. This study demonstrates that even relatively low-dose corticosterone can induce metabolic dysfunction in adrenal insufficiency. Further work is needed to determine the relative 'risk' by comparing corticosterone and cortisol, and to identify the underlying mechanisms behind potential differences.

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P604

Evaluation of the quality of life in moroccan patients diagnosed with hypoparathyroidism

Essafi Mohammed Amine[1], Handa Samira[1], Aynaou Hayat[1] & Salhi Houda[1]
[1]Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition. Hassan II University Hospital Center, Fez, Morocco

Background and aims
Hypoparathyroidism (HPt) is a rare endocrine disorder often of post-surgical origin, resulting in hypocalcaemia. Several complications have been described including impairment of quality of life (QoL). Our study aims to evaluate the effect of hypoparathyroidism on the Qol of patients diagnosed with HPt.
Methods
A cross-sectional study was conducted in the Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition of the Hassan II University Hospital of Fez. We included in our study all patients followed for chronic HPt. Well-being was assessed using the WHO 5 index, and QoL was assessed by the SF-36 questionnaire in its validated Arabic version. Data were entered into Excel and analysed using SPSS 26. Multiple linear regression was utilized to ascertain the variables linked to the QoL in individuals diagnosed with HPt.
Results
A total of 143 patients with HPt were included in the study, 86.7% of whom were female. The mean age of the patients was 44.6 17.3 years. 89.9% were of post-surgical origin. The assessment of well-being by the WHO 5 index showed a low score (<50), meaning poor well-being in 44.8%. Regarding the QoL, the assessment showed low scores in the areas of general health (41.7), limitations due to physical condition (40.5), vitality (41.4) and limitations due to psychological condition (42.6). The multiple linear regression model revealed a noteworthy association between low SF36 score and advanced age ($\beta = -5.91$ $P<0.001$), surgical origin ($\beta = 8.71$ $P<0.001$), low education level ($\beta = -10.1$ $P<0.001$), and poor compliance with medication ($\beta = -11.3$ $P<0.001$). However, the relationship between impaired QoL and achievement of normocalcemia was non-significant ($P=0.69$)

Conclusion
Our work objective that patients with HPt have a reduced and multifactorial QoL. Despite normocalcaemia. It is hypothesized that parathyroid hormone directly influences QOL. These results could serve as a basis for future research.

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P605

Title: investigating molecular mimicry between SARS-CoV-2 antigens and pancreatic islet antigens in type 1 diabetes pathogenesis using near-sequence similarity

Emmanuel Beltazar[1], Edoardo Beltazar[1], Owais Siddique[2], Tayyibah Patel[2], Honey Panchal[1] & Pravenaa Sivakumar[1]
[1]University College London, UCL Division of Medicine, United Kingdom, [2]University College London, United Kingdom

Background
Type 1 diabetes mellitus (T1DM) involves the autoimmune destruction of pancreatic islet beta cells, with recent research implicating a role for viral infections in its onset. The rise in T1D cases during the COVID-19 pandemic has sparked investigations into potential causes. Molecular mimicry between SARS-CoV-2 antigens and pancreatic islet antigens has been suggested as a plausible mechanism, yet no attempts have been made to explore this phenomenon as comparing functional protein structure remains challenging. To address this, we used pcDelta, a near-coincidence statistic originally developed for evaluating T-cell receptor (TCR) clonotype skewing following antigen exposure. Through the application of pcDelta to two sets of TCR sequences, we quantified near-sequence similarity, with higher pcDelta values indicating greater sequence similarity. The presence of similar TCR sequences suggests similar target antigens and is thus a surrogate for the degree of molecular mimicry.
Methods
CDR3 sequences of the beta chain of TCR specific to various viral antigens were sourced from the VDJ database, a meticulously curated repository of TCR sequences with annotated antigen specificities. Concurrently, islet antigen-specific CDR3 were extracted from a comprehensive review consolidating TCR clonotypes isolated from individuals diagnosed with T1D, cross-validated across multiple studies. Using pcDelta, we quantified near-sequence similarity at the amino acid level between TCR specific to islet pancreatic antigens and viral antigens. To account for different number of epitope-specific TCRs, subsampling was performed and a pcDelta value calculated for each sample.
Results
The analysis of TCR specific to Islet antigens and SARS-CoV-2 revealed a pcDelta value of (4.1310^-5), significantly exceeding the pcDelta values observed between Islet TCRs and influenza A (2.4210^-5) and HIV-1 (2.19*10^-5). This indicates a higher degree of near-sequence similarity between pancreatic islet and SARS-CoV-2 TCRs compared to other viral antigens (P-value <0.001).
Conclusion
The significant elevation in pcDelta values between SARS-CoV-2 and islet antigens TCR compared to other viral antigens indicates increased near sequence similarity between the two TCR groups. This suggests the TCRs might be targeting antigens that might be structurally similar, implying molecular mimicry between SARS-CoV-2 and islet antigens. However, the reliance on existing data sources for TCR sequences may introduce biases or incomplete representation of the T1D landscape. In addition, the study simplifies TCR binding dynamics, although the assumption has been widely used in the literature. Future investigations could employ structural modelling or functional assays to elucidate the impact of molecular mimicry in T1D and consolidate the validity of the approach.

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P606

Vitamin D status and steatohepatitis in obese diabetic and non-diabetic patients

Laura Taban (Cotoi)[1], Stoian Dana[2], Timar Bogdan[2], daniela-georgiana amzar[2], Borlea Andreea[2], Calin Adela[2], Motofelea Alexandru[2] & Laguerre Nadege[3]
[1]Centre Hospitalier de Luxembourg, Luxembourg, Luxembourg, [2]Victor Babeş University of Medicine and Pharmacy, Timişoara, Romania, [3]Metz-Thionville Hospital Mercy, Ars-Laquenexy, France

Background and Aims
The presence of steatohepatitis in obese patients can be multifactorial. The current study tries to determine the differences between diabetic and non-diabetic patients regarding the presence of steatohepatitis. We evaluated sequential liver samples and collected the times of bariatric surgery to assess the presence of NASH in patients with obesity, in the circuit of bariatric surgery.
Methods
We performed a retrospective study of 49 patients presenting high-grade obesity in the circuit of bariatric surgery, with liver biopsy. The patients underwent bariatric surgery at a single center in France and were followed for 2 years. The liver biopsies were performed intraoperatively on all 49 patients before the bariatric surgery. The primary endpoint of the study was to evaluate the relationships between steatohepatitis/liver fibrosis and the presence of diabetes and to evaluate the current relationships between the biochemical work-ups. Special importance was accorded to the correlations between vitamin D levels and the presence of hepatic steatosis, due to the antifibrogenic pattern in the liver, as shown in many important papers in the field.
Results
Significant correlations were found between the presence of liver fibrosis and the presence of diabetes ($P=0.022$), but not regarding the antidiabetic treatment. An important correlation was found between the vitamin D levels and the presence of liver fibrosis, as well as with the levels of A1C hemoglobin and LDL cholesterol levels.
Conclusion
Vitamin D deficiency presents a strong correlation with hepatic steatosis in individuals with morbid obesity. Correcting vitamin D deficiency may present a beneficial role in treating hepatic steatosis, diabetes, and cardiovascular risk in patients with morbid obesity.

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P607

Medical gender detransition is mainly associated with psychological factors

Mariana Gomes Porras[1], Mónica Tomé García[1], María Cruz Almaraz Almaraz[1], Guadalupe Cano Oncala[2] & Isabel Esteva de Antonio[1]
[1]Regional University Hospital of Málaga, Endocrinology and Nutrition, Málaga, Spain, [2]Regional University Hospital of Málaga, Psychology, Málaga, Spain

Background
Medical gender transition is a personal and complex process that can have irreversible health consequences. Detransition is the process of stopping and/or reversing partially or totally and temporarily or permanently the social, legal and/or medical changes achieved during gender transition. The current prevalence of detransition is unknown, most likely underestimated.
Aim
To determine the prevalence and describe the sociodemographic and health characteristics and factors associated with medical detransition in persons over 14 years of age with Gender Incongruence under follow-up in the Transsexual Care Unit (TCU) of a Spanish reference hospital from 1999 to February 7, 2024.
Material and methods
Cross-sectional descriptive study that included 18 transsexual people who stopped cross-sex hormone therapy (CHT). Data were obtained by review of medical records and semi-structured telephone interviews directed to those with loss to follow-up. Qualitative data were expressed as absolute value and percentage and quantitative data as range (minimum-maximum).
Results
The prevalence of medical gender detransition was 0.75% (18/2396). 14 cases (77.7%) started follow-up in the TCU in the last 6 years (2018-2024). Detransition occurred after 1-300 months from the start of medical gender transition. 11 cases (61.1%) were partial detransitions (maintained the legal and social changes) while 7 (41.2%) were total. All partial detransitions were secondary or without identity desistance while total detransitions were primary or with identity desistance. To date, 88.8% have maintained the decision to detransition, so they were considered permanent. 50% were transsexual men with onset of the identity feeling at 4-30 years of age and first visit to the TCU at 14-43 years of age. 72.2% without family support and 100% had previous psychomorbidity. 3 cases had sex reassignment surgery (SRS). 3 and 2 cases required hormone replacement therapy and non-genital reversal surgery, respectively. The psychological factor was present in 13 cases (predominantly non-binary gender identity followed by satisfaction with the changes already achieved) followed by medical (7 cases), cultural (3 cases) and social (3 cases) factors.
*c*Conclusions
Detransition is a complex process that requires assessment in specialized multidiscipslinary teams. In our series, all the detransitions presented previous psychomorbidity and 76.5% associated psychological factors. We recommend prioritizing psychosocial and identity assessment before beginning the medical transition. There is a need for health guidelines on gender detransition.

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e-Poster Presentations

Adrenal and Cardiovascular Endocrinology

EP13

Implication of serotonin in the physiopathology of aldosterone-producing adenoma

Celine Duparc[1], Margot D'Agostino[1], Antoine-Guy Lopez[2], Sylvie Renouf[1], Gilles Manceau[3], Tchao Meatchi[4], Laurence Amar[5], Estelle Louiset[1] & Hervé Lefebvre[2]
[1]Univ Rouen Normandie, Inserm, Normandie Univ, NorDic UMR 1239, Rouen, France; [2]Univ Rouen Normandie, Inserm, Normandie Univ, NorDic UMR 1239, CHU Rouen, Department of Endocrinology, Diabetes and Metabolic Diseases, ROUEN, France; [3]Department of digestive Surgery, Assistance Publique Hôpitaux de Paris, Georges Pompidou University Hospital, University Paris Cité, PARIS, France; [4]Service d'anatomie pathologique, Assistance Publique-Hôpitaux de Paris (AP-HP) Centre, Georges Pompidou University Hospital, University Paris Cité; [5]Université Paris Cité, Inserm, PARCC, Equipe Labellisée par la Ligue contre le Cancer, PARIS, France

In the human adrenal gland, serotonin (5-HT), released by subcapsular mast cells strongly stimulates aldosterone production via activation of the type 4 serotonin receptor (5-HT4R). Consistently, plasma aldosterone levels increase after administration of 5-HT4R agonists like cisapride to healthy volunteers. Previous studies performed in aldosterone producing adenomas (APA) have shown an increase in mast cells density and an overexpression of *HTR4* gene, encoding 5-HT4R, in APA tissues in comparison to normal adrenal. Moreover, administration of cisapride to patients with APA induced an exaggerated plasma aldosterone response. These results suggested that 5-HT could play a role in the pathophysiology of APA. The aim of our study was to examine expression of genes and proteins involved in aldosterone production and actors of the serotonergic pathway in a series of adenomas removed from patients with primary aldosteronism. We have also investigated the *in vitro* effect of various 5-HT4R ligands on aldosterone production by tissue explants or cultured cells derived from adenoma tissues obtained at surgery. Among the 72 tissues studied, 65% were identified as classical APAs, according to classification of the new international histopathology consensus for unilateral Primary aldosteronism. The presence of 5-HT was detected by immunohistochemistry in 75% of the classical adenomas. 5-HT was principally detected in adenoma tissues, in mast cells but also in steroidogenic cells. 5-HT4R immunostaining was widely distributed in most APA tissues, a pattern which was not exclusively noticed in AS-positive adenomas. Expression of the gene encoding the 5-HT-synthesizing enzyme tryptophan hydroxylase was similar in APA and normal adrenals. *HTR4* overexpression was more pronounced in classical than non-classical APAs and *HTR4* mRNA levels were positively correlated to those of *CYP11B2* mRNA encoding AS. Administration of 5-HT to normal adrenocortical or APA cells in culture stimulated *CYP11B2* gene expression and aldosterone production. In addition, in cultured APA cells, BIMU-8 and prucalopride, two 5-HT4R agonists, stimulated aldosterone synthesis in a dose-dependent manner with a higher efficiency than that observed in normal adrenocortical cells. Moreover, BIMU-8, strongly increased aldosterone production by perifused APA explants, an effect which was blocked by administration of GR-113808, a 5-HT4R antagonist. Administration of 48/80 compound, a mast cell degranulator, to perifused APA explants induced a 5-HT release immediately followed by an increase in aldosterone levels. These data indicate that the 5-HT signalling pathway, which is enhanced in APAs, exerts an autocrine/paracrine stimulatory action on aldosterone synthesis and may thus participate in the pathophysiology of primary aldosteronism.

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EP15

Gender-affirming hormone therapy and its impact on myocardial mass and cardiac function: a prospective magnetic resonance study on transgender men and women

Carola Deischinger[1], Dorota Slukova[1], Jürgen Harreiter[1], Stephan Nopp[2], Ivica Just[3], Martin Krssak[3], Siegfried Trattnig[3], Lana Kosi-Trebotic[1], Ulrike Kaufmann[4] & Alexandra Kautzky-Willer[1]
[1]Medical University of Vienna, Endocrinology and Metabolism, Vienna, Austria; [2]Medical University of Vienna, Hematology and Hemostaseology, Vienna, Austria; [3]Medical University of Vienna, High field MR Centre of Excellence, Department of Biomedical Imaging and Image guided Therapy, Vienna, Austria; [4]Medical University of Vienna, Department of Obstetrics and Gynaecology, Vienna, Austria

Background
The differences in cardiac parameters such as myocardial mass, left ventricular ejection fraction (LVEF), cardiac output, and brain natriuretic peptide (NT-proBNP) levels between cisgender men and women are well-established. However, no evidence exists regarding changes in myocardial mass or cardiac function parameters in transgender individuals undergoing gender-affirming hormone therapy (GAHT).
Patients and method
A prospective study enrolling 20 transgender men (TM) and 15 transgender women (TW) was conducted at the Medical University of Vienna from 2019 to 2022. A 3-Tesla electrocardiogram-gated magnetic resonance imaging was used to measure myocardial mass, LVEF and other cardiac function parameters before GAHT and at six-month follow-up. Myocardial lipid content was quantified using magnetic resonance spectroscopy.
Results
In TM, myocardial mass increased significantly after six months of GAHT from in mean ($\pm$SD) 48 ($\pm$8) g/m^2; at baseline to 54 ($\pm$7) g/m^2; at follow-up ($P=0.011$). TW showed a non-significant decrease of 4 ($\pm$14) g/m^2; in myocardial mass. In both groups, no significant changes were noted in LVEF, stroke volume, cardiac output, or peak filling rate. Neither testosterone (TM: $r=$-0.127, $P=0.679$; TW: $r=$-0.127, $P=0.679$) nor estrogen levels (TM: $r=$-0.154, $P=0.616$; TW: $r=$-0.154, $P=0.616$) were related to myocardial mass at follow-up in either group. However, testosterone levels in TM correlated with cardiac output index ($r=0.396$, $P=0.019$), and in TW, with myocardial lipid content ($r=0.579$, $P=0.007$). Notably, NT-proBNP levels in TM were significantly reduced at follow-up (from in median (IQR) 41 (26-57) pg/ml to 19 (12-34) pg/ml). Myocardial lipid content decreased in transgender men but remained similar in transgender women at follow-up.
Conclusions
Myocardial mass increased while NT-proBNP levels decreased significantly in TM after six months of GAHT. However, no significant changes in cardiac function were noted in both TW and TM. Long-term studies are needed to better understand the cardiac effects of GAHT.

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EP48

Assessing atherosclerotic risk: carotid intima-media thickness in non-functional adrenal incidentalomas

Sabrina Ayari, Nadia Khessairi, Cherchir Faten, Elyes Kamoun, Oueslati Ibtissem & Chihaoui Melika
RABTA Hospital, Tunis, Tunisia

Introduction
Carotid intima-media thickness (CIMT) is a simple and non-invasive method used to detect atherosclerosis. This measure could predict future cardiovascular events. Some studies have showed an increased cardiovascular in non functional adrenal incidentalomas (NFAI). The aim of this case control study was to determine the relationship between NFAI and CIMT.
Methods
This case control study included 40 NFAI patients (16 men, 24 women, mean age 52.9$\pm$11.2 years) and 40 individuals (17 men, 23 women, mean age 56.8$\pm$8 years) in the control group matched for age, sex, and weight. NFAI diagnosis was established according to current guidelines. Patients with mild autonomous cortisol secretion, chronic kidney disease, liver failure or under hypolipidemic drugs, combined contraceptive pills, alcohol or depression were excluded of this study. All participants underwent physical examination (waist circumference (WC), blood pressure), adrenal imaging, and biochemical evaluation including CRP-hs and baseline cortisol. All participants underwent the measurement of CIMT.
Results
The NFAI group had significantly higher CIMT (0,62mm (0.57-0.65) vs 0.46mm (0.39-0.55), $P<10^{-3}$). CIMT was positively correlated to CRP-hs ($r=0.323$, $P=0.045$), baseline cortisol ($r=0.484$, $P=0.002$) and age ($r=0.433$, $P=0.005$) in NFAI patients. No correlation was found between CIMT and systolic blood pressure, fasting blood glucose, size of the adrenal tumor, and lipid levels.
Conclusion
NFAI may in fact produce small amounts of GCs that, in consequence, may cause morphological and functional changes in vessels. Given the increased risk of subclinical atherosclerosis in NFAI patients, a more vigilant follow-up is necessary.

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EP89

Pheochromocytoma associated with pregnancy. Diagnostic difficulties and management

Zahra Ismail, moustapha ibrahim Fod, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
University Hospital Center Mohamed VI, Departement of Endocrinology, Diabetes and Metabolic Disease, Marrakech

Introduction
Pheochromocytoma is a rare cause of hypertension in pregnancy. Its prevalence ranges from 0.2% to 0.002% of cases of hypertension in pregnancy. Early diagnosis and appropriate management can reduce mortality and morbidity. Were report a case of pheochromocytoma diagnosed during pregnancy.
Observation
34-year-old diabetic patient, 29 weeks pregnant. Admitted for hypertensive peaks up to 170 mmHg of systolic, initially mistaken for pre-eclampsia. Given the 4-year history of hypertension associated with headaches and palpitations, endocrine hypertension was suspected. Urinary metanephrines were measured, and were very high (41 times upper limit for normethanephrine and 27 times for metanephrine). Abdominal MRI without gadolinium injection revealed a heterogeneous tumor above the left kidney measuring 7 cm, suggesting a pheochromocytoma. As the patient was already in her third trimester, surgery was postponed and the patient was put on alpha blockers and calcium channel blockers. Her blood pressure normalized under medical treatment. The patient had intrauterine fetal demise at 33 weeks and underwent adrenalectomy in the post partum.
Discussion
Pheochromocytoma is most common between the fourth and fifth decades of life, in both men and women. The diagnosis of pheochromocytoma in pregnant women is often difficult, and the presence of hypertension can be misleading. Persistent or paroxysmal hypertension is the most common sign of this disease. Headaches occur in up to 90% of symptomatic patients. Hypertension in pregnancy should be investigated early to differentiate pre-eclampsia from other causes. Urinary cathecolamines and metanephrines and MRI are used for diagnosis. Medical treatment with an alpha-blocker should be started as soon as the disease is diagnosed, and continued for at least 10 to 14 days before surgery. Surgery is the definitive treatment for pheochromocytoma, but the timing is controversial. Decisive criteria are gestational age, accessibility of the tumor, presence or absence of fetal distress, and the patient's response to medical treatment. If the pregnant woman is in her 24th week of gestation or more, surgical removal is postponed until or after delivery. Despite its low prevalence, pheochromocytoma during pregnancy increases maternal and fetal morbidity and mortality.

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EP90

Familial glucocorticoid deficiency type 2 – a case report

Nicoleta Chelaru[1], Cristina Cretu[1], Mariana Cabac[2] & Cristina Cristea[1]
[1]Saint Spiridon County Hospital, Endocrinology, Iasi, Romania; [2]Spitalul Orăşenesc Târgu Neamţ, Endocrinology, Romania

Background
Mutations in the ACTH receptor (MC2R) gene or in its melanocortin accessory protein (MRAP) gene disrupt receptor expression, signaling, and constitutive activity of the MC2R, leading to familial glucocorticoid deficiency (FGD) type 1 and type 2 respectively. FGD is a life-threatening, rare autosomal recessive disorder characterized by impaired cortisol synthesis and classically preserved mineralocorticoid production. There have also been described other mutations that disrupt the signaling pathways of ACTH. The clinical picture of FGD varies depending on the age of onset, the underlying genetic cause, and the severity of the deficiency and may include: recurrent hypoglycemia, seizures, hyperpigmentation, severe, recurrent infections and other symptoms linked to cortisol deficiency.
Case report
Our patient is a slightly hyperpigmented girl with no significant natal or family history and a normal psychomotor development in the first year of life. At the age of two she presented epileptic crisis, ataxia, neuropsychological delay and an autism spectrum disorder, attributed at first to a mutation in the MTOR gene, corresponding to Smith-Kingsmore phenotype. At 3 y 10 mo evaluation, she displayed a tall stature and primary hypothyroidism, therefore levothyroxine substitution was initiated. It was on the age of 6 when a second genetic study identified a homozygous mutation in the MRAP gene c.106+2dup consistent with FGD type 2. Laboratory tests showed undetectable cortisol, very high ACTH level, normal renin and aldosterone levels. Consequently, glucocorticoid substitution was initiated, then she was referred to our clinic for further follow up. It is noteworthy that she has a history of a viral meningo-encephalitis and cerebral parasitosis aspect on the MRI.
Discussions
MRAP defects have been associated with a more severe clinical picture and an early onset of the disease. Our patient's diagnosis at the age of 6 is remarkable, considering that the median age at diagnosis is typically less than 1 year. Interestingly the thyroid function substitution did not precipitate an adrenal crisis. Literature data report several cases of patients with FGD and primary hypothyroidism, but we haven't found any strong association. Another interesting fact is that tall stature associated with FGD is attributed to MC2R gene defects, and not to MRAP mutations, probably due to the early diagnosis of the latter and the lack of the prolonged effect of ACTH excess on the growth plate. We consider that early diagnosis would have improved our patient's outcome in terms of infections and seizures that could have been precipitated by cortisol deficiency.

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EP91

Identification of lipid profiles and fatty acid abundances associated with histopathology and subtypes of primary aldosteronism

Yuhong Yang[1], Yuqing Liu[1], Haifeng Zhou[2], Maoting Gao[1], Yutong Yan[1], Guodong Ma[1], Min Wang[1], Meiling Bao[3], Tao Yang[1] & Min Sun[1]
[1]The First Affiliated Hospital of Nanjing Medical University, Department of Endocrinology, Nanjing, China; [2]The First Affiliated Hospital of Nanjing Medical University, Department of Interventional Radiology, Nanjing, China; [3]The First Affiliated Hospital of Nanjing Medical University, Department of Pathology, Nanjing, China

Background
Primary aldosteronism (PA) is mainly caused by unilateral (unilateral PA) or bilateral aldosterone-producing lesions of adrenals (bilateral PA). Accumulating findings suggest distinct metabolic profiles between patients with unilateral and bilateral PA. However, the link between the metabolic features and histopathologic findings of adrenals from patients with PA remains largely unknown.
Objective
To characterize metabolic profiles with a focus on the lipid parameters, adiposity and fatty acid alterations in patients with PA with distinct histopathologic findings and subtypes.
Methods
Patient data were retrospectively collected from a single center and analyzed in 76 patients with bilateral PA and 105 with unilateral PA who were categorized into 71 of classical and 34 of nonclassical histopathology according to HISTALDO consensus. Fatty acid abundances in peripheral serum and adrenal specimens were measured by gas chromatography/mass spectrometry and liquid chromatography-tandem mass spectrometry, respectively, with human adrenocortical HAC15 cells as an *in vitro* functional validation model.
Findings
Patients of classical histopathology displayed the highest baseline serum omentin-1 levels (classical vs nonclassical vs bilateral PA: 36.13[19.95–191.45] vs 19.63[13.67–37.33] vs 13.46[9.90–29.31] ng/ml, $P < 0.001$), and the lowest leptin levels (classical vs nonclassical vs bilateral PA: 6.40[2.88–10.68] vs 13.43[4.63–21.32] vs 10.06[5.17–18.46] ng/ml, $P = 0.005$). Compared with the nonclassical group, patients of classical histopathology showed lower BMIs (25.17 ± 3.58 vs 27.03 ± 3.06 kg/m^2, $P = 0.031$) and smaller visceral adipose tissue areas (120.69[74.79-171.16] vs 155.29[127.81-197.46] cm^2, $P = 0.020$). No differences in lipid profiles and adiposity were detected between the nonclassical and bilateral PA groups. In contrast, patients of classical histopathology displayed the highest peripheral serum polyunsaturated fatty acids (PUFAs) especially ω6-PUFAs concentrations relative to the other two groups. Linear discriminant analysis demonstrated fatty acid signatures classified patients with distinct histopathology and subtypes with an accuracy of 98.7%. Combing with the findings of fatty acid abundance comparisons in aldosterone-producing adenomas vs paired adjacent cortex that identified four distinct PUFAs, C20:4 n-6 (arachidonic acid, ARA) in peripheral serum and adrenals showed a strong association with histopathology and subtypes of PA. Functional experiments demonstrated ARA decreases HAC15 cell viability via reactive oxygen species-induced apoptosis and promotes aldosterone synthase expression and aldosterone production via calcium signaling.
Interpretation
Patients with unilateral PA of classical histopathology display the least severe lipid profiles and adiposity, while showing the highest peripheral serum PUFA levels which is likely associated with their *in situ* productions in adrenal lesions, with ARA as a potential biomarker for aldosterone-producing lesions of PA.

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EP113

Audit of clinical outcomes from our nurse-led adrenal nodule clinic in a London hospital

Agathoklis Efthymiadis, Dannah Pua, Sangita Sharma, Andrew Solomon, Elaine Hui, Shivashankar Seechurn, Mushtaqur Rahman, Asjid Qureshi, Ian Seetho & Mahesh Deore
Northwick Park Hospital, Diabetes & Endocrinology, London, United Kingdom

Introduction
There is an increased number of referrals to endocrinology for adrenal nodules found on imaging. This is due to increased use and advancement in imaging modalities. Adrenal nurse-led clinics are cost-effective and safe. We established an adrenal nodule nurse-led clinic at Northwick Park Hospital in September 2022.
Methods
Retrospective data collection and analysis of patients reviewed at the clinic between September 2022-2023.
Results
Twenty-Nine patients (M = 12/F = 17) were seen. Twenty (69%) patients had left-sided adrenal nodules, five (17%) patients had right-sided adrenal nodules and four (14%) patients had bilateral adrenal nodules. Mean nodule size was 1.9 cm (range = 1.0-8.8, SD = 1.6). Four (14%) adrenal nodules were $\geq$ 4 cm. Waiting time from initial referral to clinic review was 41.5 days (SD = 29.9). Fourteen (48%) patients had hypertension, thirteen (45%) had diabetes and none had hypokalaemia. Non-functioning benign adrenal adenoma was diagnosed in seventeen (59%) of patients, primary hyperaldosteronism in three (10%), mild autonomous cortisol secretion in two (7%), myelolipoma in one (4%), Cushing's syndrome in one (4%) patient, while five (16%) patients still remain under investigation. All patients were subsequently reviewed at the endocrinology consultant-led clinic. Eleven (38%) patients were discussed at the local endocrine multidisciplinary meeting. Ten patients (34%) were directly discharged after their first consultant-led consultation, whilst three (10%) were referred to a tertiary centre for further endocrine investigations. The remaining patients were followed-up locally and four (14%) were discharged after a second consultant appointment, whilst the rest required further endocrine testing.
Discussion and conclusions
We compared our performance to the literature. The number of patients referred to our adrenal nurse-led clinic each year, the size of adrenal lesion and the final diagnosis was comparable to other centres. The timeframe from referral to clinic appointment was shorter in our clinic compared with another centre in the UK (41 days vs 3.6 months). The shorter time to testing may reduce anxiety in patients. All patients in our clinic were subsequently reviewed at a consultant-led clinic before they were discharged, whilst in other centres patients are directly discharged from the nurse-led clinic. This audit shows the importance of a local adrenal nurse-led practice that is appropriate for assessment of patients with benign adrenal nodules, facilitating early patient review, endocrine dynamic testing and prompt discharge of patients with adrenal incidentalomas, that enables reduced clinic visits and faster access to testing, using a standardised algorithm in line with the European Society of Endocrinology guidelines.

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EP114

Presentation and management of adrenal masses in a large tertiary care centre: a longitudinal study

Onnicha Suntornlohanakul[1,2], Sumedha Mandal[3], Pratyusha Saha[3], Emre Saygili[1,4], Miriam Asia[5], Wiebke Arlt[1,6,7], Yasir Elhassan[1,3,5], Alessandro Prete[1,3,5,8] & Cristina Ronchi[1,3,5]
[1]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom; [2]Endocrinology and Metabolism Unit, Division of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand; [3]Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, United Kingdom; [4]Division of Endocrinology and Metabolism, Department of Internal Medicine, Faculty of Medicine, Canakkale Onsekiz Mart University, Canakkale, Turkey; [5]Department of Endocrinology, Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom; [6]Medical Research Council Laboratory of Medical Sciences, London, United Kingdom; [7]Institute of Clinical Sciences, Imperial College London, London, United Kingdom; [8]NIHR Birmingham Biomedical Research Centre, University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

Background
Adrenal masses are detected in 5-7% of adults. The European guidelines on managing adrenal incidentalomas published in 2016[1] have standardised the management of these patients. However, evidence of the guidelines' impact on clinical care is still lacking.
Methods
We conducted a retrospective, comprehensive review of clinical presentation, radiological characteristics, final diagnosis, and outcome of a large cohort of patients with adrenal masses referred to our tertiary centre (Queen Elizabeth Hospital Birmingham, UK) between 1998 and 2022. We performed a sub-analysis comparing the characteristics and outcomes before and after implementing the 2016 guidelines.
Results
We included 1397 patients (55.7% women; median age 60 years, [interquartile range, IQR, 49-70]). Incidental discovery was the most frequent mode of presentation (67.9%). Overall, 14.7% of patients had bilateral masses, and 32.8% had masses $\geq$ 4 cm (median 2.9 cm, [IQR 1.9-4.7]). Unenhanced computed tomography (CT) Hounsfield Units (HU) were available for 763 patients; of these, 32.9% had heterogeneous tumours or HU > 20. 44.3% of patients had hormonally inactive adrenal masses. After standardised workup, the most common diagnoses were adrenocortical adenoma (ACA, 56.0%), phaeochromocytoma (12.7%), adrenocortical carcinoma (10.6%), and metastases from an extra-adrenal malignancy (5.7%). Eventually, 65% of patients referred for indeterminate masses were diagnosed as having benign lesions, while 18% remained indeterminate. At multivariable regression analysis, the significant predictors in discriminating malignant from benign lesions were HU > 20 or heterogeneous mass (odds ratio, OR, 28.40, 95%confidence interval, 95%CI [5.87-137.56]), followed by increased serum androgens (OR 27.67, 95%CI [4.05-189.00]), mass detection during cancer surveillance (OR 11.34, 95%CI [3.32-38.70]), size $\geq$ 4 cm (OR 6.11, 95%CI [2.22-16.86]) and male sex (OR 3.06, 95%CI [1.12-8.34]). After implementing the guidelines, there was no significant difference comparing patients seen before (n = 386) and after 2016 (n = 990) in the use of additional imaging in the entire cohort or among patients with indeterminate radiological appearance (HU > 20 or heterogeneous density or size $\geq$ 4 cm). Nevertheless, the proportion of patients with non-functioning benign adrenal masses that underwent multiple follow-up visits significantly decreased from 89.6% to 70.2%, while the discharge rate after the initial workup increased from 4.4 to 25.3% (P < 0.001).
Conclusion
From our extensive review of patients with adrenal masses including a high proportion of large and heterogenous lesions, ACAs remained the commonest aetiology. Implementing the European 2016 guidelines positively impacted clinical practice, reducing the number of follow-up visits, and increasing the discharge rate of benign, non-functioning masses.
Reference
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EP115

Dyslipidemia unveiled in non functional adrenal incidentalomas

Sabrina Ayari, Nadia Khessairi, Sahar Abidi, Elyes Kamoun, Oueslati Ibtissem & Chihaoui Melika
Rabta Hospital, Tunis, Tunisia

Background
Non functional adrenal incidentalomas (NFAI) constitute the majority of adrenal tumors. This entity is a result of advances in imaging techniques and their prevalent use in clinical practice. Among the associated metabolic effects of NFAI, dyslipidemia emerges as a key factor, stimulating growing interest in understanding the link between these two entities.
Methods
This case control study included 40 NFAI patients (16 men, 24 women, mean age 52.9 $\pm$ 11.2 years) and 40 individuals (17 men, 23 women, mean age 56.8 $\pm$ 8 years) in the control group matched for age, sex, and weight. NFAI diagnosis was established according to current guidelines. Patients with mild autonomous cortisol secretion, chronic kidney disease, liver failure or under hypolipidemic drugs, combined contraceptive pills, alcohol or depression, were excluded of this study. All participants underwent adrenal imaging, biochemical evaluation including triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), cholesterol total (CT), Low-density lipoprotein cholesterol (LDL-C). Dyslipidemia was defined according to the National Cholesterol Education Program (NCEP) ATP III.
Results
The prevalence of dyslipidemia was 52,5% in NFAI patients compared to 57.5% in the control group. HypoHDLemia represented the most common type of dyslipidemia in both groups, 35%and 33% respectively. Hypercholesterolemia and hypertriglyceredemia were diagnosed respectively in 20% and 18% of NFAI patients vs 25% and 18% in control group.

Conclusion
Our study didn't show a higher prevalence of dyslipedemia in NFAI patients. However, management of dyslipidemia in NFAI should be considered for primary and secondary prevention of cardiovascular risk.

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EP182

Predicting postoperative hypocortisolism in patients with non-aldosterone-producing adrenocortical adenoma: a retrospective single centre study

Ilaria Bonaventura[1], Alessandra Tomaselli[1], Francesco Angelini[1], Davide Ferrari[1], Dario De Alcubierre[1], Valeria Hasenmajer[1], Emilia Sbardella[1], Alessia Cozzolino[1], Alessandro Paganini[2], Andrea Isidori[1], Marianna Minnetti[1] & Riccardo Pofi[3]
[1]Sapienza University of Rome, Experimental Medicine; [2]Sapienza University of Rome, Department of General Surgery, Surgical Specialties and Organ Transplantation "Paride Stefanini"; [3]University of Oxford, Department of Endocrinology, Oxford Centre for Diabetes, Endocrinology and Metabolism and NIHR Oxford Biomedical Research Centre

Background
Limited information exists on postoperative hypocortisolism and hypothalamus-pituitary-adrenal axis recovery in patients with adrenal incidentaloma following unilateral adrenalectomy. We evaluated frequency of postoperative hypocortisolism and predictors for recovery in non-aldosterone- producing adrenocortical adenoma patients after unilateral adrenalectomy.
Methods
A retrospective analysis of 32 adrenal incidentaloma patients originally included in the ITACA trial (NCT04127552) with confirmed non-aldosterone- producing adrenocortical adenoma undergoing unilateral adrenalectomy from September 2019 to April 2023 was conducted. Preoperative assessments included adrenal MRI, anthropometrics, evaluation of comorbidities, adrenal function assessed via ACTH, urinary free cortisol, and 1 mg dexamethasone suppression test. ACTH and serum cortisol or Short Synacthen test were performed within 6 days, 6-week, 6-month, and a year after surgery.
Results
Six days postoperative, 18.8% of patients had normal adrenal function. Among those with postoperative hypocortisolism, 53.8% recovered by 6-week. Patients with earlier adrenal recovery (6-week) had lower preoperative 1 mg dexamethasone suppression test (median 1 mg dexamethasone suppression test 76.2 [61.8-111.0] nmol/l vs 260.0 [113.0-288.5] nmol/l, $P<0.001$). Univariate analysis showed preoperative 1 mg dexamethasone suppression test negatively related with baseline ACTH levels ($r=-0.376$; $P=0.041$) and negatively associated with the 6-week baseline ($r=-0.395$, $P=0.034$) and 30-minute cortisol levels during Short Synacthen test ($r=-0.534$, $P=0.023$). Logistic regression analysis demonstrated preoperative 1 mg dexamethasone suppression test as the only biochemical predictor for 6-week adrenal recovery: ROC curve identified a 1 mg dexamethasone suppression test threshold of 131 nmol/l predicting 6-week recovery with 89.5% sensitivity and 72.7% specificity (AUC 0.87; 95%CI 66.9-98.7, $P<0.001$). Other preoperative assessments (tumor size, ACTH levels and anthropometrics) were not associated with postoperative hypothalamus-pituitary-adrenal axis function, but the presence of diabetes was associated with a lower probability of recovery (OR = 24.55, $P=0.036$). ACTH levels increased postoperatively in all patients but did not predict hypothalamus-pituitary-adrenal axis recovery.
Conclusions
The preoperative 1 mg dexamethasone suppression test cortisol value and presence of diabetes are the only relevant predictor of hypothalamus-pituitary-adrenal axis recovery in patients with non-aldosterone- producing adrenocortical adenoma undergoing surgery, regardless other clinical and biochemical variables. Notably, pre and postoperative ACTH levels did not predict hypothalamus-pituitary-adrenal axis recovery. These findings point towards the potential for saving resources by optimizing their allocation during follow-up assessments for patients with non-aldosterone producing adrenocortical adenoma undergoing unilateral adrenalectomy.

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EP186

Undetermined masses in adrenal topography: experience of a compound by a tertiary health center

Aliny Weber kuhn[1], Victor Srougi[2], Vânia Brondani[1], Fabio Tanno[2], Ricardo de Freitas[3,4], Fernando Coelho[3,4], Maria Pereira[1], Madson Almeida[1,5,6], Ana Claudia Latronico[1,5], Jose Chambô[2], Berenice Mendonca[1,5] & Maria Candida Barisson Villares Fragoso[1,5,6]
[1]Hospital das Clínicas, University of São Paulo School of Medicine, Division of Endocrinology, São Paulo, Brazil; [2]Hospital das Clínicas, University of São Paulo School of Medicine, Division of Urology, São Paulo, Brazil; [3]Cancer Institute of São Paulo State (ICESP), Interventional Radiology, São Paulo, Brazil; [4]Hospital das Clínicas, University of São Paulo School of Medicine, Radiology Institute (InRad), São Paulo, Brazil; [5]Hospital das Clínicas, University of São Paulo School of Medicine, Laboratory of Hormones and Molecular Genetics LIM/42, Division of Endocrinology and Metabolism, São Paulo, Brazil; [6]Cancer Institute of São Paulo State (ICESP), University of Sao Paulo Medical School, Division of Endocrine Oncology, São Paulo, Brazil

Introduction
Masses in adrenal topography have been diagnosed frequently due to more available access to radiological imaging. Adrenal incidentalomas occur around 5% to 7% of patients undergoing abdominal imaging mainly over 50 years of age. The HCFMUSP is a complex tertiary center, a national reference to adrenal disorders and since 2006 around 300 adrenalectomies were performed; 8% of them corresponded to undetermined masses in adrenal topography.
Objective
We retrospectively analyzed imaging features and the definitive diagnosis of undetermined masses located in adrenal gland topography identified by abdominal CT or MRI from 2006 to 2023 ($n=49$).
Methods
All patients were undergoing an extensive hormonal evaluation, according to the European and American Society of Endocrinology guidelines. Two expert radiologists reviewed all images. Forty-nine patients were included and underwent unilateral adrenalectomy, to elucidate the etiology of the lesion on adrenal topography. Masses diagnosed as adrenocortical carcinoma were excluded from this analysis.
Results
Thirty-four (69.3%) were female. The general mean age was 48.3 years old (range 18-82yo). Abdominal or lumbar pain was the leading cause for the imaging study (42.8%), and 34.6% were identified as adrenal incidentalomas during the approach to urinary tract infection, nephrolithiasis, or pulmonary disease. None of these patients had any clinical signs of adrenal hormonal hyperfunction, neither abnormal hormonal secretion. Twenty-five patients (51%) presented a mass on the left side, and only two cases presented bilateral adrenal masses. The mean size was 8.54 cm (1.3-18 cm), with non-adrenal-neoplasia standing out for a larger average size of 11 cm (7.2-15 cm). The mean Hounsfield Units (HU) on non-contrasted CT scans were 25 HU (0-50 HU). There was no significant difference in HU concerning the size of the lesion, although non-adrenal neoplasias showed a slightly higher average, reaching 30.4 HU (3-48 HU). The etiologies were: non-adrenal cancer (15 cases) (30.6%), ganglioneuroma (9 cases) (18.3%), adrenal cysts (6 cases) (12.2%), adrenal hemorrhage (4 cases) (8.1%), infectious disease (4 cases) (8.1%), schwannoma (3cases) (6.1%), lymphangioma (2 cases) (4%), pseudocyst (2 cases) (4%), prostate cancer metastasis (1 case) (2%), arteriovenous malformation (1 case) (2%), myelolipoma (1 case) (2%), acute splenitis (1 case) (2%).
Conclusion
In this large cohort, undetermined masses in adrenal topography were more prevalent in females, with non-adrenal cancer being the most frequent cause, particularly highlighting leiomyosarcoma. Ganglioneuroma was the most frequently diagnosed benign tumor.

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EP195

Are comorbidities of patients with adrenal incidentaloma tied to sex? Results from a multicenter longitudinal study

Soraya Puglisi[1], Anja Barac Nekic[2], Valentina Morelli[3], Ylenia Alessi[4], Michele Fosci[5], Angelo Pani[5], Karin Zibar Tomšić[2], serena palmieri[6], Francesco Ferraù[4], Anna Pia[1], Giuseppe Reimondo[1], Iacopo Chiodini[7], Darko Kastelan[2] & Massimo Terzolo[1]
[1]Internal Medicine, Department of Clinical and Biological Sciences, San Luigi Gonzaga Hospital, University of Turin, Orbassano, Italy; [2]Department of Endocrinology, University Hospital Zagreb, Zagreb, Croatia; [3]Unit for Bone Metabolism Diseases and Diabetes and Lab of Endocrine and Metabolic Research, IRCCS, Istituto Auxologico Italiano, Milan, Italy; [4]Endocrine Unit, Department of Human Pathology G. Barresi, University Hospital G. Martino, University of Messina; [5]Endocrinology Unit, Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy; [6]Unit of Endocrinology, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Ca' Granda-Ospedale Maggiore Policlinico,

Milan, Italy; [7]Unit of Endocrinology, Department of Biotechnology and Translational Medicine, Ospedale Niguarda Cà Granda, University of Milan, Milan, Italy

Background
A recent cross-sectional study showed that both comorbidities and mortality in patients with adrenal incidentaloma (AI) are tied to sex. However, only few longitudinal studies evaluating the development of arterial hypertension, hyperglycemia, dyslipidemia and bone impairment in patients with AI are available. The aim of this study is to analyze the impact of sex in the development of these comorbidities during long-term follow-up.
Patients and Methods
We retrospectively evaluated 189 patients (120 females, 69 males) with AI, from four referral centers in Italy and Croatia. Clinical characteristics and hormonal data were collected at baseline and at last follow-up visit (LFUV). To compare each characteristic at baseline and at LFUV, we used the Wilcoxon test for continuous variables and the McNemar test for categorical variables. Differences between groups were analyzed with the Mann-Whitney test for continuous variables and the Chi-square test for categorical variables.
Results
Median follow-up was 52 (IQR 25-86) months. At LFUV, in both sexes arterial hypertension was more frequently reported than at baseline (females: 77.8% vs 65.8%, $P=0.002$; males: 69.1% vs 58.0%, $P=0.035$), as well as hyperglycemia (females: 39.6% vs 28.8%, $P<0.001$; males 54.0% vs 36.2%, $P<0.001$). Patients were stratified in two groups by cortisol after 1 mg-dexamethasone: 99 (62 females, 37 males) with non-functional adrenal tumors [NFAT] and 89 (57 females, 32 males) with tumors with mild autonomous cortisol secretion [MACS]. In the NFAT group, at baseline, we did not observe any difference in clinical characteristics and comorbidities between males and females. At LFUV, the NFAT group showed a higher frequency of hyperglycemia in males than in females (57.6% vs 33.9%, $p=0.03$). In the MACS group, at baseline, females were younger (60, IQR 55-69 vs 67.5, IQR 61-73, years; $p=0.01$) and presented higher rates of bone impairment (89.3% vs 54.5%, $p=0.02$) than males. At LFUV, in the MACS group, the median age remained lower (66, IQR 61-73 vs 73.5, IQR 65-78, years; $p=0.02$) and bone impairment more frequent (88.9% vs 58.8%, $p=0.01$) in females than males. Moreover, females presented a higher frequency of visceral adiposity (95% vs 60%, $p=0.01$)
Conclusions
Patients with AI frequently develop arterial hypertension and glycemic alterations and should be periodically checked for these comorbidities, regardless sex. Bone impairment was frequently reported in females with MACS, suggesting a sex-specific effect of cortisol on bones.

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EP196

Metabolic impact of dual-release hydrocortisone in patients with congenital adrenal syndrome: a retrospective study

Pierluigi Mazzeo, Filippo Ceccato, Giacomo Voltan, Irene Tizianel, Alessandro Mondin, Martina Lazzara, Alessandro Bavaresco & Mattia Barbot
Endocrine Disease Unit, Department of Medicine - DIMED, University-Hospital of Padova, Padua, Italy

Background
Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder characterized by impaired cortisol secretion and androgen excess. The mainstay of CAH treatment is glucocorticoid (GC) replacement, necessary to avoid adrenal crisis and manage androgen excess. The delicate balance between GC under/overtreatment is crucial to prevent metabolic and cardiovascular complications. Dual-release hydrocortisone (Plenadren®) is once-daily modified-release formulation of hydrocortisone (HC) approved for adrenal insufficiency. Data on its use in CAH are scarce. The aim of this study is to evaluate clinical, metabolic and hormonal characteristics of patients with CAH switched from conventional GC treatment to Plenadren.
Patients and method
Retrospective study on 29 patients followed at our Unit (M/F:17/12) with CAH; 18/29 patients were switched to Plenadren (median age 33 years, IQR 24-40). Clinical, metabolic and hormonal data were evaluated at baseline and during follow-up (at 6 months and last available visit) and compared with patients (11/29) who continued conventional GCs.
Results
There were no statistical differences between the two cohorts of patients at baseline. During follow-up, patients switched to Plenadren showed a worsening of ACTH control [123(23-307) vs 193(142-713) ng/l, $P=0.09$] despite an overall increase of daily HC equivalent dose (13 vs 20 mg/day); other parameters of disease control such as 17-OH progesterone [200 (19-433) vs 254 (99-426) nmol/l, $P=0.58$] and total testosterone levels in male [12.8 (9.0-19.1) vs 13 (10.0-16.6) nmol/l $P=0.99$] remained stable, as well as metabolic parameters like HOMA index [2.5 (1.25-2.9) vs 0.8 (0.7-2.5), $P=0.20$] and total cholesterol [178 (142-206) vs 147 (122-157) mg/dl, $P=0.11$]. However, comparing with patients on conventional GCs regimen, total cholesterol levels improved [147 (122-157) vs 200 (169-208) mg/dl, $P=0,03$], but disease control was poorer [ACTH 193 (142-713) vs 50 (19-105) ng/l, $P=0.015$ and 17-OH progesterone 254 (99-426) vs 24 (7-123) nmol/l, $P=0.004$]. Unsatisfactory disease control was the main reason for discontinuation (12/18 patients), after a median time of 29 months (6-49), but no adrenal crisis was recorded during follow-up.
Conclusions
Although dual-release HC can mimic the circadian rhythm of cortisol secretion, it provides suboptimal hormone control in CAH. The once-daily administration in the morning has a fall of cortisol level at bedtime, not avoiding the overnight ACTH-driven androgen excess. However, Plenadren is a safe treatment and tends to improve the metabolic profile compared to conventional GCs; thus it could be a reasonable choice in older CAH patients or post-menopausal women, in whom reducing cardiovascular risk factor and adrenal insufficiency are the main aims over obtaining a strict control of adrenal androgens.

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EP215

Circulating micro-RNAs are valuable biomarkers for the diagnosis and surveillance of adrenocortical tumors

Chrysoula Mytareli[1], Vasiliki Kalotychou[1], Alexandros Lafioniatis[1], Vasiliki Siampanopoulou[1], Giorgos Zografos[2], Athina Markou[3], Labrini Papanastasiou[3], Athanasios Fountas[4], Marina Mantzourani[1], Eva Kassi[5,6], Gregory Kaltsas[6] & Anna Angelousi[1]
[1]Athens Medical School, NKUA, 1st Department of Internal Medicine, Laikon General Hospital, Athens, Greece; [2]'G. Gennimatas' General Hospital of Athens, 3rd Department of Surgery, Athens, Greece; [3]'G. Gennimatas' General Hospital of Athens, Unit of Endocrinology, and Diabetes Center, Athens, Greece; [4]'G. Gennimatas' General Hospital of Athens, Unit of Endocrinology, and Diabetes Center, Athens, Greece; [5]Athens Medical School, NKUA, Department of Biological Chemistry, Athens, Greece; [6]Athens Medical School, NKUA, Department of Propaedeutic and Internal Medicine, Laikon General Hospital, Athens, Greece

Introduction
Tumor-derived material, particularly micro-RNAs, have been identified in the bloodstream and hold promise as molecular markers for diagnosing and monitoring adrenocortical incidentalomas (AIs).
Purpose
We examined selected circulating microRNAs (miR-483-5p, miR-210, miR-335, miR-22-3p), identified from microRNA profiling studies, as markers of malignancy or cortisol hypersecretion in a cohort of patients with AIs and controls in a clinical setting.
Methods
Blood samples were collected from a total of 67 patients with AIs, comprising 50 cases of adrenocortical adenomas (ACA) and 17 cases of adrenocortical carcinoma (ACC). Within the ACC group, samples were obtained either preoperatively or upon the detection of local recurrence or distant metastases in 11 cases, whereas the other 6 were collected from patients who had remained disease-free for over 3 years. Out of the 55 AI patients evaluated preoperatively, 26 had non-functioning tumors (NFAIs), 21 exhibited mild autonomous cortisol secretion (MACS) and 8 had Cushing syndrome (CS). A control group of 15 participants was enrolled for comparative analysis. Quantitative real-time polymerase chain reaction was employed to analyze microRNA expression in serum samples. Cel-miR-39-3p served as the reference gene for data normalization, and the expression levels were determined using the dCT method.
Results
Circulating miR-483-5p and miR-210 levels were considerably elevated in the group of preoperative/advanced ACC compared with ACA ($P<0.001$, $p=0.02$ respectively) and controls ($P=0.03$, ns, respectively). Interestingly, circulating miR-483-5p levels were also significantly elevated in preoperative/advanced ACC compared to disease-free ACC patients ($P=0.04$). MiR-483-5p levels demonstrated the highest sensitivity (81.8%) and specificity (92%) for distinguishing preoperative/advanced ACC from ACA (AUC=0.894, 95% CI: 0.793–0.994, $P<0.001$), while miR-335 levels did not reach sufficient diagnostic accuracy. MiR-22-3p levels effectively discriminated patients with CS from those with NFAIs (AUC=0.784, 95% CI: 0.626–0.941, $P=0.017$) reaching sensitivity up to 100% along with specificity 61.5%. MiR-22-3p levels presented a

statistically significant positive correlation with 24-hour urinary free cortisol ($rs=0.504$, $p=0.02$), as well as a significant negative correlation with adrenocorticotropic hormone ($rs=-0.351$, $p=0.01$).
Conclusion
Our study suggests that specific microRNAs could serve as valuable noninvasive biomarkers for diagnosing and monitoring AIs, complementing current diagnostic tools.

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EP217

Adrenal phenotype in multiple endocrine neoplasia type 1

Arianna Cremaschi[1], Roberta Mungari[1], Alessandra Mangone[1,2], Giulia Del Sindaco[1,2], Elisa Sala[1], Giulia Carosi[1], Veronica Lotito[1,2], Emanuele Ferrante[1] & Giovanna Mantovani[1,2]
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milano, Italy; [2]University of Milan, Department of Medical Sciences and Community Health

Background
Adrenal involvement in multiple endocrine neoplasia type 1 (MEN1) has been reported, its prevalence varying from 9 to 73%. The aim of this study was to characterize the adrenal phenotype and the prevalence and clinical significance of cortisol hypersecretion in a cohort of MEN1 patients.
Methods
We retrospectively analyzed data of 36 adult patients with germline menin mutation (20 females; mean age 50 ± 17.4 years) in regular follow-up at our Endocrinology Unit between 2000 and 2023. All study participants underwent periodical MRI abdominal imaging and evaluation of adrenal glands. If adrenal lesions were present hormonal evaluation was carried out and included: 1 mg dexamethasone overnight suppression test (DST), urinary free cortisol (UFC) levels and salivary cortisol levels assessed on 3 consecutive nights; aldosterone, renin levels and urinary metanephrines were assessed when hypertension was present. Patients were also screened for hypercortisolism-related comorbidities (cardiovascular events, hypertension, glucose and lipid metabolism, osteoporosis).
Results
13 patients (36%) had radiological evidence of adrenal lesions: 4 had hyperplasia (30.7%, 3 females) of which 2 unilateral and 2 bilateral, 4 had bilateral macronodular hyperplasia (30.7%, 3 males) and 5 had unilateral nodular lesions (38.5%, 4 males). The mean diameter of lesions was 15.7 ± 6 mm. One patient with macronodular bilateral hyperplasia had adrenal hemorrhage. Of these 13 patients, 9 (69.2%) had at least one test suggestive for hypercortisolism. 6 had serum cortisol levels after 1 mg DST ≥1.8 µg/l (mean 3.12 ± 1 µg/l), 4 had elevated UFC levels (median 1.3 IQR 1.1-1.4 ULN) and 1 had 2/3 elevated salivary cortisol levels. Median ACTH levels were 11.6 IQR 7.2-18.8 ng/l. Only one patient had both unsuppressed cortisol levels after 1 mgDST and elevated UFC on multiple occasions, thus medical therapy with metyrapone was started. One patient underwent surgical adrenalectomy. Of the 9 patients 4 had hyperplasia, 2 had macronodular hyperplasia and 3 had unilateral nodules. None had clinical signs of overt Cushing syndrome. We compared the prevalence of hypercortisolism-associated comorbidities between patients with possible cortisol autonomous secretion and without and found no significant difference (cardiovascular events 0 vs 1; hypertension 2 vs 2; mean BMI 24.6 ± 2.6 vs 27.9 ± 7.2 kg/m^2; diabetes 3 vs 1; IFG 0 vs 4; dyslipidemia 1 vs 1, osteoporosis 3 vs 1). No patients had hyperaldosteronism or pheochromocytoma.
Conclusion
Our data, with the limitation of a small series, suggest that there is a high frequency of biochemical evidence of hypercortisolism, however this does not seem to be associated with clinical signs or with increased frequency of typically related comorbidities.

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EP232

The diagnostic dilemma of benign adrenal endothelial tumors: clinical, radiological, and pathological analysis of 20 rare cases

Kimberly Coscia[1,2], Cristina Mosconi[3], Lorenzo Tucci[1,2], Giacomo Colombin[1,2], Francesca Donnarumma[1,2], Caterina Balacchi[3], Saverio Selva[4], Guido Di Dalmazi[1,2], Velentina Vicennati[1,2], Uberto Pagotto[1,2] & Antonio De Leo[5]
[1]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [2]Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Bologna, Italy; [3]Radiology Unit, Department of Specialized, Diagnostic and Experimental Medicine (DIMES), Alma Mater Studiorum University of Bologna, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [4]Division of Pancreatic Surgery, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [5]Pathology Unit - Azienda USL di Bologna, Department of Experimental, Diagnostic and Specialty Medicine, Alma Mater Studiorum University of Bologna, Bologna, Italy

Background
Adrenal endothelial tumors are mainly represented by adrenal cavernous hemangiomas (ACHs) and adrenal cystic lymphangiomas (ACLs). They are rare incidental findings, with about 160 cases of both ACHs and ACLS reported in the literature. They are usually unilateral, benign, non-functioning, and asymptomatic, although abdominal pain and life-threatening retroperitoneal hemorrhage may occur if tumor size increases. Radiological features often overlap with malignant adrenal tumors, therefore ruling out malignancy becomes mandatory. We analyzed clinical, radiological, and histopathological data to identify specific characteristics of adrenal endothelial tumors.
Methods
We conducted a retrospective review of patients admitted to our Department between 2007 and 2022 with ACHs or ACLs confirmed by histopathology. All clinical and radiological data were collected retrospectively from electronic health records.
Results
A total of 20 patients underwent elective adrenalectomy and were diagnosed with adrenal hemangiomas ($n=10$), adrenal cystic lymphangiomas ($n=7$), or undefined/combined adrenal cystic lesions ($n=3$). Six patients had no available information about preoperative workup. More than half of the cases were incidentally discovered ($n=13$) and only 2 cases were identified correctly by preoperative imaging studies. Mean age at the diagnosis was 53 years. Sex was evenly distributed (females $n=9$, males $n=11$). All tumors were unilateral. Mean preoperative tumor size was 45 mm. An upward trend in tumor size was observed in 7 cases. All tumors showed CT density values on the non-contrast series >10 Hounsfield Units (HU). Calcifications were found in 5 patients. Functional evaluation was performed in 13 patients, whereas 6 patients had no available information about hormone secretion. Hormonal studies revealed non-functioning adrenal masses in 9 cases and autonomous cortisol secretion in 2 patients, assessed by 1 mg dexamethasone suppression test. Elevated urinary metanephrines were found in 2 cases.
Conclusions
ACHs and ACLs represent a diagnostic dilemma in clinical practice due to their rarity and their misleading imaging features. Because of the heterogeneous clinical and radiological pictures, treatment should be targeted to the patient's characteristics.

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EP233

Appropriateness of patient selection for inpatient short synacthen testing in a tertiary hospital

Lyeann Tan[1], Vijay Ramadoss[1], Ada Teo[1], Kavita Narula[2], Katharine Lazarus[2], Doddabele Srinivasa Deepak[1], Li Zhen Ong[1], Karim Meeran[2], Chin Meng Khoo[1] & Pei Chia Eng[1]
[1]National University Health Systems, Endocrinology, Singapore, Singapore; [2]Imperial College London, Hammersmith Campus, United Kingdom

Background
The Short Synacthen test (SST) is commonly used in clinical practice to evaluate adrenal function. Appropriate patient selection for SST is needed to ensure accurate interpretation of the results and to mitigate increased healthcare costs associated with unnecessary testing and inappropriate glucocorticoid (GC) steroid replacement. This study aimed to investigate the indications of inpatient SSTs over a one-year period, to determine the accuracy of testing.
Method
We reviewed all relevant clinical information of all the inpatient SSTs performed between 28th February 2022 and 28th February 2023 at our institution. An SST test was considered appropriate if patients presented with symptoms suggestive of adrenal insufficiency (AI), and inappropriate if no clear indication was provided or the patient's clinical history and presenting features did not suggest AI.
Results
457 patients, with a median age of 67 years (IQR 56 to 76.5 years) underwent 485 inpatient SSTs. The common indications for SSTs were: postural hypotension

(36.70%), hyponatremia (17.1%), hypotension (16.3%) and previous or current exogenous GC use (8.1%). Of those who underwent SSTs for postural hypotension, 89.9% were symptomatic and 10.1% were asymptomatic. Of those who presented with hyponatremia, 6% had symptoms suggestive of AI and an initial presenting sodium of 127 nmol/l (IQR 124 nmol/l - 130 nmol/l). 27.9% of the patients who had hypotension had ongoing infection; 30.4% had persistent low blood pressure suggestive of AI and 33.0% had a transient hypotensive episode. 4.5% of the SSTs were carried out due to subjective feelings of giddiness and lethargy and 5.6% of SST had no documented indications. Of the 485 inpatient SSTs, 74/485 (15.3%) did not have a prior morning cortisol. 228/485 (47.0%) of SSTs did not have a measured paired baseline ACTH. Nearly half (49%) of the SSTs were performed in patients who did not have features suggestive of AI. 28 SSTs were repeated due to incorrect initial tests. Of those who underwent SSTs for suspected features of AI, 65.4% had a normal SST result. Similarly, in those who underwent SST where there was no indication for AI, 62.5% had a normal result.

Conclusion

A majority of the inpatient SSTs were inappropriately indicated. Our study demonstrates that presenting features for SST testing do not reliably predict SST outcomes in our cohort. Common errors identified insufficient pre-test cortisol testing and lack of concomitant ACTH measurement. We advocate judicious patient selection for SST testing to avoid inappropriate use of SST and subsequent life-long need for GC replacement.

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EP234

The effect of adrenalectomy on metabolic parameters in patients with primary aldosteronism

Karin Zibar Tomšić[1], Mirjana Đukić[2], Mirsala Solak[1] & Darko Kaštelan[1]
[1]University Hospital Centre Zagreb, Department of Endocrinology, Zagreb, Croatia; [2]General Hospital Sisak, Department of Endocrinology, Sisak, Croatia

Background

A few studies have shown that aldosterone has negative impact on metabolic parameters.

Objectives

The aim of the study was to evaluate metabolic parameters in patients with primary aldosteronism (PA) before and one year after adrenalectomy.

Methods

In this retrospective study, we examined 51 patients (median age 50 years, IQR 43–55; 55% male) who underwent adrenalectomy for PA between 2016 and 2022. Patients with diabetes mellitus, dyslipidemia, and autonomous cortisol secretion were excluded. We assessed differences in glucose ($n=24$), lipid profiles ($n=32$), body weight ($n=47$), and the defined daily dosage (DDD) of antihypertensives ($n=51$). Clinical remission of PA was defined according to PASO criteria.

Results

Complete clinical remission was attained by 45% of patients, while 51% achieved partial clinical remission, and 4% experienced no clinical remission. A year after surgery, there was a significant reduction in the median defined daily dosage (DDD) of antihypertensives compared to pre-surgery levels (4.5 vs 1.3, $P<0.001$). Similarly, the median fasting glucose level also showed marked improvement after surgery (5.1 mmol/l vs 4.9 mmol/l ; $P=0.035$). Conversely, no significant differences were observed in total cholesterol and triglyceride levels ($P=0.754$) and body weight ($P=0.724$) before and after surgery.

Conclusion

Adrenalectomy in patients with PA resulted in significant improvements in metabolic parameters, including reduced use of antihypertensive medications and improved fasting glucose levels one year after surgery. These results emphasise the potential metabolic benefits of adrenalectomy in the treatment of primary aldosteronism.

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EP239

Remission rate of primary aldosteronism after unilateral adrenalectomy

Mirjana Đukić[1], Karin Zibar Tomšić[2], Nikola Knežević[2,3] & Darko Kaštelan[2,3]
[1]General Hospital Sisak, Department of Endocrinology, Sisak, Croatia; [2]University Hospital Centre Zagreb, Department of Endocrinology, Zagreb, Croatia; [3]School of Medicine, University of Zagreb, Zagreb, Croatia

Background

The existing consensus for patients with primary aldosteronism (PA) after unilateral adrenalectomy recommends annual follow-up to rule out persistence or recurrence of the disease.

Objectives

The aim of the study was to assess the remission rate in patients with PA ≥ 1 year after adrenalectomy.

Methods

Of the 41 patients who underwent adrenalectomy for PA between 2016 and 2021, 24 had available follow-up data and were included in the study. To diagnose unilateral disease we used lateralization index ≥ 4 or contralateral suppression index ≤ 0.37. Biochemical and clinical remission of PA was defined according to PASO criteria.

Results

The median age of participants was 50 years (IR 42-56), 50% were women. The median follow-up time after surgery was 5 years (IR 3-5). Aldosterone concentration before and after surgery was 998 pmol/l (IR 583-1284) and 240 pmol/l (IR 194-369), $P<0.001$. Plasma renin activity before surgery was 0.15 µg/l/h (IR 0.1-0.38) whereas after surgery it was 1.5 µg/l/h (IR 0.9-5.7), $P<0.001$. Finaly, median potassium level after surgery was significantly higher compared to the level before surgery (4.3 mmol/l vs 2.9 mmol/l ; $P<0.001$). At the time of data collection, 92% of patients were in complete biochemical remission, whereas 8% were in partial biochemical remission. Regarding clinical remission, the respective rates of patients who were in complete and partial remission were 54% and 38%. Only 8% of patients did not achieve clinical remission of the disease after unilateral adrenalectomy. Both patients who were in partial biochemical remission achieved complete clinical remission.

Conclusion

Our results showed that with a lateralization index ≥ 4 or contralateral suppression index ≤ 0.37, long-term, complete or partial, biochemical remission of PA was achieved in all patients after unilateral adrenalectomy. Furthermore, long-term, complete or partical, clinical remission, was achieved in 92% patients.

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EP240

Reninoma: a rare cause of hypertension in pregnancy

Deirdre Green, Liam Plant & Domhnall O'Halloran
Cork University Hospital, Cork, Ireland

A reninoma is a tumour of the afferent arteriolar juxtaglomerular cells that secretes the enzyme renin, leading to hyperactivation of the renin-angiotensin-aldosterone system. It is a cause of pathological secondary hyperaldosteronism that results in severe hypertension and hypokalaemia. Fewer than 200 cases have been described, seven of which were associated with pregnancy. We present the case of a 29-year-old woman referred with hypertension and hypokalaemia at 10 weeks' gestation of a dichorionic twin pregnancy. She was treated with Labetolol 600 mg four times daily, Methyldopa 1g three times daily and Nifedipine LA 60 mg twice daily to maintain a blood pressure of approximately 130/90mmHg. Her medical history included hypertension, diagnosed aged 19. She had one previous uncomplicated singleton pregnancy. There was no family history of hypertension or endocrinopathy. Recumbent plasma renin concentration was elevated at 67.7 ng/l (3-6 ng/l), and plasma aldosterone was elevated at 1425 pmol/l (<440 pmol/l). Tests for hypercortisolism and catecholamine excess were negative. Echocardiography revealed borderline concentric left ventricular hypertrophy and no coarctation of the aorta. Urine protein:creatinine ratio was elevated at 53.4 mg/mmol (<45 mg/mmol). A 2.4 cm solid, right renal lesion was identified on ultrasound. Further characterisation with magnetic resonance imaging demonstrated a heterogenous high signal area that indented the renal sinus fat and extended into the medullary area of the kidney. A biopsy of the lesion was arranged, and histopathology confirmed a juxtaglomerular cell tumour. No evidence of pre-eclampsia was seen. The patient proceeded for a right total nephrectomy at 16 weeks' gestation. Macroscopically the lesion was a well circumscribed, haemorrhagic, tan-coloured mass lesion measuring $3.2\times2.5\times2.6$ cm. The tumour was microscopically characterised by diffuse proliferation of tumour cells with moderate amounts of eosinophilic cytoplasm and vesicular nuclei. The tumour cells were positive for CD34, SMA, and vimentin and negative for CD117. Electron microscopy of the tumour showed rhomboid shaped granules characteristic of renin in tumour cells. The remainder of the kidney was unremarkable. The postoperative course was complicated by hypotension, and anti-hypertensive medications were discontinued. Supine plasma renin level measurement 7 weeks postoperatively was normal at 10.3 ng/l (<16 ng/l), 15% of the original value. Two infants were born via elective Caesarean section at $33+4$ weeks gestation. Reninoma is a very rare and potentially curable form of hypertension, particularly in women of childbearing age. Plasma renin concentration was three times greater than the expected value for this stage of

pregnancy. Management in pregnancy is challenging and involvement of the multi-disciplinary team is vital.

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EP252

Biochemical diagnosis of pheochromocytoma/paraganglioma in children and adolescents

Kristin Potthoff[1], Tamara Prodanov[2], Lara Knigge[1], Sara Talvacchio[2], Angela Hübner[3], Stefan Bornstein[1], Jacques Lenders[4], Mirko Peitzsch[5], Karel Pacak[2], Graeme Eisenhofer[1] & Christina Pamporaki[1]
[1]University Hospital Carl Gustav Carus at the TU Dresden, Department of Medicine III, Dresden, Germany; [2]National Institutes of Health (NIH), Eunice Kennedy Shriver, National Institute of Child Health and Human Development, Bethesda, United States; [3]University Hospital Carl Gustav Carus at the TU Dresden, Department of Pediatrics, Dresden, Germany; [4]Radboud University Medical Center, Department of Internal Medicine, Nijmegen, Netherlands; [5]University Hospital Carl Gustav Carus at the TU Dresden, Institute of Clinical Chemistry and Laboratory Medicine, Dresden, Germany

Introduction
Currently, it is unclear whether plasma free or 24-hour urinary metanephrines are preferable for diagnosis of pheochromocytoma/paraganglioma (PPGL) in children.
Objectives
To investigate whether measurements of plasma free or 24-hour urinary fractionated metanephrines is a reliable test for screening for PPGL in children.
Methods
This retrospective study included data from 60 children with and 78 without PPGL. Data included sex, age (5-18 years), plasma concentrations of free metanephrines, and genetic test results. For a subset group of 87 children tested for PPGL, concentrations of 24-hour urinary metanephrines were also available. For patients with PPGL, data also included tumor location, size, tumor catecholamine phenotype, and presence of recurrent and/or metastatic disease.
Results
Among children with PPGL, the plasma panel presented with larger fold-normetanephrine increases above the upper cut-offs (8-fold vs 3-fold, $P < 0.001$) compared to the urinary metabolites. The plasma panel showed a diagnostic sensitivity and specificity of 100% and 93% respectively compared to 94% and 88% for the urinary panel. Measurements of plasma free metabolites offered similar diagnostic performance (AUC:0.987, 95%CI:0.969-1.00) to 24-hour urinary fractionated metanephrines (AUC:0.972, 95%CI:0.942-1.00). Sub-analysis of intra-individual temporal measurements of metabolites showed that subsequent increases larger than 35% in plasma normetanephrine over time can signal early stage development of a noradrenergic PPGL.
Conclusions
Plasma free and 24-hour urinary fractionated metanephrines are both reliable screening tests for PPGL in children and adolescents. The plasma panel may be useful for early detection of noradrenergic PPGL relevant for children tested within surveillance programs due to hereditary risk of noradrenergic tumors.

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EP254

Clinical utility of S-GRAS prognostic system in adrenocortical carcinomas: confirmatory results from a single-centre institutional registry

Erik Bényei[1], Judit Tőke[1,2], Gergely Huszty[3], Katalin Borka[4], Zoltán Sápi[5], Zsuzsanna Jakab[1], Gergely Kiss[6], Ildiko Kalina[6], Péter Resimann[1], Andrea Uhlyarik[1], Péter Igaz[1,2,7] & Miklós Tóth[1,2]
[1]Semmelweis University, Faculty of Medicine, Department of Internal Medicine and Oncology, Budapest, Hungary; [2]Healthcare Provider of European Reference Network on Rare Endocrine Conditions; [3]Semmelweis University, Department of Surgery, Transplantation and Gastroenterology, Budapest, Hungary; [4]Semmelweis University, Department of Pathology, Forensic and Insurance Medicine, Budapest, Hungary; [5]Semmelweis University, Faculty of Medicine, Department of Pathology and Experimental Cancer Research, Budapest, Hungary; [6]Semmelweis University, Faculty of Medicine, Medical Imaging Centre, Budapest, Hungary; [7]Semmelweis University, Department of Endocrinology, Budapest, Hungary

Introduction
Adrenocortical carcinoma (ACC) is a rare tumor known for its diverse biological behaviour and generally poor prognosis. Recently, the S-GRAS scoring system has emerged as an accurate prognostic model, incorporating the most frequently used clinicopathological parameters: ENSAT stage, grade, resection status, age at diagnosis, and tumor symptoms. So far, this system's efficacy has only been validated in extensive multicenter studies, proposing it as a reliable tool for predicting outcomes in ACC patients (Elhassan, 2022).
Aims
We aimed to comprehensively outline the clinicopathological characteristics of patients treated with ACC in our tertiary referral centre. We then aimed to analyse the prognostic value of the computed S-GRAS scores and compare them to prior results on patient outcomes from previous studies. Through this comprehensive demonstration, we aimed to confirm the robustness and applicability of the S-GRAS prognostic system in a single-center study.
Methods
From our ACC patient cohort of 86 patients, we analyzed data of those patients who had fully available data to calculate S-GRAS scores. 54 patients fulfilled this inclusion criteria; all were treated at our centre between January 1, 2000, and August 31, 2022. Mann-Whitney U test was used to compare patient cohort distributions, and survival correlations were analysed using Kaplan-Meier curves with log-rank tests and univariate Cox regression analyses.
Results
The distribution of our patient cohort by S-GRAS score did not differ significantly from the cohort of Elhassan *et al*. (2022). Among the studied characteristics in our analysis, hormone secretion (RR = 2.8, $P = 0.002$), higher ENSAT stages (III and IV) (RR = 9.5 $P = 0.033$ and RR = 13.5, $P = 0.011$), R1 and R2 resection states (RR = 3.0, $P = 0.002$ and RR = 4.7, $P = 0.007$), and a Ki67 index above 20% (RR = 2.7, $P = 0.026$) were associated with an increased risk of mortality. Higher S-GRAS scores (4-5 points and 6-9 points) were found to have a significant negative impact on overall survival (RR = 9.0, $P = 0.005$ and RR = 10.9, $P = 0.002$). The calculated hazard ratios corresponded well to those reported in the analyses of prior multicentre studies.
Conclusion
Preoperative hormone secretion, higher ENSAT stages, R1/R2 resection states, and a Ki67 index above 20%, were associated with an increased risk of mortality. The S-GRAS scoring system emerged as a powerful tool for prognosis, as confirmed by our single-center study with consistent results from a relatively modest patient cohort. Our findings reaffirm the reliability and applicability of the S-GRAS system in diverse clinical settings, even in limited size cohorts.
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EP258

Psychometric parameters and quality of life in patients with adrenal tumours

Elisavet Charikleia Tasouli, Chrysoula Mytareli, Evangelia Andreadaki, Foteini Thanasoula, Vasiliki Siampanopoulou, Athina Karabela, Petros Papalexis, Alexandros Lafioniatis & Anna Angelousi
Unit of Endocrinology, First Department of Internal Medicine, Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece

Introduction
Neuropsychiatric disorders are common and well-studied in patients with overt hypercortisolism. However, data regarding patients with adrenal incidentalomas (AIs) are limited. The aim of our study is to assess the psychometric and quality of life status in individuals with benign adrenal tumours.
Methods
Eighty-two patients diagnosed with AIs, encompassing 53 females and 29 males, with a total mean age of 64 years and 52controls (without AI in computed tomography scan) were included. Functional profile was based on a complete hormonal work-up including serum levels of cortisol at baseline at 8:00 am and post-1 mg overnight dexamethasone suppression test (ODST), adrenocorticotropic hormone (ACTH) levels, plasma renin activity and aldosterone levels, adrenal androgens and catecholamines levels. Psychometric analysis and quality of live status were evaluated based on established generic questionnaires, such as the European Quality of Life (EuroQoL-5D-5L) and the Depression, Anxiety, Stress Scale (DASS-21). Oncological patients were excluded.
Results
Based on the ODST cortisol levels, patients were categorized into three distinct groups: Group 1 was consisted of patients with non-functional AIs (NFAIs) exhibiting ODST cortisol levels below 1,8 μg/dl ($n = 42$), group 2 included patients with possible autonomous cortisol secretion (PACS) with cortisol levels ranging between 1.8-3 μg/dl ($n = 23$) and group 3 included patients with

autonomous cortisol secretion (ACS) with cortisol levels above 3µg/dl ($n=14$). Statistical analysis revealed a statistically significant difference in the overall DASS scores among the three groups (p-value <0.0001). Post-hoc tests revealed specific group differences, with ACS patients presenting higher total DASS score compared to NFAIs (28.5 ± 13.3 vs 10.4 ± 8.5, $P<0.001$) and compared to PACS patients (28.5 ± 13.3 vs 20.65 ± 8,63, $P=0.048$). Significant difference was also shown between NFAIs and PACS (10.98 ± 8.4 vs 20.65 ± 8.63, $P=0.04$). Controls presented lower DASS score compared to NFAIs (4.93 ± 7.37 vs 10.98 ± 8.4, $P=0.046$). These findings were corroborated by the validated EuroQoL domain reflecting compromised anxiety and depression.

Conclusion

The results of our study showed that individuals with AIs even those without overt Cushing syndrome (PACS and NFAI) might exhibit mental impairment or psychological consequences, highlighting the significance of screening for these disorders besides the well-studied metabolic abnormalities.

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EP266

In vitro differentiation of mouse pluripotent stem cells into glucocorticoid-producing adrenocortical cells

Ioannis Oikonomakos[1,2], Yasmine Neirijnck[2], Melina Tedesco[2], Fariba Jian Motamedi[2], Serge Nef[3], Stefan Bornstein[1,4], Charlotte Steenblock[1] & Andreas Schedl[2]

[1]University Hospital Carl Gustav Carus Dresden, Department of Internal Medicine III, Dresden, Germany; [2]Institute Of Biology Valrose - iBV, Nice, France; [3]University of Geneva, Department of Genetic Medicine and Development, Geneva, Switzerland; [4]King's College London, Faculty of Life Sciences & Medicine, United Kingdom

The adrenal cortex, a pivotal endocrine regulator governing body homeostasis, metabolism, and stress response through steroid hormone synthesis, presents formidable challenges for effective replacement in disorders like adrenal insufficiency and congenital adrenal hyperplasia. The limitations of current hormone replacement strategies stem from the intricate dynamics of hormonal release. This study harnesses insights derived from the analysis of a recently published single-cell atlas of the mouse to establish a robust differentiation protocol for mouse embryonic stem cells (mESCs) into adrenocortical-like cells. Key findings reveal the expression of critical adrenal progenitor markers (*Gata4, Wt1, Nr5a1, Mc2r*) during the differentiation of the cells. Furthermore, we identified Tenascin and Fibronectin as pivotal extracellular matrix proteins influencing adrenocortical development. Notably, culturing cells on Fibronectin during differentiation enhanced the expression of NR5A1, the master regulator of steroidogenesis. In parrarel, we saw that by employing 3D aggregates in microwell culture induced the expression of essential steroidogenic enzymes, including the adrenocortical-specific enzymes *Cyp21a1* and *Cyp11b1*. Importantly, these aggregates demonstrated the production and secretion of glucocorticoids, validating specific differentiation towards the adrenocortical lineage. Crucially, no gonad-specific steroids were detected in the medium, affirming the specificity of the differentiation protocol. This study provides insights into the extracellular matrix supporting adrenocortical development and outlines a step-wise protocol for differentiating mouse ES cells into glucocorticoid-producing adrenocortical cells. The directed differentiation of pluripotent stem cells offers a promising avenue for innovative cell replacement therapies, holding potential for a lasting cure in patients with adrenal disorders.

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EP267

Chronotype and sleep parameters are different in patients with primary adrenal insufficiency compared to controls

Lakshmi Kalathinkunnath[1], Jozsef Arato[1], Hannes Beiglböck[2], Michael Krebs[2], Fani Sentinella Jerbic[1], Till Roenneberg[3], Alexandra Kautzky-Willer[2], Helmut Leder[1], Kristin Tessmar-Raible[1] & Peter Wolf[2]

[1]University of Vienna, Wien, Austria; [2]Medical University of Vienna, Wien, Austria; [3]Ludwig Maximilian University of Munich, München, Germany

Background

Human chronotypes can be defined as the natural preference for specific wake and sleep times, as measured by the start and end of sleep on days without temporal restrictions. They are a consequence of the circadian clock individual periods. Cortisol is a key mediator for the rhythmic expression of circadian signals in almost all tissues. Physiological timing of cortisol levels is strictly regulated by the hypothalamic-pituitary-adrenal (HPA) axis. Diseases affecting HPA signaling might therefore have important consequences on the individual's chronotype. We therefore investigated patients with primary adrenal insufficiency with stable hydrocortisone replacement therapy.

Methods

In this exploratory pilot study, 20 patients with autoimmune adrenilitis and 40 control subjects of comparable age (54.53 ± 18.42 vs 48.56 ± 15.5 years) and sex (14f/6m vs 32f/8m) were assessed for their chronotypes using the Munich Chronotype Questionnaire for at least four times. They were also requested to constantly wear an actimetry device for 12 weeks, that monitored their sleep, temperature and light reception in this time frame. F-tests were applied to test for variability in sleep parameters and chronotypes between patients and controls, and a one-way ANOVA was applied to test for significant difference between means of sleep onset of the two cohorts.

Results

We observed high variability in sleep onset (F statistic $=1.876$, $P<0.001$) and sleep duration (F statistic $=2.496$, $P<0.001$) for patients in comparison to controls. The mean value for sleep onset were also observed to be earlier for patients (mean = 131.708 minutes) in comparison to controls (mean = 155.803 minutes) (confirmed with one way ANOVA, statistic $=29.842$, $P<0.001$). Chronotypes of patients showed high variability in comparison to controls (F statistic $=2.192$, $P=0.008$). In addition, the patient population also seemed to show a numerically later sleep onset on the weekends, which is not compensated by increased duration of sleep on the next day.

Discussion

The changes in chronotype and sleep onset in patients with primary adrenal insufficiency are likely caused by glucocorticoid replacement and possibly additional hormonal alterations. Improved awareness of their sleep variability and more controlled sleep/wake schedules, as well as illumination can likely improve the patients' life quality. Possibly associated clinically relevant effects on cardiovascular risk factors remains to be investigated in future experiments.

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EP282

Description of the x-linked adrenoleukodystrophy cohort from the csur unit of adult metabolic disorders at virgen del rocio university hospital (seville)

Lucía González Gracia, Elena Dios Fuentes, Rosa Benítez Ávila, Bothayna Oulad Ahmed, Alfonso Soto Moreno & Eva Venegas Moreno

Virgen del Rocío University Hospital, Sevilla, Spain

Introduction and Objective

X-linked adrenoleukodystrophy (X-ALD) is a rare disease caused by a mutation in the ABCD1 gene (Xq28). It is characterized by the absence of very long-chain fatty acids (VLCFAs) degradation, leading to their accumulation primarily in the central and peripheral nervous system, adrenal cortex, and gonads. It presents a variable clinical spectrum and prognosis. The aim of our study is to describe the characteristics of all X-ALD patients under follow-up at the Adult Inborn Errors of Metabolism Unit at Virgen del Rocio University Hospital (Seville).

Methods

Retrospective observational study. The following variables were collected: gender, current age and age at diagnosis, symptoms, age of symptom onset, and treatment (dietary, pharmacological, hematopoietic cell transplantation [HCT], and gene therapy). Quantitative variables are expressed as median [p25-p75], and qualitative variables as n(%).

Results

21 patients. 10 (47.6%) were males. Patients had a median age of 39.2 [23.9-53.8] years and were diagnosed at a median age of 7.1 [21.3-50.13] years. The most frequent mutation was c.971G > A (p.Arg324His). Regarding males, 7 (70%) were diagnosed as index cases, and 8 (80%) were symptomatic, with a median onset of symptoms at 14.5 [4-50.5] years: 60% adrenal insufficiency, 30% cerebral involvement, 30% myeloneuropathy, and 10% gonadal insufficiency. Concerning females, 10 out of 11 (90.9%) were diagnosed due to having an affected family member, and 4 (36.3%) had symptoms, with a median onset at 45 [41.5-56] years: 27.2% myeloneuropathy, 9.1% premature ovarian failure, and 0% adrenal insufficiency. 81% had elevated VLCFAs at diagnosis (90% of males and 72.7% of females): C22 52 [28-65] µmol/l, C24 59 [41-67] µmol/l, C26 1.51 [0.86-2.12] µmol/l, C24/C22 1.24 [0.95-1.45], and C26/C22 0.029 [0.016-0.063]. Regarding treatment, 8 (38.1%) follow a saturated fat-restricted diet, 4 (19%) take Lorenzo's oil, 6 (28.4%) hydrocortisone, 5 (23.8%) fludrocortisone, and 1 (4.8%) testosterone. One male underwent HCT, and another received gene therapy, with clinical stability of cerebral lesions in both patients. There was 1 death of a male during follow-up.

Conclusions
In our cohort, adrenal insufficiency is the most frequent symptom in males, and a high percentage of females exhibit some symptoms. Communicating data from X-ALD patient series is essential to understand the clinical spectrum of the disease and the true prevalence of symptomatic females.

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EP287

Redefining diagnostic cut-offs for the indirect water deprivation test

Yash Akkara[1], Kate Lazarus[2,3], Kavita Narula[2,3], Sirazum Choudhury[3,4], Debbie Papadopoulou[3], Niamh Martin[2,3] & Karim Meeran[2,3]
[1]Imperial College London, london, United Kingdom; [2]Imperial College London, United Kingdom; [3]Imperial College Healthcare NHS Trust, United Kingdom; [4]Imperial College London, Division of Diabetes, Endocrinology and Metabolism, Department of Metabolism, Digestion and Reproduction, United Kingdom

Background
The water deprivation test serves as a key diagnostic test to differentiate between Arginine Vasopressin Deficiency (AVP-D), Arginine Vasopressin Resistance (AVP-R), and Psychogenic Polydipsia (PP) in patients presenting with symptoms of polydipsia and polyuria, when common causes such as diabetes mellitus have been excluded. This study evaluated the established diagnostic values for serum osmolality, serum sodium, and urine osmolality.
Methods
This retrospective analysis assessed 135 patients who underwent a water deprivation test between August 2014 and August 2023. All patient diagnoses were reviewed by an expert panel. Variability and receiver operating characteristic (ROC) curves were determined for serum osmolality, serum sodium and urine osmolality, to determine the effectiveness of the current interpretation reference ranges.
Results
A total of 120 patients were included in the study analysis. Use of serum sodium demonstrated reduced variability compared with serum osmolality (0.722% vs 1.16% respectively, 37.5% reduction; $P < 0.001$). Use of the standard serum osmolality cut-off value of ≥ 300 mOsm/kg in diagnosing AVP-D, AVP-R, and PP achieved a sensitivity of 76.19% and specificity of 76.92%. Use of a serum sodium cut-off value of ≥ 148 mmol/l demonstrated 100% specificity in excluding PP. This cut-off was used in tandem with urine osmolality cut-off values of > 630 mOsm/kg (for PP) and < 383 mOsm/kg (for AVP-D and AVP-R). Review of post-desmopressin urine osmolality changes and clinical monitoring was performed in equivocal diagnostic cases ($n = 6$), achieving both 100% sensitivity and 100% specificity within the study sample.
Conclusions
This study demonstrates that use of a serum sodium cut-off value of ≥ 148 mmol/l in combination with urine osmolality yields the best diagnostic accuracy to differentiate between arginine vasopressin deficiency, arginine vasopressin resistance, and psychogenic polydipsia. Serum sodium is superior to serum osmolality, demonstrating lower total variability (including biological and analytical variability).

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EP294

Jaw Tumor syndrome revealing hyperparathyroidism: about a case report

Neima Hassan, Hind Ouakrim, Sana Rafi, El Mghari Ghizlane & Nawal El Ansari
Centre Hospitalo-Universitaire Mohammed VI Marrakech, Endocrinolgist, Marrakech

Introduction
Hyperparathyroidism is a common medical condition, but in 5-10% of cases, it is part of Jaw Tumor syndrome, an autosomal dominant syndrome linked to a mutation in the HRPT2 gene. This syndrome is characterized by the presence of mandibular brown tumors and primary hyperparathyroidism.
Case report
A 24-year-old patient with a history of severe chronic renal failure in the left single kidney, presenting ureterohydronephrosis, underwent mandibular surgery for a brown tumor exhibiting histological characteristics of bony giant cells. Clinically asthenia, nausea, abdominal pain, constipation, and bone pain, Tachycardia:110 beats/min and painless mass in the right mandible, Laboratory tests indicated primary hyperparathyroidism with corrected serum calcium: 94 mg/l, serum phosphorus of 12.41 mg/l, and PTH:790 pg/ml. Scintigraphic examination showed focal retention of MIBI-Tc99m in the left and right thyroid lobes, measuring 6.7 *4.4 mm and 4.4* 4.3 mm, respectively, suggestive of pathological parathyroid tissue. The patient underwent parathyroid tumor resection, and the histopathological study confirmed parathyroid adenoma without signs of malignancy; however, molecular genetic study could not be performed. The patient's clinical and biological conditions improved significantly during the follow-up.
Discussion
Hyperparathyroidism-Jaw Tumor Syndrome is an inherited disorder associated with increased activity of the parathyroid glands. Due to its rare diagnosis, especially considering its familial nature and the elevated risk of parathyroid carcinoma. Genetic studies should focus on identifying mutations in the HRPT2 gene. Hyperparathyroidism in individuals with HPT-JT is commonly caused by a parathyroid adenoma, leading to symptoms such as kidney stones, reduced bone mass, fatigue, muscle weakness, and bone or joint pain. Surgical removal of a parathyroid gland with a tumor, along with jaw tumor removal, may be necessary for treatment.
Conclusion
The presence of recurrent or multiple jaw lesions or the combination of jaw lesions with hyperparathyroidism bone disease on imaging should prompt consideration of HPT-JT. Early detection and treatment of hyperparathyroidism in this context allow for the timely identification of malignant disease and screening of family members.
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EP296

Adrenal insufficiency due to adrenal involvement in non-hodgkin's lymphoma

Zineb Ait Si Ali, jaddi oussama, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Centre Hospitalo-Universitaire Mohammed VI Marrakech, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction
The non-Hodgkin lymphomas (NHL) involve extralymphatic sites more often than does Hodgkin lymphoma; consequently, tumor involvement of almost every abdominal organ has been recorded. Adrenal involvement in patients with NHL may be present at the time of initial assessment. however, adrenal insufficiency as a consequence of adrenal invasion is rare. We report a case of a patient diagnosed with NHL with breast and bilateral adrenal involvement.
Case report
A 41-years-old female patient, diagnosed 2 months before with a 4 cm breast left tumor classified ACR 4, she had excisional biopsy of this tumor. Anatomo-pathological analysis revealed lymphomatous malignant tumor proliferation with immunohistochemical appearance consistent with diffuse B-type NHL. She underwent positron emission tomography (PET) scan which showed intensely hypermetabolic disease within the left mammary and bilateral adrenal glands. a computed tomography (CT) scan of adrenal glands was done showing Well-limited rounded left adrenal nodular lesion measuring 1.1x1.2 cm (42uh) right adrenal gland was normal. The patient reported asthenia with moderate weight loss and anorexia. Clinical examination noted hypotension 89/61mmhg. Blood tests showed normal natremia and kaliemia, Cortisolemia at 8am was low confirming diagnosis of adrenal insufficiency for which she was started on oral hydrocortisone. The patient received 4 courses of chemotherapy. Control PET-CT scan done after revealed complete morphological and metabolic regression of both adrenal and mammary lesions. The response of these adrenal masses to chemotherapy in a manner similar to the response of mammary masse reinforces the impression that the adrenal pathology was indeed due to the non-Hodgkin lymphoma. During follow up Cortisolemia at 8am was within normal range, oral hydrocortisone was discontinued. Regular follow up is maintained.
Discussion
Lymphoma disseminating to both the adrenals is a common cause of bilateral masses. Adrenals are involved in 24% of cases with disseminated NHL in an autopsy study. Adrenal insufficiency was reported only in four cases with adrenal involvement in a series of 127 patients with NHL. Primary NHL of the adrenal gland is extremely uncommon. Breast's malignant lymphoma can present itself as a primary mammary neoplasm or it can involve the breast as part of a generalized

process. Primary NHL of the breast is a rare disease that has been assessed to represent from 0.04–0.52% of all malignant tumors of the breast. In our case we can not propose which organ system was primarily involved, for this reason we presented our case as the NHL involvement mammary and adrenal glands.

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EP297

A rare case of antiphospholipid syndrome presenting as primary adrenal insufficiency

Catarina Dias Gama[1], Margarida Oliveira[1], Maria Leonor Guia Lopes[1], Carolina Monteiro Antunes[1], Paula Sprovera[1], Bruna Pimentel[1], Mariana Santos[2], Bernardo Marques[1] & João Manuel Sequeira Duarte[1]
[1]Centro Hospitalar de Lisboa Ocidental, Endocrinologia, Diabetes e Metabolismo, Portugal; [2]Centro Hospitalar de Lisboa Ocidental, Reumatologia, Portugal

Introduction
Antiphospholipid syndrome (APS) is a systemic autoimmune disorder known for recurrent arterial and venous thrombotic events. It may involve multiple organ systems, but its impact on the endocrine system is rare. However, the adrenal glands are one of the most susceptible endocrine organs to APS, due to thrombosis, leading to primary adrenal insufficiency (PAI). Most cases are diagnosed in patients with known history of APS.
Case Report
We report the case of 56-year-old male with history of hypertension and dyslipidemia. He was admitted to the Internal Medicine Department with a 2-week history of fatigue, anorexia, nausea, weakness and weight loss (20% in 3 months). Upon admission, he had a low blood pressure (100/54 mmHg). Blood tests revealed anemia (hemoglobin 9.9 g/dl, NR: 12.0-15.0 g/dl), thrombocytopenia (platelets 94 000×10^6/l, NR: 150-400000×10^6/l), elevated activated partial thromboplastin time (76.4 s, NR: 28-40 s) and hyperkaliemia (potassium 7.11 mmol/l, NR: 3.5-5.2 mmol/l). A thoracic computed tomography (CT) scan was performed and revealed a spiculated nodular lesion with 13x8mm, located in the superior left pulmonary lobe. A subsequent positron emission tomography (PET-FDG) scan was done to rule out malignancy but showed, instead, intense uptake in both adrenal glands, with heterogeneity and areas of necrosis, especially in the right adrenal gland. While in the hospital, the patient developed vomiting and postural dizziness. The endocrinology department was consulted, and hormonal assessments revealed a serum cortisol of 1.9 μg/dl (NR: 6.2-19.4 μg/dl) and adrenocorticotropic hormone (ACTH) of 626.0 pg/ml (NR: 7.2-63.3 pg/m). He was started on intravenous hydrocortisone (200 mg/day), with marked improvement on his blood pressure profile, well-being and appetite, as well as remission of nausea and vomiting. Additional tests showed negative 21-hydroxilase antibodies, along with a normal screening for infectious disease (including tuberculosis and human immunodeficiency virus). The remaining etiological investigation revealed positive lupus anticoagulant antibody, anti-nuclear antibody, anti-double stranded DNA antibody, and nucleosome antibody. Based on both clinical (hemorrhage/infarction of the adrenal glands) and laboratory criteria (positive antiphospholipid antibody), he was diagnosed with APS. Upon discharge, the patient was prescribed hydrocortisone (20 mg/day on divided doses), fludrocortisone 0.05 mg/day and warfarin with dose adjustments following INR (international normalized ratio) measurements. He remains asymptomatic and under regular follow-up. Subsequent MRI scans showed atrophy of the adrenal glands.
Discussion
This is a rare case of APS presenting with bilateral adrenal haemorrhage and subsequent PAI. We would like to highlight this unusual presentation of PAI, in addition to the importance of multidisciplinary teamwork in the diagnosis of such conditions.

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EP298

Knowledge assessment of patients followed for adrenal insufficiency: a study of 54 cases

Prince Ismael Mbossa Lembopo, Nassim Essabah Haraj, Siham El aziz & Asma Chadli
Faculty of Medicine and Pharmacy, Hassan II University, Endocrinology, Diabetology, Metabolic Diseases, and Nutrition, Casablanca, Morocco

Introduction
Adrenal insufficiency (AI) can pose a life-threatening risk in case of acute decompensation. The absence of specific signs of acute adrenal insufficiency (AAI) and lack of awareness about this medical emergency may lead to diagnostic and therapeutic delays, jeopardizing the patient's prognosis. Hence, the importance of well-conducted therapeutic education for adrenal-insufficient patients. The objective of this study is to assess the level of knowledge among adrenal-insufficient patients regarding the pathology and management of their replacement therapy.
Patients and Methods
A prospective descriptive study was conducted on patients with adrenal insufficiency who had already undergone therapeutic education about the disease. The reassessment was carried out during the subsequent consultation at the Endocrinology Department of the University Hospital Center of Casablanca between 2021-2023. Data analysis was performed using Excel 2017 software.
Results
The study included 54 adrenal-insufficient patients, of whom 64.8% were women. The average age was 38.9 years. Adrenal insufficiency was of peripheral origin in 51.85% (Addison's disease 37%, autoimmune adrenalitis 4.7%, tuberculosis 3.7%, and bilateral adrenalectomy 3.7%) and secondary in 48% (post-corticosteroid therapy 33.33%, antehypopituitarism 14.8%). The definition of adrenal insufficiency was correct in 36% of cases, insufficient in 48%, and no response in 16% of cases, correlating with the level of education. The vital need for treatment was known in 88%, triggers for AAI and management were known in 37%. The average hydrocortisone dose was 30 mg. Episodes of AAI were found in 79.6%, with 44.44% occurring upon treatment cessation. Knowledge of a normosodic diet was present in 33.33%, and awareness of medications to avoid, especially diuretics and laxatives, was observed in 18.5%. All patients received an Addison's card. Therapeutic adherence was observed in 59.2%.
Conclusions
The knowledge of adrenal-insufficient patients remains insufficient. The establishment of a therapeutic education program is necessary to enhance patient understanding.

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EP299

Prevalence and significance of hypokalemia in primary aldosteronism: a retrospective study

Siddiqa Soomauroo[1], Faten Hadjkacem[1], Abdelmuhaymen Missaoui[1], Ahmad Ridwaan Auckburally[2], Souhir Maalej[1], Wiem Feki[2], Zeinab Mnif[2], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Radiology, Sfax, Tunisia

Introduction
Primary hyperaldosteronism (PA) is the autonomous production of aldosterone by a disease primarily affecting the glomerular zone of the adrenal gland. It is one of the most frequent causes of secondary hypertension. The diagnosis should be suspected in the presence of the classic clinico-biological triad in patients presenting with hypertension, low plasma renin activity (PRA), with or without hypokalemia.
Patients and Methods
Retrospective and descriptive study concerning 40 patients with PA, collected in the endocrinology department of the Hedi Chaker University Hospital of Sfax, over the period of 10 years from January 2010 to December 2022.
Results
The average age of our patients was 55.4 years. They were composed of 16 men and 24 women. In 32% of cases, hypertension was recent, evolving for less than than 5 years. Severe hypertension was found in 11 cases. Hypokalemia was noted in 19 cases (47.5%), symptomatic of asthenia in the majority of cases (60%). Analytical study of the correlation between serum potassium levels and plasma aldosterone concentration (PAC) showed that 15 of these patients had PAC above 200 pg/ml. As PAC increased, so did the number of patients with hypokalemia, with a correlation coefficient $r=$-0.350, $P=0.027$. The threshold of the PAC was studied by the ROC curve. A PAC level above 199 pg/ml was predictive of hypokalemia with a sensitivity of 78.9% and specificity of 66.7%. Following specific treatment of the PA (surgery or spironolactone), a significant increase in mean kalemia was observed during patient follow-up ($P<0.001$) compared with kalemia on admission.

Conclusion
Contrary to initial data, normokalemic rather than hypokalemic PA is the most frequent form of hyperaldosteronism. Hypokalemia is neither a sensitive nor a specific marker for the diagnosis of PA. Nevertheless, its presence can help to identify a severe form of the disease, and therefore recognise patients at particularly high cardiovascular risk.

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EP300

Primary aldosteronism: insights from a single center cohort

Siddiqa Soomauroo[1], Faten Hadjkacem[1], Abdelmuhaymen Missaoui[1], Ahmad Ridwaan Auckburally[2], Souhir Maalej[1], Wiem Feki[2], Zeinab Mnif[2], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Radiology, Sfax, Tunisia

Introduction
Primary aldosteronism (PA) is commonly identified as the main cause of secondary hypertension. It is becoming increasingly wide-spread, affecting between 1 and 30% of people suffering from hypertension. We aim to describe the epidemiological, clinical and paraclinical characteristics of PA and to analyse its therapeutic and evolutionary aspects.
Patients and methods
Retrospective and descriptive study concerning 40 patients with PA, collected in the endocrinology department of the Hedi-Chaker University Hospital of Sfax, over the period of 10years from January 2010 to December 2022.
Findings
The average age of our patients was 55.4 years. They were composed of 16 men and 24 women. In 32% of cases, hypertension was recent, evolving for less than than 5 years. Severe hypertension was found in 11 cases and resistant hypertension in 4 others. Hypokalaemia was noted in 47.5% of cases, symptomatic of asthenia in the majority of cases (60%). The mean plasma aldosterone concentration was 250 pg/ml. The mean plasma renin concentration was 3.98 pg/ml, below 4.6 pg/ml in 28 cases. The aldosterone to renin ratio was greater than 23 in all cases, with a mean level of 41. The etiology of PA was dominated by bilateral adrenal hyperplasia (BAH) in 20 cases, aldosterone-producing adenoma in 17 cases and unilateral adrenal hyperplasia in 2 cases. One patient had a malignant adrenocortical carcinoma secreting aldosterone (ACC). Fourteen patients had cardiovascular involvement, characterized by electrical left ventricular hypertrophy and/or hypertrophic cardiomyopathy on echocardiography, and/or evidence of coronary insufficiency. Surgical treatment consisted of unilateral adrenalectomy in 8 cases. Twenty-eight patients were treated medically with spironolactone. The course of the disease was favourable with a reduction in the number of antihypertensive treatments. Follow-up of patients observed blood pressure control and normalization of potassium levels in all cases except the case of the malignant ACC, who died of a massive pulmonary embolism.
Conclusion
PA is an underdiagnosed cause of hypertension. Although it is traditionally associated with hypertension and low potassium levels, many patients with PA do not exhibit hypokalemia. The recommended treatment for those with unilateral disease is adrenalectomy. However, individuals who are unfit for surgery or have BAH can undergo medical treatment using mineralocorticoid antagonists alongside antihypertensive medications to better manage blood pressure. We highlight the need for early detection of PA and appropriate management of all hypertensive patients with cardiovascular comorbidities and/or metabolic syndrome, among others, in order to attenuate the harmful effects of excess aldosteronism.

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EP304

Do non-functional adrenal incidentalomas present a higher cardiovascular risk?

Sabrina Ayari, Nadia Khessairi, Cherchir Faten, Elyes Kamoun, Fatma Chaker, Meriem Yazidi, Oueslati Ibtissem & Chihaoui Melika
RABTA Hospital, Tunis, Tunisia

Introduction
Non-functioning adrenal incidentaloma (NFAI) is a frequently diagnosed since the increased use of radiological examinations. The recent studies have shown that NFAI might have negative cardiometabolic effects and increased cardiovascular risk. The aim of this case control study was to determine the relationship between NFAI, CRP-hs, uric acid and cardiovascular risk (CVR) based on GLOBORISK algorithm of Tunisia.
Methods
This case-control study included 40 NFAI patients (16 men, 24 women, mean age 52.9 ± 11.2 years) and 40 individuals (17 men, 23 women, mean age 56.8 ± 8 years) in the control group matched for age, sex, and weight. NFAI diagnosis was established according to current guidelines. Patients with mild autonomous cortisol secretion, chronic kidney disease, liver failure or under hypolipidemic drugs, combined contraceptive pills or alcohol were excluded of this study. All participants underwent physical examination, adrenal imaging, biochemical evaluation including baseline cortisol, CRP-hs, lipid profile, uric acid, and fasting plasma glucose (FPG). All participants underwent the assessment of the 10-year risk of cardiovascular mortality based on the GLOBORISK algorithm of Tunisia.
Results
NFAI presented higher basal cortisol level (10.4 µg/dl (8.0-13.2) vs 8.0 µg/dl (7.0-10.6), $P=0.007$), higher uric acid level (51.8 ± 15.3 mg/l vs 43.3 ± 11.2 mg/l $P=0,009$) and higher CRP-hs (2.5 mg/l (1.3-4.6) vs 0.9 mg/l (0.43-1.98), $P<10^{-3}$) compared to control group. Using the GLOBORISK algorithm, NFAI didn't present a higher cardiovascular risk compared to controls. Age ($r=0.692$, $P<10^{-3}$) and systolic hypertension ($r=0.384$, $P=0.014$) were positively correlated to a higher CVR in NFAI patients. Basal cortisol level superior to 10 µg/dl and uricemia superior to 55 mg/l were associated with elevated CVR with odds ratios of 3.73 (95% CI:1.02-14.23) and 5.14 (95% CI:1.29-20.52) respectively.
Conclusion
This study confirms that cardiovascular remodelling in asymptomatic patients with NFAI can be detected in early stages. Therefore, NFAI having higher cardiovascular risk should be monitored regularly.

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EP311

Impact of 10 years of conventional steroids vs dual-release hydrocortisone on metabolic, cardiovascular, and bone outcomes in treatment-naïve patients with adrenal insufficiency

Valentina Guarnotta, Claudia Di Stefano, Laura Tomasello, Giuseppe Pizzolanti, Giorgio Arnaldi & Carla Giordano
Università degli Studi di Palermo, PROMISE Department, section of endocrinology, Palermo, Italy

Patients with adrenal insufficiency show higher mortality than in the general population, mainly due to non-physiological daily glucocorticoid overexposure and to inadequate cortisol exposure during stress-related events and illness. The aim of the current study is to compare the impact of 10 years of conventional glucocorticoid (GC) replacement treatment and dual-release hydrocortisone (DR-HC), on anthropometric, metabolic, cardiovascular and bone outcomes in treatment-naïve patients with primary adrenal insufficiency (PAI) and secondary adrenal insufficiency (SAI). Forty patients (19 with PAI and 21 with SAI) were randomly allocated to conventional GCs (cortisone acetate or hydrocortisone) administered two or three times a day and 43 (20 with PAI and 23 with SAI) on dual-release hydrocortisone (DR-HC). Anthropometric, metabolic, cardiovascular and bone parameters were evaluated at baseline and after 5 and 10 years of follow-up. All patients enrolled completed the study. Among patients with PAI, one patient developed hypothyroidism after 2 years from the diagnosis of adrenal insufficiency and another patient developed type 1 diabetes mellitus after 1 year from diagnosis of adrenal insufficiency. Patients with SAI mainly had stable control for other pituitary insufficiencies during 10 years of treatment. In patients treated with conventional GCs, a trend of significant increase in BMI ($P=0.040$), waist circumference (WC) ($P=0.001$), systolic and diastolic blood pressure ($P=0.017$ and $P=0.035$), HOMA-IR ($P=0.035$), area under curve-2 hours (AUC_{2h}) of insulin and glucose ($P=0.018$ and $P=0.003$), and a trend of significant decrease in oral disposition index (DIo) ($P=0.025$) and Isi-Matsuda ($P=0.043$) were observed at 5 and 10 years of follow-up. In patients treated with DR-HC, a trend of significant decrease in triglycerides and LDL cholesterol ($P=0.034$ and $P=0.032$, respectively) was observed after 5 and 10 years of follow-up compared to baseline. At 10 years of follow-up, patients with conventional GCs had significantly higher values of BMI ($P=0.031$), WC ($P=0.047$), systolic blood pressure ($P=0.039$), total and LDL cholesterol ($P=0.041$ and $P=0.042$), HbA1c ($P=0.040$), HOMA-IR ($P=0.006$), AUC_{2h} of glucose ($P<0.001$), thickness of the interventricular septum in diastole and of the posterior wall (both $P<0.001$) and significantly lower values of DIo ($P=0.001$) and ISI-Matsuda ($P<0.001$), lumbar spine T score ($P=0.036$) and

femoral neck Z score ($P=0.026$), compared to patients treated with DR-HC. In patients with treatment-naïve AI, 10 years of therapy with conventional GCs was associated with a worsening of metabolic, cardiac and bone outcomes, while DR-HC had no impact on them achieving a lower risk of developing comorbidities.

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EP315

Incidence and features of adrenal crisis in patients with Addison's Disease

Alberto Scala[1], Marianna Torchio[1], Fabio Presotto[2], Caterina Mian[1], Filippo Ceccato[1], Scaroni Carla[1], Corrado Betterle[1] & Chiara Sabbadin[1]
[1]University Hospital of Padua, Endocrine Unit, Padua, Italy; [2]Ospedale Dell'Angelo, Unit of Internal Medicine, Mestre-Venice, Italy

Introduction
Adrenal crisis (AC) is the most severe manifestation of adrenal insufficiency, still responsible for a high mortality of affected patients, especially with primary adrenal insufficiency (PAI). Its presentation is insidious, leading to a delayed diagnosis and treatment. Patient education is crucial in the prevention and self-management of AC.
Aim of the study
We want to evaluate the incidence, features (symptoms, signs, laboratory findings), precipitating and predisposing factors of AC.
Methods
A total of 132 patients with PAI were enrolled. Patients' characteristics and information on their previous AC were collected through a questionnaire and clinical documentation, supplied by patients or retrieved from archives of the Hospitals of Padova and Venice-Mestre.
Results
Among our patients, the most frequent cause of PAI was autoimmune adrenalitis (92.4%), mainly associated with other autoimmune comorbidities. The 65.9% of patients experienced at least one AC, with an incidence of 10.5/100 patient-years. In 55% of cases, AC occurred after the diagnosis of PAI. The most frequent symptoms and signs of AC were fatigue (96%), gastrointestinal disorders (39-85%), hypotension (57%), and hyperpigmentation (57%). Hyponatremia and hyperkalemia were found respectively in 77% and 32% of cases of AC. The most frequent trigger factors were vomiting and diarrhea (65%), infections (38%) and emotional stress (29%). Patients with a high number of autoimmune comorbidities and those with premature ovarian insufficiency (POI) had a significantly higher risk of AC ($P<0.02$).
Conclusions
AC is still a frequent complication of patients with PAI, especially when affected with other autoimmune comorbidities or with POI. AC awareness among clinicians, patients, and their care-givers is critical to prevent, recognise and adequately treat this life-threatening complication.

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EP325

Circadian fluctuation of amino acids and biogenic amines in health and in hypercortisolism states

Guido Di Dalmazi, Flaminia Fanelli, Lorenzo Tucci, Valentina Bissi, Greta Galante, Ilaria Improta, Alessandro Perrone, Kimberly Coscia, Giacomo Colombin, Valentina Vicennati, Uberto Pagotto & Guido Di Dalmazi
University of Bologna, Department. of Medical and Surgical Sciences, Bologna, Italy

Background
Chronic hypercortisolism is known to alter the circadian rhythm and to impair protein metabolism. Altered amino acid (AA) and biogenic amine (BA) levels were found in basal blood in patients with hypercortisolism. However, poor information is available on the physiologic circadian fluctuation of these molecules. Furthermore, the potential derangement caused by hypercortisolism was never investigated.
Aim
To characterize diurnal levels and fluctuations of AA and BA in convenient dried blood spots (DBS) from finger-prick in healthy subjects (HS) and in patients affected by autonomous cortisol secretion (ACS) or Cushing syndrome (CS).
Methods
HS (38.0 ± 15.5 y; $n=9$), ACS (64.8 ± 8.4 y; $n=6$) and CS (53.4 ± 8.0 y; $n=5$) patients underwent a 7-days standardized isocaloric Mediterranean diet. On the 7th day, subjects collected DBS at 7 time-points: 30 min before and 2 h after breakfast, lunch and dinner, and at bedtime. 21 AA and 21 BA were measured in DBS by LC-MS/MS.
Results
Compared to HS, ACS patients had lower His ($P=0.026$), while CS patients had lower Asn ($P=0.030$) and higher spermidine ($P=0.003$). CS also had higher spermine ($P=0.028$) and t4-OH-Pro ($P=0.032$) compared to ACS patients. A daily rhythm was detected in HS for 11 AA (Met, Leu, Ile, Arg, Cit, Glu, His, Pro, Trp, Val; P:0.001-0.037) and Met-SO (P:0.010), mostly with levels higher at awakening and bedtime, and lower in the morning (positive quadratic trend). Of these, some maintained their rhythm also in ACS (Ile, Leu, Trp, Val, Met-SO; P:0.043); however, only Leu maintained a similar rhythm in CS patients (P:0.006). Fluctuation of other compounds were found in ACS (Gly, His, Lys, Orn, Phe, Ser, Thr, t4-OH-Pro; P:<0.001-0.006) and in CS (asymmetric-dimethylarginine (ADMA), creatinine, spermine; P:0.003-0.018) with variable trends. AUCs of Arg (R:0.632, P:0.037), spermidine (R:0.743, P:0.009), spermine (R:0.729, P:0.011) and taurine (R:0.788, P:0.004) were directly correlated with post-dexamethasone test cortisol. AUCs of ADMA (R: -0.513, P:0.030) and Orn (R:-0.573, P:0.013) were negatively associated with fat free mass.
Conclusions
A panel of AA displayed a physiologic diurnal fluctuation consistent with day/night protein anabolic/catabolic processes. Daily fluctuations were revealed in ACS for a different panel of AA, and were almost all lost in CS. ACS and CS also showed disease specific fluctuations in some BA. Finally, ACS showed a deranged histidine metabolism, whereas CS showed an enhanced polyamine pathway.

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EP326

Radiomics for immunohistochemistry prediction in pheochromocytoma: a pilot study

Lorenzo Tucci[1,2], Antonio De Leo[1,3], Giulio Vara[4,5], Kimberly Coscia[1,2], Saverio Selva[6], Claudio Ricci[1,6], Laura Alberici[6], Caterina Balacchi[7], Donatella Santini[3], Valentina Vicennati[1,2], Uberto Pagotto[1,2], Cristina Mosconi[1,7], Giovanni Tallini[1,3] & Guido Di Dalmazi[1,2]
[1]Alma Mater Studiorum - Bologna University, Medical and Surgical Sciences Department, Bologna, Italy; [2]IRCCS S. Orsola-Malpighi Polyclinic, Endocrinology and Diabetes care and Prevention Unit, Bologna, Italy; [3]IRCCS S. Orsola-Malpighi Polyclinic, Anatomic Pathology Unit, Bologna, Italy; [4]Alma Mater Studiorum - Bologna University, Biomedical and Neuromotor Sciences Department, Bologna, Italy; [5]Civil Hospital "Umberto I", Radiodiagnostic Unit, Lugo, Italy; [6]IRCCS S. Orsola-Malpighi Polyclinic, Division of Pancreatic and Endocrine Surgery, Bologna, Italy; [7]IRCCS S. Orsola-Malpighi Polyclinic, Diagnostic and interventional abdominal-pelvic radiology Unit, Bologna

Background
Radiomics, or texture analysis, is gaining growing interest for its high prediction performances, mainly for clinical purposes. Radiomics application for pheochromocytoma immunohistochemistry (IHC) and molecular biology prediction is still unexplored.
Aim
To evaluate radiomics ability to predict pheochromocytoma IHC.
Methods
We retrospectively enrolled 38 pheochromocytoma who underwent surgery at Sant'Orsola-Malpighi Polyclinic since 1999 to 2023 with availability of pre-surgery basal computerized tomography (CT) scan and post-surgery IHC results on formalin-fixed, paraffin-embed tissues. IHC for Succinate Dehydrogenase Subunit A (SDHA), B (SDHB) and Somatostatin Receptor 2 (SSTR2A) was performed using Ventana Benchmark Ultra (©Roche Ventana Medical System, USA). IHC scores ranged from 0 (negative) to 3 (strongly positive). Texture analysis was performed on CT basal scan with LifeX software (version 7.2.0, ©LITO, France). Logistic regression was used to assess texture analysis ability to predict IHC scores. Sensitivity, specificity, negative (NPV) and positive predictive value (PPV) of significant predictors were estimated through receiver operating characteristic curve analysis.
Results
0 patients displayed SDHA negativity, 5 patients displayed SDHB negativity, 27 patients displayed SSTR2A IHC positivity. A model including Maximum Grey

Level and Strength predicted SDHB negativity (Odds Ratio (OR): 2.743; 95% Confidence Interval (CI): 1.544 – 4.873; $P<0.001$) with sensitivity 100.0%, specificity 60.6%, NPV 100.0%, PPV 28.0%. A model including Zone Percentage predicted SSTR2A positivity (OR: 2.718; CI: 1.435 – 5.149; $P<0.001$) with sensitivity 77.8%, specificity 80.0%, NPV 57.0%, PPV 91%. A model including Joint Maximum predicted SSTR2A score equal to 3 (OR: 2.718; CI: 1.509 – 4.896; $P<0.001$) with sensitivity 87.5%, specificity 65.5%, NPV 95.0%, PPV 41.2%. A model including Maximum Grey Level and Strength predicted the combination of SDHB negativity and SSTR2A positivity (OR: 2.689; CI: 1.439 – 5.024; $P<0.001$) with sensitivity 75.0%, specificity 93.0%, NPV 96.9%, PPV 75.0%.

Conclusion

Radiomics has shown good performance in predict pheochromocytoma IHC. These findings, if confirmed with wider and prospective studies, may open a new scenario for radiomics. Hence, in the context of pheochromocytoma, texture analysis may reflect pathological molecular pathways, absence or presence of somatic mutations and the individuation and selection of potentially sensitive tumours to nuclear medicine test or treatment.

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EP327

Emerging role of IGF1R and IR expression and localisation in adrenocortical carcinomas (ACC)

Rosa Catalano[1], Emma Nozza[1,2], Emanuela Esposito[1,2], Anna Maria Barbieri[4], Giorgio Croci[3], Barbara Altieri[4], Anna Angelousi[5], Michaela Luconi[6,7], Hantel Constanze[8,9], Sandra Sigala[10], Laura-Sophie Landwehr[4], Guido Di Dalmazi[11,12], Elisa Cassinotti[13], Ludovica Baldari[13], Serena Palmieri[14], Alessandra Mangone[14], Emanuele Ferrante[14], Cristina Ronchi[15,16], Giovanna Mantovani[1,14] & Erika Peverelli[1,14]

[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]University of Milan, PhD Program in Experimental Medicine, Milan, Italy; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Pathology Unit, Milan, Italy; [4]University Hospital, University of Würzburg, Division of Endocrinology and Diabetes Department of Internal Medicine I, Würzburg, Germany; [5]National and Kapodistrian University of Athens, 5First Department of Internal Medicine, Laikon General Hospital, Medical School, Athens, Greece; [6]University of Florence, Endocrinology Unit, Department of Experimental and Clinical Biomedical Sciences 'Mario Serio', Florence, Italy; [7]AOU Careggi, Centro di Ricerca e Innovazione sulle Patologie Surrenaliche, Florence, Italy; [8]University Hospital Zurich and University of Zurich, Department of Endocrinology, Diabetology and Clinical Nutrition, Zurich, Switzerland; [9]University Hospital Carl Gustav Carus Dresden, Medical Clinic and Policlinic III, Dresden, Germany; [10]University of Brescia, Section of Pharmacology, Department of Molecular and Translational Medicine, Brescia, Italy; [11]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Division of Endocrinology and Diabetes Prevention and Care, Bologna, Italy; [12]Alma Mater Studiorum University of Bologna, Department of Medical and Surgical Sciences (DIMEC), Bologna, Italy; [13]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Surgery, Milan, Italy; [14]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [15]University of Birmingham, Institute of Metabolism and System Research, Birmingham, United Kingdom; [16]Birmingham Health Partners, Centre for Endocrinology, Diabetes and Metabolism (CEDAM), Birmingham, United Kingdom

Adrenocortical carcinomas (ACC) overexpress the insulin-like growth factor 2 (IGF2) that drives a proliferative autocrine loop by binding both IGF1R and isoform A of insulin receptor (IRA). However, the contribution of these receptors in mediating ACC cell growth has been poorly investigated. The aim of this study was to investigate IGF1R and IR expression and localisation in ACC and adrenocortical adenomas (ACA) samples, and to test their involvement in mediating IGF2 tumorigenic effects in ACC cells. To this end, we used four available cell lines and ACC primary cultures. Immunohistochemistry analysis on a cohort of ACC ($n=116$) and ACA ($n=17$) revealed that IGF1R was expressed in 85.3% of ACC and in all ACA. No difference in mean percentage of IGF1R positive cells, but a higher IGF1R plasma membrane localisation was observed in ACC (47.5%) compared to ACA (17.6%) ($P<0.05$). In ACC, IGF1R plasma membrane localisation was associated with a higher Ki67 ($P<0.01$), Weiss score ($P<0.001$) and among Weiss criteria, with a higher mitotic rate, presence of atypical mitoses and venous invasion. Moreover, IGF1R plasma membrane localisation showed a 7.5-fold increased risk of having Ki67 ≥ 10 ($P<0.01$). IR protein expression was found in 45.65% of ACC and in all ACA ($P<0.001$). In ACC, IR immunopositivity was associated with higher ENSAT stage, Ki67, Weiss score and a major risk of having a Ki67 ≥ 10 ($P<0.05$). RT-qPCR revealed that the prevalent isoform of IR was IRA in ACC ($n=8$), but not in ACA ($n=8$) ($P<0.05$). In ACC cell lines double IGF1R + IR silencing reduced cell proliferation in JIL2266 (-44.95 (16.04)%, $P<0.05$), MUC-1 (-46.31 (13.58)%, $P<0.001$) and TVBF-7 (-42.12 (15.89)%, $P<0.001$), but not H295R. The single IGF1R or IR knockdown inhibited cell growth only in MUC-1 cells. In ACC primary cultures ($n=3$), expressing higher levels of IRA than IRB, cell proliferation was reduced after IR but not IGF1R knockdown ($P<0.05$). In conclusion, we demonstrated that IGF1R plasma membrane localisation is more frequent in ACC than in ACA and is associated with a worse tumour behaviour in ACC. We further found in ACC an association between immunopositivity to IR, whose prevalent isoform is IRA, with more aggressive features. We first demonstrated a role of IR in mediating cell growth in ACC cells. Overall, these data suggest that: 1) IGF1R plasma membrane localisation and IR expression could represent biomarkers of more aggressive tumours; 2) IR, and in particular the spliced isoform IRA, might constitute a novel ACC therapeutic target.

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EP328

Low sodium diet affects microbiome and immunophenotype in patients with primary aldosteronism in a sex-dependent manner

Hanna F. Nowotny[1], Tingting Zheng[2], Thomas Marchant Seiter[1], Jing Ju[1], Holger Schneider[1], Kroiss Matthias[1], Anna-Lina Sarkis[1], Lisa Sturm[1], Vera Britz[1], Andreas Lechner[1,3], Anne Potzel[3,4,5], Sonja Kunz[1], Martin Bidlingmaier[1], Klaus Neuhaus[6], Adrian Gottschlich[7,8,9], Sebastian Kobold[7,10,11], Nicole Reisch[1], Melanie Schirmer[2], Martin Reincke[1] & Christian Adolf[1]

[1]Department of Medicine IV, LMU University Hospital, LMU Munich, Munich, Germany; [2]Translational Microbiome Data Integration, Technical University of Munich, Freising, Germany; [3]German Center for Diabetes Research (DZD), Neuherberg, Germany; [4]Physicians Association for Nutrition e.V, Munich, Germany; [5]CCG Type 2 Diabetes, Helmholtz Zentrum München, Munich, Germany; [6]ZIEL - Institute for Food & Health, Technical University of Munich, Freising, Germany; [7]Division of Clinical Pharmacology, LMU University Hospital, LMU Munich, Munich, Germany; [8]Bavarian Cancer Research Center (BZKF), Munich, Germany; [9]Department of Medicine III, University Hospital, LMU Munich, Munich, Germany; [10]German Cancer Consortium (DKTK), partner site Munich, a partnership between DKFZ and University Hospital LMU, Munich, Germany; [11]Einheit für Klinische Pharmakologie (EKLiP), Helmholtz Munich, Research Center for Environmental Health (HMGU), Neuherberg, Germany

Background

It is known that excessive dietary sodium intake increases cardiovascular risks and contributes to elevated blood pressure. Additionally, a high-salt diet is linked to unfavorable inflammatory immune responses. Notably, individuals with primary aldosteronism (PA) commonly exhibit elevated sodium intake. Despite treatment with mineralocorticoid receptor antagonists (MRA), PA patients do not experience a complete reduction in excess cardiovascular risk compared to hypertensive controls. Hence, this study aims to explore the impact of moderately reducing sodium intake on the gut microbiome composition and immunophenotype in PA patients.

Methods

Conducted as a prospective two-stage clinical trial, we compared 15 PA patients before start of MRA therapy with appropriately matched healthy controls (cohort A). Furthermore, in 31 PA patients on stable MRA treatment for at least three months, we evaluated standardized blood pressure measurements, performed laboratory tests, analyzed peripheral blood mononuclear cells using flow cytometry and collected stool samples for microbiome analysis before and after a three-months intentional reduction in dietary sodium (cohort B).

Results

Our findings unveiled alterations in the immunophenotype of PA patients following a median sodium reduction of 3.7 g/d. In cohort A, we could observe an upregulation of regulatory T cells in patients with PA compared to normotensive controls ($P=0.0072$) as well as a downregulation of Tc2 cells. Abundance of *Bacteroides uniformis* was higher in the subgroup of patients with PA compared to the matched control cohort ($P=0.0123$), while abundance of *Lactobacillus*

species was reduced compared to controls ($P=0.0052$). Sodium reduction in cohort B led to a decrease in the percentage of pro-inflammatory and pro-hypertensive Tc17 cells ($P=0.0008$) with major effects in male PA patients ($P=0.0012$) and in Tc17/Treg ratio ($P=0.0007$). While sodium reduction did not lead to changes in microbiota abundance, abundance of *Bacteroides uniformis* was higher in female compared to male PA patients throughout the study. Abundance of *Bacteroides uniformis* showed a trend to decrease upon MRA treatment and sodium reduction.

Conclusion

Our study suggests a less pronounced inflammatory phenotype in patients with PA treated with moderate dietary sodium restriction. This observed immune modulation could potentially contribute to effective blood pressure reduction and positively impact cardiovascular risk. Recognizing the interplay between sodium intake, immune responses, and cardiovascular health underscores the potential therapeutic implications of dietary interventions in the management of PA and associated cardiovascular risks.

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EP329

Phenotype variability in intron2 splice variant of CYP21A2 gene – a single-centre pilot study on children and adolescents

Iuliana Gherlan[1,2], Procopiuc Cameliua[2], Madalina Vintila[1,2], Radomir Lidia[2], Andreea Cristiana Brehar[2], Elena Braha[2], Suzana Vladoiu[2], Dana Manda[2], Andrei Muresan[2], Poalelungi Catalina[2] & Sorina Schipor[2]
[1]Carol Davila University of Medicine and Pharmacy, Bucure?ti, Romania; [2]C.I. Parhon National Institute of Endocrinology, Bucure?ti, Romania

Introduction

Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21OHD) is caused by mutations in the CYP21A2 gene, located on the short arm of chromosome 6. Approximately 11 point mutations are responsible for over 90% of cases, with good genotype-phenotype correlations. Depending on the residual 21-hydroxylase activity, three distinct phenotypes (classic salt wasting – SW, classic simple virilising – SV and non-classic - NC) with 4 corresponding genotypes have been described (null, A, B, C). Although usually associated with SW forms, higher variability in phenotype has been described in patients with intron 2 (I2) splice (c.293-13A>G) variant.

Aim

To describe the genotype-phenotype correlation in 21OHD patients with I2 splice variant.

Methods

Between January 2021 and December 2023, 40 children and adolescents with 21-hydroxylase deficiency referred to our centre were clinically and genetically characterised. Multiple ligation-dependent probe amplification (MLPA) method using the MRC-Holland SALSA MLPA P050-C1 kit and Coffalyser.net software were used for the evaluation of copy number variations and several point mutations of the CYP21A2 gene. We used Sanger sequencing (CEQ 8000 Genetic Analysis System, Beckman Coulter) to confirm these variants and to analyse the entire gene sequence in probands and their parents.

Results

I2 splice variant was described in 11 patients (27.5% of 21OHD patients) for a total of 17 alleles (21.25% of all alleles). It was observed in 5 patients in a homozygous state and in another 6 patients in a compound heterozygous state. From the homozygous patients, 3 cases were clinically SW, and the other 2 related patients were clinically expressing NC CAH. The compound heterozygous patients had the same predicted and observed salt-wasting phenotype in patients with I2 splice/p.Arg357Trp and I2 splice/p.Gln319Ter genotype. A case with an expected SV predicted phenotype (I2 splice/p.Ile173Asn genotype) had the same clinically expressed one. The association between I2 splice on one allele and p.Pro454Ser and p.Pro31Leu on the other one led to a predicted NC phenotype, but SV-type clinical manifestations. Instead, patients with I2 splice/p.Pro454Ser and I2 splice/p.Pro31Leu, p.Val282Leu had the same predicted and observed NC phenotype. As a result, the relative frequency of predicted phenotype is 0.71 for SW, 1 for SV and 0.66 for NC phenotype, respectively.

Conclusion

In our group of patients I2 splice allele had a similar incidence to other European populations and a good genotype-phenotype correlation.

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EP372

Association of X-linked adrenoleukodystrophy with Gitelman syndrome: a hypothesis to be confirmed by genetics

Najoua Lassoued, Elloumi Yassmine, Baha Zantour, Alaya Wafa & Sfar Habib
Taher Sfar University Hospital, Endocrinology Department, Mahdia, Tunisia

Background

X-linked adrenoleukodystrophy (X-ALD) is the most common peroxisomal disorder. The clinical spectrum in males with X-ALD ranges from isolated adrenal insufficiency (AI) and slowly progressive myelopathy to devastating cerebral demyelination. Gitelman syndrome (GS) is a rare autosomal recessive inherited tubular disease which is caused by mutation in the SLC12A3 gene. It is characterized by hypokalemic alkalosis with hypomagnesemia and hypocalciuria. We report the association of these two rare syndromes in a 17-year-old male patient.

Case Presentation

A 17 years old male patient, intellectually disabled, with familial history of an intellectual disability and deaths at a young age, is hospitalized in the Endocrinology Department for acute AI with good evolution under hydrocortisone. The patient had presented several similar episodes since the age of 2 months. Nevertheless the diagnosis of AI hadn't been made by the pediatricians because of the presence of normokalaemia during the acute episodes and the persistent of hypokalaemia after administration of hydrocortisone. The patient had melanoderma on examination. The neurological examination was normal. The brain MRI was normal. Faced with the male sex and mental debility, a dosage of very long chain fatty acids was requested, returning positive. The diagnosis of X-ALD was therefore retained. The evolution was marked by the persistence of hypokalemia with hyperkaliuresis, hypomagnesemia, hypocalciuriaand metabolic alkalosis raising suspicion of the diagnosis of GS. The genetic study in search of the mutation of the SLC12A3 gene is in progress. The patient was discharged on hydrocortisone and potassium supplementation.

Conclusions

The association of X-ALD with GS has never been reported in the literature. Genetic confirmation should be done before discussing the genetic and molecular mechanisms behind this association.

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EP375

Backpain as first manifestation of malignant pheochromocytoma. Could stable adrenal incidentaloma transform into malignant pheochromocytoma?

Aleksandra Czapla-Iskrzycka[1], Anna Babińska[1], Tomasz Szmuda[2], Maciej Śledziński[3], Grzegorz Romanowicz[4], Anna Lewczuk-Myślicka[1] & Renata Świątkowska-Stodulska[1]
[1]Medical University of Gdansk, Department of Endocrinology and Internal Diseases, Gdańsk, Poland; [2]Medical University of Gdansk, Department of Neurosurgery, Gdansk, Poland; [3]Medical University of Gdansk, Division of General, Endocrine and Transplant Surgery, Gdansk, Poland; [4]Medical University of Gdansk, Division of Nuclear Medicine, Gdansk, Poland

Malignant pheochromocytomas (MP) are rare form of catecholamine-producing tumours that are usually associated with tachycardia, hypertension and diaphoresis. MP are typically diagnosed by symptoms, elevated catecholamine levels and characteristic radiological imaging. Metastases to the vertebrae are extremely rare and usually appear at late stage of the disease, sometimes years after the diagnosis. Backpain as a first manifestation of MP is unusual, especially with history of stable adrenal mass described as adenoma. A 44-year-old male patient was admitted to endocrinology clinic in November 2023 because of backpain since March 2023. Previously patient sought help at least 3 times at neurologists because of increasing backpain (VAS 9/10) and paraesthesia. He was treated for sciatica. The lumbar spine MRI was prescribed in October – in L1 vertebrae large pathological mass causing spinal canal narrowing with nerve compression and pathological mass of right adrenal gland 64x50mm. Patient was scheduled for neurosurgical decompression, which was cancelled due to pheochromocytoma suspicion, eventually confirmed in vertebral mass biopsy. One-day clinic endocrinological assessment proved elevated chromogranin, catecholamines in evaluation. Patient had a history of stable 15mm right adrenal gland tumour described as adenoma. Due to the backpain worsening and being

bedridden the patient was admitted to our endocrinology clinic. He negated any pheochromocytoma symptoms. Elevation of serum normetanephrine was confirmed. In FDG-PET scan – right adrenal gland tumour with infiltration of inferior vena cava (IVC) and metastases to L1 vertebrae, sacrum, left VII rib, Th1 vertebrae and IV liver segment. Somatostatin analogue (SSA) scintigraphy described primary tumour 84x56mm with metastases in previously found sites and at least 9 more lytic lesions in bones – ribs, vertebrae, skull and pelvic bones, which were not visible in FDG-PET scan. SSA was administered. Patient was transferred to neurosurgery clinic – decompression with carbon implant placement was performed. Then, the patient was admitted to general surgery department –right adrenalectomy with a 130mm-tumour infiltrating the IVC and liver metastasectomy was conducted. The PRRT is scheduled for January 2024. For the time being the patient is walking and without severe pain. The clinical presentation of MP might be atypical and not associated with catecholamine overproduction. It should be remembered that first symptoms might derive from the mass of the metastasis. The treatment of patients with MP needs to be multidisciplinary and requires various and sometimes not standardized approaches. The patient's quality of life must be the most important goal during planning all diagnostic and therapeutic procedures.

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EP376

Pembrolizumab-induced secondary adrenal insufficiency and thyroid dysfunction in an 81 year old male with metastatic cutaneous melanoma - A Case Report

Kurt Bryan Tolentino[1], Sheryl Tugna[2] & Edison So[2]
[1]St. Luke's Medical Center - Global City, Endocrinology, Taguig, Philippines; [2]St. Luke's Medical Center - Global City, Taguig, Philippines

Immune-checkpoint inhibitors have been increasing used in the field of medical oncology for treatment of various early to late-stage malignancies, however, rare occurrences of adrenal insufficiency and thyroid dysfunction may occur. Pembrolizumab, a PD-1 inhibitor, has been associated with adrenal insufficiency in 1-2% of patients, while thyroid related adverse events occurred in 3.2-10.1%. This is a case report of an 81 year-old male, known to have a cutaneous melanoma stage IV (CTxN0M1A of the muscle), with a prolonged use of Pembrolizumab eventually developing both Pembrolizumab-induced hypothyroidism and adrenal insufficiency. This patient had a wide excision with split-thickness skin graft of the right lower extremity back in June 2022 showing a histopathology of melanoma. He was then started on Pembrolizumab therapy on July 2022. Routine laboratories done showed normal TSH. On the 15th cycle (February 2023), there was an incidental finding of an elevated TSH of 17.632, with normal FT4 (1.11 ng/dl) and FT3 (2.56 pg/ml). the patient was then started on Levothyroxine 25 mg once daily. On the 16th cycle of Pembrolizumab showed persistence of an elevated TSH 8.355 uIU/ml, with normal FT4 (1.24 ng/dl) and FT3 (2.47 pg/ml). Levothyroxine supplementation was continued with TSH serially monitored prior to immunotherapy. On his scheduled 24th cycle of Pembrolizumab (Dec 7, 2023), he developed a 1-week history of productive cough, generalized weakness, and exertional dyspnea, managed as pneumonia and was given Azithromycin 500 mg but due to persistence, prompted further evaluation. Vital signs were normal, thyroid function test showed nonthyroidal illness syndrome (TSH 3.383 uIU/ml, FT4 1.16 ng/dl, FT3 1.97 pg/ml), sodium and potassium were normal (142 mEg/l, 4.1 mEq/l respectively), Creatinine was slightly elevated (1.29 mg/dl), Cortisol level was low at 1.82 (mg/dl). Due to low cortisol levels, referral to endocrinology service was done where an ACTH stimulation test was subsequently done. Baseline cortisol was at 1.68 mg/dl, cortisol 30 minutes and 60 minutes post cosyntropin were 7.79 mg/dl and 11.19 mg/dl respectively. Baseline ACTH was low prior to ACTH stimulation test at 3.51 pg/ml. He was diagnosed to have secondary adrenal insufficiency and was initially started on Hydrocortisone 50 mg q6 and was sent home with tapering doses of Prednisone. Both thyroid dysfunction and adrenal insufficiency can occur in patients treated with Pembrolizumab. Thyroid related dysfunction may occur earlier compared to adrenal insuffiency and must be monitored in patients being treated with Pembrolizumab. Levothyroxine and Steroid supplementation still remain to be the treatment of choice.

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EP385

A case of ectopic adrenal tissue in the fallopian tube

Bruna Pimentel[1], Margarida Oliveira[1], Catarina Gama[1], Paula Sprovera[1], Carolina Monteiro Antunes[1], Maria Leonor Guia Lopes[1], Clara Cunha[1], Ana Brandão[2], Helena Oliveira[3] & João Manuel Sequeira Duarte[1]
[1]Egas Moniz Hospital, Endocrinology, Lisbon, Portugal; [2]Hospital de Cascais, Gynecology and obstetrics, Lisbon, Portugal; [3]Hospital de Cascais, Pathology, Lisbon, Portugal

Introduction
Ectopic adrenal tissue (EAT) occurs in less than 1% of adults, more commonly in males. It may be found anywhere along the path of embryogenic migration, usually in the kidney and retroperitoneal fat. We report a case of EAT in the fallopian tube, a particularly rare localization.
Case
We present a 57-year-old female with a known medical history of nephrolithiasis and previous ectopic pregnancies. The patient was submitted to a laparoscopic right adnexectomy due to a paratubal cyst. The histopathological evaluation of the surgical specimen showed a 7 cm fallopian tube partially adherent to the ovary, with a cystic structure in its distal half measuring 6.5 x 5 x 3.8 cm. A 3 mm nodule composed of clear cells was identified, immunoreactive to calretinin, inhibin, vimentin, ki67 1%, and negative for chromogranin, synaptophysin, S100, CD10, RCC and AE1/AE3 markers, suggesting an ectopic adrenal nodule. The patient had no symptoms of adrenal hyperfunction. On physical examination there was no evidence of hypertension or signs of Cushing's syndrome.
Conclusion
EAT is usually clinically silent, found incidentally, and the diagnosis is made only by histopathological examination, like in our case. Very rarely, some ectopic EAT can become hormonally functional or undergo a malignant transformation. Hence, awareness is important and if detected resection is recommended.

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EP387

Patient with immune checkpoint inhibitor Pembrolizumab associated endocrine dysfunctions: a report of clinical case

Viktorija Preobrazenska[1,2], Laura Stirane[1,2] & Una Gailisa[1,2]
[1]Pauls Stradins Clinical University Hospital, Endocrinology, Riga, Latvia; [2]University of Latvia, Riga, Latvia

A 38–year-old female was diagnosed with right breast cancer cT2mN0M0G3 with positive BRCA + gene mutation. The patient was treated with neoadjuvant chemotherapy plus one dose immune checkpoint inhibitor Pembrolizumab following bilateral radical mastectomy, extirpation of the right sentinel lymph nodes and bilateral reconstruction with an implant. Approximately one month after using Pembrolizumab the patient noticed extreme fatigue, decreased blood pressure, accelerated pulse, weight loss of 4 kilograms. The blood test showed hyperthyroidism with thyroid stimulating hormone (TSH) <0.011 mU/l [reference range: 0.4 – 4.0], free thyroxine (FT4) – 34.6 pmol/l [reference range: 11.5 – 22.7] and free triiodothyronine (FT3) – 7.9 pmol/l [reference range: 3.5-6.5] without presence of anti-thyroid peroxidase and thyrotropin receptor antibodies. In addition, in blood test repeatedly was revealed adrenal insufficiency with cortisol 3.0 nmol/l [reference range: 166 – 507] and adrenocorticotropic hormone (AKTH) $<$ 1.5 pg/ml [reference range: 7.2 – 63.3]. The therapy with Prednisolone 7.5 mg daily (5 mg in the morning and 2.5 mg in the afternoon) and Thiamazole 10 mg was started immediately. Three weeks after therapy initiation Thiamazole dose was reduced to 5 mg daily. After two more weeks the blood test showed hypothyroidism with TSH 9.7 mU/l [reference range: 0.4 – 4.0], FT4 – 11.1 pmol/l [reference range: 11.5 – 22.7] and Thiamazole was discontinued. The patient was observed, in three months with no medication thyroid hormones stabilized and no more therapy was needed in further observation period. Pituitary MRI showed no convincing indications of pathological changes in the pituitary gland. The therapy with prednisolone was continued in the same dose, a gradual improvement in clinical manifestations was observed. We hypothesize that immune checkpoint inhibitor Pembrolizumab caused permanent secondary adrenal insufficiency and transient hyperthyroidism.

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EP389

Adrenocortical carcinoma and addison's disease. Is it possible?: a case report

Jose Antonio Ariza Jimenez[1], Isabel Manoja Bustos[2] & Jorge Marín Martín[2]
[1]Hospital la Merced, Endocrinology and Nutrition, Osuna (Sevilla), Spain; [2]Hospital la Merced, Internal Medicine, Osuna (Sevilla), Spain

Introduction
Adrenocortical carcinoma is a rare tumour, with an annual incidence of 1 to 2 case per million. Hypercortisolism constitutes the predominant clinical manifestation in patients with hormone excess, presenting in 50% to 80% of all adrenocortical carcinomas. Non-functioning tumors are even rarer, comprising only 20% of adrenal carcinomas in the largest reported series. Conversely, Addison's disease is also an infrequent disorder, with estimated incidence rates in Europe ranging from 4.4 to 6.2 new cases per million per year. Currently, autoimmunity stands as the prevailing etiology of Addison's disease in Europe, accounting for 75-96% of all cases. Herein, we present an unprecedented case involving a woman diagnosed with both adrenocortical carcinoma and Addison's disease.
Case report
A 45-year-old woman with a medical history marked by multiple allergies and autoimmune disorders, including vitiligo, autoimmune vasculitis, and myasthenia gravis underwent thymoma surgery in 2013. An incidental finding on CT revealed a 52 x 44 mm right adrenal adenoma with suspected malignancy. Functionality studies demonstrated normal 24-hour urine metanephrines and slightly elevated 24-hour urine cortisol. Subsequently, a right adrenalectomy was performed, yielding biopsy results indicative of carcinoma staged as T2N0M0. No oncological treatments were administered during ten years of follow-up, with no evidence of recurrence or hormonal abnormalities. After a decade without issues, the patient was referred to our clinic due to significant asthenia and weight loss. Physical examination unveiled marked cutaneous and mucosal hyperpigmentation, accompanied by a propensity toward hypotension. In light of suspected adrenal insufficiency, blood tests and a CT scan were conducted. The CT scan revealed no abnormalities in the contralateral adrenal gland, but analysis confirmed primary adrenal insufficiency, reflected in decreased cortisol levels (1.86 µg/dl, reference range: 4.8-20.00 µg/dl) and elevated ACTH (1835 pg/ml, reference range: 3.6-60.5 pg/ml). Aldosterone and DHEA levels were also diminished. Positive 21-OHAbs (3.35, reference range: 0.00-1.00) confirmed autoimmune adrenal insufficiency. Treatment commenced with hydrocortisone 20 mg/24h and fludrocortisone 50 mg/24h, resulting in notable improvement in asthenia and hyperpigmentation, enabling the patient to resume her usual activities.
Conclusions
Addison's disease should be consistently contemplated in the differential diagnosis of adrenal insufficiency. Prompt initiation of corticosteroid therapy is imperative in the management of adrenal insufficiency.

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EP390

Endocrinopathys in poems syndrome – what's its clinical implications?

Carolina Peixe, José Vicente Rocha, Mariana De Griné Severino, Marta Lopes, Ana Raquel Gomes, Maria Inês Alexandre & Ana Paula Barbosa
Hospital de Santa Maria, Lisboa, Portugal

Introduction
POEMS syndrome is a rare multisystem disorder characterized by polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma-proliferative disorder and skin changes. Different endocrinopathies are found in 58-80% of patients, however, its pathophysiology remains unknown. Hypogonadism (primary and secondary) is the most common endocrinopathy (79% of patients), with other abnormalities including hyperprolactinemia (56%), primary hypothyroidism (54%), abnormal glucose metabolism (24%), primary adrenal insufficiency (17%), and elevated IGF-1 levels (14.8%). We present two cases of endocrinopathy in POEMS syndrome.
Clinical Cases
Patient 1, 59-year-old female, and Patient 2, 52-year-old male, diagnosed with POEMS Syndrome, initiated follow-up in our clinic due to the potential risk of associated endocrinopathies. Patient 1 presented fatigue and cutaneous hyperpigmentation. The initial assessment revealed primary hypothyroidism and suspicion of primary adrenal insufficiency - TSH 15.6 µU/ml (RR:0.30-4.20), FT4 0.74 ng/dl (RR:0.85-1.70); ACTH 66.3 pg/ml (RR:0-46), cortisol 6.3 µg/dl (RR:4-23), confirmed by the Synacthen® test with a cortisol peak of 10.6 mg/dl at 30 min. Treatment with hydrocortisone followed by levothyroxine was initiated. Five years after, in the period post-menopause, asymptomatic hyperprolactinemia and hypogonadotropic hypogonadism (HH) were observed - prolactin 131.4 ng/ml (RR:4.7-23.0), FSH 5.3 U/l (RR:25.0-134.9), LH 2.43 U/l (RR:7.7-58.5). The pituitary MRI showed an empty sella turcica. Patient 2 had decreased libido, fatigue, and muscle weakness. The initial endocrine evaluation revealed HH and subclinical hypothyroidism – FSH 2.8 U/l (RR:1.5-12.9), LH 1.8 U/l (RR:1.3-9.8), total testosterone 55.7 ng/dl (RR:190-740); TSH 13.8 µU/ml, FT4 1.03 ng/dl. It was also suggestive of primary adrenal insufficiency - ACTH 164 pg/ml, cortisol 9.6 µg/dl, later confirmed by the Synacthen® test – cortisol peak 10.6 mg/dl at 60 min. Hydrocortisone treatment was initiated but testosterone replacement therapy was not due to the associated thrombotic risk.
Discussion
Both patients presented HH, the most common endocrinopathy in POEMS Syndrome. The association between hypothyroidism and POEMS Syndrome remains unclear, considering its prevalence in the general population. Although rare, primary adrenal insufficiency was observed in both cases. The literature suggests a potential association between POEMS Syndrome and an empty sella turcica, as seen in Patient 1. Despite this evidence, the only pituitary deficit identified in this patient was HH, without any relation with hypothyroidism and adrenal insufficiency.
Conclusions
Unrecognized endocrinopathy poses a significant risk for morbidity in POEMS syndrome. A multidisciplinary approach is crucial for systematic endocrine assessment in these patients to enhance early detection and management.

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EP391

Pheochromocytomas are most commonly detected as Adrenal Incidentalomas

Debbah Wissame, Mezoued Mouna, Bessaid Khadidja & Azzouz Malha
Endocrinology-diabetology department of the public hospital establishment (EPH) of Bologhine Ibn Ziri-, Algiers, Algeria

Introduction/objective
Pheochromocytomas are increasingly diagnosed in incidentally detected adrenal masses, with the advent of modern imaging modalities and increased access to imaging. The proportion of pheochromocytomas in adrenal incidentalomas is relatively low, ranging from 7% to 25% of cases recently. Given the evolution of the presentation of pheochromocytomas, we sought to evaluate the proportion and clinical, biochemical and radiological characteristics of incidental pheochromocytomas and compare them to pheochromocytomas whose mode of discovery was adrenergic symptoms and/or uncontrolled hypertension.
Patients and methods
A retrospective descriptive and analytical study including 48 patients hospitalized for pheochromocytoma in the endocrinology-diabetology department of the public hospital (EPH) Bologhine Ibn Ziri - Algiers, Algeria, spread over a period of 20 years.
Results
After excluding pheochromocytomas diagnosed via screening of genetically predisposed individuals ($n=7$; 14.6%), we individualized two groups: group 1, pheochromocytoma diagnosed in a context of adrenal incidentaloma (63.4% of patients) and group 2, pheochromocytoma diagnosed by adrenergic symptoms and/or uncontrolled hypertension (36.6% of patients). Patients detected by incidentaloma were older (median age 48 years) than those detected due to clinical suspicion (30 years) ($P=0.006$). Tumors identified by incidentaloma were significantly larger (median size 65.7 mm) than tumors detected due to adrenergic symptoms/uncontrolled hypertension (55 mm) ($P<0.05$). There was no difference in catecholamine secretion in the two groups ($P=0.13$) (the median increase in metanephrines is: 13× ULN in group 1, and 10× ULN in group 2).
Conclusion
Due to the better availability and more frequent use of complementary examinations, the prevalence of incidental pheochromocytomas continues to increase. It would be legitimate to follow a diagnostic approach and adequate care so as not to ignore them.

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EP392

Stress cardiomyopathy secondary to pheochromocytoma

Isabel Losada Gata, Alberto García Piorno, Mónica Gómez-Gordo Hernanz, Gloria Collado González, Ignacio Jiménez Hernando, Marta Pérez Noguero, Amaya Morales Jaurrieta, Blanca Farache Suberviola, Laura González Fernández & Olga González Albarrán
Gregorio Marañón General University Hospital, Endocrinology, Madrid, Spain

Introduction
Pheochromocytoma, a rare catecholamine-secreting tumor, typically presents with paroxystic hypertension, tachycardia, headache, and diaphoresis. Less frequently, symptoms imply substantial hemodynamic compromise and cardiogenic shock may occur. The delay time in diagnosis is approximately 3 years.
Case Presentation
This is a 41-year-old woman with no relevant history or cardiovascular risk factors, who presented with stress-induced cardiomyopathy or TakoTsubo syndrome, associated with intense headache. The hemodynamic study revealed normal coronary arteries and a reduced left ventricular ejection fraction (LVEF) of 40%, with altered segmental contraction on cardiac magnetic resonance. A year later, she required a new admission due to angina refractory to diltiazem and nitrates; a diagnosis of Prinzmetal's angina was made. A CT scan was performed to rule out non-coronary etiology, and an 8 cm adrenal mass compatible with pheochromocytoma was incidentally found. The study was completed with metanephrines in urine and PET-CT, confirming the diagnosis. Prior to the intervention, alpha blockade with doxazosin was started, with notable difficulties in management, requiring a multidisciplinary approach with cardiology and intensive medicine for dosing, due to the patient's symptomatic hypotension when the dose was increased, and rest angina associated with alterations in repolarization with its decrease. After beta blockade with metoprolol, right adrenalectomy was performed, without incident. The patient's evolution was favorable, with recovery of the LVEF and disappearance of arterial hypertension and headache, although maintaining some occasional episodes of vasospastic angina. Postoperative urinary metanephrines were normal. The genetic study was negative for MEN-1, VHL, NF-1, RET, SDHAF2 SDHB, SDHC, SDHD, TSC1, TSC2.
Discussion and Conclusions
Endocrine causes should be taken into account and ruled out in the differential diagnosis of angina, given that catecolamine-induced cardiomyopathy is potentially reversible.

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EP393

Solitary abdominal pain unveiling pheochromocytoma in a young patient: a case report

Romana Marušić[1,2], Ines Bilić-Ćurčić[2,3], Ivana Prpić-Križevac[2,3], Ema Schönberger[2,3], Kristina Steiner[3], Klara Ormanac[2,3] & Silvija Canecki-Varžić[2,3]
[1]General Hospital Vukovar, Department of Internal Medicine, Vukovar, Croatia; [2]Faculty of Medicine Osijek, Osijek, Croatia; [3]Clinical Hospital Center Osijek, Department of Endocrinology, Osijek, Croatia

Introduction
Pheochromocytomas are rare neuroendocrine tumors originating from chromaffin cells in the adrenal medulla, secreting catecholamines and causing symptoms such as hypertension, anxiety, panic attacks, palpitations, and headaches. An adrenal gland incidentaloma is identified as an unintentional discovery in approximately 3 - 4 % of computed tomography (CT) abdomens performed. Pheochromocytoma is diagnosed in about 5% of adrenal incidentalomas. Diagnosing pheochromocytoma is challenging due to symptoms overlapping with other medical conditions.
Case report
We present a 33-year-old patient evaluated in the emergency department for abdominal pain. Ultrasound revealed a 12 cm oval heterogeneous formation near the lower spleen pole of unclear origin and inflammatory changes at the descending to sigmoid colon transition. A subsequent upper abdomen CT revealed a left adrenal gland formation measuring 11 $\times$ 8.8 $\times$ 11 cm with a native density of 30 Hounsfield units (HU), with 60 % absolute wash-out and 40 % relative wash-out. An irregular hypervascular zone (21 $\times$ 20 $\times$ 25 mm) in the left kidney's lower pole mesentery prompted gastroenterological examinations (esophagogastroscopy, colonoscopy, magnetic resonance (MR) enterography), all yielding normal results. The patient had normal blood pressure; his only symptom was mild abdominal pain. Laboratory findings showed slightly elevated normetanephrine in serum (0.80 nmol/l, reference interval 0.13-0.62 nmol/l) and twice-elevated normetanephrine in urine (0.48 umol/dU, reference interval $<$0.24 umol/dU). Metanephrine values in serum and urine were within reference intervals. Repeated urine metanephrine and normetanephrine findings were normal as well as androgen and cortisol levels. Therefore, the differential diagnosis included pheochromocytoma and adrenocortical carcinoma which was considered as more plausible option. Surgery was recommended, however perioperative preparation according to the protocol for pheochromocytoma was not performed since the biochemical findings were not confirmatory for the diagnosis of pheochromocytoma. The patient underwent a left-sided adrenalectomy without complications. Pathohistological analysis confirmed a composite pheochromocytoma with a ganglioneuroma component in 5 - 10 % of tumors, a PASS score (a pheochromocytoma of the adrenal gland scaled score) $>$4, and a GAPP score (the grading of adrenal pheochromocytoma and paraganglioma) of 5/10. Follow-up adrenal gland MRI revealed no disease recurrence.
Conclusion
The diverse clinical presentations of pheochromocytoma, ranging from asymptomatic to displaying atypical symptoms, underscore the diagnostic challenges posed by this rare neuroendocrine tumor. Given its potential to precipitate hypertensive crises, arrhythmias, and myocardial infarctions, early recognition and prompt intervention become imperative for mitigating severe complications.

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EP394

Adrenal incidentalomas and arterial hypertension

Oumayma Zarrouk, ACH Taieb, Ghada Saad, Asma Ben Abdelkarim, Molka Chadli Chaieb & Koussay Ach
University Hospital of Farhat Hached, Endocrinology departement, sousse

Introduction
Endocrine hypertension is the most common cause of secondary hypertension affecting nearly 3% of the population. Adrenal etiologies play a significant role in these cases. An adrenal incidentaloma is an asymptomatic adrenal tumor, at least one cm in diameter, discovered incidentally during a medical imaging examination. It requires an investigation into its secretory or malignant nature leading to the development of arterial hypertension.
Materials and Methods
This is a retrospective descriptive study focusing on patient records where an adrenal incidentaloma was discovered during hospitalization for hypertension. We documented clinical and biological presentation, etiological profile as well as diagnostic and therapeutic methods.
Results
Our series included 22 patients:2males and 20 females, aged between 29 and 76 years, with a mean age of 52 years. Family history revealed familial hypertension in 18 patients (81.8%), 3 cases of early stroke and 1 case of myocardial infarction. At the time of diagnosis, 6 patients had type 2 diabetes(average duration of 4 months) and a standard deviation (SD) of 3 months. Only one patient was a smoker, and one had dyslipidemia treated with statin. The discovery of hypertension occurred with headache in 7 patients (31.8%), Menard triad (headache, palpitations and sweats) in 5 patients (22.7%), tinnitus in 2 patients (9.1%)and was incidental in 8 patients (36.4%). Among these, 4 cases had refractory hypertension (18.2%) and 2 cases had malignant hypertension (9.1%). No patient experienced complications. The mean systolic blood pressure was 16.1mmHg and the mean diastolic blood pressure was 9.1mmHg. The average weight of the population was 79.8 kg, the average height of 159.19 cm, the average BMI of 31.13 kg/m^2; and the average waist circumference of 105 cm with a SD of 26.6 cm. Biologically, the average blood glucose was 6.57 mmol/l and the average serum potassium was 3.8 mmol/l with a SD of 0.57 mmol/l. Ten patients had a confirmed hypokalemia. A CT scan focused on the adrenals revealed an incidentaloma with an average size of 21.5 mm and a standard deviation of19.21mm. The etiological diagnosis included pheochromocytoma in 7 patients(31.8%), clinically and biologically confirmed hypercortisolism in 9 cases (27.3%)of which6 were adenomas, 1 corticosurrenaloma and 2 bilateral adrenal hyperplasia. There were also 4 cases of primary hyperaldosteronism (18.2%). Two patients did not have hormonal secretion and thus had essential hypertension. For etiological treatment, 18 patients underwent unilateral adrenalectomy for endocrine hypertension (81.8%), while 4 patients received medical treatment(18.2%). Medical treatment for hypertension included ACE inhibitors in 5 patients (22.7%) calcium channel blockers in 4 patients (18.2%), angiotensin receptor antagonists in 2 patients (9.1%), and 1 patient received thiazide diuretic alone. Combination therapy was used in 6 patients, and triple therapy in 4 patients.
Conclusion
Adrenal hypertension is a treatable cause of secondary hypertension. The clinical signs resulting from hyperadrenergic activity, hypercortisolism, or hyperaldosteronism are not specific, but they disappear after surgery, which remains the only curative treatment.

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EP405

Adrenal lesions in in patients with MUTYH syndrome

Joaquin de Carlos[1], Lucia Zabalza[2], Ana Irigaray[1], Maria Rosario Aznarez[1], Jon Yoldi[1], Miguel Marti[1], Xabier Ayarza-Marien[1] & Emma Anda Apiñariz[1]
[1]Hospital Universitario de Navarra, Endocrinology, Pamplona, Spain; [2]Hospital Universitario de Navarra, Gastroenterology, Pamplona, Spain

Introduction
MUTYH (MutY homolog Escherichia coli, homolog of MYH, hMYH) is a repair enzyme with a crucial role in the correction of DNA errors, being considered a protective factor of the cell. MUTYH mutations have been linked to MUTYH-associated polyposis syndrome (MAP), an autosomal recessive disorder characterized by multiple colorectal adenomas. Patients with MAP show a much higher lifetime risk of gastrointestinal cancers as an additional role of MUTYH, it appears to contribute in the involvement of pathologies based on oxidative stress damage, as well as in the prevention of inflammatory and degenerative based disorders. Although the development of extraintestinal pathology is not fully defined, it seems to increase the risk of tumors and endocrinological pathology.
Materials and methods
Prospective study, selecting 27 living patients diagnosed and registered with MUTYH syndrome under follow-up from the Digestive Department of the Hospital Universitario de Navarra (HUN) with current or past follow-up in the Endocrinology Department. Radiological tests, clinical, and analytical variables were analyzed.
Results
The study population included 14 men (51.8%) and 13 women (48.2%), with a mean age of 56 years. The median age at diagnosis of FAP was 48 years, with a mean follow-up time of 8 years. All patients had an abdominal imaging study (CT or MRI), detecting lesions in 3/27 (11.11%). The average size was 2 cm. One of the patients had bilateral adenomas, while the other two were unilateral. Of note, one of them showed calcifications in both glands in the CT scan. All were incidental findings presented as non-functioning adenomas in the analytical tests performed. The study consisted of the overnight 1 mg dexamethasone suppression test, catecholamine/metanephrine determination, adrenal androgen production, and if appropriate, screening of primary hyperaldosteronism. No major endocrinological alterations (defined as nodular disease or thyroid carcinoma, thyroid autoimmunity, diabetes, obesity) were detected when comparing both groups. There were also no differences in gender, age, or time since diagnosis.
Conclusions
Adrenal lesions are common in patients with MUTYH who undergo abdominal imaging. They appear to follow a benign and slowly progressive course, presenting clinically and analytically as non-functioning lesions.

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EP406

Adrenal venous sampling in patients with bilateral adrenal lesions and ACTH-independent cushing's sydrome

Zydrune Visockiene[1,2], Jogaile Gudaite[1], Gintare Naskauskiene[1,2], Valentinas Jakubkevicius[1,2], Nida Jugulyte[1], Domas Grigoravicius[1] & Marius Kurminas[1,2]
[1]Faculty of Medicine of Vilnius University, Vilnius, Lithuania; [2]Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Background
ACTH-independent Cushing's syndrome (AICS) due to bilateral adrenal lesions (BAL) is a challenge as determining whether autonomous cortisol secretion is unilateral or bilateral is crucial in guiding the treatment strategy.
Aim
To analyse the usefulness of adrenal venous sampling (AVS) in differentiating between unilateral and bilateral cortisol secretion in patients with AICS and BAL.
Methods
We performed a retrospective single center analysis of 6 patient cases with AICS who had AVS done at Vilnius University Hospital Santaros Klinikos between 2018 and 2023. AICS diagnosis was clarified by 1 mg dexamethasone suppression test as well as testing late night cortisol, 24 h urine cortisol and ACTH. Successful cannulation was defined as adrenal to peripheral vein ratio of aldosterone >2. Unilateral cortisol secretion was defined as side-to-side lateralization index >2 using aldosterone as a reference hormone.
Results
Concomitant diseases were diagnosed as follows: hypertension – in all 6 patients, dyslipidemia – in 4, osteoporosis – in 2 (with multiple fractures in one case), cardiovascular diseases – in 1, diabetes – in 1 patient. Two out of six patients presented with overt Cushing's syndrome. Both had BAL on computed tomography (CT). Based on the AVS results, one of these patients had unilateral secretion and percutaneous radiofrequency ablation of the functioning tumor was performed. Following the ablation the patient developed transient adrenal insufficiency and was treated with hydrocortisone for two years. The other patient underwent bilateral adrenalectomy. Mild autonomous cortisol secretion was diagnosed in four other patients – all of which showed BAL on CT. One of these patients had unilateral cortisol secretion based on the AVS results and is scheduled for a unilateral adrenalectomy. The remaining three patients had different treatment strategies - one of them underwent unilateral adrenalectomy which did not result in adrenal insufficiency. Furthermore, this led to the discontinuation of antihypertensive treatment as blood pressure normalized. The second patient underwent a two-stage bilateral laparoscopic adrenalectomy with a break of 3 months between operations when hypercortisolism remained after the first one. The third patient had bilateral adrenalectomy.
Conclusions
AVS is an important procedure that may contribute to appropriate treatment in patients with AICS and BAL. In our case, AVS helped to avoid unnecessary bilateral adrenalectomies in 2 out of 4 cases. However, the rare clinical scenario of BAL needs an individualised treatment approach based on the agreement of both the patient and the medical team.

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EP407

Unusual cause of cushing's syndrome

Mayet Roxana Padilla Segura[1], Maria del Carmen De Mingo Alemany[2], Maria Francisca Moreno Macian[2], Begoña Pla Peris[1], Pablo Abellan Galiana[1], Alicia Rizo Gellida[1], Esther Serisuelo Meneu[1], Angela Bono Velilla[1], Francisco Javier Maravall Royo[1] & Agustin Ángel Merchante Alfaro[1]
[1]Hospital General Universitario de Castellon, Endocrinology and Nutrition, Castellon de la plana, Spain; [2]Hospital Universitario y Politecnico La Fe de Valencia, Pediatric Endocrinology, Valencia, Spain

Introduction
Carney Complex (CNC) is a rare syndrome characterized by multiple endocrine and non-endocrine tumors, which may be accompanied by macular pigmentation of the skin. This is an autosomal dominant disorder with high penetrance and heterogeneous expression. It is caused by inactivating pathogenic variants in the PRKAR1A gene in over 70% of cases which encodes the regulatory type 1 alpha subunit of protein kinase A. Diagnosis is made by identifying specific criteria. At least two criteria are necessary, but only one is needed if the patient or a first-degree relative has the genetic alteration.
Case report
An 11-year-old girl with a history of polycystic kidney disease with dysplastic, nonfunctional left kidney and compensatory enlargement of right kidney. She also had a history of melanotic shwannomas on the abdomen, scalp, and lower eyelid. She was referred for suspicion of Cushing's syndrome (CS) due to a one-year history of weight gain, moon face, truncal obesity, purplish streaks, dorsocervical fat pad, and mild hirsutism. On biochemical study, 24 h urinary cortisol (24hUC) was inconsistent: 3.397 ->132->1270 mg reference range (RR:21-143) and midnight salivary cortisol 0.75 mg/dl (RR: <0.27). We found a nonsuppressible serum cortisol (SC): 6.7 mg/dl (RR:6-18), after dexamethasone (DST) 1 mg followed by administration of DST 8 mg finding SC remained high after 48h: 12.10 mg/dl, with also elevated 24 hUC: 403 mg, undetectable serum ACTH <5 pg/ml (RR:5-60), and low dehydroepiandrosterone sulfate: 25.9 mg/dl (RR:33.9-280), confirming an ACTH-independent CS (ACTHICS) with a cyclic pattern. In addition, a paradoxical increase in 24 hUC was detected at day 6, measuring 6,137 mg/24 h. This finding is consistent with primary pigmented nodular adrenocortical disease (PPNAD), which is the most common endocrine neoplasm in CNC and one of the main diagnostic criteria, in addition to the mentioned schwannomas. A contrast-enhanced CT scan of the abdomen revealed normal-appearing adrenal glands, and genetic testing identified a likely pathogenic variant in heterozygosis of the PKRAR1A gene (Chr17: c.658_659 of p(Asn220 Cysfs*12). Histopathological confirmation of PPNAD was obtained after performing bilateral adrenalectomy and left nephrectomy. A search for potential relatives was conducted, but yielded no results.
Conclusion
CNC should be considered in the differential diagnosis of ACTHICS, especially if it has a cyclic pattern and the imaging studies appear to be normal. We present a novel variant of the PKRAR1A mutation, with pathogenic implication. Timely diagnosis and treatment of the patient, in conjunction to screening first-degree relatives who may be affected, can help prevent further complications.

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EP408

Pseudo cushing syndrome with gastrointestinal sarcoidosis: case report

Hemmet Al Hadad[1], Ahmed Fayed[2], Ihab Sameh[2], Mohamed Nagy[2], Sheriff Hamdy[3], Hesham El Makzangy[3], Reem Hamdy[4], mirette makram[1,5,6] & Randa Salam[1]
[1]Cairo University, Internal medicine, endocrinology, Cairo, Egypt; [2]Cairo University, Internal medicine, Cairo, Egypt; [3]Cairo University, Tropical medicine and gastroentrology, Cairo, Egypt; [4]Cairo University, Rheumatology, Cairo, Egypt; [5]Cairo University, Internal Medicine, Endocrinology, Egypt; [6]Faculty Of Medicine Kasr Al-Ainy, Cairo University

Introduction
Pseudo Cushing syndrome (PCS) is caused by non-neoplastic over activity of the hypothalamic-pituitary-adrenal axis. Differentiating between PCS and Cushing disease (CD) can be challenging because of their overlapping clinical and biochemical features.
Case presentation 15 year old male presenting with watery diarrhea of 2 months duration occurring 3 times per day with lower limb weakness No rectal bleeding, fever, or weight loss
Physical examination
Blood pressure: 125/90 mm Hg. Pulse: 125 /mint, normal RR and temperature. BMI: 41 kg/m2 and no cushingoid features. The abdominal examination showed hepatomegaly. The neurological examination showed nystagmus and decreased motor power of both L.L (grade 1) with intact sensations. The Cardiac and chest examination were normal. Investigations: Labs: Infectious work-up including ova and parasites, culture were negative (Hb 9.9 gm/dl), microcytic hypochromic anemia hypokalemia (2.5 mEq/l) (3.5-5.5 mEq/l) hypoalbuminemia (2.7 mmol/l), Normal liver and kidney functions Anti-transglutaminase, and anti-endomysial antibodies, ANA, ANCA, LKMA, ASMA were also negative. Colonoscopy revealed erythematous mucosa in the transverse colon, Esophagogastroduodenoscopy (EGD) revealed diffuse gastric erythema with erosions and duodenitis, cortisol was done to exclude adrenal insufficiency instead it was markedly elevated Serum cortisol 9 am: 48.23 mg/dl (4.3-22.4), cortisol 9 pm: 40.73 mg/dl ($>$ 10), ACTH: 89.3 pg/ml (7.2-63.3), free urinary cortisol $<$ 1140 mg/24 hr Serum cortisol 9 am after low dose dexamethasone suppression test:30.2 mg/dl Serum cortisol 9 am after high dose dexamethasone test: 3.18 mg/dl Imaging: Abdominal CT with oral and I.V contrast: hepatomegaly (27 cm), enlarged celiac and porta hepatis lymph node (largest 1.7 cm) Biopsy of porta hepatis lymph node: non-caseating microgranulomas picture of sarcoidosis Angiotensin-converting enzyme (ACE) was elevated at 93 U/l (8-52), Chest CT was unremarkable and the patient started to receive 40 mg prednisone Outcome and follow up: The diarrhea stopped, L.L weakness improved (grade 4) as well as the anemia (Hb 12 gm/dl). Morning cortisol 14.5 mg/dl. ACTH 37.2 pg/ml
Conclusion
We present a case of PCS with severe hypercortisolism mimicking CD in critical ill adolescent with GIT sarcoidosis that improved spontaneously with the treatment of underlying aetiology

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EP410

Impact of sampling device on quantification of 11-oxygenated androgens in saliva by liquid chromatography tandem mass spectrometry

Sonja Kunz[1], Ilja Dubinski[2], Katharina Schiergens[2], James Hawley[3], Brian Keevil[3], Nicole Reisch[1], Martin Reincke[1], Heinrich Schmidt[2] & Martin Bidlingmaier[1]
[1]University Hospital, Ludwig Maximilian University Munich, Department of Medicine IV, Munich, Germany; [2]Dr. von Hauner Children's Hospital, University Hospital, Ludwig Maximilian University Munich, Department of Pediatrics, Division of Pediatric Endocrinology, Munich, Germany; [3]Manchester University Foundation NHS Trust, Manchester Academic Health Sciences Centre, Department of Clinical Biochemistry, United Kingdom

Introduction
11-ketotestosterone (11KT) and 11β-hydroxyandrostenedione (11OHA4) are new biomarkers for hyperandrogenic disorders. Steroids can be measured in saliva, allowing non-invasive sampling by patients. We modified a published LC-MS/MS method[1] for quantification of 11-oxygenated androgens in saliva with respect to sample volume, extraction procedure and equipment, and assessed the potential impact of different sampling devices on results.
Method
Calibrators were prepared from primary standards (Merck KGaA, Steraloids Inc.) in artificial saliva. Samples were extracted by supported-liquid-extraction with dichloromethane without online solid-phase-extraction. 11-oxygenated androgens were quantified using a 1290 Infinity II HPLC (Agilent Technologies; injection volume 20 µL) coupled to a 6500+ QTRAP mass spectrometer (AB Sciex) via gradient elution and multi-reaction monitoring in positive ESI mode. After method validation, 30 samples from volunteers and patients with adrenal diseases covering a broad concentration range were measured in parallel at our laboratory and the laboratory which originally described the method. To test a potential impact of the sampling device, spiked artificial, and individual or pooled native saliva was applied to three sampling tools (Salivette® and Salivette® Cortisol (Sarstedt), SalivaBio Infant's Swab (Salimetrics)), or used directly. Sample volumes of 20-300 µL were compared.
Results
Performance characteristics were largely comparable to the original method, although our limits of quantification were higher (11KT: 30 vs. 5 pmol/l; 11OHA4: 60 vs. 50 mol/l). Measured concentrations correlated well (intercept 3.18/10.19, slope 1.14/1.54 for 11KT/11OHA4, respectively). Bias between the methods was 17% for 11KT, but 59% for 11OHA4. At very high cortisol and low 11OHA4 concentrations we observed a weak interference from cortisol on 11OHA4 that was not described for the original method. Results from measurement by our method did not differ for saliva volumes between 50 and 300 µL. Measured concentrations were significantly affected by the choice of the sampling tool. Samples collected by the SalivaBio Infant's Swab exhibited the least deviation (-/+6%) from sampling without tool.
Conclusion
We transferred and modified an established method for quantification of 11-oxygenated androgens to allow application if no online SPE is available. While results for 11KT agreed, a significant bias in results for 11OHA4 was observed, perhaps relating to differences in calibrators. To avoid interference from extreme cortisol concentrations on 11OHA4 signals we recommend sampling before hydrocortisone intake. Required volume can be reduced to 50 µl, facilitating analysis of samples from newborns. The impact of sampling devices on measured concentrations must be considered for future studies.
Reference
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EP412

The incidence of cancers in patients with non-functional adrenal tumors: a swedish population-based national cohort study

Jekaterina Patrova[1], Buster Mannheimer[1], Jonatan D. Lindh[2] & Henrik Falhammar[3]
[1]Karolinska Institutet, Department of Clinical Science and Education, Södersjukhuset, Stockholm; [2]Karolinska Institutet, Department of Laboratory Medicine, Division of Clinical Pharmacology, Stockholm, Sweden; [3]Karolinska Intitutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden

Importance
It is unclear if non-functional adrenal tumors (NFAT) are associated with higher cancer incidence.
Objective
To analyze the cancer incidence in patients with NFAT.
Design, Settings and Participants
A national retrospective register-based study involving cases with NFAT diagnosed in Sweden 2005-2019 and controls was conducted. Both cases and controls were followed until death or 2020. Individuals with diagnosed adrenal hormonal excess or malignancy were excluded. Follow-up started after 3-months malignancy-free survival following the date of the NFAT diagnosis. Sensitivity analyses were performed in subgroups of individuals in whom we would presume controls would also have had a CT: those with acute appendicitis (in whom we would also assume there was no concern of cancer), and in patients with a combination of gallbladder/biliary tract/pancreas disorders, and 6- and 12-months malignancy-free survival following the date of the NFAT diagnosis.
Setting
A national retrospective register-based study.
Exposures
NFAT diagnosis.
Main outcomes and measures
The primary outcome was all types of cancer, after adjustment for sex, age and comorbidities. Secondary outcomes were specific types of cancer.

Results
Among 17,726 cases, 10,777 (60.8%) were women, and the median (IQR) age was 65 (57;73) years. Among 124,366 controls, 69,514 (55.9%) were women, and the median (IQR) age was 66 (58;73) years. The incidence of any cancer was higher in patients with NFAT compared to controls (hazard ratio (HR) 1.35, 95%CI 1.29-1.40, adjusted HR (aHR) 1.31, 95% CI 1.26-1.37), slightly higher among females than males (HR 1.44, 95% CI 1.36-1.52, aHR 1.34, 95% CI 1.26-1.41 vs. HR 1.28, 95% CI 1.20-1.36, aHR 1.29, 95% CI 1.21-1.37). The incidence of thyroid, lung, stomach and small intestine, kidney, and pancreatic cancer were increased in cases. The thyroid and kidney cancer incidences were particularly high in cases younger than 65 years. Sensitivity analyses did not change the overall results.
Conclusions and Relevance
The incidence of cancer in NFAT was increased. Long-term follow-up is indicated.

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EP413

Modified release hydrocortisone, a new treatment for congenital adrenal hyperplasia due to 21-hydroxylase deficiency: a single center 'real-world evidence' preliminary study

Chiara Simeoli[1], Erminio M. Crescenzo[1], Augusta M. Pulci Doria[1], Angelica Larocca[1], Nicola Di Paola[1], Claudia Pivonello[2], Mariarosaria Negri[3], Annamaria Colao[1] & Rosario Pivonello[1]
[1]Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia, Andrologia e Nutrizione, Università Federico II di Napoli, Naples, Italy; [2]Dipartimento di Sanità Pubblica, Università Federico II di Napoli, Naples, Italy; [3]Dipartimento di Scienze Umanistiche, Università Telematica Pegaso, Naples, Italy

Life-long glucocorticoid (GC) treatment is needed in patients with congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency, to replace GC deficiency and to control androgens excess. Multiple daily immediate-release-hydrocortisone (IR-HC), characterized by GC overexposure, peaks and troughs, is frequently associated with a suboptimal androgen control, due to ACTH overnight increase. Once daily dual-release-HC (DR-HC), approved for adrenal insufficiency and, despite a near-physiological daily cortisol profile, characterized by suppressed evening cortisol levels, appears not able to avoid ACTH overnight increase and consequent morning androgens excess. A novel twice daily modified-release-HC (MR-HC), recently approved for CAH patients >12 years, simulating the overnight increase of cortisol, appears able to control ACTH overnight increase and consequent morning androgens excess. The current study aimed at investigating the impact of the switch from IR-HC/DR-HC to MR-HC on 3-month metabolic and androgen profiles, and quality of life in 15 CAH females. Nine (60%) patients with classic-form [four (44.4%) with salt-wasting and five (55.6%) with simple-virilizing] and six (40%) with non-classic form, aged 30.1±11.1,15-60 yrs, were enrolled. Seven (46.7%) patients treated with thrice daily IR-HC (23.4±8.2 mg/day) and eight (53.3%) treated with DR-HC (14.4±8.2 mg/day) were switched to equivalent doses of twice daily MR-HC (20.7±7.8 mg/day). The primary outcome was the change from baseline to 3 months of MR-HC in the percentage of patients with good disease control, defined as morning 17OH-progesterone (17OHP)<3 times the upper limit of normal (ULN) and androstenedione within the reference range, according to the phase3 study. Secondary outcomes included changes in hormones and metabolic parameters. Lastly, a questionnaire focusing on asthenia, sleep quality, hyperandrogenisms signs, stress doses and adrenal crises, was administered to all patients before and after the switch. The percentage of patients with controlled disease was 20% (3/15) at baseline and 73.3% (11/15) 3 months after the switch to MR-HC ($P=0.0034$). Particularly, a significant decrease in testosterone (0.4±0.6 *vs* 1.3±2.5ULN at baseline, $P=0.011$) and 17OHP (2.5±3.1 *vs* 22±21.6ULN at baseline, $P=0.005$) was observed. No changes were observed in the other evaluated parameters. Considering patients with alterations at baseline, MR-HC resulted in patient-reported benefits including menses restoration (4/4=100%), asthenia (7/9=77.8%), sleep quality (4/8=50%) and hirsutism (1/11=9.1%). In the 3 months before the switch, twelve patients [12/15 (80%)] adjusted their GC doses for fever/surgery/stress events compared with one [1/15 (6.7%)] patient in the 3 months after the switch. No adrenal crises were observed both 3 months before and after the switch. In conclusion, these preliminary data showed that MR-HC improved disease control in CAH females, with overall patient-reported benefits, mainly in menses, asthenia and sleep quality.

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EP414

Osilodrostat in cushing's disease: Risk of adrenal insufficiency should be monitored

Fatma Ben Abdessalem[1], Hamza ELFEKIH[1,2], Ghada Saad[1,2], Koussay Aich[1,2] & Molka Chadli-Chaieb[1,2]
[1]Faculty of Medicine Ibn El Jazzar, University of Sousse, Sousse, Tunisia; [2]Endocrinology-Diabetology Department, Farhat-Hached University Hospital, Sousse, Tunisia

Introduction
Endogenous Cushing's disease is a serious and rare endocrine disorder. Medical therapy is mostly used as second-line treatment after failed surgery or recurrence and comprises several pituitary-directed drugs, glucocorticoid receptor blocker and adrenal steroidogenesis inhibitors such as osilodrostat. We here describe a case of a Tunisian patient with uncured cushing's disease who developed iatrogenic adrenal insufficiency in the setting of Osilodrostat treatment.
Case Presentation
A 46-year-old female presented to our department with invalidant asthenia and abdominal pain. She has an uncured cushing's disease, following transsphenoidal surgery, complicated with diabetes and hypertension. There was no visible residue on the post operative pituitary MRI. Adrenal CT-scan showed: Nodule of the external arm of the left adrenal gland of 30x17 mm with spontaneous density 7UH, Nodule of the external arm of the right adrenal gland of 15×9 mm with spontaneous density 7UH. She was proposed for bilateral adrenalectomy which was not performed; hence she was given osilodrostat with an initiation dose of 2 mg *2/day. The patient wrongly took a dose of 7 mg *2/day for 13 days then consulted us with an acute adrenal insufficiency: asthenia, vomiting and abdominal pain. Physical examination showed melanoderma with low blood pressure at 80/60 mm Hg. Basal cortisol was low at 17 ng/ml. Natremia and kaliemia were in the normal ranges. Osilodrostat was stopped and hydrocortisone was commenced (200 mg/day). The dose of hydrocortisone was rapidly decreased to 20 mg/day, and osilodrostat was reinitiated (5 mg in the morning, 5 mg in the evening) on Day 7.
Discussion
The effective cortisol inhibition achieved by osilodrostat therapy in Cushing's disease has been demonstrated by several studies. Detailed education of patients treated with osilodrostat should be systematically performed. Titration should be very progressive, or the dose increase could be more rapid in patients for whom a 'block and replace' approach may appear necessary. Given the risk of adrenal insufficiency in this setting of a highly effective drug, our case suggest that 'block and replace' approach should be systematically considered in patients treated with osilodrostat.

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EP415

Adrenal specific functional imaging with 123I-IMAZA for non-invasive diagnostic evaluation of TART - a case series

Stefanie Hahner[1], Schirbel Andreas[2], Schlötelburg Wiebke[2], Carmina Teresa Fuss[1], Ann-Christin Welp[3], Matthias Auer[3], Christian Lottspeich[3], Britta Heinze[1] & Nicole Reisch[3]
[1]University Hospital Würzburg, Division of Endocrinology and Diabetology, Würzburg; [2]University Hospital Würzburg, Department of Nuclear Medicine, Würzburg; [3]LMU University Hospital, Department of Medicine IV, Munich

Background
Distinction of benign testicular adrenal rest tumours (TART) and potentially malign Leydig cell tumors (LCT) is challenging but important to prevent unnecessary surgery of TART. Ultrasound or magnetic resonance imaging can reliably detect but not distinguish between both tumour entities.
Methods
Functional imaging results using the specific CYP11B1/2-inhibitor ^{123}I-IMAZA were investigated in seven adult male patients with classic congenital adrenal hyperplasia and incidentally detected testicular masses and in one patient with seminoma. Planar whole body images and in part additional SPECT images were acquired 4 hours after injection of 130-180 MBq ^{123}I-IMAZA. Uptake was compared with testicular uptake in 20 males receiving ^{123}I-IMAZA imaging for other adrenal diseases. Operated testicular lesions were stained for expression of CYP11B1 and 2.
Results
In four cases, scintigraphy showed significant scrotal and adrenal uptake with depiction of even small testicular masses below one cm of diameter. In these patients, no surgical intervention was performed. In two patients with missing tracer uptake, tumour resection showed a Leydig cell tumour not expressing

CYP11B. In one, we suspect low detection limit of scintigraphy being responsible for missing tracer uptake. As this patient had very small and for many years known and stable tumour, the likelihood of benign TART was extremely high and surgical intervention was not performed.
Conclusion
This is a unique, first time report of adrenal specific functional imaging for non-invasive diagnostic evaluation of TART.

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EP416

Idiopathic unilateral genycomastia in a child

Neima Hassan, Hind Ouakrim, Sana Rafi, El Mghari Ghizlane & Nawal El Ansari
Centre Hospitalo-Universitaire Mohammed VI Marrakech, Endocrinolgist, Marrakech

Introduction
Gynecomastia, marked by mammary gland hypertrophy, arises from an imbalance between androgens and estrogens. Notable etiologies include hypogonadism, tumors, iatrogenic causes, and idiopathic factors.
A case report
A patient aged 8 years and 10 months, with no pathological history, was admitted for further management of right unilateral gynecomastia. The functional signs included unilateral right hypertrophy in the retroareolar region. On physical examination, firm unilateral palpation of 3 cm on the right, eccentric, with no signs of hyperthyroidism or hypercorticism, and the right and left testicular size measuring 4 ml. The diagnosis of idiopathic gynecomastia was confirmed by examination results, revealing a nodular tumefaction, well-limited, regular in contour, hypoechoic, finely heterogeneous, measuring $3\times3\times0.6$ cm. Testicular ultrasound showed no abnormalities. Additional tests, including TSH:1.6 uui/ml, renal and hepatic tests without abnormalities, FSH:1 mui/l, LH:0.12 mui/l, Testosterone:0.10 mg/l, BHCG:0.11 mui/l, and estradiol:2 pg/ml, were within normal ranges. Due to aesthetic discomfort, the patient was referred to the plastic surgery department for further care.
Discussion
In contrast to gynecomastia in adolescents and adult men, prepubertal gynecomastia is a rare occurrence. The primary objective of the interview and clinical examination is to identify warning signs of non-physiological gynecomastia. Various drugs, whether toxic or topical, are linked to gynecomastia and warrant investigation before any additional work-up. The key etiological emergencies to rule out involve tumoral origins, including germinal testicular and adrenal causes. To biology of renal, hepatic, and thyroid function, alongside a hormonal workup (LH, FSH, estradiol, total and free testosterone, SHBG, β-HCG), is necessary. Management relies, on one hand, on reconstructive surgery in cases of significant discomfort. Aromatase inhibitors can also contribute to preventing recurrence.
Conclusion
Gynecomastia represents an infrequent clinical scenario that may signify an underlying disease. A thorough clinical evaluation, paired with an initial work-up, guides the etiological diagnosis. A specific cause is seldom identified, and in 90% of cases, prepubertal gynecomastia is classified as idiopathic
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EP417

Plasma cortisol measurement: ordering practices

Mohamed Chaher Rabah[1], Rim Marrakchi[1], Dhouha Zouari[1], Mariem Boudaya[1], Kamel Jamoussi[1], Mohamed Abid[2] & Mouna Turki[1]
[1]Laboratory of Biochemistry, Hédi-Chaker Hospital, Sfax, Tunisia; [2]Endocrinology departement, Hedi Chaker Hospital, Sfax, Tunisie

Introduction
Cortisol level measurement is required in the diagnosis and management of adrenal, pituitary and hypothalamic pathologies.
Aim
The aim of this study was to evaluate clinician's practice in ordering cortisol test.
Methods
A retrospective study concerning 63 cortisol requests data collected by the laboratory computer system (Health Lab) between January 2024 and February 2024. Only requests of 0800 hours plasma cortisol were included. We collected age, sex and ordering's origins. Cortisol tests were performed based on electrochemiluminescence immunoassay (eCLIA) by Dxi600® Beckman Coulter. Frequencies of cortisol requests were classified according to the reasons and origins of ordering.
Results
The mean age of patients was 38.8 years, with extremes ranging from 6 months to 85 years with a male/female sex ratio of 0,8. The majority of cortisol requests were from the endocrinology department (54%) followed by the paediatrics department (17.5%) and the internal medicine department (14.3%). Reasons for prescribing a cortisol test were as follows: 66.7% for suspecting of adrenal insufficiency, 4.8% for following-up of a confirmed adrenal tumour and 7.9% for following-up of pituitary and hypothalamic pathologies. Among cortisol requests 11.1% were not renseigned. Among cortisol test requests with clinical indications of suspecting adrenal insufficiency, following-up adrenal insufficiency and following-up of pituitary and hypothalamic pathologies only 31%, 25% and 40% were pathological respectively.
Conclusion
There was an over-ordering for cortisol tests in our hospital practice. This suggests this request should be more rational in order to limit healthcare costs

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EP418

Clinical and hormonal characterisation of 71 patients with bilateral macronodular adrenocortical disease (BMAD)

Andreea Vladan[1], Ionela Baciu[1,2], Nicoleta Baculescu[1,2], Iulia Burcea[1,2], Cristina Capatana[1,2], Ramona Dobre[1,2], Roxana Dusceac[2], Simona Galoiu[1,2], Radu Iorgulescu[3], Dan Niculescu[1,2], Raluca Trifanescu[1,2], Anda Dumitrascu[2], Larisa Buduluca[2], Mircea Diculescu[1,4], Serban Radian[1,2] & Catalina Poiana[1,2]
[1]Carol Davila University of Medicine and Pharmacy; [2]Parhon National Institute of Endocrinology; [3]Sf Ioan Emergency Hospital, Bucharest; [4]Fundeni Clinical Institute

Background
BMAD is defined as development of multiple large nodules, >1 cm diameter, with bilateral involvement of the adrenal glands. It is typically associated with endogenous Cushing's syndrome (CS) and occurs in adults, in the 4th-7th decade of life.
Aim
To describe the clinical presentation, the biochemical peculiarities and the management of 71 patients diagnosed with BMAD in a tertiary endocrinology centre.
Results
We described 71 patients with BMAD (54F/17M), aged 65 years old (32-82, median/range), age at onset 61 years old (30-78, median/range). 59 patients were diagnosed incidentally by computed tomography (47), MRI (8) or abdominal ultrasound (4), while 9 of them were referred to the endocrinologist with high suspicion of CS and 2 to be screened for endocrine causes of hypertension. 46 patients were overweight or obese, with a median BMI of 27 kg/m^2 (17.5-44.2), 28 patients had diabetes or prediabetes and 56 patients presented hypertension. 37 patients presented CS, 3 of whom associated primary aldosteronism – 19 patients with MACS, 32 patients presented nonfunctional bilateral macronodular adrenocortical disease and one single patient was diagnosed with adrenocortical carcinoma. Cortisol after dexamethasone 1 mg overnight was 3.43 mg/dl (1.04-23.75) in patients with CS. UFC was high in 3 patients with CS. Median ACTH was 5.19 pg/ml (1-19.98) in patients with CS. All patients had done an enhanced computed tomography, the maximum diameter of the adrenal nodule was 2.8 cm (1.19-7.8). 15 patients with CS were screened for aberrantly expressed hormone receptors, 7 patients presented a positive response after a mixed meal, suggestive for GIP expression, 1 patient presented a positive response after Diphereline administration suggestive for GnRH/l H/FSH/beta-hCG expression. 19 patients were submitted to adrenal surgery, 4 of whom needed bilateral adrenalectomy, while the other patients were followed-up. The median follow-up was 3 years (0-19). During follow-up, 2 of the 15 patients who were submitted to unilateral adrenalectomy had inefficient suppression of cortisol in dexamethasone suppression tests.
Conclusions
Diagnosis of BMAD in our cohort was done mainly by imaging. CS due to BMAD is frequently pauci-symptomatic, warranting biochemical screening in patients

with metabolic syndrome and atypical Cushing's. Bilateral adrenalectomy is curative. Management depends on the severity of Cushing's and availability of medical therapy (requiring biochemical aberrant adrenal receptor profiling). Patients subjected to conservative management need long-term follow-up.

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Correlation of hypothalamic-pituitary-adrenal axis parameters with the size of adrenal incidentaloma

Sanja Ognjanovic, Bojana Popovic, Valentina Elezovic Kovacevic, Dusan Ilic, Milica Opalic Palibrk, Lena Radic, Katarina Krstic & Djuro P. Macut
Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Department for Endocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia

Introduction
The majority of adrenocortical incidentalomas (AIs) are nonfunctional adenomas. Some of them demonstrate an autonomous cortisol secretion (ACS), a pathologic condition defined as biochemical evidence of hypercortisolism without typical signs or symptoms of Cushing's syndrome.
Subjects and methods
In this cross-sectional study, we evaluated 152 consecutive patients, aged 58.3 years (range, 25-84 years) of whom 105 (69.1%) with unilateral adrenal incidentalomas (UAIs) and 47 (30.9%) with bilateral adrenal incidentalomas (BAIs). The hypothalamic-pituitary-adrenal (HPA) axis activity was evaluated using basal cortisol and ACTH levels, midnight cortisol level, 24-h urinary free cortisol (UFC), and post 1 mg overnight dexamethasone suppression test (1 mg-DST) cortisol level. We measured the maximum adrenal nodule diameter on CT and MRI.
Results
There was no significant difference between the longest diameter of the largest adrenal nodule between BAI and UAI patients (3.2 $\pm$ 1.0 *vs* 3.0 $\pm$ 1.2mm $P=0.254$). We found that the maximum adrenal nodule diameter negatively correlated with the ACTH level ($r=-0.213$; $P=0.009$), and positively correlated with midnight serum cortisol level ($r=0.274$; $P=0.001$), UFC ($r=0.264$; $P=0.044$), post DST-1 mg cortisol level ($r=0.206$; $P=0.011$), and probability for ACS ($r=0.276$; $P=0.001$). Multivariate Logistic Regression for ACS showed, after controlling for age, waist circumference, Body Mass Index, UAI *vs* BAI, that adrenal adenoma size was an independent predictor of occurrence of ACS (OR = 1.055, 95% CI 1.017-1.094, $P=0.004$).
Conclusion
These results suggest that critical adrenal tumor mass is required to increase the capacity of steroidogenesis and to result in mild cortisol excess, but probably different pathogeneses are also involved.

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EP420

Does tenascin-X correlate with adrenal dysfunction in patients with Ehlers–Danlos syndrome?

Domański Jan[1,2], Babula Emilia[1,2], Poprawa Iga[1,2], Żuk-Łapan Aleksandra[1,2], Podstawka Jakub[1,2], Julia Latocha[1,2], Zuzanna Szymańska[1,2], Zagozda Małgorzata[3], Wilk Juliusz[3], Korcz Tomasz[3], Cicha-Brzezińska Małgorzata[3], Siejka Anna[4], Mruk Bartosz[5], Walecki Jerzy[6], Bernadetta Kaluza[1,2] & Franek Edward[1,2,7]
[1]National Medical Institute of the Ministry of the Interior and Administration, Department of Internal Medicine, Endocrinology and Diabetology, Warsaw, Poland; [2]National Medical Institute of the Ministry of the Interior and Administration, Students Scientific Group of the Medical University of Warsaw at the Department of Internal Medicine, Endocrinology and Diabetology, Warsaw, Poland; [3]National Medical Institute of the Ministry of the Interior and Administration, Laboratory Diagnostic Center, Warsaw, Poland; [4]The Children's Memorial Health Institute, Department of Clinical Biochemistry, Diagnostic of Metabolism and Steroidogenesis Disorders Lab, Warsaw, Poland; [5]National Medical Institute of the Ministry of the Interior and Administration, Department of Radiology, Warsaw, Poland; [6]National Medical Institute of the Ministry of the Interior and Administration, Department of Radiology, Centre of Postgraduate Medical Education, National Institute of Medicine of the Ministry of the Interior and Administration, Warsaw, Poland., Warsaw, Poland; [7]Mossakowski Medical Research Centre Polish Academy of Sciences, Warsaw, Poland, Department of Human Epigenetics, Warsaw, Poland

Background
Ehlers–Danlos syndrome is a group of genetic conditions characterized by alterations in connective tissue structure, which produces various symptoms. Some subtypes of this syndrome are associated with structural alterations of tenascin-X, an extracellular matrix glycoprotein encoded by the TNXB gene, which partially overlaps the CYP21A2 gene, which encodes adrenal 21-hydroxylase. The purpose of this study was to assess the relationship between tenascin-X levels and adrenal hormones in female patients with Ehlers–Danlos syndrome.
Material and methods
The purpose of this study was to prospectively assess 30 female patients, aged 20–53 years, with hypermobile or classical Ehlers–Danlos syndrome. All patients underwent tests of their tenascin-X levels as well as adrenocorticotropic hormone (ACTH), cortisol, androstendion, and 17-hydroxyprogesterone levels, and urine steroid profile, and magnetic resonance imaging of the adrenal glands.
Results
The study showed no statistically significant correlation between tenascin-X levels and either of the following: 17-hydroxyprogesterone (r_s -0.02, $P=0.933$), cortisol (r_s 0.18, $P=0.346$), ACTH (r_s 0.22, $P=0.233$), androstendion (r_s 0.244, $P=0.194$). There was a positive correlation between tenascin-X levels and dehydroepiandrosterone sulfate (DHEA-S) (r_s 0.362, $P=0.049$). Univariate logistic regression demonstrated that tenascin-X cannot be a predictor of late-onset congenital adrenal hyperplasia (OR 0.49, 95% CI 0–1.3, $P=0.99$).
Conclusions
Tenascin-X levels show no significant correlation with 17-OH-progesterone levels and show a positive correlation with DHEA-S levels. However, the study did not demonstrate tenascin-X to be a predictor of late-onset congenital adrenal hyperplasia in women with Ehlers–Danlos syndrome.

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EP540

Clinical, biological, radiological and therapeutic profiles of pheochromocytomas/paragangliomas

Debbah Wissame, Mezoued Mouna, Bessaid Khadidja & Azzouz Malha
Endocrinology-diabetology department of the public hospital establishment (EPH) of Bologhine Ibn Ziri-, Algiers, Algeria

Introduction
Pheochromocytomas-paragangliomas are rare neuroendocrine tumors that secrete catecholamines from chromaffin cells of the adrenal medulla, sympathetic or parasympathetic ganglia. Unrecognized pheochromocytomas are associated with high mortality, most often due to cardiovascular disorders.
Objective of the study
The objective of our work is to study the clinical, biological, radiological and therapeutic characteristics of pheochromocytomas/paragangliomas
Patients and methods
This is a retrospective descriptive and analytical study spread over a period of 20 years involving 48 patients hospitalized for pheochromocytoma/PPGL in the endocrinology-diabetology department of the public hospital (EPH) Bologhine ibn ziri - Algiers, Algeria.
Results
The analysis of our series finds a clear female predominance, with a mean age at diagnosis of 39 $\pm$ 16.02 (13-76) years. The circumstances of discovery were dominated by adrenal incidentaloma in 26 patients (54.2%). We observed in our cohort: arterial hypertension in 81.2% of our patients including 13 cases of resistant hypertension, 35.4% of patients are diabetic with 41% of cases with cardiovascular complications such as left ventricular hypertrophy in the majority of cases. The determination of urinary methoxylated derivatives was carried out in 75% of cases, with a mixed secretory predominance of 58%. An adrenal CT scan was performed in 95.83% of cases, apart from two patients in a pregnancy context. The mean size of the tumor was 65.7 $\pm$ 30 (10-150) mm with a mean spontaneous density (SD) (specified in 32.6% of cases) of 40.3 $\pm$ 19 (18 -98) HU. A significant positive correlation was observed between the size of the tumor and the rate of MN These pheochromocytomas were included in the context of MEN 2a in 9 cases, Von Hippel Lindau disease (VHL) in 2 cases and neurofibromatosis 1 (NF1) in 2 cases. Pathological examination confirmed the diagnosis in all cases. An average PASS score of 4.7 and a Ki 67 of 3.7%. A malignant form was observed in 6 cases. The postoperative evolution was marked by a normalization of blood pressure figures in 17 patients (58%) and normalization of the glycemic cycle in 04 patients (33.3%).
Conclusion
Most pheochromocytomas were diagnosed incidentally in our cohort. The clinical characteristics and management of our patients are consistent with those in the literature. Pheochromocytoma requires long-term monitoring.

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EP541

Management of adrenal incidentalomas: a single-centre experience

Furhana Hussein[1], Haneen Eltayeb[2], Samrah Ejaz[2,3,3], Alida Akter Ani[2], Gideon Mlawa[2], Belayet Hossain[2] & Edel Casey[2]
[1]Queen's Hospital, Endocrinology and Diabetes/Acute Medicine, London, United Kingdom; [2]Queen's Hospital, London, United Kingdom; [3]Queens Hospital, Endocrinology, London, United Kingdom

Introduction
An adrenal incidentaloma is an adrenal mass lesion greater than 1 cm in diameter, which is incidentally discovered by radiological investigation. The prevalence of adrenal incidentalomas increases with age, increasing to around 3% at aged 50years and 10% in the elderly. The majority of these lesions are benign >80%. Adrenal incidentalomas fall into one of three categories: Non-functioning tumours: these lesions are benign e.g. adenomas, adrenal cysts, haematomas, etc. Functioning tumours: these lesions produce excess of hormones that the adrenal gland normally produces such as in phaeochromocytoma, Cushing's, Conn's, etc. Malignant tumours: these could include adrenocortical carcinoma and metastatic disease.
Aim
of this study was to look at the diagnosis and management of patients referred for adrenal incidentalomas at Queen's Hospital, London, UK (BHRUT–Barking, Havering and Redbridge University Hospitals NHS Trust) in 2014-2020 (7 years).
Method
Retrospective single-centre study looking at patients referred for adrenal incidentaloma between 2014-2020. 154 patients were identified and data was collected on investigations, diagnosis and management. This was compared to the European Society of Endocrine guidelines 2023.
Results
154 patients identified of which 61% female and 39% male. Initial scan showing adenoma leading to referral were CT 84% and MRI 16% Age of presentation more common in the age range of 61-70years (30%) and the least common was age range 20-30years (1%). Majority of the adrenal incidentalomas were non-functioning (65%). The second most common was cortisol secreting adenomas which included 28 patients with 21 possible autonomous cortisol secreting adenomas (PACS) and 7 autonomous cortisol secreting adenomas (ACS). Looking further at these patients and their co-morbidities such as hypertension, diabetes mellitus, dyslipidaemia; 100% had dyslipidaemia and 81% of PACS and 57% ACS had 2 or more co-morbidities. The remaining adrenal incidentalomas consisted of 8% Conn's, 4% Cushing's, 3% Phaeochromocytoma, 3% myelolipoma, 3% malignancy and 5% had no diagnosis. No diagnosis was either due to patient's wishes for not having further investigations or patient passed away before completing investigations.
Conclusion
Our single-centre study showed that majority of adrenal incidentalomas are non-functioning (65%) which correlates with the literature. However, it is important not to miss relevant diseases such as phaeochromocytoma, adrenocortical carcinoma, etc. It is important to send relevant investigations including hormone profile. It is important to have an MDT approach which is individualised for each patient.

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EP560

How concordant is cardiovascular risk stratification using various risk scoring system compared with coronary artery calcium scoring in asymptomatic Thai people with diabetes mellitus?

Yotsapon Thewjitcharoen, Waralee Chatchomchuan, Soontaree Nakasatien, Sirinate Krittiyawong & Thep Himathongkam
Theptarin Hospital, Diabetes and Thyroid center, Bangkok, Thailand

Background
People with type 2diabetes (T2D) often referred as cardiovascular disease (CVD) risk equivalent. However, CVD risk in diabetes varies greatly and substantial proportion of people with T2D have low CVD risk as with the general healthy population. The latest European Society of Cardiology (ESC) guidelines 2023 endorsed the T2D-specific CVD risk score (SCORE2-Diabetes) for people with T2D. However, current prediction models are developed from non-Asian populations, and their utility in other parts of the world is unknown.
Objectives
This study aims to compare various CVD risk prediction tools and validate their performances with the severity of subclinical coronary atherosclerosis assessed by coronary artery calcium (CAC) risk scoring system in asymptomatic Thai people with T2D.
Methods
This cross-sectional study included asymptomatic Thai people with DM who underwent CAC measurement at Theptarin Hospital, Bangkok, Thailand. Four CV risk scores (Thai CV risk score, SCORE2 model, SCORE2-Diabetes model, and UKPDS risk score) were applied and estimated risk scores were correlated with the severity of CAC. Both low-risk and moderate-risk countries were applied in SCORE2 and SCORE2-Diabetes models.
Results
A total of 83 participants (female 39.8%, mean age 59.0±7.2 years, mean DM duration 10.0±8.9 years, BMI 26.5±5.1 kg/m^2, A1C 7.3±1.7%, insulin usage 24.1%) were studied. Zero calcium score was found in 25.3% and CAC score ≥ 100 AU was found in 49.4% of all participants. In people with a duration of diabetes ≥ 10 years, zero calcium score was also found in 6.1%. The Thai CV risk score classified the highest proportion of patients into very high-risk category of CVD (28.9%), followed by SCORE2 (9.6%), SCORE2-Diabetes (9.6%), and UKPDS (7.2%). Spearman correlation coefficients for CAC score with various CV scores ranged from 0.314 to 0.419 with SCORE2-Diabetes performed the best.
Conclusions
Our data showed that when CAC measurements were done in asymptomatic people with DM, almost one-fourth of subjects were found to have zero score, indicating very low-risk for CVD in the future. Although there had been many efforts to create CV risk scoring systems both general population and diabetes-specific risk scores for CVD risk stratification, currently available CVD risk scores (both non-DM and DM-specific risk scores) did not accurately predict the severity of CAC burden in Thai people with T2D.

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EP582

Lipid risk factors for cardiovascular mortality and chronic inflammation in functionally dependent elderly persons

Olga Vasovic
Euromedic General Hospital, Belgrade, Endocrinology, Belgrade, Serbia

Introduction
Many studies have pointed to the importance of chronic inflammation and dyslipidemia in the development of atherosclerosis, but data related to the elderly population are still inconsistent. The aim of the work: To determine the importance of determination of markers of inflammation (C-reactive protein - CRP) and lipid status in elderly (≥65 years), functionally dependent persons.
Methods
A prospective study that included 257 patients (aged 65-99 years, 76.9% women) of the City Institute for Gerontology, Belgrade. At the beginning of the study patients were divided into three groups based on CRP values: group A (CRP<1 mg/l, n= 70), group B (CRP 1-3 mg/l, n= 69) and group C (CRP >3 mg/l, n=69). Patients with CRP>10 mg/l were excluded from the study. Lipidogram, glycemia, HbA1c, then anthropometric measurements, blood pressure and pulse were measured in each patient. After a two-year follow-up, mortality and the factors that influenced its occurrence were analyzed.
Results
CRP showed a significant positive correlation with waist circumference (P=0.005), hips (P=0.012), HbA1c (P=0.033) and triglycerides (P=0.028), and a negative correlation with Hdl-cholesterol (P=0.013). Of the lipid risk factors, only the ratios total cholesterol/Hdl (P=0.019) and triglycerides/Hdl (P=0.045) were significantly lower in group A compared to group B, and without differences compared to group C. However, elevated cholesterol is an independent risk factor for Mt only in group C: OR=3.71 (95%C:1.09-12.63).
Conclusion
Determination of CRP helps to identify old people who are at high risk and in whom the treatment of hyperlipidemia is most important in the prevention of mortality.

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EP593

Safety and efficiency of short-term glucocorticoid treatment in laryngological patients – pilot study

Lucyna Papierska[1], Wiktor Miechowski[2], Karolina Dżaman[2] & Wojciech Zgliczynski[1]
[1]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland; [2]Centre of Postgraduate Medical Education, Department of Otolaryngology, Warsaw, Poland

Patients with chronic sinusitis with polyps are prepared for surgery (FESS) in one of two ways: through intranasal steroid therapy or oral preparation. The high-dose oral glucocorticoids are not often used in Poland, because of the due to the risk of developing side effects including pituitary-adrenal axis inhibition with the need for steroid cover during surgery. The 30 patients before FESS were randomly divided into two equal-sized groups. Patients in the first group received intranasal fluticasone propionate at a dose of 800 µg /day for 8 consecutive weeks before surgery. Patients in the second group received oral prednisone at a dose of 0.5 mg/kg/day for 7 days. The degree of polyposis assessed by sinus CT decreased statistically significantly only after treatment with oral steroid (13.14 (95%CI 8.95-15.92) vs. 8.0 (95%CI 4.05-10.59) $P=0.000012$ on a Lund-Mackay scale). There was no statistically significant difference in ACTH levels (14,73 (95%CI 11,85-19,49) vs. 21,09 (95%CI 12,28-41,08) and in morning cortisol levels before and after oral steroid treatment 1.41 (95%CI 8.44-14.20) vs. 8.16 (95%CI 6.69-14.2) $P=0.39$) and this effect did not differ from that observed after intranasal therapy. Electrolytes, glucose, and insulin levels also did not change significantly after this treatment. The operation was performed without hydrocortisone cover and no complications were observed. In conclusion, we have stated that our data confirmed the lack of inhibition of the pituitary-adrenal axis after short-term high-doses GCS therapy. We are planning further research in this area with the goal of introducing oral GCS into the standard preparation for FESS.

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EP599

Ophthalmic artery doppler as a test for gut-brain axis modulation: feasibility study

Rostyslav Bubnov[1] & Mykola Spivak[2]
[1]Clinical hospital`Pheophanià, Ultrasound, Kyiv, Ukraine; [2]Zabolotny Institute of Microbiology and Virology, National Academy of Sciences of Ukraine, Kyiv, Ukraine

Introduction
The Gut-Brain Axis (GBA) is implicated in various conditions, including migraine, headache disorders, Irritable Bowel Syndrome (IBS), hypertension, and vascular dysregulation. While ophthalmic artery Doppler shows promise in conditions like migraine and stroke prevention [2], effective treatments targeting these mechanisms are still under exploration. Probiotic therapy, as a potential molecular and cellular modulator, may balance regulatory systems leading to pathological conditions.
Aim
To explore the relevance of ophthalmic artery Doppler as a test for the efficacy of probiotic therapy in potentially modulating the gut-brain axis.
Methods
A cohort of 10 patients diagnosed with migraine, headache disorders, seasonal dizziness, nausea, IBS, and hypertension underwent general clinical, lab tests, and radiology tests for a metabolic biomarker panel. Probiotic strains, including Lactobacillus and Bifidobacterium genera, were administered at a dose of 10^9 CFU per day for ten days was based on symptoms [3-5]. Ophthalmic artery Doppler analysis was conducted before and after interventions to assess changes in blood flow parameters. Standardized scales evaluated improvements in eye symptoms. Kidney Doppler, blood flow resistive index in segmental arteries, and parameters like visceral fat were also tested.
Results
Analysis revealed significant changes in ophthalmic artery Doppler parameters post-interventions. Peak systolic velocity increased from 25 cm/sec to 35 cm/sec ($P<0.05$), indicating enhanced blood flow, accompanied by a decrease in resistivity index from 0.78 to 0.65 ($P<0.01$), suggesting reduced vascular resistance. Similar trends were noted in ciliary and other ophthalmic parameters. Effective outcomes were observed in kidney blood flow, with decreased IR. Low and normal BMI patients experiencing treatment effects exhibited increased visceral fat. Other symptoms related to GBA, including IBS, asthma, and hypertension, showed alleviation.
Conclusion
Microbiome modification via probiotic therapy may impact certain diseases in both short-term and long-term scales. The Gut-Brain Axis emerges as a potential mechanism, urging further exploration and clinical consideration. Future research should delve into mycobiome, neuromodulators, interleukins (IL-6), cortisol levels, metabolites, Short-Chain Fatty Acids (SCFA), serotonergic agents, CGRP-signaling, hypoxic signaling, and the modulation of calcitonin gene-related peptide (CGRP) within the trigeminal system [1-3].
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EP629

Epidemiological data of primary and secondary adrenal insufficiency in southern province of seville

Pavle Puzigaca, Eyvee Arturo Cuéllar Lloclla, José Álvaro Romero Porcel, Sara Hami Gil & María Victoria Cózar León
Virgen de Valme University Hospital, Department of Endocrinology and Nutrition, Seville, Spain

Objective
Evaluate the prevalence of adrenal insufficiency (AI) in Southern Province of Seville that comprises around 400.000 people.
Materials and methods
Retrospective descriptive study that includes patients diagnosed with primary (PAI) and secondary (SAI) adrenal insufficiency that are followed up at Virgen de Valme University Hospital.
Results
Out of the 125 patients with AI, 51 patients (40,8%) had PAI and 74 patients had SAI (59.2%). PAI was diagnosed in 30 men (59%) and 21 women (41%). Age at diagnosis was 32 $\pm$ 21 years. The most common cause was of autoimmune origin (51%), followed by adrenalectomy (31%), congenital adrenal hyperplasia (16%), and tuberculosis (2%). Among patients with autoimmune origin of PAI, 15 (58%) had at least one associated autoimmune disease, most commonly Hashimoto's thyroiditis (80%), type 1 DM (27%), pernicious anemia (13%), celiac disease (7%), Grave's disease (7%), Goodpasture's syndrome (7%), and psoriasis (7%). As for adrenalectomy, the cause of surgery were pheochromocytoma (37.5%), Cushing's syndrome (37.5%), and metastasis (25%). Regarding treatment, the mean dose of hydrocortisone was 23.2 $\pm$ 7.9 mg and of fludrocortisone 0,08 $\pm$ 0.5 mg. SAI was diagnosed in 41 men (55%) and 33 women (45%). Age at diagnosis was 48 $\pm$ 21 years. The main etiology was non-functioning pituitary macroadenoma (25.7%), followed by craniopharyngioma (10.8%), functioning pituitary adenoma (8.1%), Sheehan syndrome (6.8%), pituitary apoplexy (6.8%), empty sella turcica (6.8%), traumatic head injury (5.4%), immunotherapy (4.1%), hypophysitis (4.1%), exogenous corticosteroids (4.1%), radiotherapy (2.7%), idiopathic panhypopituitarism (2.7%), pituitary hypoplasia (2.7%), pituitary carcinoma (1.4%), and other causes (8.1%). The mean hydrocortisone dose for treatment was 18.8 $\pm$ 5.3 mg.
Conclusions
In our study population, it was observed that AI occurs more frequently in men. SAI is more common and occurs almost 15 years after PAI, with the dose of hydrocortisone being almost 5 mg less than in PAI. The most common cause of SAI was non-functioning pituitary macroadenoma, while in the case of PAI, it was of autoimmune origin and most commonly associated with Hashimoto's thyroiditis.

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EP630

Long term management of adult bilateral adrenal hyperplasia with mild autonomous cortisol secretion - data from a Romanian tertiary center

Vlad Radulescu[1], Anastasia Stanescu[1], Cristina Stancu[1], Monica Gheorghiu[1,2], Dana Manda[1], Anda Dumitrascu[1] & Corin Badiu[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Bucureşti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania

Introduction
Adrenal hyperplasia is found in more than 15% of abdominal imaging procedures in adults, unrelated to endocrine disorders, especially after the COVID era. Adrenal management is consequently recommended.
Aim
To retrospectively evaluate the adrenal status in terms of morphological progression and functional impairment of adrenal function, in a cohort of cases admitted at least yearly in the National Institute of Endocrinology, Bucharest, Romania, between 2019-2023.

Patients and Methods
141 patients (104 women, 37 men) were evaluated for bilateral adrenal hyperplasia. Adrenal function was assessed by basal and dynamic cortisol (suppression tests) and ACTH, testosterone, DHEA-S, aldosterone and renin as well as urinary and plasma metanephrines and normetanephrines.
Results
There were recorded 18 (12.8%) cases of ACTH dependent Cushing, 14 (9.9%) cases of ACTH independent Cushing, 9 (6.3%) cases of Non Classical congenital adrenal hyperplasia (CAH), 7(4.9%) cases of pheochromocytoma/PPGL, 4 (2.8%) cases of primary hyperaldosteronism, 3 (2.1%) cases of metastatic adrenals, 3 (2.1%) of CCAH and 3(2.1%) paraneoplastic Cushing and 2 (1.4%) of each: adrenal carcinoma and androgens secreting tumors; 58 (41.1%) cases remained non-functional. All PPGL cases underwent surgery with one case of bilateral adrenalectomy. Bilateral adrenal surgery was performed for ACTH independent Cushing ($n=2$) while unilateral surgery was performed for 7 cases. For ACTH dependent Cushing there was only one case of bilateral adrenalectomy, 7 cases of pituitary surgery and 4 cases of pituitary + bilateral adrenal surgery with only 2 cases where unilateral adrenalectomy was chosen. Only 4 cases of non-functional adrenal lesions underwent unilateral surgery because of their higher growth rate. From those with mild autonomous cortisol secretion ($n=18$, 12.8%), a number of ($n=6$) were submitted to unilateral adrenal surgery and declared cured; the site of surgery was decided upon size. From those MACS followed up without surgery, the cortisol autonomy increased during follow-up in 2, remained similar in 8 and diminished in other 2. Several comorbidities (diabetes, high blood pressure, dyslipidemia, osteoporosis) were also subject to follow-up in MACS cases.
Conclusion
The detailed follow-up at 6-12 months of patients with nodular or non-nodular adrenal hyperplasia is required, for proper and individualized management

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EP631

Haematuria as an atypical presentation of pheochromocytoma: a case report

Ana Matijaca[1] & Magdalena Kujundžić[2]
[1]Clinical Hospital Dubrava, Department of Endocrinology and Diabetology, Zagreb, Croatia; [2]Dom zdravlja Zagreb

Pheochromocytomas are rare catecholamine-producing tumors that arise from chromaffin cells located in the adrenal medulla. They are usually benign, but approximately 10% of pheochromocytomas are malignant. The most common clinical features include Menard triad: headache, sweating and palpitations, and permanent or paroxysmal hypertension. Haematuria as a presenting feature of adrenal pheochromocytoma is rarely seen. We report a case of pheochromocytoma in a 61-year-old female patient who presented with haematuria, sporadic left-sided lumbar pressure with some diaphoresis, and well-regulated permanent hypertension. Due to the suspected left adrenal mass seen on the ultrasound, abdominal computed tomography (CT) was done and revealed a 70 mm large left adrenal gland mass. Subsequently, a left-sided adrenalectomy was performed in 2015. Pathohistological examination confirmed pheochromocytoma with an increased risk of malignant behavior. Annual follow-up in 2019. detected elevated urinary metanephrines and normetanephrin. CT scan confirmed 30x24 mm tumor recurrence in left kidney hilus and the patient was submitted to reoperation. Two years after – in 2021. slightly increased values of urinary normetanephrine were noticed although the patient didn't have any symptoms related to excessive catecholamine level once again. Contrast-enhanced thorax CT scan of the abdomen didn't show any suspected lesions but multiple 7 mm large solid lung nodules at bilateral lung basis were noticed. Further, thoracic CT set suspicion of lung metastases so following PET/CT as well as SPECT- CT – MIBG 131 confirmed the suspected metabolically active spread of malignant pheochromocytoma and the patient was referred to an oncologist. Clinical feature of pheochromocytoma are primarily associated with excessive catecholamine production with levels that are expected to be proportional to tumor size. In this case report we wanted to show patient who, except of haematuria as first symptom to be evaluated for, pheochromocytoma was clinicaly silent, as well as the reccurence of tumor or presence of (lung) metastases. Patient did not have any adrenergic symptoms before surgical removal as well as after reaccurance of tumor or lung metastases. Early diagnosis accompanied by lifelong anual follow-up is essential to enable early detection of recurrence and potential malignant complications and in our case report we wanted to emphasis the importance of urinary catecholamine metabolites measurment in follow-up of these patients.

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EP632

A thousand faces of pheochromocytoma: Insights from a case series

Romana Marušić[1,2], Ines Bilić-Ćurčić[2,3], Ema Schönberger[2,3], Kristina Steiner[3], Klara Ormanac[2,3], Eduard Oštarijaš[4] & Silvija Canecki-Varžić[2,3]
[1]General Hospital Vukovar, Department of Internal Medicine, Vukovar, Croatia; [2]Faculty of Medicine Osijek, Osijek, Croatia; [3]Clinical Hospital Center Osijek, Department of Endocrinology, Osijek, Croatia; [4]General Hospital Virovitica, Department of Internal Medicine, Virovitica, Croatia

Introduction
Pheochromocytomas, rare neuroendocrine tumors originating from adrenal medulla chromaffin cells, excessively secrete catecholamines, manifesting diverse symptoms. With an incidence of 2-9 per million inhabitants, these tumors pose diagnostic challenges due to their varied clinical presentation.
Case Description
We present five patients diagnosed with pheochromocytoma at the Clinical Hospital Center Osijek. The incidentaloma of the adrenal gland was discovered while diagnosing unrelated conditions, and none of the patients displayed typical pheochromocytoma symptoms. While one patient reported abdominal pain, others remained asymptomatic. CT was performed, and all patients exhibited significantly elevated normetanephrine levels in serum and urine, with only one showing marginally elevated metanephrine in urine. Patients' characteristics are shown in Table 1.

Table 1. Clinical Profile Summary

Patient	1	2	3	4	5
Age (years)	34	76	67	67	57
Sex (male/female)	male	female	male	male	female
Body mass index (kg/m^2;)	21.5	34.1	26.6	25.8	28.4
Prior cardiovascular disease	-	-	yes	-	-
Hypertension	-	yes	yes	-	yes
Number of antihypertensives	0	2	1	0	1
Beta - blocker	-	-	yes	-	yes
Positive family history	-	-	-	-	-
CT* characteristics Side, size (cm), native density (**HU), absolute wash - out/relative wash - out (%))	left, 11x8.8, 30, 60/40	left, 3.8x4.6, 32	left, 3.5x3.1, 35, 71/56	right, 1.6x1.4, 30, 38/54	left, 3.8x3.4, 20, 59/69
Plasma metanephrine (pmol/l), reference range	0.22 (0.01-0.3)	-	0.34 (0.05-0.36)	0.27 (0.05-0.36)	0.29 (0.05-0.38)
Plasma normetanephrine (pmol/l), reference range	0.80 (0.13-0.62)	-	3.87 (0.14-1.05)	1.68 (0.14-1.05)	3.20 (0.14-0.75)
Urinary metanephrine (umol/dU), reference range	0.20 (<0.27)	0.18 (<0.17)	0.19 (<0.27)	0.12 (<0.27)	0.86 (<1.62)
Urinary normetanephrine (umol/dU), reference range	0.48 (<0.24)	3.96 (<0.19)	0.95 (<0.24)	0.38 (<0.24)	5.34 (<2.13)
Tumor type pheochromocytoma/paraganglioma	pheochromocytoma	pheochromocytoma	pheochromocytoma	pheochromocytoma	
Size of tumor (cm) - PHD	12x11.5	5x3.8	4.2x2.7	1x1.2	3x2.5
AJCC*** staging	pT2	pT2	pT1	pT1	pT1
PASS score****	7/20	4/20	1/20	-	0/20
Ki-67 (%)	1 - 3	1	<1	< 1	2
Treatment	surgery	surgery	surgery	surgery	surgery
Follow - up	complete response	complete response	complete response	complete response	complete response

*CT: computed tomography; **HU: Hounsfield Units; ***AJCC: American Joint Committee on Cancer Staging for Pheochromocytoma, ****PASS Score: Pheochromocytoma of the Adrenal Gland Scaled Score

Conclusion
Pheochromocytoma, lacking specific symptoms, often evades recognition. If there is a clinical suspicion or imaging finding of incidentaloma of the adrenal gland, biochemical testing for pheochromocytoma is crucial.

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EP633

Pseudopheochromocytoma in a patient with depression: a case report

Sawsen Nouira, Hamza Elfekih, Fatma Ben Abdessalem, Asma Gorchene, Kussay Ach, Yosra Hasni & Molka Chaieb
University Hospital Farhat Hached, Endocrinology-Diabetology Department, Sousse

Introduction
Pseudopheochromocytoma is a poorly comprehended entity believed to arise from an overstimulated sympathetic nervous system. Individuals with pseudopheochromocytoma seem to demonstrate heightened cardiovascular reactivity to catecholamines, along with an increased release of epinephrine from the adrenal glands in response to stimulation from the sympathetic nervous system. This clinical report presents an observation of pseudopheochromocytoma in a patient diagnosed with a depressive disorder.
Case Presentation
A 29-year-old patient was admitted to our endocrinology department for the evaluation of hypertension. The onset of his medical history dates to the age of 18-year-old, when he was receiving psychiatric care for depression. The patient's clinical course revealed a sudden-onset hypertension, palpitations, and headache lasting for few minutes followed by spontaneous resolution. He noted a worsening of blood pressure while on antidepressants medications. We conducted a 24-hour ambulatory blood pressure monitoring, revealing consistently normal blood pressure levels interspersed with two episodes of elevated systolic blood pressure reaching 140 mmHg. Investigations have ruled out renal artery stenosis. Aldosterone (257 pg/ml [42-209]) and direct renin (17.7 pg/ml [2.7-16.5]) levels were in favor of secondary hyperaldosteronism. Urinary normetanephrines were mildly elevated, below twice the upper limit of normal (Metanephrines: 276 nmol/24 h [$<$159 nmol/24 h]). 3-methoxytyramine were mildly elevated. Repeating metanephrines in the plasma after 30 min rest showed normal result and the abdominal CT-scan eliminated adrenal tumors.
Discussion
Pseudopheochromocytoma is characterized by the presence of symptoms of catecholamine excess and is commonly considered as a diagnosis of exclusion, yet it possesses distinct characteristics. It is strongly linked to psychiatric disorder, which may not be immediately apparent. Pharmacological approaches for managing this condition encompass antihypertensive medications, antidepressants, and anxiolytics. Additionally, psychotherapeutic interventions prove beneficial in addressing this association. The management of pseudopheochromocytoma is frequently challenging.

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EP703

Vitamin D status in young healthcare workers: association with lipid parameters

Zeineb Rekaya, Samir Mekaouer, Meriem Yazidi, Nadia Khessairi, Elyes Kammoun, Ibtissem Oueslati, Fatma Chaker & Melika Chihaoui
La Rabta university hospital, Endocrinology

Introduction
Vitamin D deficiency is an emerging concern that has the potential to impact one's health, even in sunny Mediterranean countries like Tunisia. This issue is particularly notable among indoor workers in the healthcare sector, who experience minimal sun exposure. The aim of this study was to describe the Vitamin D profile within this specific population and to establish its association with lipid parameters.
Methods
This cross-sectional observational study, conducted from August 2022 to October 2023, involved 64 young and healthy hospital-based healthcare workers. Exclusions were made for individuals with medical conditions that might impact phosphocalcic metabolism. Vitamin D levels were classified as Deficiency ($<$10 ng/ml) and Insufficiency (10-29 ng/ml).
Results
The study participants had a mean age of 29.51 $\pm$ 7.064 years, with 57% being women and 43% men. Among women, 28.6% wore veils. The mean vitamin D level was 21.05 ng/ml [12.87; 21.05]. A vitamin D deficiency was present in 16.7% of cases, and an insufficiency in 62.5% of cases. Women had a lower Vitamin D level compared to men (15.5 vs 16.4 ng/ml, $P=0.57$). The frequency of vitamin D deficiency was higher in women than in men (29.6% vs 0% $P=0.007$). A positive correlation was found between Vitamin D and Ldl levels ($P=0.042$), and between vitamin D and total cholesterol level ($P=0,024$). Healthcare workers with vitamin D deficiency had lower Hdl levels than workers with vitamin D insufficiency. (1.41 vs 1.24 mmol/l, $P=0.028$).
Conclusion
This study revealed a significant prevalence of vitamin D deficiency and insufficiency among young healthcare workers, with women exhibiting a higher deficiency rate. The positive correlations with Ldl and total cholesterol levels emphasize potential links with lipid metabolism. The lower level of Hdl observed in workers with a vitamin D deficiency highlight the need for targeted interventions to improve the vitamin D status among healthcare professionals.

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EP705

Clinical significance of adrenal venous sampling in primary hyperaldosteronism: a case report

Natia Katamadze
clinic ENMEDIC, endocrinology, tbilisi, Georgia

Primary hyperaldosteronism represents a current and underdiagnosed cause of secondary hypertension, characterized by inordinate and independent aldosterone production. While adrenal venous sampling (AVS) has surfaced as the gold standard for lateralization of aldosterone excess, its operation in cases of grueling primary hyperaldosteronism remains less explored. In this unique case history, we present the clinical script of a case with suspected primary hyperaldosteronism, flaunting atypical biochemical and imaging findings. This case of a 45- year old male who presented to the clinic with complaints of high blood pressure, rhythm disturbances, palpitaions, dyspnea and muscle cramps. While all the symptoms were experiences unexpectedly, he had no memory of these symptoms in the past. He was being managed in an outpatient department for hypokalemia and hypertension since the age of 38. He has been taking three antihypertensives (amlodipine, enalapril, labetalol) and supplemental potassium (2 tablets of 10 mEq three times a day). Initial investigations revealed normal hematological and renal parametres but sodium showed 135 mmol/l and potassium 2.5 mmol/l. ECG performed at the time of admission were unremarkable as well. Serum Aldosterone and renin levels were 97 ng/dl and 0.19 ng/ml/hour, respectively, and cortisol levels were 11.7 g/dl. The Aldosterone-Renin ratio was calculated to be 510 ng/dl per ng/(mg/hour). These markers were obvious in stating that there are some discrepancies in some of these levels of some parametres listes above. The abdominal contrast-enhanced Computed Tomography scan showed nodular lesions in the adrenal glands ; 7mm on the right and 37mm on the left which were probably adenoids with low lipid substrate (32 HU- hounsfield unit densities). A selective Adrenal Venous Sampling with Adrenocorticotropic Hormone Stimulation tests were performed. While the aldosterone and cortisol levels in the left adrenal vein were 97 ng/dl and $>$120 µg/dl, the levels in the right adrenal vein were 4086 ng/dl and $>$120 µg/dl, suggesting a diagnosis for Unilateral Adrenal Hyperplasia. Sarcastically, in this case, size didn't matter but infact the hyperactivity did the work. A right adrenelectomy was done to the patient and medications such as spironolactone and oral potassium chloride were given orally during his hospital stay. His electrolytes and blood pressure were corrected 5th day after the surgery and he was subsequently discharged with verapamil, hydralizine, doxasozin and spironolactone. The aldosterone-renin ratio levels came 125 ng/dl(ml/hour)

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EP707

Primary adrenal carcinoma: review and experience of 8 cases in the hospital of málaga

Maria Jose Vallejo Herrera, Veronica Vallejo Herrera, Stella Gonzalez Romero & Viyey Kishore Doulatram Gamgaram
Hospital Regional Málaga, Malaga

Introduction
Primary adrenal carcinoma is a very rare pathology, its treatment is fundamentally surgical and adjuvant treatment with mitotane can prevent recurrences. The prognosis

varies depending on the patient, the stage and the histopathological diagnosis. We present the case mix of patients diagnosed with adrenal cortex carcinoma in our center between 2012-2022 and review the management of this pathology.
Patients and Methods
Retrospective study on adult patients diagnosed with adrenal carcinoma in our center between 2012-2022. We include hormonal study, imaging tests, treatment, histopathological findings and evolution. In carrying out this work we have followed the ethics rules for publication, informed consent has been obtained from the patients and it has been approved by the corresponding ethics committee.
Results
We included eight patients (Table 1), five women and three men, with a mean age of 47 years (range 25-68 years). Three consulted for locoregional symptoms, 4 for functional syndrome and one was diagnosed incidentally. The majority had hyperproduction of sex hormones and cortisol and one case turned out to be non-functioning. Half of the tumors were located on the left adrenal gland and the other half on the right. Two patients had metastasis at diagnosis and one case had a second concomitant primary lung neoplasia. The sites of metastases were liver, lung and bone. Of the eight cases presented, 6 patients underwent adrenalectomy with radical intent. Surgery was not performed in the two patients with stage IV disease; In both cases, metastasis of adrenal carcinoma was confirmed by biopsy of liver metastasis. The patient with a second primary lung tumor first underwent adrenalectomy and then resection of the lung tumor. Regarding the histological study of the surgical specimens, in all cases it was described the Weiss score and the Ki67. Three were low grade and three were high grade. Five patients received treatment with mitotane, due to high grade to prevent recurrence (3 cases) or due to advanced stage of the disease (2 cases). One patient received chemotherapy with EDP (etoposide, doxorubicin and cisplatin) with partial response. In follow-up, until 2022-2023, four patients are in remission, three Patients presented a recurrence of the disease and 3 patients died (one after a recurrence and the other two -stage IV- one month and one year after diagnosis).

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EP708

Familial congenital adrenal hyperplasia (CAH) presenting as addisonian crises – case series

Man Yan Hamilton, Furhana Hussein, Keiko Carter, Bashir Mahamud, Mohammad Saleki, Ayan Mohamed & Gideon Mlawa
[1]Queens Hospital, Endocrinology and Diabetes, Romford, United Kingdom

Introduction
This case series consist of three brothers who are aged 24, 27 and 28. The eldest brother was diagnosed with CAH at 18 days when he presented with poor weight gain, vomiting and persistent jaundice with hyponatraemia. The parents received genetic counselling for the next two pregnancies and all three children were managed with hydrocortisone and fludrocortisone maintainence therapy. They were closely monitored for their growth rates, signs of precocious puberty and any preciptious weight gain during their childhood.
Recurrent admissions
Their care were transferred from paediatric endocrinologists to the adult service since 2016. From 2016-2024, there were more than 28 acute admissions between the 3 brothers. They often present with gastrointestinal symptoms such as recurrent vomitting, abdominal pain and most of them were treated for gastroenteritis with addisonian crisis. None of them wore a steroid alert bracelet nor carry a steroid emergency card and we noted that their emergency steroid ampules sometimes expired. Repeated counselling were held with the patients and their families to highlight the importance of the above issues and sick day rules. At times there were delays with fluid and intravenous hydrocortisone treatment due to London Ambulance Service having limited understanding of CAH. We created an emergency plan to notify these 3 brothers to the ambulance service to ensure timely treatment will be given in future cases.
Routine monitoring and symptoms management
Testicular screening and Vitamin D levels with bone density scans were regularly carried out. Their weights were monitored with periodic steroid day curves to ensure there was no over-replacement of cortisol. We provide regular counselling regarding health and lifestyle choices to avoid the development of metabolic syndrome. Secondary hypogonadism was managed with a trial of testosterone replacement therapy. Patients were referred to reproductive endocrinologist or a fertility specialist early, whilst checking sperm count and discussing possibility of sperm cryopreservation.
Conclusion
A MDT approach is crucial in supporting paediatric CAH patients transitioning to adult services. The team involves paediatric endocrinologists, geneticists, endocrinologists, fertility specialists, dietitians, physiotherapists and the local ambulance service. In this case we highlight the importance of clear communication between teams to support the early recognition and treatment of adrenal crisis in adults prior to admission. Following the establishment of emergency care plan, the family of 3 brothers are able to receive their treatment in a timely matter and potentially reduce their length of stay at the hospital.

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EP717

Adrenocortical carcinoma revealed by pulmonary embolism

Oumeyma Trimeche, sana abid, Ines Bayar, Bilel Ben Amor, Ekram Hajji, Héla Marmouch, Hanene Sayadi & Inès Khochteli
Fattouma Bourguiba University hospital, Endocrinology, Monastir, Tunisia

Introduction
Adrenocortical carcinoma is a very rare tumor with a heterogenous prognosis.
Case report
Patient R.B is a 58-year-old female patient with no particular familial history. She had a personal history of hypertension, discovered 6 months ago well controlled with beta blockers and amlodipine. Two weeks before her admission to the hospital, she reported having constantly worsening abdominal pain followed by frequent vomiting few days later. The patient consulted a gastroenterologist and an abdominal CT was performed. It revealed the presence of a massive 12×11 cm heterogenous right adrenal mass, invading the IV segment of the liver along with the inferior cavernous vein. She also had bilateral and proximal pulmonary embolism with a right thrombus in her right atrium from tumor extension and suggestive signs of pulmonary metastasis on thoracic CT. Upon her admission in the intensive care unit, clinical examination revealed excessive hirsutism notably in her face and deepening of her voice. Those symptoms were insidious and neglected by the patient for 5 months. She had no evident clinical signs of Cushing syndrome in spite of cutaneous fragility. Laboratory exams showed cytolysis and persistent biological inflammatory syndrome despite the absence of infection. She had no hypokalemia. Hormonal assessment revealed normal Metanephrines and preserved cortisol nychthemeral rhythm as well as urinary free cortisol level. However, she had an extremely high testosterone level: 117 ng/ml, increased dehydroepiandrosterone sulfate: >27 µmol/l (normal level $<$ 6.6) and high 17 alpha hydroxy-progesterone. Few days later, the patient deceased from cardiac arrythmia.
Discussion
Pulmonary embolism in the setting of adrenocortical carcinoma is a rather rare finding. Hypercoagubality associated with Cushing syndrome, cancer thrombi and direct tumor invasion are the pathophysiological mechanisms explaining this finding. The latter hypothesis is the most likely to be the cause of embolism in our case. Albeit, non-secreting adrenal cancer are the most incriminated, our report suggest otherwise.

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EP720

Emerging endocrine complications in cancer immunotherapy

Ruxandra Paula Ristea[1], Teodora Puscas[1], Claudiu Zaharia[1], Serghei Tutovan[1] & Mihaela Stanciu[1,2]
[1]County Clinical Emergency Hospital of Sibiu, Endocrinology, Sibiu, Romania; [2]'Lucian Blaga' University of Sibiu, Faculty of Medicine, Endocrinology, Sibiu, Romania

Introduction
Immune-checkpoint inhibitors (ICIs) have revolutionised cancer treatment, offering superior efficacy compared to traditional chemotherapy. The use of immune checkpoint inhibitors has been associated with the occurrence of multiple endocrine immune-related adverse events (irAEs), such as primary hypothyroidism, thyroiditis, primary adrenal insufficiency, type 1 diabetes mellitus, and hypophysitis. In certain instances, these irAEs may necessitate the discontinuation of treatment.
Case Report
We present a 50-year-old female patient with a history of multinodular goiter and previously treated Graves' disease who was diagnosed with malignant melanoma in 2020. Immune checkpoint blockade therapy was initiated using anti-PD-1 antibodies and anti-CTLA-4. Within 2 months, the patient developed multiple immune-related endocrine complications. Clinical evaluation and laboratory investigations revealed autoimmune thyroiditis with elevated thyroid peroxidase antibodies (TPO), resulting in hypothyroidism requiring levothyroxine substitution (50 mg/day). Additionally, the patient was diagnosed with type 1 diabetes

and autoimmune hepatitis. Subsequently, she presented with symptoms like asthenia, significant weight loss, hypotension, loss of appetite, nausea, and vomiting, leading to the diagnosis of primary adrenal insufficiency. Corticosteroid treatment was initiated.
Conclusions
This case highlights the importance of monitoring patients undergoing immune checkpoint blockade therapy for the emergence of immune-related endocrine complications. Routine assessment of hormone levels and pre-treatment baseline evaluations are crucial for timely intervention. Prompt intervention and appropriate therapeutic approaches successfully controlled the patient's immune-related endocrine adverse events, allowing the continuation of immune checkpoint blockade therapy for melanoma.

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EP721

ACTH-independent cushing's syndrome in a patient with bilateral adrenal tumors: complete remission after unilateral adrenalectomy

Larisa Nicoleta Chetan[1], Andreea Vladan[2], Cretoiu Rebeca[2], Radu Iorgulescu[3], Serban Radian[2,4] & Poiana Catalina[2,4]
[1]C.I. Parhon National Institute of Endocrinology, Pituitary and Neuroendocrine Pathology, Bucureşti, Romania; [2]C.I. Parhon National Institute of Endocrinology, Pituitary and Neuroendocrine Pathology, Bucharest, Romania; [3]Sf. Ioan Clinical Emergency Hospital, Bucureşti, Romania; [4]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania

Introduction
Bilateral adrenal tumors in patients with adrenal Cushing's syndrome (CS) are rare, lending to differential diagnosis which includes bilateral macronodular adrenal disease (BMAD), synchronous adrenal adenomas and even adrenocortical carcinoma. The treatment consists of unilateral adrenalectomy, followed by contralateral adrenalectomy, if warranted by persistent significant CS.
Aim
To present a case highlighting unilateral adrenalectomy as an effective treatment of CS in patients with bilateral adrenal tumors.
Case Report
A 54 year old woman with a history of arterial hypertension, and incidentally discovered bilateral adrenal tumors presented to our clinic with minimal clinical signs of CS. Serum cortisol did not suppress after 1 mg dexamethasone overnight, showing mild autonomous cortisol secretion (cortisolemia 3.8 mg/dl). 24-hour urinary free cortisol showed two increased values, midnight serum cortisolemia was mildly elevated and ACTH was suppressed ($<$ 5 pg/ml). Co-secretion of adrenal androgens was absent and 17 HO-progesteron was low. Aldosteronoma and pheochromocytoma were excluded. Family history was negative for endocrine tumors and biochemical screening for hyperparathyroidism and pituitary disease was negative, making MEN1 syndrome unlikely. Adrenal CT scan demonstrated a large heterogenous right adrenal tumor (6/6.75 cm), with native density $>$10 HU and peripheral calcification and a left adrenal homogeneous macronodule (1.91/2.79 cm) with density $>$10 HU. We tested cortisol response to stimuli, to detect the expression of aberrant adrenal receptors and observed responses to ortostatism and partially to GnRH analog. Right laparoscopic adrenalectomy was performed and while initial pathology reported an adrenal endothelial vascular cyst, the immunohistochemical diagnosis was of adrenal cortical adenoma with cystic-hemorrhagic changes. Basal cortisolemia was normal and ACTH unsuppressed one week postoperatively and we discontinued glucocorticoid replacement. Later testing demonstrated complete cortisol suppression after overnight 1 mg dexamethasone and normal midnight cortisolemia, consistent with CS remission.
Conclusion
Unilateral adrenalectomy was curative for our patient. Interestingly, adrenal function resumed rapidly. Regular follow-up of the left adrenal nodule is mandated.

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EP723

Pericarditis as a presentation of adrenal crisis in non compliante patient with congenital adrenal hyperplasia

Marianna Bystrianska[1], Adrian Bystriansky[2], Marcela Sýkorová[3], Lýdia Opravilová[4], Dušan Kapusta[4] & Ľubomír Skladaný[4]
[1]University Hospital Banska Bystrica, Department of Internal Medicine, Banská Bystrica; [2]Institute of Cardiovascular Disease Banská Bystrica, Department of Arrhythmology, Banská Bystrica, Slovakia; [3]Institute of Cardiovascular Disease Banská Bystrica, Department of Cardiology, Banská Bystrica, Slovakia; [4]University Hospital Banska Bystrica, Department of Internal Medicine, Banská Bystrica, Slovakia

Background
Pericarditis as a presentation of sever adrenal insufficiency (AI) is very rarely documented. We would like to present a rarely case of sever AI whose first clinical presentation was pericarditis with heart failure and cardiac tamponade.
Case presentation
A 35 years old man was hospitalized on Department of Internal Medicine for chest pain, shortness of breath and hypotension. On ECG was documented sinus tachycardia with diffuse ST elevation. Cardio specific enzymes were negative, D-Dimers increased, serum hyponatremia and hyperkalemia. Urgent CT pulmonal angiography ruled out suspected pulmonary embolism and revealed pleural and pericardial effusion. Bedside echocardiography confirmed severe cardiac tamponade. Despite of urgent pericardiocentesis in emergency settings with a total amount of 1,000 ml, hypotension continued without adequate effect od high dose of vasopressors' therapy. The prolonged shock status was based on unmeasured plasmatic concentration of cortisol: 20 nmol/l (185- 624). In addition, we found out that the patient was treated for congenital adrenal insufficiency (CAH) in childhood, unfortunately without compliance for treatment as an adult (12 years did not used glucocorticoids). On abdominal CT scan has been detected bilateral adrenal hyperplasia. In the next 6 months he was repeatedly hospitalized for relapsing pericardial effusion accompanied with shock as well as hepatic and renal failure. The definitive clinical stabilization was achieved after adequate substitution therapy (glucocortiocoids and fludrocortisone). Genetic test confirmed the deficiency of 21 – hydroxylase.
Conclusion
Pericarditis and cardiogenic shock, or prolonged hypotension without vasopressors effects can be sign of unknown adrenal insufficiency. Early diagnosis and urgent treatment with supplementation of glucocorticoids is important to avoid morbidity and mortality.

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EP726

Adrenal vs pituitary hypercortisolism: population characteristics and metabolic complications

Miruna-Viorela Nacu[1], Carmen Sorina Martin[1,2], Ana-Maria Simonescu[3], Anca Sirbu[1,2], Carmen Barbu[1,2], Luminita Cima[1,2], Iulia Stoian[1,2] & Simona Fica[1,2]
[1]"Elias" Hospital, Department of Endocrinology, Diabetes Mellitus, Nutrition and Metabolic Disorders, Bucharest, Romania; [2]'Carol Davila' University of Medicine and Pharmacy, Department of Endocrinology, Diabetes, Nutrition and Metabolic Disorders, Bucharest, Romania; [3]CF 1 'Witting' Hospital, Ophthalmology Department, Bucharest, Romania

Introduction
Cushing's syndrome (CS) is associated with a plethora of metabolic consequences. Current literature regarding the impact of different aetiologies on metabolic complications is scarce, and results are inconsistent. More studies are needed to validate previous findings.
Aim and methods
In order to compare the outcomes of pituitary and adrenal CS, we conducted an observational retrospective study, investigating the medical records of 72 patients diagnosed with CS between 2010-2021. Mean time of follow-up was 5.53$\pm$4.27 years (median 5 years).
Results
We included 35 patients (91.4% females) with pituitary CS and 37 (83.7% females) patients with adrenal CS. Patients with Cushing's disease were diagnosed at a younger age (37.77$\pm$13.04 vs 53.49$\pm$13.33 years, P $<$0.01) and were more likely to present with clinical signs of hypercortisolism, including central obesity, hirsutism, and purple striae (P=0.002). At diagnosis, cortisol levels, evaluated by early morning and midnight serum cortisol, were similar between our groups (p value was 0.61 and 0.07) and there were no statistically significant differences regarding body mass index, systolic and diastolic blood pressure, lipid profile, fasting plasma glucose, glycated haemoglobin and personal history of arterial hypertension, type 2 diabetes, or osteoporosis. Neither lumbar nor femoral bone mineral density and T scores differed between the two aetiologies. Comparing datasets from first admission with their recent counterparts, a significant reduction in systolic blood pressure was found (134.14$\pm$19.29 vs 121.66$\pm$14.87 mmHg, P=0.01) in patients with Cushing's disease, while their diastolic blood pressure was stationary. In patients with adrenal adenoma, this reduction was not significant (140.33$\pm$25.54 vs 132.86$\pm$18.47 mmHg, P=0.06), although the groups were similar in terms of active disease (P=0.176) and use of antihypertensive medication (P=0.722).

Conclusions
In line with previous studies, Cushing's disease is diagnosed at an earlier age and is more frequently associated with clinical signs of hypercortisolism as opposed to adrenal CS, despite similar cortisol levels. Conversely, the impact on glucose, lipid and bone metabolism appears to be comparable in these groups. Systolic blood pressure seems less likely to improve overtime in adrenal vs pituitary Cushing's syndrome.

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EP727

Developing of a clinico-biological score to predict the diagnosis of cushing's syndrome

Ameni Terzi[1], Ibtissem Ouesleti[1], Elyes Kammoun[1], Yesmine Merhbene[1], Meriem Mabrouk[1], Arige Abid[1], Meriem Yazidi[1] & Mélika Chihaoui[1]
[1]Rabta, Endocrinology, Tunis

Introduction
Cushing's syndrome (CS) has relevant morbidity and mortality and poses several diagnostic challenges underlining the need for a prompt diagnosis in order to initiate earlier treatment. The aim of the present study was to develop a new clinical and biological score to predict the diagnosis of CS.
Methods
This was a monocentric retrospective study including patients who were admitted to the Department of Endocrinology of La Rabta Hospital, Tunis for suspicion of CS. Clinical and biological data were collected from medical records. Univariate analysis was conducted to assess CS associated signs.
Results
One hundredtwo patients (69 women and 33 men) were enrolled in this study. Their mean age was 56.6 $\pm$ 14.7 years. The CS's diagnosis was established in 63 patients (62%) and ruled out in 39 patients (38%). Proximal amyotrophy (OR : 9.88, IC95% : 1.2-78.8, $P=0.010$), headache (OR :2.93, IC95% :0.99-8.66, $P=0.045$), sleep disorders (OR = 9.22, IC95% : 2.02-42.06, $P=0.001$), and cortisol level after 1-mg dexamethasone suppression test (DST) $>$ 5µg/dl (OR : 2.5, IC95% : 1.02-6.12, $P=0.042$) were associated with the diagnosis of CS. We developed a new score to predict CS based on four items including proximal amyotrophy (10 points), headache (3 points), sleep disorders (9 points) and cortisol level after DST $>$ 5 µg/dl (2 points). The total score was 24 points. The total score median was 3 (Interquartile interval:0-12) in patients with CS and 0 (Interquartile interval:0-2) in patients without CS ($P<0.001$). This score had an area under the ROC curve of 0.746 (95%-CI: 0.65-0.842, $P<0.001$). A total score $\geq$12 points was positively associated with the diagnosis of CS (OR = 12.9, 95% CI: 1.64-102.01, $P=0.003$). This cut-off had a specificity of 97% but a sensitivity of 25%.
Conclusion
In the present study, we generated a new score to establish the diagnosisof CS. This score was positively associated with the diagnosis of CS with a good specificity but a very low sensitivity.

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EP728

17 alpha hydroxylase deficiency, a case report

Youcef Sellami[1], Khadidja Bessaid[2], Mouna Mezoued[2] & Malha Azzouz[2]
[1]Algeria, EPH bologhine ibn ziri, Alger, Algeria; [2]EPH bologhine Ibn ziri, Endocrinology, Alger, Algeria

Introduction
Congenital adrenal hyperplasia (CAH) due to 17-alpha-hydroxylase deficiency is a very rare form of CAH characterized by glucocorticoid deficiency, hypergonadotropic hypogonadism and hypertension with hypokalemia. It is an autosomal recessive disorder with an estimated incidence of one in 1,000,000 newborns. Over 100 mutations in the CYP17A1 gene have been identified with combined 17-hydroxylase/17,20-lyase deficiency, but in some authentic cases no mutation has been found.
Case report
Our patient was 24 years old, with no specific pathological history, referred to us for investigation of impuberty associated with arterial hypertension. Clinically, the patient presented an impuberty and severe hypertension onset at the age of 17, with no clinical signs of adrenal insufficiency or hyperandrogenism. Biochemical: hypokalemia of around 3 meq/l Hormonal investigation was in favor of hypergonadotropic hypogonadism, E2 : 11.53 pg/ml(12.5-166) FSH : 46.67 Mui/ml(25.8-21.5) LH : 31.28 Mui/ml(1.0-11.4) With 46 XX karyotype. We found primary adrenal insufficiency, CP at 0800 h :19 nmol/l (154-638) vs ACTH:165 pg/ml In this context, 17 hydroxylase deficiency was evoked, confirmed by a DOC: 5015 pg/ml(40-170) Corticosterone: 657 nmol/l (0.8-59) Morphologically, we realized an abdominal scan, which revealed bilateral adrenal nodules measuring 16$\times$14 mm on the left and 14$\times$10 mm on the right, consistent with adrenal adenomas. A genetic study is underway. Therapeutically, we introduced spironolactone at a dose of 75 mg/d. We opted for Hydrocortisone at a dose of 10 mg/d in the evening, as a brake, and gradually introduced estradiol valerate. Various reassessments revealed normalization of blood pressure and kalemia, with satisfactory breast development.
Conclusion
The diagnosis and management of 17-alpha-hydroxylase block is a challenge, given the rarity of this entity. Early diagnosis is very important, enabling appropriate treatment to reduce the severity of disorders and improve quality of life.

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EP729

The cost burden of hospitalisation for adrenal insufficiency patients in the NHS in england

Leonardo Ruiz[1], Beate Ritz[1], Robert Murray[2], Matthew Beckett[3] & Janet Wild[3]
[1]Advanz Pharma, United Kingdom; [2]Leeds General Infirmary, United Kingdom; [3]CSL, United Kingdom

Introduction
Adrenal Insufficiency (AI) is a heterogeneous condition comprising primary, secondary and tertiary disease. Individuals with AI suffer more frequent infections and take longer to recover. Adrenal Crises (ACs), most commonly precipitated by infections, are an acute life-threatening complication with a reported mortality of 6%. ACs are, at least in part, potentially preventable and outcomes are improved by early initiation of high-dose glucocorticoids. Currently, there is a scarcity of information concerning the burden of AI episodes. We therefore utilised 'Hospital Episode Statistics' (HES) data to understand current practices and resources associated with AI patients.
Materials and Methods
The HES dataset contains details of all admissions and outpatient appointments at NHS hospitals in England after translating clinical information into a standardised set of codes. Spells between 1st April 2018 and 31st March 2023, focusing on HES codes E27.1 (Primary AI) [$n=57,125$], E27.2 (Adrenal Crisis) [$n=12,640$] and E27.4 (Other and unspecified AI) [$n=79,965$] were analysed for admissions, length of stay, costs, follow-up, and readmissions.
Results
The data reveal stable admissions for E27.2, reduced E27.1 admissions during COVID-19, and steadily increasing E27.4 admissions. The largest number of patients were coded as E27.4 rising consistently since 2018/2019. Length of stay was between 10 and 18 days and increased for E27.2 by 44% since 2018/19. Patients with primary pneumonia and concomitant AI had a longer mean duration of admission than those without AI; and were more likely to require critical care. Overall, $<$3% of patients were admitted to ICU. The mean cost per hospital stay increased over the analysis period, with the most marked increase being for E27.2 which rose 26% since 2019/20. Average costs in 2022/23 were £4,409 for E27.1; £6,579 for E27.2; and £4,726 for E27.4 Ten percent of patients had more than one non-elective readmission within 12 months of initial admission. Specialist Endocrinology follow-up following admission was low. Centres treating $>$400 episodes a year followed-up between 19% and 30% of patients with primary or secondary AI within 26 weeks. Only 33% of patients admitted with AC in 2022/23 were followed up.
Conclusion
The number of patients admitted to hospital with AI has increased since 2018/19. Costs and length of stay have risen significantly. Patients with AI and concomitant disease are more likely to have longer duration of admission and be re-admitted than those without AI. Follow-up of these patients by endocrinologists appears surprisingly low.

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EP730

11-DOC secreting adrenal lesion as a cause of mineralocorticoid induced hypertension

Lina Alomari[1,2] & David Hughes[1]

[1]University Hospitals Derby & Burton NHS Trust, Department of Endocrinology, United Kingdom; [2]Royal Derby Hospital

Background
It is well recognised that the most frequent cause of mineralocorticoid induced hypertension is primary hyperaldosteronism. Excess 11-deoxycorticosterone (11-DOC), which is a precursor molecule for the production of aldosterone, may in rare cases be the cause of the mineralocorticoid induced hypertension in patients with normal or low aldosterone levels.
Case
We describe a 70 year old female patient with a background of treated breast cancer who was referred to the endocrinology team in 2019 by her GP with a two-year history of mild hypokalaemia with hypertension requiring two antihypertensive agents for blood pressure control. Further assessment in the endocrinology clinic revealed low renin and low aldosterone levels, normal overnight dexamethasone suppression test, normal metadrenalines, testosterone and DHEAS levels. She underwent CT adrenal which showed a 1.6×1.9 cm indeterminate right adrenal mass (HU = 50). MRI adrenal confirmed the presence of a right adrenal mass with restricted diffusion, described as "not a simple adenoma". Spironolactone was added to her antihypertensives and a plan for right adrenalectomy was made. Due to the COVID pandemic pressures, her surgery & follow upwas delayed. A repeat CT adrenal in 2021 showed no change in size of the adrenal lesion. The patient was no longer keen to proceed with surgery and preferred a more conservative management approach. At that point, she had her hormonal profile repeated which again revealed low renin with low aldosterone, A post low dose dexamethasone suppression test revealed that the 11 deoxycorticosterone remaining elevated at 12 nmol/l, mildly elevated cortisol at 99 nmol/l, normal androstenedione and normal 17 OHP. A urine steroid profile confirmed a marked increase corticosterone metabolite compared to cortisol metabolites and hence a diagnosis of DOC secreting adrenal adenoma was confirmed. An FDG PET CT showed low uptake with stability in size over two years suggesting the adenoma was non-cancerous. A PET 11C metomidate scan performed at Cambridge hospital confirmed increased activity in the right adrenal adenoma.
Conclusion
11-DOC is a mineralocorticoid precursor with a weaker effect than aldosterone. While a lesion secreting 11-DOC is rare, It is an important cause to consider in patients with hypertension with suppressed aldosterone and renin levels. Serum 11-DOC level and urine steroid profile are essential to aid diagnosis, but there may also be a role for PET 11C metomidate scan in localisation.

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EP731

Prevalence of metabolic syndrome in non functional adrenal incidentaloma: a case-control study

Sabrina Ayari[1], Nadia Khessairi[1], Sahar Abidi[1], Elyes Kamoun[1], Oueslati Ibtissem[1] & Chihaoui Melika[1]
[1]Rabta Hospital, Endocrinology, Tunisia

Background
The diagnosis of adrenal incidentaloma (AI) is becoming more common with the rising use of radiological tests. Most of AI are nonfunctional adrenal incidentalomas (NFAI) that may produce small amounts of glucorcorticoids that, in consequence, may cause metabolic disorders. Metabolic syndrome being a significant health concern should be evaluated in patients with NFAI. The objective of the study was to assess metabolic syndrome (MS) prevalence and characteristics in NFAI patients according to International Diabetes Federation (IDF) criteria compared to a control group.
Methods
This case-control study included 40 NFAI patients (16 men, 24 women, mean age 52.9 ± 11.2 years) and 40 individuals (17 men, 23 women, mean age 56.8 ± 8 years) in the control group matched for age, sex, and weight. NFAI diagnosis was established according to current guidelines. Patients with mild autonomous cortisol secretion, chronic kidney disease, liver failure or under hypolipidemic drugs, combined contraceptive pills, alcohol or depression, were excluded of this study All participants underwent physical examination (waist circumference (WC), blood pressure), adrenal imaging, and biochemical evaluation including triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), cholesterol total (CT) and fasting plasma glucose (FPG). All participants underwent the assesment of characteristics of the metabolic syndrome according to IDF.
Results
The NFAI group had significantly higher WC ($P < 0.02$), higher obesity ($P = 0.025$) higher fasting plasma glucose ($P = 0.014$), higher score of metabolic syndrome according to IDF (3 (2-3) vs 2 (1-3), $P = 0.076$) and higher prevalence of metabolic syndrome (21 patients (53%) vs 12 patients (30%); $P = 0.041$) compared to the control group. NFAI was positively associated with metabolic syndrome (OR = 2.58; 95% confidence interval (CI): 1.03-6.46; $P = 0.041$). Obesity (OR = 7.29, IC: 1.74-30.56, $P = 0.001$) and female genre (OR = 7.29; IC: 1.74-30.56; $P = 0.004$) were positively correlated to metabolic syndrome in NFAI patients. In multivariate analyses including gender, WC, hypertension and diabetes, NFAI was not a factor independently associated with metabolic syndrome ($P = 0.862$).
Conclusion
NFAI are common and they are associated with adverse metabolic changes. Threshold, NFAI should be considered as an innovative factor for metabolic syndrome.

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EP732

Hypothalamic-pituitary-adrenal axis, type 1b glycogen storage disease & pregnancy

Fotini Pouliasi[1], Ioannis Ilias[2], Vasiliki Papadopoulou[1], Konstantina Barouti[1] & Eftychia Koukkou[1]
[1]Elena Venizelou, Endocrinology, Diabetes and Metabolism, Athina, Greece; [2]Ippokrateio General Hospital of Athens, Endocrinology, Athina, Greece

Introduction
Individuals with glycogen storage disease type 1b (GSD1b) usually have low blood glucose and are at constant risk of hypoglycemia. We recently hospitalized a pregnant woman with GSD1b, where despite nutritional management, her glycemia values were almost unwaveringly towards the lower physiological limits. In a recent study (Rossi *et al*. Orphanet Journal of Rare Diseases 2020; 15: 99, https://doi.org/10.1186/s13023-020-01377-w) it was reported that under resting conditions and after stimulation with corticotropin (ACTH), individuals with GSD1b (n:7) show lower cortisol levels compared to a control group.
Aim
Considering that the stimulus of hypoglycemia is strong for the hypothalamic-pituitary-adrenal (HPA) axis, we investigated the postpartum diurnal variation of salivary cortisol (sF) in a woman with GSD1b.
Methods
Postpartum, in a 35-year-old woman with GSD1b, we assessed the diurnal variation in sF (5 samples per day) for two days, the first week postpartum and after three months. Corresponding sampling was performed in two, age-matched healthy women, 2-4 months postpartum, who formed the control group. The sF determinations were performed using the Elecsys Cortisol II assay (Roche) with electrochemiluminescence. The Sign test was applied for statistical analysis.
Results
The diurnal profile of sF changes was similar in shape for the patient and control group, with a peak at wake-up and nadir at 20:00-midnight. Overall, the patient's early sF measurements were higher than her late ones (*P*:0.03). The patient's late sF measurements were higher than those of the control group on the first day (*P*:0.05). On the second day, the patient's late cortisol awakening response (CAR, sF at 08:00 - sF at 08:30) was marginally lower, compared to the control group (*P*:0.06).
Discussion
The early sF measurements of the GSD1b patient point towards a stimulation of the HPA, however this is also a finding in normal women postpartum, where within a few days after delivery, plasma total and free F values gradually return to pre-pregnancy levels after increasing, especially in the third trimester of pregnancy (Jung *et al* J Clin Endocrinol Metab 2011; 96:1533-1540 & Mistry *et al*. Reproductive Biology and Endocrinology 2015; 13:101). According to our results, in GSD1b, no particular effect of the sustained stimulus of hypoglycemia on HPA is found.

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EP733

Adrenal Insufficiency Detection Challenges in Adult Beta-Thalassemia

Seda Hanife Oguz[1], Alperen Onur İşler[1] & Uğur Unluturk[1]
[1]Hacettepe University School of Medicine, Division of Endocrinology and Metabolism, Department of Internal Medicine, Ankara, Turkey

Background
Adult beta-thalassemia patients experience various endocrine complications associated with iron deposition. However, data regarding adrenal insufficiency (AI) are limited.

Subjects and Methods
A total of 104 beta-thalassemia patients examined between 2015 and 2024 in our outpatient clinic had at least one measurement of morning serum ACTH and cortisol levels. At the time of presentation, two male patients had already been diagnosed with primary AI. Twenty-two additional patients opted for screening with a 250 mg-tetracosactid stimulation test. Among them, 20 tests were performed on 18 patients who agreed to be tested in a median follow-up period of 3 years.
Results
The mean age in the test group was 30.6 ± 6.7 years. Sixteen patients had beta-thalassemia major (5 F, 11 M), while the remaining three had beta-thalassemia intermedia (all F). All patients were transfusion-dependent except the patients with beta-thalassemia intermedia. Three patients showed maximum cortisol responses of less than 18 mg/dl (16.6%). Two of the three patients with inadequate cortisol responses had thalassemia intermedia. Four additional patients had less than 20 mg/dl peak cortisol responses. Only two patients in the test group had ACTH levels higher than twice the upper normal limit at baseline, with peak cortisol responses of 14.8 mg/dl and 20.6 mg/dl, respectively. None of the patients had baseline morning cortisol levels of less than 5 mg/dl, and none exhibited typical symptoms or signs of AI except for mild fatigue. All patients remained asymptomatic during a median of 3-years' follow-up, with no glucocorticoid requirement. The mineralocorticoid axis was evaluated in ten patients: none had low aldosterone levels; however, seven revealed high renin levels. Among these seven, three had peak cortisol responses <18 mg/dl, while the remaining four had responses >20 mg/dl. All patients but one had additional beta-thalassemia-related endocrinopathies, bone metabolism disorders being the most common (84.2%), followed by hypogonadism (73.7%).
Conclusions
Subclinical AI may be more common than overt AI in beta-thalassemia patients. Our findings highlight the difficulty of detecting AI in beta-thalassemia patients, indicating that standard symptoms, signs, and laboratory parameters might be unreliable. The discordance between the pituitary and adrenal glands may further complicate the diagnostic process. Moreover, iron accumulation in the adrenal gland might not involve all regions, but only the glomerulosa region in some patients. Our study proposes the utilization of the 250 mg-tetracosactid stimulation test, as a more accurate method to diagnose adrenal insufficiency in patients with beta-thalassemia, regardless of transfusion dependence and disease severity.

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EP734

Hydrocortisone vs prednisolone for treatment of adrenal insufficiency disease (HYPER-AID Study) – interim results from a single, tertiary care centre

Bianca Maria Leca[1], Puja Thadani[1], Dineesha Dineesha Kumarathunga[1], Vindya Wellala[1], Allan Davasgaium[1], Rojet George[1], Parminder Seehra[1], Rajan Mattu[1] & Harpal S. Randeva[1]
[1]University Hospital Coventry & Warwickshire, Warwickshire Institute for the Study of Diabetes, Endocrinology and Metabolism (WISDEM), United Kingdom

Introduction
Adrenal insufficiency (AI) requires lifelong steroid replacement therapy, traditionally with hydrocortisone (HC), which, taken in divided doses, mimics the normal daytime cortisol profile. Prednisolone, with its longer duration of action, presents a cost-effective, once-daily alternative, yet its comparative efficacy and safety profile in AI management still need to be explored. Therefore, the current study aims to assess the metabolic and cardiovascular outcomes in AI patients transitioning from HC to prednisolone.
Methods
The study was conducted following the protocol for 'Hydrocortisone vs Prednisolone for the Treatment of Adrenal Insufficiency Disease' (HYPER-AID Study), IRAS ID: 234243. Patients diagnosed with AI according to the standard diagnostic criteria, on stable HC replacement (for a minimum of four months), were recruited. Baseline assessments were conducted before switching to prednisolone, and a follow-up visit was scheduled after at least four months on the new regimen. Measurements included anthropometric data, cardiovascular risk factors, glycaemic control markers, and safety profiles. Statistical analysis was performed using SPSS statistics version 29.0, considering $P<0.05$ statistically significant.
Results
Fifteen patients with AI were recruited. Two patients withdrew due to altered mood and fatigue. Of 13 participants, 7 were male (53.8%), with a mean age of 60.69 ± 11.56 years. The majority (92.3%) had secondary AI. The total daily HC dose ranged between 17.5 and 25 mg and was substituted by 3 to 5 mg of prednisolone. Notably, 61.5% of patients were effectively replaced with a 4 mg dose. At follow-up, the mean body mass index (BMI) showed a marginal decrease from 31.56 ± 7.01 kg/m^2 to 30.87 ± 6.97 kg/m^2 ($P=0.016$). Similarly, the waist circumference slightly decreased from 106.11 ± 11.94 cm to 103.26 ± 10.6 cm ($P=0.011$). Furthermore, no marked changes were observed in blood pressure, heart rate, lipid profiles, glycaemic control, serum electrolytes, renal and liver function, or haematological parameters. Interestingly, all participants opted to continue treatment with prednisolone, highlighting a preference potentially linked to the simplified administration regimen.
Conclusion
Switching from HC to prednisolone in patients with AI appears safe and results in minor yet statistically significant reductions in BMI and waist circumference, suggesting possible metabolic benefits. The absence of adverse effects on cardiovascular risk factors further supports prednisolone as a feasible, cost-effective alternative to HC in AI management. Nevertheless, further studies with larger sample sizes are required to validate these findings and assess the long-term treatment implications.

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EP735

Heart failure and its reversibility in patients with cushing's syndrome

Raisa Kosharnaia[1], Zhanna Belaya[1], Elizaveta Mamedova[1], Elena Przhiyalkovskaya[1], Zamira Zuraeva[1], Marina Michurova[1] & Victor Kalashnikov[1]
[1]Endocrinology Research Centre, Moscow, Russian Federation

Myopathy is a common complication of Cushing's syndrome (CS), which predicts the possibility of heart muscle damage and may be a cause of heart failure. Goal of this study is to evaluate the prevalence of heart failure in patients with active CS and the probability of recovery after achieving a remission.
Materials and methods
We enrolled patients with CS hospitalized in our clinic from October 2018 to December 2022. To confirm the diagnosis of CS we measured: late-night salivary cortisol (LNSC) (reference range 0.5-9.65 nmol/l); 24 hours urine free cortisol (reference range 100-379 nmol/day)., midnight serum cortisol levels (reference range 46.0-270.0 nmol/l). All patients underwent clinical investigation including expert echocardiography with speckle tracking and evaluation of N-terminal pro–B-type natriuretic peptide (NT-proBNP) (reference <125 pg/ml Cobas 6000) and Soluble suppression of tumorigenicity 2 (ST2) (reference <35 ng/ml ; Presage ST2 Assay Kit (Critical Diagnostics, USA) at the baseline and 6 months after surgical treatment. In patients with preserved ejection fraction the H2FPEF and HFA-PEFF heart failure diagnostic algorithms were used.
Results
The study included 70 patients with active CS ($n=54$ women, 24h urine cortisol = 1193.5 [690.9; 2034.6] nmol/24h, LNSC 21.57 [13.03; 43.89] nmol/l. The causes of CS were Cushing' disease in 51 patients; Ectopic-ACTH-syndrome in 9 cases and benign cortisol-secreting adrenal adenoma in 10 cases. The diagnosis of heart failure was verified in 46 (65.7%) patients. According to the results of echocardiography, 16 (22%) patients revealed dilation of the left atrium, 3 (4.3%) - left ventricle (LV), 37 (52.9%) patients had LV hypertrophy, 4 patients - decrease of LV ejection fraction (LVEF 40-50%); impaired diastolic function was detected in 37 (52.9%) patients. A decrease in global longitudinal myocardial strain was detected in 28 (39.4%) patients. Remission was confirmed in 52 patients 6 months after surgical treatment. Among 36 re-examined patients with 6 months remission of CS, the heart failure was confirmed in 26 patients, whereas in 16 of them heart failure regressed. The initially elevated NT-proBNP 132.8 [49.2; 444.4] and ST2 31.9 [22.7; 72.6] decreased to 71.8 [13.4; 163.2] $P=0.004$ and 25.9 [19.9; 33.3] $P=0.031$ respectively, supporting the reversibility of heart failure.
Conclusion
CS causes heart muscle damage with the development of heart failure in 65.7% of patients. Achieving CS remission led to regression of heart muscle myopathy in 44.4% of the recorded cases after 6 months of observation, which supports the reversibility of this damage.

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EP736

Polygenic risk score for autoimmune Addison's disease combined with whole-genome sequencing identifies patients with undiagnosed monogenic primary adrenal insufficiency

Maribel Aranda-Guillen[1], Ileana R. Botusan[1,2], Venuja Fernando[1], Ellen Røyrvik[3,4,5], Anette Susanne Bøe Wolff[3,4,6], Stefan Johansson[3,7],

Eystein Sverre Husebye[1,3,4,6], Sophie Bensing[2,8], Olle Kämpe[1,2] & Daniel Eriksson[1,9]
[1]Karolinska Institutet, Center for Molecular Medicine, Department of Medicine, Solna, Stockholm, Sweden; [2]Karolinska University Hospital, Department of Endocrinology, Stockholm, Sweden; [3]University of Bergen, Department of Clinical Science, Bergen, Norway; [4]K.G. Jebsen Center for Autoimmune Disorders, Bergen, Norway; [5]Norwegian Institute of Public Health, Department of Genetics and Bioinformatics, Bergen, Norway; [6]Haukeland University Hospital, Department of Medicine, Bergen, Norway; [7]Haukeland University Hospital, Department of Medical Genetics, Bergen, Norway; [8]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [9]Uppsala University, Department of Immunology, Genetics and Pathology, Uppsala, Sweden

Background
Primary adrenal insufficiency (PAI) is sometimes misdiagnosed as autoimmune Addison's disease (AAD), affecting clinical management and genetic counselling. We tested a polygenic risk score (PRS) for AAD ($PRS14_{AAD}$) as a tool to reevaluate disease etiology and identify patients misdiagnosed with AAD.
Methods
We calculated the $PRS14_{AAD}$ in a cohort of patients diagnosed with AAD but lacking 21-hydroxylase autoantibodies ($n=124$). Patients with low genetic susceptibility to AAD were selected for whole-genome sequencing to detect potential monogenic causes ($n=35$).
Results
Among the 35 patients, monogenic PAI was found in 5 (14%) and suspected in 3 additional cases (9%). Three out of the 5 rediagnosed patients developed the disease in adulthood, indicating late-onset monogenic disease associated with hypomorphic genetic variants.
Conclusion
A PRS for AAD can help identify potential monogenic cases, regardless of the age at diagnosis. Early identification of the underlying cause of PAI enables accurate management and correct genetic counselling

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EP737

Measurement of cortisol in hair using a commercial ELISA

Nico Rauchschwalbe[1], Lucia Maß[1], Elisabeth Schmitter[1], Thomas Neiße[1], Kristin Meyer-Schlinkmann[1] & Michael Doelle[1]
[1]Labor Krone GbR, Bad Salzuflen, Germany

Increased cortisol production (Cushing's syndrome) is a rare disease that is sometimes very difficult to diagnose. Cyclical Cushing's syndrome in particular is a major challenge. In this case of hypercortisolism, which is not always present, longitudinal diagnostic methods are advantageous. In the past, it has already been shown several times that the measurement of cortisol in the scalp hair shows significantly increased values in patients with Cushing's syndrome. However, the measurement of cortisol in hair is not yet widely available. Our aim was therefore to use a commercially available assay for the determination of cortisol in saliva for the determination of cortisol in hair. Our study introduces a cutting-edge method for quantifying cortisol levels in scalp hair through the utilization of an commercially available automated Enzyme-Linked-Immunosorbent Assay (ELISA). For the analysis of cortisol in hair, 25 mg of washed and milled scalp hair were extracted within 3 hours using methanol and ultrasound-assisted extraction. The supernatant was transferred to a glass vial and evaporated to dryness at 50 °C under a constant stream of nitrogen. The dry residue was redissolved in deionized water and vortexed for 30 seconds. Cortisol concentrations were determined using a commercially available cortisol-saliva ELISA from IBL International GmbH. The test protocol was modified for this purpose by reducing the sample volume used and adjusting the calibration points to a range of 40 pg/mg to 600 pg/mg to meet the expected concentrations of cortisol in hair. Processing and analysis were performed on a fully automated ELISA processor (Analyzer 1 from Euroimmun). For further development, individual reference values for healthy individuals, mild autonomous cortisol secretion and Cushing's syndrome still need to be determined. Our study outlines the successful adaptation and optimization of a saliva cortisol measurement protocol for assessing cortisol level in scalp hair. Unlike existing techniques primarily restricted to research applications, we aim for commercial viability of an automated processed protocol, providing an efficient and reproducible means for routine analysis, paving the way for broader applications in clinical and diagnostic setting.

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EP738

Adrenal lesions prevalence and hormonal profiles in a tertiary endocrinology center from romania

Carmen Barbu[1,2], Luana Zuga[2], Suzana Florea[2], Roxana Bunghez[2], Sorina Martin[1,2], Anca Sîrbu[1,2], Luminita Cima[1,2], Alice Albu[1,2], Iulia Stoian[1,2] & Simona Fica[1,2]
[1]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [2]Elias Hospital, Bucharest, Romania

Backround
The increased frequency of performing imaging investigations in the period following the SARS-COV-2 pandemic has led to more frequent identification of adrenal lesions in patients who subsequently required further endocrine evaluation.
Objective
To compare the functional profile of the newly diagnosed lesions vs those coming for follow up over 2023.
Methods
Retrospective observational study aiming all of the patients admitted in our endocrinology department for adrenal lesions evaluation within the 2023 year. Variables such as age, sex, chronic diseases (arterial hypertension, diabetes, dyslipidemia, obesity, osteoporosis), laboratory investigations (adrenal hormones: cortisol, aldosterone, metanephrines, normetanephrines), the results of imagistic investigations used to diagnose the adrenal lesion and the choices of treatment were collected from 160 patients's medical records. Comparisons were made between the newly diagnosed patients (85) and those who had already previous evaluations (75).
Results
160 patients were included with comprehensive evaluation for adrenal lesions in our department over the whole 2023 year: 85 newly diagnosed patients and 75 patients with previous evaluation (diagnosed between 2007-2022) with a majority of women (65/85, and 62/75 respectively), aged between 23 and 80 (mean age 58.8 y). The diagnostics were as follows : unilateral adenoma 53 out of 85 in new cases vs 51 out of 75 in 'old' cases (NS), bilateral adrenal hyperplasia (30/85 in new vs 24/75 in old cases group, NS) and two adrenal carcinomas (both cortisol-secreting, one of them also secreting androgens) only in the newly diagnosed cases. Functional profile was present in 24/85 in new cases vs 28/75 in old cases ($P<0.05$) as following: hypercortisolism 11 out of 24 functional lesions vs 10 out of 27 functional lesions in old cases, subclinical hypercortisolism 3/24 vs 2/27 cases, hyperaldosteronism 7/24 vs 9/27 cases, paraganglioma 5/24 vs 7/27 cases. Sixty of the 85 new cases and 51 of the 75 reevaluated patients were hypertensive. The most frequent management decision was periodic imagistic and hormonal reevaluation. Surgery was recommended in 10 of the new cases and 20 of the cases diagnosed between 2007-2022.
Conclusions
In the newly diagnosed group (over 2023), a functional profile was present in a smaller proportion than in those with previous evaluation. Among new patients, functional lesions were more frequent in men. Out of all 160 patients in the study, there was a correlation between secretor status and lesion distribution. More bilateral adrenal hyperplasias appear secretory than unilateral adenomas, but a larger sample is needed.

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EP739

Surgical management of adrenal masses: experience of a tertiary center

Sara Santos[1], Miguel Saraiva[2], Francisca Marques Puga[2] & Isabel Palma[2]
[1]Instituto Português de Oncologia do Porto, Porto, Portugal; [2]Unidade Local de Saúde de Santo António, Porto, Portugal

Introduction
Adrenal masses (AM) are being increasingly diagnosed but only a small portion will need surgical treatment.
Methods
We retrospectively reviewed patients referred to the Endocrinology Clinic that underwent adrenalectomy between 1996 and 2023.
Results
We included 57 patients. Most AM were diagnosed incidentally (53%) and had a median size of 32 (25) mm. Forty (70%) patients had hormonal hypersecretion (HH): pheocromocytoma (PC) (15; 37%), primary hyperaldosteronism (PHA) (15; 37%), ACTH independent Cushing's syndrome (CS) (6; 15%), mild autonomous cortisol secretion (MACS) (3; 8%) and cortisol and androgens co-secretion (1; 3%). Patients with PC were initially referred to our clinic for incidentaloma (10; 71%), hypertension (HT) (3; 22%) or as a part of screening for a genetic syndrome (1;

7%). Patients with PHA had HT with (7; 54%) or without (6; 46%) hypokalemia. Patients with CS presented with an incidentaloma (4; 67%) or features of hypercortisolism (2; 33%). Reasons for surgery included HH (39; 68%), imaging features not suggestive of benign adenoma (NB) (9; 16%) and others (9; 16%). All masses described as adenoma (23; 40%) on imaging exams had a benign diagnosis after surgery. AM described as NB (21; 37%) were later diagnosed as PC (8; 40%), cortical adenoma (CA) (2; 10%), ganglioneuroma (2; 10%), oncocytic CA (1; 5%), tumor of uncertain malignant potential (1; 5%), myelolipoma (1; 5%), nodular hyperplasia (1; 5%), black adenoma (1; 5%) and infarcted adrenal neoplasia (1; 5%). Two patients (10%) had AM with features suggestive of adrenal carcinoma: 1 was diagnosed with an infarcted cavernous hemangioma, and 1, deemed irresectable. AM with a diagnosis of PC after surgery and an accessible imaging exam (12; 26%) were initially described as NB (8; 67%), PC (3; 25%) or myelolipoma (1; 8%). All patients with PC and CS were biochemically cured after surgery. Of the 15 patients with PHA, 13 (87%) were biochemically cured, with resolution of HT and hypokalemia, when present. Of the remaining 2 (13%), 1 (50%) had an imaging exam describing an adenoma and bilateral hyperplasia, and 1 (50%) had a diagnosis of nodular hyperplasia after surgery.

Conclusions

Imaging exams were accurate in detecting benign lesions. All patients with PHA had relevant clinical manifestations of HH while most patients with PC and CS presented with an incidentaloma. Surgery was effective in most cases and the patients who were not cured likely had bilateral HH.

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EP740

Significance of screening and confirmatory tests in identifying primary hyperaldosteronism among patients investigated for secondary endocrine hypertension

Raluca Bocai[1], Găloiu Simona Andreea[1,2], Trifanescu Raluca Alexandra[1,2], Dana Alice Manda[1] & Catalina Poiana[1,2]
[1]Endocrinology Institute "C.I.Parhon", Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Introduction

Delayed diagnosis of secondary hypertension, notably primary aldosteronism, challenges healthcare. Inconsistent guideline adherence hampers detection rates and diagnostic uniformity, emphasizing the imperative for improved diagnostic strategies in identifying primary hyperaldosteronism. Our study directly addresses this critical gap in clinical care, underscoring the need for enhanced diagnostics in patients undergoing investigation for secondary endocrine hypertension.

Methods

A retrospective study at a Bucharest tertiary center analyzed 83 consecutive medical records between January 2023 and December 2023 during screening for secondary hypertension. Diagnosing primary hyperaldosteronism involved aldosterone-to-renin ratio (ARR) measurements, with confirmatory saline infusion or captopril suppression tests aligned with the 2016 European Society guideline for hyperaldosteronism. Sensitivity, specificity, and predictive values for ARR cutoffs (38, 57, 77 pg/ml/pg/ml) and confirmatory tests were calculated. Receiver operating characteristic (ROC) curve analysis and the area under the curve (AUC) assessed the diagnostic performance.

Results

In the cohort of 83 patients undergoing screening for secondary hypertension, the gender distribution revealed 31 men (37%) and 52 women (63%), with a median age of 45 years. Of these, 24 cases (28.9%) were diagnosed as primary hyperaldosteronism. Additional diagnoses included 1 case (1.2%) of acromegaly, 13 cases (15.6%) of Cushing syndrome, and 4 cases (4.8%) of pheochromocytoma, while the remaining cases tested negative for secondary endocrine hypertension. At ARR cut-off of 38, the study observed a sensitivity of 88%, specificity of 90%, positive predictive value (PPV) of 78%, and negative predictive value (NPV) of 95%. At ARR cut-offs of 57 and 77, sensitivities were 75%, with specificities of 92% and 98%, respectively. The corresponding positive predictive values (PPV) were 78% and 95%, and negative predictive values (NPV) were 90% and 91%, respectively. In the confirmatory phase, 15 patients underwent the saline infusion test, resulting in 9 positive confirmations (sensitivity: 69%, specificity: 100%, PPV: 100%, NPV: 33%). Nine patients underwent the Captopril suppression test, obtaining 5 positive confirmations and 4 negative results, hindering reliable sensitivity and specificity calculations due to the limited sample size. After ROC curve analysis, the optimal cutoff was 37.25, exhibiting the best balance of sensitivity and specificity ($AUC = 0.929$, $P < 0.001$) in our data set.

Conclusion

The identified cutoff value of 37.25 in our study aligns closely with literature findings, affirming its relevance in diagnosing primary hyperaldosteronism. However, to enhance diagnostic accuracy, additional confirmation tests and a larger patient cohort are crucial, ensuring broader clinical validation.

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EP741

Clinical and biochemical data for the diagnosis of endogenous hypercortisolism: the "Cushingomic" approach

Filippo Ceccato[1], Alessandro Bavaresco[1], Eugenio Ragazzi[1], Mattia Barbot[1], Marco Boscaro[1], Daniela Basso[1], Scaroni Carla[1] & Giorgia Antonelli[1]
[1]University of Padova, Italy

Background

The recommended first-line screening tests for Cushing's syndrome (CS) are serum cortisol after 1-mg dexamethasone suppression test (F^{DST}), urinary free cortisol (UFC), and late-night salivary cortisol (LNSC). CS is often diagnosed late: the clinical presentation of endogenous hypercortisolism overlaps with common clinical conditions.

Methods

We analyzed the diagnostic test accuracy of F^{DST}, UFC, and LNSC in patients without CS (263 suspected CS, 319 adrenal incidentaloma, and 33 pituitary incidentaloma) and 40 with CS. Non-parametric multivariate methods (principal component analysis, K-means clustering, random forest, and supervised learning algorithm) were used to compute an integrated analysis among screening tests (sF^{DST}, UFC, LNSC), cortisol-related comorbidities and signs-symptoms of CS.

Findings

The three tests were able to individuate CS, F^{DST} and UFC were slightly superior to LNSC. The threshold of F^{DST} should be adapted to the population considered, especially in adrenal incidentaloma with mild autonomous cortisol secretion. The diagnostic accuracy of UFC and LNSC was independent of the group or high-risk condition considered. Some cortisol-related chief complaints (diabetes, hypertension, and obesity) were more common in patients without CS: the direction of their vectors was not aligned and their correlation with screening tests was poor. A neural network model that combined screening tests and clinical presentation was able to predict the CS diagnosis in the validation cohort with 99% sensitivity, 86% specificity, 99% precision, and 86% accuracy.

Interpretation

Screening tests for CS performed adequately. The presence of cortisol-related comorbidities and mild autonomous cortisol secretion should be interpreted carefully.

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EP742

Cushing's syndrome in a patient with non-hodgkin's lymphoma

Iuliana Ilie[1], Lidia Felicia Mihai[2], Gabriel Lepadat[3] & Madalina Musat[4,5]
[1]Gral Medical Clinic, Endocrinology Department, Bucuresti, Romania; [2]Clinical Hospital Colentina, Hematology Department, Bucureşti, Romania; [3]Clinical Hospital Colentina, Department of Surgery,, Romania; [4]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania; [5]CI Parhon Institute of Endocrinology, Bucuresti, Romania

Endogenous Cushing's syndrome is a rare disease, with an incidence of 0.7–2.4 per million people per year. Adrenal origin is described in approximately 20 percent of all cases. Adrenal lymphoma presenting as adrenal incidentaloma with autonomous cortisol production has recently been described, though this is a rare condition. We report a rare case of adrenal Cushing's syndrome in a patient diagnosed with a low-grade non-Hodgkin's lymphoma. Female patient, age 53, was diagnosed in 2018 with low grade follicular lymphoma (biopsy from a inguinal adenopathy) with no indication of hematological treatment. The patient had multiple CT scans in the follow up of her lymphoma; which revealed a left heterogeneous adrenal mass of 29/32 mm; relatively stable since 2018. Recently she presented to the endocrinology department with a history of progressive weight gain of approx. 10 kg in the last year, hypertension, dyslipidemia, decreased muscle strength and right leg pain with recent swelling; At presentation she had facial plethora, central obesity with a BMI of 36 kg/m^2; moon face, bilateral varicose veins with signs of thrombosis in the right lower leg. Diagnosis of Cushing's syndrome was based on demonstrating hypercortisolism, disturbed circadian rhythms of salivary a cortisol and non-suppressible cortisol by a low dose dexamethasone suppression test (LDST). ACTH and DHEAS levels were low, which confirmed the adrenal origin. CBC was normal and HBA1C was 5.8%. Plasmatic metanephrines and normetanephrines were normal. The venous doppler revealed right saphenous vein thrombosis and the patient was commenced on oral

anticoagulants. Two months later, right laparoscopic adrenalectomy was performed with intra and postoperative glucocorticoid replacement. The pathology report is in progress. Very few cases of lymphoma and Cushing's syndrome are described in literature and some report Cushing's masking the diagnosis of Lymphoma with progression of hematological disease following treatment of Cushing's syndrome. In conclusion, if immunohistochemical analysis for steroidogenesis enzymes expression in neoplastic B-cells will be demonstrated this would require a personalized approach for the succesful management of the patient with Cushing's syndrome.

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EP743

Radiological characteristics of adrenal incidentalomas followed in the endocrinology department

Prince Ismael Mbossa Lembopo[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital, Endocrinology, Diabetology, Metabolic Diseases, and Nutrition, Casablanca

Introduction
Adrenal incidentaloma refers to an adrenal mass discovered incidentally during imaging for another indication, most commonly through a CT scan. The discovery of an adrenal incidentaloma has become frequent with the use of imaging studies. CT scans play a crucial role in characterizing adrenal incidentalomas, allowing for better management. The aim of the study is to determine the contribution of CT scans in exploring adrenal incidentalomas in patients followed in the endocrinology department.
Patients and Methods
A retrospective descriptive and analytical study was conducted, including all patients seen in consultation or hospitalized in the endocrinology department with adrenal incidentalomas over a period of 5 years (2017-2022). Criteria for determining the nature of the adrenal incidentaloma included histology and the absence of size progression after one year of follow-up. CT scan characteristics for the diagnosis of adrenal incidentalomas included size, spontaneous density (SD), absolute washout (AW), and relative washout (RW). Statistical analysis was performed using Excel 2017.
Results
The study included 43 patients, of whom 59% were women, with a mean age of 48 years. All patients underwent endocrine hormonal assays for adrenal incidentalomas. The size of the mass was less than 40mm in 32 patients and greater than or equal to 40mm in 11 patients. Adrenalectomy was performed in 20 patients, and 23 non-operated patients underwent medical follow-up. Histology revealed adenoma in 11 cases, pheochromocytoma in 2 cases, myelolipoma in 3 cases, lymphoma in 2 cases, and adrenal hyperplasia in 1 case. Adenoma was confirmed histologically, and the size did not change after one year of follow-up in non-operated cases, in 92.4% of adrenal incidentalomas with a size <40 mm, SD ≤ 15 HU, RW $\geq 40\%$, and AW $>60\%$.
Conclusions
Characterizing adrenal incidentalomas with CT scans is a crucial step in the management of these incidentalomas.

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EP744

Unlocking the metabolic mysteries: exploring metabolic syndrome in primary aldosteronism

Siddiqa Soomauroo[1], Faten Hadjkacem[1], Abdelmuhaymen Missaoui[1], Souhir Maalej[1], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Primary aldosteronism (PA) is associated with increased prevalence of metabolic disorders such as impaired glucose and lipid metabolism and insulin resistance. Individuals with PA have an increased risk of cardiovascular events. The aim of this study is to determine the characteristics of metabolic syndrome (MS) in patients with PA.
Patients and methods
Retrospective study concerning 40 patients with PA over the period of 10 years from January 2010 to December 2022. The MS was diagnosed according to the worldwide definition of the International Diabetes Federation (IDF).
Findings
The average age of our patients was 55.4 years. There were 16 men and 24 women. Hypertension was present in 39 patients. Severe hypertension was found in 11 cases and resistant hypertension in 4 others. The average Body Mass Index (BMI) was 29.7 kg/m^2. Obesity was documented in 42.5%. It was classified as grade I in the majority of instances. The android distribution was present in 90% of cases. The mean waist circumference (WC) was 102 cm. In terms of lipid profile, dyslipidemia was diagnosed in 30 of our patients, with 7 patients already undergoing treatment. Mixed dyslipidemia was the most common type (35%), followed by isolated low HDL-cholesterol (10%). Among our 40 patients, 16 had diabetes. The exploration of glucose homeostasis diagnosed 9 new cases of impaired glucose tolerance. Metabolic syndrome was present in 82.5% of cases. Among them, 13 patients met all the diagnostic criteria according to the IDF. An analytical study of MS in PA revealed that among anthropometric parameters, only WC was significantly higher in patients with MS ($P=0.005$). Biochemically, triglycerides levels were higher in patients with MS (1.7 vs 0.9 mmol/l; $P=0.002$), while HDL-cholesterol levels were higher in patients without MS (1.1 vs 1.4 mmol/l; $P=0.024$). Bilateral adrenal hyperplasia was the most frequent aetiology of PA among the patients presenting with MS.
Conclusion
Recent studies have shown that MS is more common in hypertensive individuals with PA than in those with essential hypertension. These findings suggest the possibility of aldosterone effects on carbohydrate metabolism through insulin secretion and/or insulin resistance. Indeed, hypokalemia is a factor contributing to decreased insulin production. Additionally, chronic potassium depletion observed in PA is responsible for insulin resistance that persists even after correction of hypokalemia. This implies a direct action of aldosterone on insulin receptors, associated with development of MS.

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EP745

Association of cognitive-behavioral disorders with a 21-hydroxylase deficiency

Hamza Elfekih[1], Nassim Ben Hadj Slama[1], Amira Yanes[1], Taieb ACH[1], Koussay El Euch[1], Yosra Hasni[1] & Molka Chadli Chaieb[1]
[1]University hospital of Farhat Hached, Endocrinology, Soussa, Tunisia

Introduction
Congenital adrenal hyperplasia encompasses a spectrum of autosomal recessive disorders marked by enzymatic deficiencies in cortisol biosynthesis. The prevailing etiology predominantly involves a deficit in 21-hydroxylase. This pathophysiological state gives rise to a myriad of complications, with acute adrenal insufficiency standing out as the most critical. Nevertheless, it is noteworthy that less-explored are the intricacies of additional complications, particularly those pertaining to the psycho-behavioral domain.
Case présentation
We present the case of a 16-year-old female patient who has been under medical surveillance since early childhood due to the discovery of a 21-hydroxylase block, identified in the context of precocious puberty and virilization. The patient, born of consanguineous parentage, has a a twin brother exhibiting cognitive disorders. The diagnosis of 21-hydroxylase block was established based on elevated levels of 17-hydroxyprogesterone at 10.7 ng/ml. Genetic analysis revealed a heterozygous composite mutation Q318X and duplication of exons 1, 3, 4, 6 inherited from the father, along with exon 8 duplication inherited from the mother. Pituitary imaging, however, showed no abnormalities. The patient was subsequently initiated on appropriate replacement therapy. In addition to the endocrine manifestations, she exhibits psychomotor retardation, language disorders, and challenges in socialization. She has also experienced recurrent major depressive episodes, necessitating ongoing psychiatric management.
Discussion
Deficiency in 21-hydroxylase can manifest as either a salt-wasting or a simple virilizing form. Both forms have the potential to result in cognitive impairment. The relationship between hormones and cognition is intricate and lacks a clear definition. The disturbance of the hypothalamic-pituitary- adrenal axis characteristic of congenital adrenal hyperplasia due to 21-hydroxylase deficiency is likely to affect brain development, yet neuroanatomic work is only beginning. Specific learning disabilities have been rarely reported in congenital adrenal hyperplasia. The impact of hormones on cognition is still not clearly defined, but it is postulated that females with this condition have excess prenatal androgen stimulation, which increases the risk for cognitive impairment. Furthermore, numerous studies have reported a high prevalence of anxiety and depressive disorders among patients with congenital adrenal hyperplasia, notably attributed to challenges in gender identity. Elevated levels of corticotropin-releasing hormone have also been documented in various episodes of melancholic depression. Cognitive and psychiatric disorders should be systematically investigated from the initial diagnosis of congenital adrenal hyperplasia.

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EP746

When two rare conditions come together

Francisca Leitão, Ana Quítalo, Maria Carlos Cordeiro & Luísa Raimundo
Hospital Garcia de Orta

Introduction
Deficiency of 11-beta hydroxylase (11-HD) accounts for 5% of the causes of congenital adrenal hyperplasia (CAH), with an incidence of 1:100,000. The classic form phenotype consists in an excess of androgens and mineralocorticoids, which clinically translates into hypertension and hypokalaemia. In boys, there may be an increase in penis size, early adrenarche, increased growth velocity, and advancing bone age.
Clinical case
We present a case of a 31-year-old male diagnosed with HCS due to 11-beta-hydroxylase deficiency. At the age of 4, he presented with early penile development (penis 7 cm long) and pubarche, hypertension, with an increase in bone age of 6 years compared to chronological age. At diagnosis, he had an increase in 11-deoxycorticol, 17-hydroxyprogesterone (OHP), and androgens, with low cortisol. A Synacthen test was carried out highlighting the HCS (at 60 minutes cortisol 8.1 mg/dl). The genetic study confirmed the diagnosis, with a reference to his parents and 2 siblings as carriers. Medicated and symptomatically controlled with prednisolone and fludrocortisone. With a personal history of osteoporosis, generalized anxiety, social phobia, and nocturnal facial paresis followed in Rheumatology, Psychiatry, and Neurology, respectively. Medicated with calcium carbonate, D vitamin, and ibandronic acid. At the age of 23, he started manifesting symptoms of decreased libido, loss of appetite, adynamia, epigastralgia, diarrhea, and significant weight loss (14 kg, more than 10% of his weight). Blood tests showed a decrease in dihydroepiandrostenedione sulphate, free and total testosterone. Also, a decreased follicle-stimulating hormone and luteinizing hormone was noted, highlighting hypogonadotropic hypogonadism. Subclinical hypothyroidism was also diagnosed. An upper gastrointestinal endoscopy was performed due to his gastrointestinal complaints, with no alterations. Finally, a magnetic resonance imaging of the sella was also performed to exclude space-occupying lesions, without alterations, and a scrotal ultrasound scan, also normal. He started supplementation with levothyroxine and testosterone. Later, he was admitted to the psychiatry department for anorexia nervosa, indicating hypogonadotropic hypogonadism secondary to eating disorders.
Conclusions
This case highlights the complexity of the overlap between two extremely rare pathologies: HCS due to 11-HD deficiency and anorexia nervosa in men.

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EP755

Allgrove syndrome: a case report

Ines Mezghani[1], Marrakchi Rim[1], Hadjkacem Faten[2], Boudaya Mariem[1], Jammoussi Kamel[1], Rekik Nabila[2], Abid Mohamed[2] & Turki Mouna[1]
[1]Hedi-Chaker University Hospital, Biochemistry Departement, sfax, Tunisia; [2]Hedi-Chaker University Hospital, Endocrinology Departement, sfax, Tunisia

Introduction
Allgrove syndrome or Triple A (3A) syndrome is a rare autosomal recessive disease characterized by alacrima, esophageal achalasia and adrenocorticotropic hormone-resistant adrenal insufficiency.
Observation
A 3-year-old and 9 months patient, from a consanguineous marriage, consulted for melanoderma, with family history: sisters with an heterozygous mutation of the AAAS gene, two paternal cousins, 5 years and 22 years, followed for autism and profound encephalopathy with epilepsy, respectively. The diagnosis of Allgrove syndrome was based on the association of alacrima confirmed by the Schirmer test, adrenal insufficiency and achalasia following digestive exploration (TOGD and esophageal manometry). The genetic study revealed the IVS14 + 1G > A mutation of the AAAS gene: mutation of intron 14 of the AAAS gene (chromosome 12: 12q13). The child received hydrocortisone and Fludrocortisone. The neurological development was marked by microcephaly at (-3SD), distal wasting with bone deformation (pathological exaggeration of the arch of the foot), facial and bulbar deficiency with a nasal voice. The onset of a growth delay from -0.5 to -2.5 SD, G2 P1 puberty at the age of 14 years 9 months and school failure. The appearance of dysphagia required two esophageal dilations. Macroscopic hematuria appeared at the age of 10 due to calyx microstones.
Conclusions
Allgrove syndrome is a rare, serious and multi-systemic pediatric condition requiring multidisciplinary care and genetic counseling among siblings

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EP759

Clinical profile of patients with adrenal tumors in a tertiary endocrine center in Kathmandu, Nepal

Ansumali Joshi, Srijana Karmacharya, Puspa Dahal & Rama Rana
Kathmandu Diabetes and Thyroid Centre

Adrenal tumors are not uncommon in endocrine practice. We collected retrospective data from our clinical records of our patients with adrenal tumors from 2021 January to 2023 January. There were a total 20 patients; males 10 (50%) and females 10 (50%). Mean age was 47.4 ± 10.65 years and average BMI was 26.57 ± 4.94. Hypertension was seen in 13 patients (65%) and diabetes in 9 patients (45%). Nonfunctioning adrenal adenomas (NFAAs) were seen in 12 patients (60%) and functioning adenomas seen in 8 patients (40%). Among NFAAs, 9 patients (75%) had left sided, 2 patients (16.6%) had right sided and 1 patient (8.3%) had bilateral adrenal adenomas. All NFAAs were detected as incidentalomas. Mean size of NFAA was 21.92 mm (in greatest dimension). Among patients with NFAAs, 1(8.33%) went for surgery and other 11 patients (91.67%) underwent conservative management. Among functioning adrenal adenomas, 7 patients (87.5%) had left sided and 1 patient (12.5%) had right sided adrenal adenoma. All functioning tumors were unilateral. Pheochromocytoma was seen in 2 patients (10% of all adrenal tumors), aldosterone producing tumor (Conn's syndrome) was seen in 3 patients (15% of all adrenal tumors), cortisol secreting tumor (nonACTH dependent Cushing's syndrome) was seen in 3 patients (15% of all adrenal tumors). Mean size of pheochromocytoma tumors was 35.55 mm (in greatest dimension), aldosterone producing tumors was 14.5mm (in greatest dimension) and cortisol secreting tumors was 26.67mm (in greatest dimension). One patient had MEN 2A syndrome (medullary thyroid carcinoma and pheochromocytoma). Of functioning adrenal adenomas, 6 patients (75 %) went for surgery. All the patients underwent laparoscopic surgery. Cure was achieved in all patients who underwent surgery. One patient with an aldosterone producing tumor was managed with medical treatment (spironolactone) and the patient with MEN 2A syndrome had undergone total thyroidectomy for medullary thyroid carcinoma but died before pheochromocytoma surgery could be done.

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EP760

Challenges of endocrine hypertension

Tea Khurodze[1], Sopo Javelidze[2], Ana Pruidze[2] & Vitali Vashakidze[2]
[1]David Tvildiani Medical University, Endocrinology, Tbilisi, Georgia; [2]David Tvildiani Medical University, Tbilisi, Georgia

Background
Endocrine pathologies are a common cause of secondary hypertension. Most patients with primary aldosteronism and primary hyperparathyroidism suffer from hypertension. Although the coexistence of parathyroid adenoma and cones syndrome in the same patient is uncommon, the occurrence of these two adenomas at the same time can have significant implications for the patient's clinical presentation, diagnostic evaluation, and treatment approach.
Case Presentation
A 64-year-old Caucasian female was referred by her cardiologist to our clinic due to uncontrolled hypertension for 10-11 years, dyslipidemia and hypokalemia, case-typified resistant hypertension-related target organ damage symptoms, and a history of cardiovascular events. The patient's medical history is remarkable for lithotripsy due to nephrolithiasis in 2017-2018; In 2019 a coronary bypass was performed. History revealed that she was prescribed ace inhibitor in combination with thiazide diuretic and beta blocker for hypertension, atorvastatin for dyslipidemia. In her family history, none of her first-degree relatives had malignancy, her mother died at 50 years of age due to thromboembolism. On her P/E: BP 140/90 mm/hg pulse 90. The laboratory examinations reported: CBC, Urea, Creatinine, OH-vit-D3, cortisol catecholamine and its metabolites in 24 h urine, sodium, thyroid function tests, ACTH, PRL were normal, Potassium 2.0 mmol/l -L, ionized Calcium 1.7 mmol/l -H, Phosphorus: 0.7 mmol/l -L aldosterone level was measured after normalization of potassium level aldosterone 251,11 pg/ml-H, renin 5.91 pg/ml-L/N renin-Aldosterone ratio 40.34-H, Abdominal MRI revealed 1.6 -2.0 cm right adrenal adenoma. Thyroid ultrasound revealed a 22/14/12 mm hypoechogenic nodule at the lower part of the left lobe and a 16/9/7 mm iso echogenic nodular lesion at the lower posterior part of the right lobe. After biochemical confirmation of hyperparathyroidism technetium -99m sestamibi scintigraphy SPECT- CT confirmed the diagnosis of parathyroid adenoma, the mass was adjoined the lower pole of the left lobe of the thyroid gland. Followed by biopsy malignancy was excluded. Subsequent examinations, including densitometry identified osteoporosis. Based on these findings, a diagnosis of primary hyperparathyroidism associated with

aldosterone-secreting adenoma was made. The patient was provided 50 mg of spironolactone daily, BP and potassium were normalized and the patient was operated for parathyroid adenoma. PTH, Ca, and phosphorus normalized after surgery. Blood pressure is controlled with spironolactone, osteoporosis is treated with denosumab, and in 2-3 months adrenalectomy is planned

Conclusion

In this unique case report, we present the clinical details, diagnostic evaluation, and management approach of a rare case involving the coexistence of an adrenal adenoma and a parathyroid adenoma.

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EP768

Metastatic giant pheochromocytoma and primary hyperparathyroidism: Association or coincidence: about a case report and literature review

Benabdelatif Katia[1], Aicha Lachkhem[1], Abdelkader Yahi[1], Redhouane Longo[2], Ould Kablia Samia[1] & Bensalah Meriem[1]
[1]Endocrinology department, Central Military Hospital, Algiers, Algeria.; [2]Endocrinology department, Regional university Military Hopsital of Oran, Algeria.

Introduction

Pheochromocytomas and paragangliomas (PPGLs) are chromaffin cell tumors that arise from neuroectodermal cells. These tumors are characterized by a very heterogeneous natural history and an unpredictable ability to metastasize. The rate of metastatic disease ranges from lessthan 1% to 79%, depending on tumor site and size, age at diagnosis and genotype.30% are considered to be hereditary. Primary hyperparathyroidism can be associated with PPLGs. We report a case of a metastatic giant pheochromocytoma measuring 15 cm associated to an asymptomatic primary hyperparathyroidism

Case report

64-year-old female, with no significant past medical, family and psychosocial history, admitted for management of a right adrenal lesion measuring 153×100 mm, revealed by deep asthenia, anorexia, weight loss and recurrent *abdominal pain*. Clinical examination reveals an anorexic patient without clinical signs of mineral, androgen or catecholamine tumoral hypersecretion. Screening test for hypertension revealed low blood pressure with a mean of 90/56 mmHg. Biochemical tests revealed a high level of catecholamines (Noradrenaline). Laboratory investigations on three occasions showed a high level on calcium adjusted for albumin (2.67–2.88 mmol/l), parathyroid hormone (102-198 pg/ml) and low phosphor (0.6 mmol/l), which confirm the diagnosis of primary hyperparathyroidism. Neck ultrasound and 99mTc-MIBI scintigraphy revealed a superior right parathyroid adenoma. Morphological exploration revealed a large right adrenal mass measuring 153×100 mm with a suspicious appearance, with liver and lung metastases. MIBG -131 scintigraphy confirms the neuroectodermic tumor of adrenal with pulmonary and hepatic localizations. The patient underwent surgery. The anatomopathological and immunohistochemical study shows an aggressive pheochromocytoma with PASS score 10, expressing synaptophysin and chromogranin A with positive PS100. Unfortunately, she died following surgery.

Conclusion

Metastatic pheochromocytoma and primary hyperparathyroidism are two endocrine entities which can occur in an isolated form or as a part of a syndromic association. The prognosis of metastatic PPGL is heterogeneous, depending on local invasion, associated with a high mortality rate and several complications. Treatments includes medications helping control blood pressure and heart rate, but surgical removal of the tumor is the main curable treatment.

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EP877

Clinical, biological and anatomopathological profile of pheochromocytomas

Marwa El Arem[1], Bilel Ben Amor[1], Ekram Hajji[1], Sana Abid[1], Ines Bayar[1], Héla Marmouch[2], Hanene Sayadi[2] & Inès Khochteli[3]
[1]Hospital Fatouma Bourguiba, endocrinology, Monastir, Tunisia; [2]Hospital Fatouma Bourguiba, endocrinology, Monastir; [3]Hospital Fatouma Bourguiba, endocrinology

Introduction

Pheochromocytoma is a rare tumour of the adrenal medulla. The aim of our work is to describe the clinical, biological and anatomopathological profile of pheochromocytomas.

Material and method

Retrospective descriptive study carried out in the endocrinology department of the Fattouma Bourguiba University Hospital, Monastir, Tunisia.

Results

Analysis of a series of 13 cases found 9 women and 4 men with an average age of 55.3+/-11 years, 12 patients were hypertensive, 46% of whom had paroxysmal hypertension. The circumstances of discovery were mainly suggestive symptoms ($n=8$), an adrenal incidentaloma ($n=4$) and resistant hypertension ($n=1$). The symptoms described were a Menard's triad (61%), abdominal pain (23.7%) and weight loss (15.3%). The nosological setting was NF1 in two cases and VHL syndrome in one case. The topographical diagnosis was made by abdominal MRI ($n=5$), abdominal CT ($n=5$) and MIBG scintigraphy ($n=2$) with an average size of 5 cm. Methoxylated derivatives were elevated in all patients with a majority increase in normetanephrines with an average level 12 times normal.

Conclusion

The clinical presentation of pheochromocytoma is variable. It should be considered in the presence of any adrenal incidentaloma and resistant hypertension and/or associated with hypokalaemia.

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EP905

Assessing the Metabolic profile of young healthcare professionals: a cross-sectional study

Zeineb Rekaya, Samir Mekaouer, Meriem Yazidi, Elyes Kamoun, Nadia Khessairi, Ibtissem Oueslati, Fatma Chaker & Melika Chihaoui
La Rabta university hospital, Endocrinology Department, Tunis, Tunisia

Introduction

The prevalence of metabolic syndrome (MS) is constantly increasing, particularly among young individuals with sedentary professions. Identifying individuals with MS is crucial for implementing personalized interventions to prevent cardiovascular events. Our study aimed to assess the metabolic profile of young and healthy healthcare professionals, considering the specific lifestyle linked with their professional roles.

Methods

This cross-sectional observational study, conducted from August 2022 to October 2023, involved 64 young and healthy hospital-based healthcare workers, aged between 18 and 45 years. Each participant underwent a physical examination to determine anthropometric parameters and blood pressure. A fasting biological sample was collected for the analysis of fasting blood glucose and lipid parameters. The diagnosis of metabolic syndrome followed the criteria established by the International Federation of Diabetes (IDF 2009).

Results

The study participants had a mean age of 29.5±7.1 years, with 57% being women and 43% men. 33.8% were overweight, and 13.3% were obese. Smoking was reported by 21.2% of participants. Regular physical activity was reported by 22.2% of participants. Lipid profile analysis revealed total cholesterol at 4.6 mmol/l [4;4.9], Hdl cholesterol at 1.26 mmol/l [1.02;1.41], Triglycerides at 0.89 mmol/l [0.72;1.277], and Ldl cholesterol at 2.82 mmol/l [2.41;3.23]. Android obesity was present in 13.8% of men and 15% of women. The mean systolic blood pressure was 116.3±9.6 mmHg and the mean diastolic blood pressure was 73.5±7.7 mmHg. 7.4% of participants had high triglyceride levels. HypoHdlemia was noted in 31.6% of women and 40% of men. None had fasting glycemia ≥6 mmol/l. The prevalence of metabolic syndrome among all the study participants was 8.8%, with a distribution of 13.8% in men and 5.1% in women.

Conclusion

Despite their young age, the frequency of metabolic disorders among healthcare workers was high in our study. These findings underscore the need for targeted interventions to prevent metabolic and cardiovascular diseases among healthcare professionals.

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EP915

Adrenal incidentaloma: A case of pheochromocytoma with sub-clinical Cushing's syndrome

Sana Rafi[1], Meryam Alahyane, El Mghari Ghizlane & El Ansari Nawal
Mohammed VI university hospital of Marrakesh, Department of Endocrinology, Diabetes, Metabolic diseases and Nutrition, Marrakesh, Morocco

Background
An adrenal incidentaloma (AI) is defined as an adrenal lesion that is discovered when a radiological study is performed for indications other than suspected adrenal disease. All patients with an AI should be evaluated for endocrine adrenal functioning and malignancy potential features. A combination of pheochromocytoma and Cushing's syndrome in same adrenal gland is extremely rare. We report a case of AI with the evidence of both pheochromocytoma and sub-clinical Cushing's syndrome.
Case report
A 68 year old female patient presented with an acute respiratory SARS-CoV2 infection. To stratify severity and disease extension, a Computed tomography was performed revealing chest ground-glass opacities, as well as a Right adrenal mass measuring 27×26×25 mm, a spontaneous density of 33UH, Absolute Wash out >50%. Left adrenal gland was normal; Without any clinical symptoms or biological hormonal findings suggesting of a functioning adrenal tumor. On endocrine evaluation a year later, the patient remains asymptomatic, however the laboratory data demonstrated 4 times raised 24-h urinary fractionated metanephrines with non-suppressible serum cortisol after 1 mg dexamethasone suppression test. She underwent right-sided adrenalectomy. The Anatomopathologic report confirmed a pheochromocytoma with a pass score at 3; a proliferative KI index of 5%; staining positive for chromogranin and synaptophysin. The Patient was discharged in good clinical condition.
Discussion
There are few case reports suggesting the different etiologies for this association, namely, pheochromocytoma secreting adrenocorticotropin hormone (ACTH) or its precursors, corticomedullary mixed tumors and focal adrenocortical hyperplasia. Pheochromocytoma may secrete various substances in addition to catecholamines. There are few cases reported of Cushing's syndrome due to ACTH-secreting pheochromocytoma. In some of them, there was predominance of hyperpigmentation, hypokalemic alkalosis and evidence of contralateral adrenal gland hyperplasia on imaging, but these features were absent in our case. Mixed tumors involving the cortical and medullary components of the adrenal gland are quite rare. On histochemical staining, patient's tumor was not a corticomedullary mixed tumor, but a pure pheochromocytoma. In some cases adrenocortical hyperplasia resulting from the pheochromocytoma's paracrine stimuli was the source of autonomous cortisol production. As we do not have plasma ACTH levels, this hypothesis could not be completely ruled out.
Conclusions
The clinical aspects of this case suggest the importance of proper pre-operative recognition of the dual hormone secretion from adrenal mass, which, if goes unnoticed could lead to adrenal or hypertensive crisis in perioperative period.

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EP916

Value of low-dose short synacthen test (1μg) vs high-dose synacthen test (250 μg) for assessment of the adrenal axis

Anastasia Patricia Stanescu-Smocot[1], Vlad George Radulescu[2], Cristina Stancu[2], Dana Manda[2] & Corin Badiu[2]
[1]C.I. Parhon National Institute of Endocrinology, Clinical Endocrinology IV, Bucureşti, Romania; [2]C.I. Parhon National Institute of Endocrinology, Bucureşti, Romania

Introduction
Assessment of adrenal insufficiency (AI) is done routinely through Synacthen test. However, the conventional high dose (250 μg) stimulation is supra-physiological, therefore 1 μg low dose test was developed.
Aim
to investigate the utility of the Low-dose test vs the High-dose test, in patients with suspected central AI, in a tertiary centre of endocrinology, in the National Institute of Endocrinology, Bucharest, Romania.
Material and methods
We performed a retrospective study spanning the period from 2019 to 2023. This study focused on patients presenting diverse disorders leading to central AI. The aetiology was: pituitary adenomas ($n=35$), basal or postsugery, adrenal Cushing after surgery ($n=31$), congenital hypopituitarism ($n=11$), patients previously on corticosteroids ($n=10$), after stopping the GC treatment and oncologic patients under immunotherapy ($n=9$). After basal sampling between 8-10 AM, a dose of synthetic ACTH (Synacthene) was injected iv, 250 μg for high dose and 1 μg for low dose test. Cortisol was sampled at 30 and 60 min.
Results
Among the participants ($n=117$), 36.8 % were male and 63.2 % were female. Complete recovery is considered if serum cortisol levels after stimulation rises over a minimum of 18 μg/dl (12-18 μg/dl is considered incomplete response, values lower than 12 μg/dl is considered diagnostic for AI). Out of the 117 patients 23 (31.9%) were found to have AI in Low-dose testing (cortisol 0' = 6.78 mg/dl ± 4.2, T1 = 16.19 mg/dl ± 8.5, T2 = 16.09 ± 9.04) vs. 4 (cortisol 0' = 11.92 mg/dl ± 6.19, T1 = 31.76 ± 12.45, T2 = 27.46 ± 13.07) (3.3%) in the High-dose test therefore, they required ongoing treatment. Subclinical AI with incomplete response was present in 14 patients, requiring treatment in stress conditions. Among all patients in the low-dose test 10 (13.9 %), respectively 16 (35.6%) in the high-dose test achieved normal adrenal function.
Conclusion
Low dose Synachtene revealed more cases of AI, who required substitution treatment. The findings highlight the need for further research to optimize treatment strategies and improve outcomes for individuals with central hypocorticism.

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EP917

Evaluation of late-night salivary cortisol diagnostic accuracy for Cushing's syndrome in the clinical setting

Daniela Dadej, Ewelina Szczepanek-Parulska & Marek Ruchała
Poznan University of Medical Sciences, Department of Endocrinology, Metabolism and Internal Medcine, Poznań, Poland

Introduction
The diagnosis of Cushing's syndrome (CS) is often challenging and requires the use of several diagnostic methods. Late-night salivary cortisol (LNSC) offers an easy, non-invasive screening method for CS. However, its availability is still limited and the cut-off values vary widely between laboratories. The aim of this study was to assess the diagnostic value of LNSC for CS in comparison with late-night serum cortisol (LNSerC) and 24-hour urinary free cortisol (UFC). We also aimed to verify the accuracy of manufacturer-provided cut-off value for LNSC.
Methods
Patients with suspected CS hospitalized in our department were retrospectively reviewed. Saliva was collected at 11 p.m. using a Salivette. At the same time blood samples for the determination of serum cortisol were obtained. Additionally, 24-hour urine collection for free cortisol assessment was performed. Salivary cortisol was determined using automated electrochemiluminescence assay - Elecsys Cortisol II (Roche Diagnostics). Upper reference limit for LNSC provided by the manufacturer was 11,3 nmol/l.
Results
A total of 69 patients were included in the study. 19 patients were diagnosed with endogenous CS (pituitary: 10, ectopic: 2, adrenal: 7), among them 2 were already treated and presented normal cortisol values. CS was excluded in the remaining 50 patients. 86% of the cohort were women. The mean age was 45,9, and mean BMI was 29.9 kg/m^2. Obesity was present in 40% of patients. Cortisol concentrations assessed with all analysed methods were significantly higher in patients with active CS compared to patients in whom CS was excluded: salivary cortisol (15 nmol/l vs 2.985 nmol/l, $P<0.001$), serum cortisol (523 nmol/l vs 170 nmol/l, $P<0.001$), and UFC (594.5 nmol/24 h vs 130 nmol/24 h, $P<0.001$). LNSC was not related to sex, BMI, smoking status or oral contraceptive (OC) use (however only 4 patients were using OC). Significant correlations between LNSC and LNSerC ($P<0.001$; $r=0.832$), and UFC ($P<0.001$; $r=0.526$) were identified. ROC curves comparison demonstrated no superiority of any of the analysed methods in the diagnosis of CS (LNSC vs LNSerC $P=0.905$; LNSC vs UFC $P=0.619$; LNSerC vs UFC $P=0.623$). AUC for LNSC was: 0.93043, $P<0.001$, for LNSerC: 0.933258, $P<0.001$, and for UFC: 0.901563, $P<0.001$. The cut-off point 11.3 nmol/l for LNSC provided sensitivity of 88.24% and specificity of 88.46%.
Conclusions
LNSC is a valuable method in the diagnosis of CS providing the accuracy comparable to LNSerC and UFC. Cut-off value provided by the manufacturer offers high accuracy in the diagnosis of CS.

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EP918

Identification of risk factors and indications for performing an ACTH-Test in cases of suspected adrenal insufficiency

Janine-Marie Eggers[1], Catharina Bullmann[2] & Birgit Harbeck[1]
[1]University Medical Center Hamburg-Eppendorf, III. Department of Medicine, Hamburg, Germany; [2]MVZ Amedes Experts, Endocrinology, Hamburg, Germany

Introduction
Adrenal insufficiency can result in a life-threatening situation if undetected. This pathology is diagnosed by performing an ACTH-Test. Most symptoms like fatigue, loss of weight or arthralgia are rather unspecific. Therefore it is difficult to assess which patients really need an ACTH-Test. Aim of this study was to identify risk factors and indications in order to specify which patients actually require it.
Material and methods
324 patients who received an ACTH-Test from 14th October 2011 to 2nd December 2022 were included. They were compared in terms of gender, age, BMI, blood pressure, symptoms, diagnoses, glucocorticoid medication, laboratory parameters and reasons for testing. A test result was considered as pathological if the basal cortisol level had not increased by at least 100% or >150 ng/ml after 60 minutes despite stimulation with Synacthen. Statistical analysis were executed by using SPSS.
Results
262 of the included patients were female, 61 were male and 1 was transsexual. 87 patients had a pathological test result by definition. No patient with a previously diagnosed hyponatremia had a pathological test result. There was also no significant difference between the test groups for a low sodium value in the laboratory (9.2% (pathological) vs. 8.4% (normal), $P=0.807$). Statistically significant risk factors were myalgia ($P=0.014$), an adrenalectomy ($P=0.014$) and the oral intake of a cortisone-containing drug at time of the test ($P=0.010$), especially of prednisolone ($P=0.029$) and hydrocortisone ($P=0.023$). Statistically significant indications were an elevated ACTH value ($P=0.002$) and a borderline to low cortisol value ($P=0.012$) in the routine laboratory. It was also useful to carry out the test while discontinuing or tapering off hydrocortisone substitution ($P=0.047$).
Conclusions
The patient's symptoms or clinical situation as the only reason for performing an ACTH-Test seems to be too unspecific. Other risk factors or indications like corresponding aberrances in the laboratory parameters should be taken into account.

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EP919

Primary unilateral macronodular adrenal hyperplasia with concomitant glucocorticoid and androgen excess and KDM1A inactivation

Yasir Elhassan[1], Silke Appenzeller[2], Laura-Sophie Landwehr[2], Juliane Lippert[2], Dillon Popat[3], Lorna C. Gilligan[1], Lida Abdi[3], Edwina Goh[1], Salvador Diaz-Cano[1], Stefan Kircher[2], Susanne Gramlich[2], Robert Sutcliffe[1], Shakila Thangaratinam[1], Li Chan[3], Martin Fassnacht[2], Wiebke Arlt[3] & Cristina L Ronchi[1]
[1]Birmingham, Birmingham, United Kingdom; [2]Würzburg, Würzburg, Germany; [3]London, London, United Kingdom

Background
Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a rare cause of Cushing's syndrome. Primary unilateral macronodular adrenal hyperplasia with concomitant glucocorticoid and androgen excess has never been studied before.
Methods
We investigated a woman with a large, heterogeneous 7 cm adrenal mass (with a radiologically normal contralateral adrenal) and adrenocorticotropic hormone (ACTH)-independent glucocorticoid and androgen excess, a presentation typically suggestive of adrenocortical carcinoma. We undertook detailed histopathological examination in addition to a comprehensive molecular analysis of the resected adrenal mass as well as of the patient and the parent's leukocyte DNA.
Findings
Histopathological examination revealed macronodular adrenal hyperplasia without evidence of malignancy. Interval imaging 24 months after surgery persistently showed normal contralateral adrenal gland. At whole-exome sequencing of four representative nodules, we detected inactivating germline variants p.G46S and p.R269Dfs*7 in *KDM1A*; inactivating *KDM1A* variants have been described in 90% of PBMAH associated with ectopic expression of the gastric inhibitory polypeptide receptor (GIPR) leading to food-dependent Cushing syndrome. Copy number variation analysis demonstrated an additional somatic loss of the *KDM1A* wild-type allele on chromosome 1p36.12 in all nodules. RNA-sequencing on a representative nodule showed low/absent expression of *KDM1A* and a high expression of *GIPR* compared to an available dataset of 52 unilateral sporadic adenomas and 4 normal adrenal glands. Sanger sequencing confirmed germline *KDMIA* p.R269Dfs*7 variant in the father and *KDM1A* p.G46S variant in the mother. Clinical assessment of the parents showed no features of glucocorticoid or androgen excess.
Conclusion
We investigated the first case of primary unilateral macronodular adrenocortical hyperplasia (PUMAH) associated with severe Cushing's syndrome and concomitant androgen excess and suggest pathogenic mechanisms involving *KDM1A*, but without features of food-dependent Cushing's syndrome.

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EP920

Adrenal lesions do matter in the course of primary aldosteronism: a comparative analysis of Conn's adenoma vs bilateral adrenal hyperplasia

Siddiqa Soomauroo[1], Faten Hadjkacem[1], Ahmad Ridwaan Auckburally[2], Abdelmuhaymen Missaoui[1], Souhir Maalej[1], Wiem Feki[2], Zeinab Mnif[2], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Radiology, Sfax, Tunisia

Introduction
Primary aldosteronism (PA) is commonly identified as the main cause of secondary hypertension. It is becoming increasingly wide-spread, affecting between 1 and 30% of people suffering from hypertension. We aim to determine the different characteristics between aldosterone-producing adenoma (APA) and bilateral adrenal hyperplasia (BAH).
Patients and methods
Retrospective descriptive and analytical study concerning 40 patients with PA, collected inthe endocrinology department of the Hedi Chaker University Hospital of Sfax, over the period of 10 years from January 2010 to December 2022. In an endeavour to determine the distinct characteristics of the 2 main aetiologies, we defined 2 groups: the first group APA ($n=17$) and the second group BAH ($n=20$).
Findings
The mean age of our patients was 55.4 years old. The aetiology of PA was dominated by BAH in 20 cases. The sex ratio (M/F) in the group APA was 0.55 whereas in the group BAH, the sex ratio was 1. Statistical analysis between these two groups revealed no significant differences in epidemiological and clinical data, with the exception of asthenia, which was more prominent in the BAH group, with a significant difference (75% vs. 41.2%; $P=0.037$), and fasting blood glucose was significantly higher in the BAH group than in the APA group ($P=0.018$). In terms of hormonal profile, serum aldosterone and renin levels, as well as aldosterone to renin ratio (ARR) were higher in the APA group, but the difference did not reach statistical significance for these parameters. We found no significant difference in the incidence of metabolic syndrome between the 2 groups (APA = 82.4% vs BAH = 80%).
Conclusion
APA is generally observed in individuals between the third and fifth decade of life. The symptoms associated with this entity are generally more severe, with higher blood pressure levels and more pronounced hypokalemia compared with other forms of PA.

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EP923

Adrenoleucodistrofia ligada al cromosoma X con genética atípica

Rocio Dominguez Rabadan[1], Rossana Manzanares Cordova[2] & Luna Florencio Ojeda[2]
[1]Hospital Juan Ramón Jiménez, Endocrinology, Huelva; [2]Hospital Universitario Juan Ramón Jiménez, Endocrinology, Huelva, Spain

Background
X-linked adrenoleukodystrophy (X-ALD) is a hereditary disease that occurs in boys in childhood and adolescence, with cases being rarer in adulthood. Primary

adrenal insufficiency (PSI) is present in more than 50% of patients and in 10% it is the only manifestation
Case report
24-year-old male, diagnosed with primary adrenal insufficiency as a child. The pathological history included dyslipidemia, obesity, prediabetes and parietospastic gait as possible involvement of the 1st motor neuron. Family history of the index case: Maternal family without any living male, mother had 5 brothers, males who died from vomiting, hyperpigmentation, dehydration. When reviewing his medical history, the etiology of PSI was not identified, so additional tests were requested. Anti-21 hydroxylase (anti-21OH) antibodies were negative and abdominal CT showed a mildly hypoplastic right adrenal gland. Given the negativity of these 2 tests in a man with neurological involvement and a family history, genetic etiology was suspected and very long chain fatty acids (LCGML) in plasma were requested: still pending. The genetic study demonstrated the ABCD1 gene mutation (NM_000033.4). Identified variant: c.355G>C (pAla119Pro). This variant is classified as probably pathogenic because: it is located in a gene where missense-type variants are usually pathogenic; and is described in the ClinVar database (ID: 585356) as a variant of uncertain clinical significance. As of the date of issuance of this report, it has not been described in the scientific literature consulted

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EP929

Angiomyolipoma of right adrenal gland

Mariyah Ahmed[1], Sheeba Shaikh[2], Aziz Gulamhusein[3], Pedro Oliveira[4] & Safwaan Adam[2,5]
[1]The Christie Hospital, Department of Endocrinology, Manchester, United Kingdom; [2]The Christie Hospital, Department of Endocrinology, Manchester, United Kingdom; [3]The Christie Hospital, Department of Urological Surgery, Manchester, United Kingdom; [4]The Christie Hospital, Department of Pathology, Manchester, United Kingdom; [5]The University of Manchester, Faculty of Biology, Medicine and Health, Manchester, United Kingdom

We describe the case of a 52-year-old female, with a body mass index of 32 kg/m^2 and without significant co-morbid illness who initially presented acutely, with self-resolving abdominal pain. During that admission, an abdominal computed tomography (CT) scan demonstrated a right-sided heterogeneous and contrast enhancing adrenal mass (measuring 59×41 mm) with a 15 mm focus of cystic degeneration. Based on the scan appearances, the patient was suspected as having a phaeochromocytoma and referred to our centre. She did not report any symptoms of catecholamine excess however was found to be hypertensive. Initial blood test screening revealed a diagnosis of type 2 diabetes mellitus (glycated haemoglobin 55 mmol/mol). She underwent biochemical screening for adrenal hormone excess with normal values of plasma metanephrines (<38 pmol/l [0-510]), normetanephrines (233 pmol/l [0-1180]), 3-methoxytyramine (<75 pmol/l [0-180]), aldosterone (161 pmol/l with an aldosterone to renin ratio of 146) and a normal post-overnight dexamethasone suppression test cortisol (<50 nmol/l). On the basis of initial investigations, the patient was worked up for the possibility of a 'non-functioning' phaeochromocytoma and underwent functional imaging with positron emission tomography (PET) scans; she initially underwent a fluorodeoxyglucose (FDG) and then a gallium^{68} dotatoc PET scan. Both PET scans showed moderate-to-high intensity localised tracer uptake and consequently the patient was diagnosed as having a non-functioning phaeochromocytoma. Her hypertension was managed with doxazosin which was uptitrated to achieve consistent normotension. She underwent a right-sided robot-assisted laparoscopic adrenalectomy with an uneventful post operative course. A short synacthen test performed a week after surgery was normal with a peak cortisol of 780 nmol/l (>450). Postoperative histopathology and immunohistochemistry demonstrated features consistent with an epithelioid angiomyolipoma of the adrenal gland, without any evidence of necrosis, mitotic activity or vascular invasion. There was strong positivity for Cathepsin K and alpha smooth muscle actin (SMA) and negativity for Human Melanoma Black 45 (HMB45). Cytokeratins, neuroendocrine markers, CD34 and signal transducer and activator of transcription 6 (STAT6) were also negative. The Ki67 was less than 1%. Our case demonstrates a rare and unusual benign adrenal tumour type which had the preoperative radiological appearances of a phaeochromocytoma. Angiomyolipomas (AMLs) usually consist of smooth muscle cells, adipose tissue, and thick-walled blood vessels and are commonly found in the kidneys. Extrarenal AMLs are rare with the liver being the commonest site. There have been less than 30 cases reported in the English literature for adrenal AML.

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EP930

Silent yet aggressive: a case of large adrenocortical carcinoma with asymptomatic hypercortisolism

Robu Larisa, Ilona Beatrice Blesneac, Otilia Tarcau, Anca Matei, Laura Teodoriu, Alexandru Florescu & Cristina Preda
Saint Spiridon County Hospital, Iasi, Romania

Introduction
Adrenocortical carcinoma (ACC) is a rare endocrine malignancy arising from the adrenal cortex often with unexpected biological behavior. It can occur at any age, with two peaks of incidence: in the first and between fifth and seventh decades of life. Although ACC are mostly hormonally active, precursors and metabolites may be also produced by dedifferentiated and immature malignant cells.
Case report
We report a rare and challenging case of adrenocortical carcinoma (ACC) in a 40-year-old male with no previous pathological history, presenting with severe abdominal pain, significant weight loss, and hypercortisolism. The patient was admitted to the Endocrinology Clinic for evaluation of an adrenal mass, initially suspected to be an adrenal hematoma of approximately 6 cm based on abdominal CT findings. Clinical examination revealed pale skin, minimal adipose tissue, and a large, hard, painful mass in the right flank. Hormonal evaluation confirmed hypercortisolism, indicated by increased cortisol levels (CLU at 590 mg/dl), a lack of suppression with 1 mg dexamethasone, and only partial suppression with a high-dose dexamethasone test. Notably, DHEAS levels were markedly elevated (>1000 mg/dl), along with increased 17-OH-Progesterone, whereas urinary metanephrines remained normal. The patient also exhibited hypogonadotropic hypogonadism, likely secondary to hypercortisolism. Further imaging with an abdominal CT scan revealed a large retroperitoneal mass centered at the right adrenal lodge, measuring 149/118/168 mm. This mass had heterogeneous components, showing no clear demarcation from adjacent vital structures including the liver, kidney, and inferior vena cava, and exerting a mass effect. Multiple nodular lesions in the right hepatic lobe suggested metastases. A biopsy from the adrenal mass confirmed the diagnosis of adrenocortical carcinoma with a high Ki67 proliferation index of 70-80%. Given the tumor's extensive size, mass effect, and evidence of hepatic metastases, surgical intervention was deemed unfeasible – stage IV. The patient was commenced on Mitotane and protocol-based chemotherapy.
Conclusions
This case of adrenocortical carcinoma exemplifies the unique and complex nature of this malignancy, particularly in its long-term evolution without overt clinical signs of hypercortisolism. Despite the absence of initial symptoms typically associated with hypercortisolism, the patient's condition rapidly deteriorated, underlining the unpredictable and aggressive course of ACC. The long asymptomatic progression of ACC in this patient raises important questions about the underlying mechanisms of tumor growth and hormonal activity, suggesting a potential area for further investigation in the field of endocrine oncology.

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EP974

The 1-mg overnight low-dose dexamethasone suppression test cut-off in establishing the diagnosis of Cushing's syndrome

Amani Terzi, Ibtissem Oueslati, Yasmine Merhbène, Elyes Kamoun, Cyrine Chehaider, Meriem Yazidi & Melika Chihaoui
La Rabta University Hospital, Department of Endocrinology, Tunisia

Introduction
The 1-mg overnight low-dose dexamethasone suppression test (DST) has been used to screen for mild autonomous cortisol secretion and Cushing's syndrome (CS). The aim of the present study was to determine the DST discriminatory threshold confirming the diagnosis of CS.
Methods
This was a monocentric retrospective study including patients who were admitted to the Department of Endocrinology of La Rabta Hospital, Tunis between 2014 and 2023 for suspicion of CS. All patients underwent 1-mg DST followed by the 4-mg DST. A serum cortisol level <1.8 µg/dl at 08h after DST exclude the diagnosis of CS.
Results
One hundred two patients (69 women and 33 men) were enrolled in this study. Their mean age was 56.6 ± 14.7 years. The diagnosis of CS was confirmed in 63 patients (62%) and ruled out in 39 patients (38%). The mean serum cortisol level after the 1-mg DST was 7.4 ± 6.9 µg/dl in patients with CS and 4.4 ± 4.7 µg/dl in those without CS ($P=0.019$). It was 10.1 ± 8.8 µg/dl in patients with CS clinical features and 4.4 ± 3.3 µg/dl in patients without CS clinical features ($P<$

0.001). The area under the ROC curve of serum cortisol level after the 1- mg DST was 0.726 ($P<0.00$). A cut-off value of 1.8 μg/dl had a sensitivity of 100% and a specificity of 10%. A cut-off value of 10 μg/dl was associated with the diagnosis of Cushing syndrome (Odds Ratio = 4.5, $P=0.034$) with a specificity of 95%. A cut-off value of 24 μg/dl confirmed the diagnosis of CS in 100% of cases.
Conclusion
This study provides evidence that with a higher cutoff for serum cortisol level as 24 μg/dl, the 1-mg DST establishes the diagnosis of CS without the need for other tests.

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EP978

A middle aged man presented with hypertension and adrenal incidentaloma diagnosed with pheochromocytoma

Mohammad Salah Uddin & Fathi Abourawi
Diana princess of Wales hospital, Endocrinology, Grimsby, United Kingdom

Pheochromocytomas are rare tumors located in the adrenal medulla, that derive from the chromaffin cells and produce catecholamines. They are an uncommon cause of hypertension, and only 50% of the patients present symptoms compatible with this pathology. Here we describe the case of a 67-year-old man who was referred with h/o mild headache, hypertension and adrenal incidentaloma detected by CT abdomen and pelvis which showed 4.5 cm indeterminate nodule in the left adrenal gland. PMH includes T2DM, prostate cancer treated with radical prostatectomy and salvage radiotherapy. His BP was 177/100 mmhg in the clinic and other systemic examinations were unremarkable, no palpable mass was found in neck or abdomen. There was no family history of any adrenal, thyroid, parathyroid or pituitary gland problem. Subsequently, MRI scan of adrenal gland showed 5.5 cm indeterminate nodule in left adrenal gland though in-phase/out-phase sequence couldn't be done. Laboratory studies revealed an elevated plasma non metanephrine of 10,506 pmol/l (normal limit up to 1180), plasma metanephrine level was 272 pmol/l (normal limit up to 272), plasma 3-methoxytyramine was 211 pmol/l (normal limit up to 180). Other blood tests including overnight dexamethasone suppression test, plasma aldosterone and renin ratio, serum calcium, TSH, urea and electrolytes, PSA were in acceptable normal limit. A diagnosis of pheochromocytoma was made and the patient was started on phenoxybenzamine to control his blood pressure with the aim of adding betablocker subsequently. The case has been discussed in adrenal MDT and decided for left sided adrenalectomy after discussion with the patient. He is currently waiting for the left adrenalectomy. This case highlights the importance of having a high index of suspicion to diagnose this rare tumor presented with very subtle clinical findings and adrenal incidentaloma on imaging. Early diagnosis and subsequent interventions with surgery and antihypertensive medications can reduce morbidity and mortality.

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EP979

Pheochromocytoma with an atypical presentation

Ilir Gjermeni, Irida Kecaj, Ediola Hysa & Ergita Nelaj
University Hospital Center "Mother Teresa", Internal Medicine, Tirana, Albania

Introduction
Pheochromocytoma is a rare tumor of adrenal gland tissue. It results in the release of too much epinephrine and norepinephrine, hormones that control heart rate, metabolism, and blood pressure. The clinical manifestations of patients with pheochromocytoma are diverse, ranging from asymptomatic, paroxysmal hypertension, episodic anxiety to devastating acute heart failure and acute pulmonary edema, which all increase the difficulty of identifying and diagnosing it.
Case presentation
We report the case of a 51-year-old man, with a 4-year history of resistant arterial hypertension, type 2 diabetes mellitus, and post-ischemic stroke. The patient complaints abdominal pain in the right iliac fossa, which is suspected as acute appendicitis, complicated with hypertensive crisis, headache and sweating. Abdominal ultrasound shows a round hypoechoic formation, 29 mm, in the superior pole of right kidney. Computed tomography scan of abdomen shows a dense formation in the right suprarenal gland, 30 x 30 mm, with densification of the surrounding tissue, suspicions for pheochromocytoma. Laboratory tests revealed elevated urinary metanephrine excretion of 1030 mg/24 hours (rate < 375 mg/24 hours) and elevated urinary normetanephrine of 835 mg/24 hours (rate <780 mg/24 hours. Open surgical excision of the pheochromocytoma was performed. The histological analysis of the mass confirmed diagnosis. The symptoms releated to pheochromocytoma were relieved and the blood pressure returned to normal after surgery.
Conclusion
Pheocromocytoma is a rare tumor of the adrenal gland that is responsible for a small percentage of all patients with hypertension. However, it should always be suspected in patients with resistant and unstable hypertension.

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EP980

Neurofibromatosis type 1: rare cause of pheochromocytoma - a report of 2 cases

Karimi Meryem[1], Hajar Azagouagh[1], Mustapha Asfour[2], Rifai Kaoutar[1], Iraqi Hind[1] & Mohamed Elhassan Gharbi[1]
[1]ibn Sina rabat, Endocrinology, Morocco; [2]Hôpital militaire d'instruction Mohammed V, Endocrinology, Morocco

Introduction
Neurofibromatosis type 1 is a multi-organ genetic disease, commonly occurring with variable severity. Pheochromocytoma is a rare manifestation in NF1, affecting 1-15% of NF1 patients according to studies.
Case Report
We present 2 cases: - Patient 1: 28 years old, with personal history of café au lait spots, cutaneous and subcutaneous neurofibromas, axillary lentigines. Referred for endocrinology consultation due to an adrenal mass discovered during an ultrasound for abdominal pain. Further CT scan revealed right adrenal masses measuring 25*22mm and 39*34mm, with estimated absolute washout of 62% and 37%. Elevated methoxylated derivatives in hormonal assessment. The patient underwent laparoscopic surgery. - Patient 2: 26 years old, with similar personal history. Discovered through a similar presentation as the first patient, adrenal CT scan revealed a tissue mass measuring 50*57*40mm, with tissue density of 49ui. Elevated methoxylated derivatives in hormonal assessment. The patient underwent laparoscopic surgery.
Discussion and Conclusion
In NF1, 80% of pheochromocytomas are asymptomatic, with over half being non-secreting. When secretory, they are often asymptomatic but can become symptomatic acutely, especially during surgical procedures. These findings underscore the importance of screening for pheochromocytoma in the NF1 population around the age of 35 to 40.

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EP1014

Adrenal cavernous hemangioma: a diagnostic challenge

Alberto García Piorno, Isabel Losada Gata, Mónica Gómez-Gordo Hernánz, Gloria Collado González, Marta Pérez Noguero, Ignacio Jiménez Hernando, Alejandra Rivas, Gilberto Pérez Lopez & Laura González Fernández
Gregorio Marañón General University Hospital, Endocrinology, Madrid, Spain

Introduction
Cavernous hemangiomas (CH) are benign vascular tumors that frequently involve the skin, central nervous system or liver. Rarely, they can also affect adrenal glands. Adrenal cavernous hemangiomas are mostly unilateral lesions, typically discovered incidentally on radiological imaging. They generally present in the sixth to seventh decade of life and tend to be asymptomatic and non-functioning tumors. Preoperative differential diagnosis from malignant neoplasms owing to imaging features remains challenging.
Case report
A 58-year-old woman was referred for the evaluation of a left adrenal mass incidentally discovered during an ultrasound conducted for the assessment of acute ureteric colic. The patient was asymptomatic, with no reported headache, palpitations or diaphoresis. Physical examination was unremarkable. A contrast enhanced CT scan of the abdomen revealed a solid exophytic left adrenal mass that measured 4 x 3.5 cm and exhibited heterogeneous contrast enhancement. Imaging characteristics were suggestive of adrenal adenoma with hemorrhagic degeneration. Subsequently, an abdominal magnetic resonance imaging (MIR)

was performed, revealing non-specific features. Tumor functionality was explored through a series of laboratory investigations. Analysis revealed an increase in dopamine and noradrenaline levels in a 24-hour urine sample on a single occasion, which was not confirmed in subsequent assessments. No abnormal hormone levels were detected in blood tests. 123I-Metaiodobenzylguanidine (123I-MIBG) scintigraphy showed absence of radiotracer uptake in the adrenal gland. Given the non-specific radiological findings and the exclusion of functionality, it was decided to monitor the lesion, which remained stable in successive radiological follow-ups. In the latest TC scan, performed 6 years after the initial diagnosis, the adrenal mass exhibited an increase in dimensions to 5 x 5.4 cm. Imaging characteristics were suspicious for adrenal myelolipoma as the tumor displayed macroscopic fat. Additionally, a newly appeared 5 mm focal calcification was observed. Due to diagnostic uncertainty and the observed growth, the patient was offered resection, and a retroperitoneal laparoscopic adrenalectomy was performed. The histopathological examination revealed a benign adrenal cavernous hemangioma with extensive thrombosis. The patient recovered without surgical related complications.
Conclusion
Cavernous adrenal hemangiomas are rare tumors that should be considered in the differential diagnosis for nonfunctioning adrenal incidentalomas. They are radiologically heterogeneous, often presenting as hypodense lesions with variable calcification, macroscopic fat or necrosis. These findings can be common to other adrenal lesions such as angiomyolipoma, pheochromocytoma or adrenal carcinoma. Thus, surgical resection is often required to exclude malignancy and the final diagnosis is largely established after histopathological analysis.

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EP1019

[131I]6ß-iodomethyl-19-norcholesterol SPECT/CT in the localization of cortisol-producing adrenal adenoma

Annamaria Erdei[1], Laura Koroskenyi[1], Eszter Daniel[2], Monika Andrasi[3], Sandor Barna[3] & Endre Nagy[1]
[1]Faculty of Medicine, University of Debrecen, Divison of Endocrinology, Department of Internal Medicine, Debrecen, Hungary; [2]Faculty of Medicine, University of Debrecen, Department of Surgery, Debrecen, Hungary; [3]Faculty of Medicine, University of Debrecen, Department of Nuclear Medicine, Debrecen, Hungary

Introduction
Adrenal scintigraphy using [^{131}I]6ß-iodomethyl-19-norcholesterol has been available since 1975, primarily for the diagnosis of hyperaldosteronism helping to distinguish between unilateral adenoma and bilateral hyperplasia. First line treatment of ACTH-independent form of Cushing syndrome is surgery after localization of the cortisol-producing adrenal tumour.
Case report
A 31-year-old woman has been referred to the endocrine clinic with suspected Cushing syndrome in 2020. Tonsillectomy, lactose intolerance, allergic rhinitis and epilepsy were present in her medical history. She complained of weight gain (30 kg during one year), secondary amenorrhoea, and elevated blood pressure. Physical examination revealed round face, central obesity, oedema on the legs and striae on the skin of the abdomen. Laboratory examinations proved hypercortisolism with suppressed ACTH level. We diagnosed her with hypertension, osteoporosis and impaired glucose tolerance as complications of Cushing syndrome. Adrenal CT showed bilateral adrenal adenomas, with 30 mm diameter in the right side and 17 mm in left side. Iodo-methyl-norcholesterol SPECT/CT proved cortisol-secreting adenoma in the right adrenal gland. Coronavirus pandemic-driven restrictions prevented immediate surgery; this was postponed to an uncertain date in the future. We decided to start metyrapone treatment until surgery, which partially controlled her hypercortisolism. Laparoscopic adrenalectomy in the right side was performed one year later. Histology confirmed cortisol secreting adenoma. After operation, the patient had transient adrenal insufficiency for a few weeks, then normal cortisol levels resumed spontaneously as expected. Clinical features of Cushing syndrome gradually disappeared, her body weight decreased from 126 kg to 78 kg.
Conclusions
In Cushing syndrome with bilateral adrenal lesions, it may be challenging to lateralize the hormone source. Iodo-methyl norcholesterol SPECT/CT is a feasible non-invasive method to localize the cortisol-secreting adrenal adenoma preoperatively.

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EP1056

Administration of high dose vitamin E in female rabbits with hypercholesterolemia increases acutely androgen levels: an animal model study

Ioannis Vlachos[1], Sofia Chatzi[2], Konstantinos Kontzoglou[1] & Georgios Boutzios[2]
[1]National and Kapodistrian University of Athens, Nikolaos Christeas Laboratory of Experimental Surgery and Surgical Research, Medical School, Athens, Greece; [2]National and Kapodistrian University of Athens, Department of Pathophysiology, Medical School, Athens, Greece

Introduction
Only few studies were observed, supporting the hypothesis that the administration of high doses of vitamin E in people with elevated serum total cholesterol levels leads to increased adrenocortical hormone secretion. There are only limited data concerning androgen or estrogen levels. The aim of this study is to investigate the possible effect of Vitamin E on adrenal and sex hormones in rabbits with hypercholesterolemia, as an animal model for the research.
Methods
The study was designed with 4 rabbits, 2 males and 2 females. High cholesterol diet was administered to all subjects for 13 days. When total cholesterol levels were $\geq$597 mg/dl high cholesterol diet was discontinued. We administered vitamin E 1000IU on the study group (1 female and 1 male rabbit, subject 1 and 2 respectively) for 30 days while female subject 3 and male subject 4 did not receive any supplement. Serum samples were tested at baseline when high total cholesterol levels were achieved and 2, 4, 5, 10, 20, 30 after vitamin E supplementation for total cholesterol, SGPT, gGT, estradiol, testosterone, cortisol and DHEA. The animals were then euthanized and were sent for histological examination.
Results
The initial measurements of liver enzymes were: SGPT = 50 IU/l for subject 1, 60 IU/l for subject 2, 47 IU/l for subject 3 and 56 IU/l for subject 4 and gGt = 16 U/l, 20 U/l, 17 U/l, 15 U/l respectively. After vitamin E supplementation SGPT values were 32 IU/l, 35 IU/l, 38 IU/l, 32 IU/l and gGt 6 U/l, 4 U/l, 5 U/l, 4 U/l for each subject respectively. Plasma morning cortisol levels at baseline were 45 mg/dl, 9.49 mg/dl, 1.33 mg/dl, 1.72 mg/dl demonstrating a wide variance in the subsequent measurements, reaching 754 mg/dl for subject 1 on the fifth day of vitamin E administration. Testosterone levels at baseline were 0.0636 ng/dl, 5.58 ng/dl, 0.0933 ng/dl, 5.53 ng/dl and after supplementation 0.0497 ng/dl, 7.49 ng/dl, 0.0783 ng/dl, 6.71 ng/dl. Interestingly, testosterone and DHEA levels increased acutely only in female rabbits, the first day after administration of vitamin E. Estradiol levels at baseline were 13 pg/ml, 8.47 pg/ml, 11.3 pg/ml, 13.2 pg/ml and after supplementation for 30 days 1.84 pg/ml, 11.7 pg/ml, 4.4 pg/ml 4.54 pg/ml.
Conclusions
Administration of high dose vitamin E in female rabbits with hypercholesterolemia increases testosterone and DHEA levels, but not estrogen levels. Further studies are needed to support or verify a claim.

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EP1057

Malignant mesenteric paraganglioma: a case report

Mohamed Samir Merad & Fatiha Mohammedi
Oran, Algeria Oran 1 Ahmed Ben Bella Medical University, Endocrinology and Diabetology departement -Larribere Clinic – university Hospital Dr Benzerdjeb, Oran, Algeria

Introduction
Paragangliomas are neuroendocrine tumors that develop from the paraganglia of the sympathetic and parasympathetic nervous systems. They are benign in approximately 80% of cases and are usually localized. However, in rare situations, they can be malignant, which is defined by the presence of tumor cells in nearby tissues or at a distance (metastases). Most parasymphathetic paragangliomas are located in the skull base and along the vagus and glossopharyngeal nerves, while the majority of sympathetic paragangliomas are found in the belly. Paragangliomas found in the mesentery are extremely rare.
Observation
A 44-year-old man with no previous pathological history arrived with widespread abdominal pain extending to the left shoulder. An abdominal CT scan revealed an intra-abdominal tissue mass, paramedian, on the right below the pancreas, measuring 86/74 mm, with multiple secondary adenopathies, the largest of which was 26 mm. The tumor could not be removed (inoperable tumor), and a biopsy revealed a malignant mesenteric paraganglioma, which is why it was referred to us for care. The patient's general condition was satisfactory, and he was normotensive with no other clinical symptoms suggesting multiple endocrine

neoplasia type 2. In the 24-hour ambulatory blood pressure test, the blood pressure profile was normal, and the ophthalmological examination was normal. Hormonal evaluation: 24-hour plasma and urine methoxylates are normal; calcitonin levels and phosphocalcic assessment are also normal. Extension exploration: a cervico-thoraco-abdomino-pelvic CT scan showed a well-limited (40×10×40 mm) polylobed mesenteric intraperitoneal development with a necrotic segment VII liver nodule measuring 14×13 mm and no bone lesions. MIBG scintigraphy was negative. The patient was later sent to the Oncology Department for combined follow-up, and chemotherapy was advised as palliative treatment.

Conclusion

Non-secreting mesenteric paragangliomas with malignant potential are commonly detected inadvertently and have a poor prognosis.

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EP1058

Norepinephrine-only secreting pheocromocytoma: case report

Elena Dragan
Reteaua Privata de Sanatate Regina Maria, Endocrinology, Bucharest, Romania

Introduction

Pheocromocytomas are catecholamine-secreting tumors that arise from cromaffin cells of the adrenal medulla, probably occurring in less than 0.2% of pacients with hypertension. The objective of this report is to describe a case of norepinephrine-only secreting pheocromocitoma.

Case description

A 43-year-old female pacient presented with hypertension, recent onset diabetes and right adrenal mass measuring 3.5×2.7 cm on a CT scan. Hormonal tests showed normal basal cortizol level, normal cortisol level after 1 mg Dexamethasone test, high levels of aldosterone and renin, elevated normetanephrine levels (12xN) with normal metanephrine levels, high levels of chromogranin A. The normal metanephrine levels with elevated normetanephrine may be a characteristic of VHL syndrome. Thyroid ultrasound, thyroid hormones levels, PTH, calcitonin were normal. Genetic testing for VHL syndrome was made, results being not available for now. The pacient was treated with alpha blockers for several days, the beta-blocking drug was added and she underwent total adrenalectomy. The histological + IHC report confirm benign pheocromocitoma. Postoperative, the pacient had complete resolution of symptoms with normal blood pressure and resolution of diabetes.

Conclusion

A pheocromocytoma is a rare catecholamine secreting tumor. About 30% of pheocromocytomas occur as part of hereditary syndromes. The characteristic of pheocromocytomas associated with VHL syndrome is normetanephrine-only secretion. Genetic testing is important because can set appropriate follow-up and surveillance.

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EP1059

A case of silent giant pheochromocytoma

Sofia-Maria Lider-Burciulescu[1,2], Cristina Stancu[3], Maria Anghel[3], Vlad Radulescu[3] & Corin Badiu[3,4]
[1]Carol Davila University of Medicine and Pharmacy, Endocrinology IV, Bucureşti; [2]"Ana Aslan" National Institute of Geriatrics and Gerontology, Endocrinology, Bucharest, Romania; [3]National Institute of Endocrinology, Endocrinology IV, Bucureşti; [4]Carol Davila University of Medicine and Pharmacy, Endocrinology, Bucureşti

Introduction

Pheochromocytoma is a rare tumor, representing a cause of secondary endocrine hypertension. Traditionally, prior to the widespread availability of imaging investigations, pheochromocytoma was diagnosed based on the triad: headache, palpitations and sweating. Diagnosis is crucial, as 40-50% of pheochromocytoma patients exhibit genetic mutations associated with multiple syndromes, such as MEN2 syndrome, succinate dehydrogenase enzyme mutations, neurofibromatosis type 1 and von Hippel-Lindau syndrome. Management inevitably involves surgery, preceded by appropriate α-blockade. Lifelong monitoring is necessary due to the risk of recurrence and malignancy.

Case description

We present the case of a 50-year-old Caucasian woman, smoker of 30 pack-years, diagnosed with hypertension in 2022 for which she is currently undergoing treatment with Perindopril/Indapamide 5/1.25 mg. The patient describes three hypertensive crises associated with stressful events and hyperhidrosis for the past 3 months. In november 2023 she underwent an abdominal CT scan that revealed a nodularly transformed right adrenal gland, with dimensions of 90/66/81.2 mm, featuring an iodophilic tissue component, cystic areas and several central necrotic areas, suggestive for a giant right adrenal pheochromocytoma. Upon examination, the patient has hyperpigmentation on the anterior thorax, intermittent headache and a blood pressure of 150/98 mmHg. Calcitonin is within normal range. Plasma metanephrines and normetanephrines present values of 1770 pg/ml (>23 UNL) and 4860 pg/ml (>31 UNL), respectively. Markers specific of neuroendocrine tumors are elevated, such as chromogranin A (981 ng/ml; >9.5 UNL) and neuronal specific enolase (19.8 mg/l; >1.5 UNL). Urinary metanephrines and normetanephrines have elevated values of 2600 mg/24 h (>8.5 UNL) and 3900 mg/24 h (>7 UNL), respectively. Urinary 5-HIAA has normal values. The mean blood pressure after ambulatory blood pressure monitoring is 122/80.2 mmHg. Based on these results, the patient underwent surgery after receiving treatment with phenoxybenzamine for 3 weeks. The histopathology report is pending as well as the RET gene analysis.

Discussion

This case describes the management of a patient with giant oligosymptomatic pheochromocytoma. The particularity of the case is given by the large dimensions of the tumor (9 cm) and the unusual clinical picture of the patient.

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EP1091

Caae report of rare hormonally active adrenocortical oncocytoma: two-year follow-up

Khatuna Chakvetadze[1] & tamar shervashidze[2]
[1]JSC Georgian Hospitals- Kutaisi Referral Hospital, Outpatient, Kutaisi, Georgia; [2]David Abuladze Clinic, Outpatient, Tbilisi

Introduction

Adrenocortical oncocytomas, made up of specific epithelial-origin cells, are rare neoplasms, generally without hormonal activity. Most of them are considered to be benign tumors, with the size of generally 4-8 cm and lack of pathognomonic radiological features.

Case Report

This is a 2 year follow up of a 43-year-old woman, who first referred to the endocrinologist in 2021 due to weight gain, resistant arterial hypertension and menstrual irregularities for several years. After 10-years of infertility 7-years ago she delivered a preterm healthy baby-girl. Physical examination revealed cushingoid characteristic features: dorsal cervical fat pad, moon facies, fragile skin and thin extremities. Cushing's syndrome was confirmed by an overnight 1-mg dexamethasone-suppression-test, an elevated free cortisol on a 24-hour urine collection, suppressed ACTH level and low DHEA-S level. Primary hyperaldosteronism was excluded by an oral salt loading test. Urinary metanephrines were normal. HBA1C-6.0%. Abdominal CT and MRI revealed left-sided adrenal heterogeneous lesion measuring 2.3×2.8×2.2 cm with a calcification focus in the periphery. She was also revealed small liver hemangiomas and NAFL-disease. In July 2021 the patient underwent laparoscopic left adrenalectomy. To prevent postoperative adrenal insufficiency, the patient was medicated with hydrocortisone. The operative adrenal gland measured 6×2.5×2.5 cm, with a nodule of 2.5×2.2×2.0 cm of well-defined limits, yellowish. The histological/immunohistochemical analysis revealed the diagnosis of adrenocortical neoplasm with predominance of oncocytic cells in solid-trabecular-structures (adrenocortical oncocytoma), having uncertain malignant potential. The doses of hydrocortisone were tapered slowly and stopped 3 months later. 6,12 and 24 months after surgery her cortisol, DHEA-S, electrolyte levels, HBA1C were normal, without any radiologic evidence of recurrence. In March 2023 she delivered a healthy baby-girl through C-section, without any gynecological or intraoperative complications. She is currently in follow up.

Discussion

Hormonally active adrenocortical oncocytomas are extremely rare tumors, about 17.0% of adrenal oncocytomas may have hormonal activity. By origin oncocytomas are epithelial-tumors composed of large eosinophilic cells, having mitochondria-rich cytoplasm and large nucleoli. The frequency of non-functioning oncocytomas is higher in females. The diagnosis of these neoplasms is mostly based on histological/immunohistochemical analysis. The Lin-Weiss-Bisceglia risk system is used to distinguish malignant oncocytic tumors, with major and minor criteria for differentiation. Small oncocytomas are commonly benign tumors, but in our clinical case oncocytoma expressed with Cushing's syndrome, with its two minor criteria (necrosis and capsular invasion), was classified as having uncertain malignant potential, thus suggesting important prognosis. Two-years close follow-up did not reveal any abnormalities.

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EP1092

A rare association of salt-wasting congenital adrenal hyperplasia and type 1 diabetes mellitus

Ahmet Soyer[1], Hatice Aksu[1], Esma Ayrancl[1], Bilge Dibeklioglu[1], Sefika Polat[2], Oya Topaloglu[2], Reyhan Ersoy[2] & Bekir Cakir[2]
[1]Ankara City Hospital, Department of Endocrinology and Metabolism, Turkey; [2]Ankara Yildirim Beyazit University, Department of Endocrinology and Metabolism, Turkey

The co-occurrence of congenital adrenal hyperplasia and type 1 diabetes mellitus (T1DM) is a rare phenomenon in existing literature. The primary cause of congenital adrenal hyperplasia (CAH) is often 21-hydroxylase deficiency (21OHD), a condition associated with the CYP21A2 gene located on chromosome 6p21.3 within the major human leukocyte antigen (HLA) histocompatibility locus. Various gene polymorphisms, particularly in HLA-DQalpha, DQbeta, and DR genes on chromosome 6p21.32, are known to influence the risk of type 1 diabetes. Although the genetic loci for T1DM and 21-OH CAH are close, these conditions typically manifest independently, we present a case involving a man in his 20s who visited the emergency department with symptoms such as nausea, vomiting, headache, fatigue, and excessive sleepiness. This individual had a history of both classic salt-wasting congenital adrenal hyperplasia and type 1 diabetes mellitus. Over the past decade, the patient had experienced recurrent hospitalizations for diabetic ketoacidosis, with recent complications arising from the malfunction of an insulin pump due to technical issues. Initial treatment included insulin infusion, intravenous hydration, and an increased hydrocortisone dose. Once acidosis resolved, the patient transitioned to basal-bolus therapy and resumed insulin pump use. Carb counting was introduced, and dietary adjustments were made. An abdominal computed tomography scan revealed bilaterally thickened adrenal glands, and scrotal ultrasound detected an adrenal rest tumor. The patient was discharged with oral hydrocortisone (30 mg once daily), oral fludrocortisone (0.2 mg once daily), and continued use of an insulin pump. Repeated ketoacidosis episodes were potentially linked to hydrocortisone use, prompting consideration of a connection between T1DM and 21OHD, necessitating further investigation through additional studies.

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EP1093

Metyrapone treatment for mild autonomous cortisol secretion (MACS) - a case report

José Manuel Ruiz-Cánovas[1], Eider Pascual-Corrales[1,2], Estefanía Aracely Achote-Rea[1], Imanol Madrid-Egusquiza[1], María Noelia Sánchez-Ramírez[1], Cindy Anabel Idrobo-Zambrano[1], Carlos García-Regal[1], José María Jiménez-Cassinello[1], Arturo Vega-Beyhart[1] & Marta Araujo-Castro[1,2]
[1]Ramón y Cajal Hospital, Endocrinology and Nutrition, Madrid, Spain; [2]Instituto Ramón y Cajal de Investigación Sanitaria - IRYCIS, Madrid, Spain

A 68-year-old man with history of non-muscle-infiltrating bladder tumor and atrial fibrillation was referred to the Endocrinology Department in November 2020 for a functional study of a left adrenal incidentaloma. Furthermore, the patient had a history of arterial hypertension diagnosed at the age of 45 years, on treatment with 3 drugs (enalapril 20 mg B.I.D., amlodipine 5 mg B.I.D., hydrochlorothiazide 12.5 mg/day), achieving usual blood pressure (BP) levels of 150/90 mmHg. At the first evaluation (November 2020) in the Endocrinology Department, headaches, frequent palpitations and non-weight gain in recent years were reported, BMI of 26 kg/m2 and no specific clinical data of hypercortisolism. Functionality study was requested, after replacing antihypertensive medication for at least 4 weeks with doxazosin 4 mg, obtaining the following results: plasma ACTH <3.8 pg/mL (normal range 7.7-48.8); serum basal cortisol 18.7 mg/dl (normal range: 3.7-19.4); urinary free cortisol (UFC) 75.00 mg/24 h (normal $<$ 140); Late-night salivary cortisol 4.62 nmol/l ($<7,56$); Cortisol after suppression with 1 mg of Dexamethasone 7.10 mg/dl. Aldosterone/renin ratio and metanephrines were normal. HbA1c was 6.1%. In September 2020, non-enhanced CT scan has showed radiological stability of the adrenal lesion with respect to 2018 imaging tests: 41x37mm, oval, sharp-edged, heterogeneous, with majority component of low-density value, compatible with lipid-rich adenoma. The study was extended to norcholesterol scintigraphy, and the findings were consistent with hyperfunctioning left adrenal adenoma. The patient refused adrenalectomy, opting for conservative management. During follow-up, home BP values were around 150/90 mmHg. Glycemic control worsened, HbA1c increasing over 6.5%. Treatment with metformin/empagliflozin was initiated. No osteopenia/osteoporosis was detected. Given patient's refusal of surgery and coexistence of two comorbidities potentially associated with hypercortisolism, one of them poorly controlled, metyrapone treatment (currently off-label) following the Debono protocol was proposed. Upon approval by the hospital pharmacy, metyrapone was started at a night dose of 250 mg. After 2 weeks, BP improved notably, reaching 120/70 mmHg, and amlodipine was suspended. Metyrapone night dose was increased to 500 mg and BP continued falling, so enalapril was discontinued. After 3 months on treatment, pathology tests showed basal cortisol at 15.7 mg/dl; UFC at 31.20 mg/24 h; Late-night salivary cortisol at 3.18 nmol/l ; HbA1c at 6.6%. No secondary side effects were developed. We can conclude that metyrapone is a useful and safe treatment for patients with MACS and associated comorbidities, offering a better control of hypertension.

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EP1094

Subclinical hypercortisolism revealed by a resistant hypertension

Nouhaila Essafir, Nada Ait Kassi & Anas Guerboub
Military Hospital Mohammed V Rabat, Endocrinology

Introduction
Hypercortisolism is considered to be a rare condition with an estimated incidence between 0.4 and 2.4 cases per million per year, typically manifests as the clinically and biochemically evident Cushing's syndrome. However, a more subtle form, known as subclinical hypercortisolism (SH) or autonomous cortisol secretion (ACS), poses diagnostic challenges. It is defined as excessive cortisol secretion without the classic manifestations of clinically overt Cushing syndrome.
Case presentation
We report the case of a 33-year-old female patient, who has been followed for secondary amenorrhea, dyslipidemia, and hypertension since the age of 24, controlled with a triple therapy. Given the secondary nature of hypertension, a CT scan was performed, revealing a right adrenal mass measuring 38x19mm with a spontaneous density of 25 HU. A secretory assessment was conducted: 24-h urinary fractionated metanephrines and vanillylmandelic acid levels were measured ruling out pheochromocytoma. Plasma aldosterone/renin ratio was examined to exclude primary aldosteronism. Regarding hypercortisolism, 24-hour urine free cortisol levels were normal. Additionally, the cortisol circadian rhythm was disrupted with a value of 265 ng/ml. The standard dexamethasone suppression test showed an elevated morning cortisol level at 221 ng/ml (**not suppressed**). The morning plasma ACTH concentration was low, less than 3 ng/l. The diagnosis of cortisol adenoma was made, hence the indication for adrenal surgery.
Conclusion
Subclinical hypercortisolism is a relatively newly discussed and understood disease. Unfortunately, it is highly **under-diagnosed** and **under-treated**. Subclinical Cushing's syndrome is described as 'hidden hypercortisolism' since it is typically asymptomatic. Even though, the condition still leads to long-term consequences of cortisol excess (**hypertension, type 2 diabetes, hyperlipidemia and osteoporosis**). The timely diagnosis of such cases allows for appropriate management and prevention of associated complications.

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EP1095

Adrenal insufficiency revealing multifocal tuberculosis

Meryam Alahyane, Sana Rafi, Manar Bari, Ghizlane El Mghari & Nawal El Ansari
Mohammed VI university hospital of Marrakesh, Department of Endocrinology, Diabetes, Metabolic diseases and Nutrition, Marrakesh, Morocco

Background
Multifocal tuberculosis is defined as the involvement of at least two extra-pulmonary sites, with or without pulmonary involvement. The most commonly involved endocrine organ is the adrenal gland. We report a case of adrenal insufficiency revealing multifocal tuberculosis.
Case report
A 65 year old female patient with no context of immunosuppression, presented to emergency department with Consciousness disturbance associated with severe hyponatremia, revealing a primary adrenal crisis confirmed with low plasma cortisol and high ACTH levels. Computed tomography (CT) revealed Bilateral adrenal masses with calcifications measuring 20 mm and 16 mm for the left and the right mass respectively. Both have a spontaneous density of 33 UH, and absolute wash of 27% and 11%. CT chest revealed micronodules in the posterior upper lobe of the left lung, multiple calcification zones and mediastinal lymph nodes. The patient presented also a skin temporal lesion, having the clinical

presentation of tuberculosis lupus. The biopsy showed a giant epithelioid cell granuloma without caseating, with a positivity of Gene-Xpert. HIV serology and viral hepatitis were negative The diagnosis of multifocal tuberculosis including pulmonary, adrenal and skin localisation was established. The symptoms of primary adrenal insufficiency gradually subsided after the initiation of Hydrocortisone replacement in addition to antituberculous therapy.
Discussion
Although autoimmune adrenalitis is the most common cause of primary adrenocortical insufficiency, Tuberculous Addison's disease (TAD) is still common particularly in endemic countries. This condition could be inaugurated by an Addisonian crisis, as it is the case for our patient. Tuberculosis may directly involve the adrenal glands which classically appears after more than 90% of the adrenocortical destruction by tuberculosis. Following Hematogenous and lymphatic dissemination, the adrenal localisation is often not apparent for as many as 10 years after tuberculosis infection. Generally, in the early and active stages of tuberculosis, adrenal glands are enlarged, while long-term disease will have small, atrophic adrenals, and calcification due to degeneration process. Multifocal tuberculosis is a severe form of the disease, usually affecting immunocompromised individuals who already have a pulmonary localization. However, it can also affect immunocompetent subjects with or without pulmonary involvement. It is therefore necessary to systematically carry out an exhaustive assessment of the dissemination of the tuberculosis germ, in order to improve the disease management. Prognosis is often favorable, depending on the type of the disease localisation and the early initiation of anti-tuberculosis drugs.

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EP1097

The complex intersection of congenital adrenal hyperplasia, antiphospholipid syndrome, and infertility: a successful pregnancy journey

Aiste Cemerkaite & Vita Lizdeniene
Lithuania, Lithuanian University of Health Sciences Kaunas Clinics, Kaunas, Lithuania

Congenital Adrenal Hyperplasia (CAH), a genetic adrenal gland disorder, can disrupt hormonal balance, leading to fertility issues in females. Timely interventions, like hormone therapy, are essential for managing fertility concerns and ensuring a safe pregnancy for individuals with CAH. A 28-year-old patient consulted an endocrinologist for a detailed examination due to infertility issues persisting for 2 years. Prior to this, the patient had given birth to a 22-week-old newborn who died within the first day due to infection. During the investigation of infertility causes, 17-OH was incidentally tested despite the absence of hyperandrogenism symptoms (regular menstrual cycle, no hirsutism, no acne). A significantly elevated 17-OH level was found (63.81 nmol/l). Suspecting congenital adrenal hyperplasia, a Synacthen test was performed, but the diagnosis was ruled out (Synacthen test results: 17-OH 0' 11.9 nmol/l, 30' 11.8 nmol/l, 60' 9.06 nmol/l). The patient consulted with a geneticist, and two pathogenic variants of the CYP21A2 gene were identified. Upon repeating the Synacthen test, CAH was diagnosed (Synacthen test results: 17-OH 0' 37.3 nmol/l, 30' 154 nmol/l, 60' 199 nmol/l). Treatment with dexamethasone 0.25 mg/p was prescribed, assisted fertilization was recommended, and the male partner was advised to undergo CYP21A2 mutation screening (not detected). The patient underwent intrauterine insemination, but it was unsuccessful: at 13 weeks, a single embryo reduction was performed, and at 17 weeks, there was a miscarriage of the second fetus. Two days later, with no remaining fetal cardiac activity, an abortion was performed. After the unsuccessful pregnancy, the patient was reevaluated by a geneticist, and antiphospholipid syndrome was confirmed (anti-cardiolipin antibodies (IgM) - 99.96). The patient underwent a second intrauterine insemination and one successfully implanted. Due to CAH, dexamethasone was discontinued, and hydrocortisone 5 mg was started three times a day. Aspirin and low-molecular-weight heparin were prescribed for antiphospholipid syndrome. During pregnancy, the patient consulted with a geneticist again, and it was assessed that the risk of CAH for the fetus was minimal (the fetus is an obligate carrier of one pathogenic variant of the CYP21A2 gene). Chromosomal anomaly testing (PRISCA) was performed with low-risk results. A healthy male newborn was delivered via cesarean section at 38 weeks (APGAR 9). Stress doses of hydrocortisone were administered during delivery, and the postoperative period was uneventful. In conclusion, despite complexities involving congenital adrenal hyperplasia, antiphospholipid syndrome, and infertility, a multidisciplinary approach, including genetic consultations, resulted in the successful delivery of a healthy newborn.

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EP1098

Testosterone producing adrenal cortical carcinoma in a post-menopausal woman

Mitra Moazzami, Melanie Lyden & Irina Bancos
Mayo Clinic, Rochester, United States

Introduction
In post-menopausal women, the differential diagnosis of hirsutism caused by testosterone excess includes ovarian and adrenal sources. Bilateral ovarian hyperthecosis is a common cause of testosterone excess in post-menopausal women and the diagnosis is confirmed by histopathological examination of the ovaries. Adrenal tumors causing testosterone excess is exceedingly rare. In fact, most causes of hirsutism secondary to adrenal tumors is due to dehydroepiandrosterone sulfate (DHEAS) and androstenedione excess. Further, the median tumor size of an adrenal cortical carcinoma (ACC) is 10 cm. We present a case of a post-menopausal women with ACC of 1.2 cm with testosterone excess.
Case report
A 60-year-old female presented to the clinic in October 2023 with a two-year history of isolated hirsutism. In September 2022 patient had investigations showing an elevated serum testosterone (172 ng/dl), a normal dehydroepiandrosterone sulfate (DHEAS) of 68 mg/dl, and a normal androstenedione 78 ng/dl. Her local endocrinologist recommended bilateral oophorectomy. Surprisingly, after the oophorectomy, her testosterone levels did not drop (testosterone 138 ng/dl). Pathology of the ovaries were normal. Computed Tomography (CT) of abdomen done showed 1.2 cm right adrenal nodule with unenhanced density of 20 Hounsfield units (HU) and a normal left adrenal. Contrast washout characteristics showed an absolute washout of 61.6% and relative washout of 51.7%. Subsequently, the identified source of testosterone production was suspected to be associated with the adrenal mass. The patient was treated with a right laparoscopic adrenalectomy. Post-operatively, testosterone concentrations dropped. Ultimately, the pathology had features of low-grade ACC which included 6 mitotic figures/50 high power fields (HPFs), Ki-67: 5.13%.
Conclusions
We describe a patient with a testosterone-secreting adrenal mass with findings consistent with a low-grade ACC. The workup of a post-menopausal women with hyperandrogenism includes androgen secreting ovarian or adrenal tumors, Cushing's syndrome or iatrogenesis. The adrenal cortex produces the androgens: DHEAS, androstenedione, and a small amount of testosterone. When only the testosterone level is elevated, it typically indicates an ovarian source. Therefore, isolated elevation of testosterone is rarely due to an adrenal source. Further, most cases of testosterone producing adrenal masses are benign. Moreover, the median size of an ACC is usually 10 cm. Therefore, finding an ACC of 1.2 cm that exclusively secretes testosterone is very rare. This highlights the importance of considering adrenal sources of isolated testosterone secretion.

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EP1099

Gonadal impact of congenital adrenal hyperplasia in adulthood: a follow-up study

Hamdi Frikha[1], Yassmine Abdelkafi[1], Nesrine Dhieb[1], Mouna Elleuch[1], Mahdi Kamoun[1], Thouraya Kamoun[2], Mongia Hachicha[2], mouna mnif[1], Habib Sfar[3], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology; [2]Hedi Chaker University Hospital, Department of Pediatrics; [3]Tahar Sfar University Hospital, Department of Endocrinology

Introduction
Advances in diagnosis and treatment over the years have improved the life expectancy and quality of life for individuals with congenital adrenal hyperplasia (CAH). The inevitable alteration of the hypercortisolism-hyperandrogenism balance with current CAH therapy could be responsible for several anomalies in the gonadotropic axis and compromise fertility. This study aims to investigate this aspect in an aging Tunisian population of patients with CAH.
Methods
A retrospective and descriptive study was conducted on patients with CAH followed at the endocrinology department of Hedi Chaker University Hospital in Sfax.
Results
Twenty-six patients (11 men and 15 women; mean age: 27.4 $\pm$ 8.2 years) were recruited. Evaluation of gonadal function in male subjects showed preserved

Leydig function (Testosterone 5.23 ± 2.34 ng/ml; LH 2.8 ± 1.3 mUI/ml), Sertoli axis abnormalities in 50% of patients (Inhibin B 117.7 ± 75.2 pg/ml), and spermatogenesis abnormalities (Azoospermia = 2, oligoasthenospermia = 1, oligo-astheno-teratospermia = 1). Furthermore, adrenal rest tissue in the testicular tissue (TART) was observed in 6 patients with an ultrasound appearance of vascularized hypoechoic areas. In female subjects, hormonal exploration did not reveal ovarian dysfunction; however, a decrease in follicular reserves, evidenced by a low AMH level, was found in 33% of patients. Additionally, 6 out of 15 patients met at least two diagnostic criteria for polycystic ovary syndrome (PCOS). While infertility was present in only one patient, we observed 4 spontaneous pregnancies in 2 of our patients, resulting in the birth of 2 female newborns without genital anomalies.

Conclusion

The data from our series align with literature findings, although studies on aging CAH populations are infrequent. This underscores the importance of regular monitoring of gonadotropic function in both sexes, especially for the occurrence of TART in men and PCOS in women, which may compromise fertility.

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EP1100

Cardiovascular and cerebrovascular burden associated with primary aldosteronism: a monocentric study

Siddiqa Soomauroo[1], Faten Hadjkacem[1], Abdelmuhaymen Missaoui[1], Ahmad Ridwaan Auckburally[2], Souhir Maalej[1], Wiem Feki[2], Zeinab Mnif[2], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik[1]

[1]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Radiology, Sfax, Tunisia

Introduction

Primary aldosteronism (PA) is commonly identified as the main cause of secondary hypertension. It is becoming increasingly wide-spread, affecting between 1 and 30% of people suffering from hypertension. A prolonged exposure to high aldosterone concentrations has a deleterious effect on cardiovascular tissues and is associated with target organ damage, independently of blood pressure, so a higher risk of cardiovascular events has been reported in patients with primary aldosteronism,

Aim

The aim of this study was to evaluate the prevalence of cardiovascular and cerebrovascular events in patients with PA.

Patients and methods

Retrospective and descriptive study concerning 40 patients with PA, collected in the endocrinology department of the Hedi Chaker University Hospital of Sfax, over the period of 10 years from January 2010 to December 2022.

Results

The average age of our patients was 55.4 years. Fourteen patients had cardiovascular disease consisting of electrical left ventricular hypertrophy and/or hypertrophic cardiomyopathy on transthoracic echocardiogram and/or coronary artery disease. Four patients had cerebrovascular ischemic stroke. Analytical study showed that there was no significant statistical difference between plasma aldosterone concentration (PAC) in patients with and without cardiovascular disease (median PAC = 226 pg/ml vs 199 pg/ml; $P = 0.856$). Similarly, the PAC was higher in patients with cerebrovascular disease but the difference was not significant (median PA: 337 pg/ml vs 207 pg/ml; $P = 0.223$). Twelve out of 40 patients (30%) with cardio and/or cerebrovascular disease had PAC above 200 pg/ml. The evolution of the cardiovascular risk after specific treatment of PA was not carried out in our study.

Conclusion

In addition to the classic role of aldosterone, which acts via the reabsorption of water and sodium in the kidney to induce volume expansion, several studies have shown that aldosterone has direct effects on the vascular system, even in the absence of hypertension. A recent meta-analysis of 31 studies demonstrated that patients with PA had an increased risk of stroke, coronary heart disease and heart failure compared with essential hypertension.

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EP1101

Giant adrenal masses during congenital adrenal hyperplasia: a case report

Hamdi Frikha, Oumeyma Trimeche, Wiem Gherissi, Dhoha Ben Salah, Khouloud Boujelben, Fatma Mnif, Mouna Mnif, Mohamed Abid & Nabila Rekik Majdoub

Hedi Chaker University Hospital, Department of Endocrinology

Introduction

Congenital adrenal hyperplasia (CAH) in its classical form is an early-onset and challenging-to-treat condition with long-term evolution associated with significant morbidity, typically involving metabolism, bone, and gonadal aspects. Through this specific case study, we illustrate one of the rare complications of CAH in adulthood.

Case Report

A 24-year-old patient, born of consanguineous parents, has been monitored since birth for classical virilizing CAH. The patient is treated with suppressive doses of dexamethasone, but due to poor treatment adherence, the disease remains in chronic imbalance (17OHP consistently > 15 ng/ml). An abdominal CT scan conducted to investigate abdominal pain revealed two large bilateral adrenal masses measuring 6 cm (right) and 5.8 cm (left) with loss of the fatty rim. Hormonal assessment did not reveal hormonal hypersecretion. Functional imaging with PET-FDG showed no increased metabolism in relation to the masses, and the extension study was negative. A right adrenalectomy was performed, and pathological examination revealed a benign-looking tumor. Evaluation at 3 months postoperatively showed persistent disease imbalance (17OHP = 57 ng/ml and ACTH > 2000 pg/ml) with a 40% increase in the size of the left adrenal confluent tumor.

Discussion

This case illustrates an unusual complication of CAH with a long course. Prolonged exposure to excess ACTH appears to be the primary etiopathogenic factor for adrenal tumorigenesis in the context of CAH. Malignant transformation and the simultaneous presence of two masses of different histological and functional nature are situations rarely described in the literature but remain plausible in our patient given the rapid increase in size. This concern highlights the importance of careful monitoring.

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EP1102

Clinical features and complication profile of arterial hypertension in patients with primary aldosteronism

Siddiqa Soomauroo[1], Faten Hadjkacem[1], Abdelmuhaymen Missaoui[1], Ahmad Ridwaan Auckburally[2], Souhir Maalej[1], Wiem Feki[2], Zeinab Mnif[2], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik[1]

[1]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Radiology, Sfax, Tunisia

Introduction

Primary aldosteronism (PA) is frequently recognized as the main cause of secondary hypertension. Its prevalence is on the rise, impacting a range of 1 to 30% among individuals with hypertension.

Patients and methods

Retrospective and descriptive study concerning 40 patients with PA, collected in the endocrinology department of the Hedi Chaker University Hospital of Sfax, over the period of 10 years from January 2010 to December 2022.

Results

The average age of our patients was 55.4 years. Among the 40 patients, 39 (16 men and 23 women) presented with hypertension. In 32% of cases, the hypertension was recent, evolving for less than 5 years. Severe hypertension was found in 11 cases and resistant hypertension in 4 others. Ten patients (25.6%) were on at least a triple anti-hypertensive therapy. The therapeutic classes most used were calcium channel blockers prescribed in 25 cases (64.1%), followed by ACE inhibitors in 12 cases (30.8%). The assessment of target organ damage revealed hypertensive retinopathy ($n = 4$), hypertensive cardiopathy ($n = 8$), microalbuminuria ($n = 26$), proteinuria ($n = 3$) and renal failure ($n = 8$). In our study, we noted a statistically significant reduction of antihypertensive drugs in 36 patients who had received treatment, whether by surgery or spironolactone ($P = 0.001$).

Conclusion

Sodium and water retention constitute the primary pathophysiological mechanism behind the elevation of blood pressure in PA. This hypervolemia, combined with other factors, accounts for the nearly constant presence of hypertension in patients with PA. This type of hypertension has no particular semiological features. Its severity is not perfectly correlated with the degree of hyperaldosteronism whereas the prevalence of PA is correlated to the degree of severity of hypertension. Some

studies have reported a prevalence of PA that may exceed 20% in cases of resistant hypertension.

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EP1103

Clinical and biological study of adrenal incidentaloma

Hayfa Farid[1], Taieb ACH[1,2], Asma Ben Abdelkarim[1,2], Hamza Elfekih[1,2], Yosra Hasni[1,2], Amel Maaroufi[1,2] & Molka Chedli Chaieb[1,2]
[1]Farhat-Hached University Hospital, Department of Endocrinology and Diabetology, Sousse, Tunisia; [2]Faculty of Medicine of Sousse, University of Sousse, Tunisia

Introduction
The adrenal incidentaloma is an asymptomatic tumor measuring at least one cm, discovered incidentally during a medical imaging examination. The adrenal incidentaloma continues to grow with technological advances and improved radiological examinations. Any adrenal incidentaloma involves the search for a secretion or malignant character. The objective of our study is to study the clinical, biological and etiological aspects of adrenal incidentalomas.
Patients and Methods
This was a retrospective, descriptive study carried out in an Endocrinology department, on records of patients in whom an adrenal incidentaloma has been discovered. The following parameters were identified: Clinical and biological presentation, etiological profile, diagnosis and therapeutic means.
Results
Our study covered 22 patients: 2 men and 20 women, aged between 29 years and 76 years with an average of 52 ± 14 years. Family history in these patients was familial hypertension in 18 patients (81.8%), 3 had a history of early stroke and 1 had a history of myocardial infarction. Beyond them, 6 patients had type 2 diabetes with an average duration of 4 ± 3 months. Only one patient was smoking and only one was dyslipidemic under statin. Hypertension was found in 12 patients (54.5. Of these patients, 4 had a refractory hypertension (18.2%), 2 had a malignant hypertension (9.1%). The mean systolic blood pressure was 16.1 ± 2.1 mmHg and the average diastolic blood pressure was 9.1 ± 1.3 mmHg. The mean weight of the population was 79.8 ± 15.06 Kg, the mean size of 159.19 ± 7.6 cm, an average BMI of 31.13 kg/m^2; and an average waist of 105 ± 26.6 cm. Biologically, the mean blood glucose was 6.57 mmol/l, the mean serum potassium level was 3.8 ± 0.57 mmol/l. 10 patients had proven hypokalemia. An adrenal-centered scan showed an incidentaloma of an average size of 21.5 ± 19.21 mm. The etiologic diagnosis was a pheochromocytoma in 7 patients (31.8%) attested by an elevation of the metanephrine blocks, clinical and biological hypercorticism in 9 cases (27.3%) including 6 adenomas, 1 case Of adrenal cortex and 2 cases of bilateral adrenal hyperplasia, 4 cases of primary hyperaldosteronism (18.2%). 2 patients had no hormonal secretion. For etiological treatment, 18 patients had unilateral adrenalectomy in (81.8%). 4 patients received medical treatment (18.2%).
Conclusion
The adrenal incidentaloma continues to grow with technological advances and increased abdominal radiological examinations. In the majority of cases, it will be a non-secreting benign adenoma. However, the clinician must ensure that there is no disease requiring specific management by performing a baseline hormonal assessment.

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EP1105

Clinical case: manifestation of primary adrenal insufficiency in Addison's crisis

Justina Bieliauskienė
Lithuania University of Health Sciences, Hospital of Lithuanian University of Health Sciences, Kaunas clinics, Endocrinology department, Kaunas, Lithuania

Introduction
An Addison's crisis is a life-threatening situation that usually results hypotension/hypovolemic shock, nausea or vomiting, fever, loss of consciousness, hyponatremia (Na ≤ 132 mmol/l), hyperkalemia and hypoglycemia.
Case description
33 years old patient was found at home after firefighters broke down the door, with a lot of stomach contents around. The last contact with relatives was a day ago, when the patient complained of fever and vomiting. The patient was unconscious, hypotensive (BP 72/48mmHg), glycemia 5.2 mmol/l, hyperkalemia 6.5 mmol/l, normonatremia 137 mmol/l, increased uremic indicators (creatinine concentration in serum 1439 mcmol/l ; urea 29.3 mmol/l), increased CRB 284.8 mg/l, elevated creatine kinase activity 981 IU/l was found. CT of the head, Ro of the lungs, ultrasound of the abdomen - without changes, and neuroinfection was ruled out. The patient was hospitalized in the intensive care unit, treatment with dexamethasone, infusion and antibiotic therapy was started. Renal replacement therapy was started due to significant uremic indicators. Hyperpigmentation of the patient's skin was observed, so primary adrenal insufficiency was suspected, ACTH was 6.7 pmol/l (n. 1.63 - 14.15 pmol/l) and cortisol in the morning was 25.7 nmol/l (less than 12 hours after dexamethasone injection). After the hypovolemic shock regressed, without administering glucocorticoids for 2 days, the tests were repeated: ACTH - 374.5 pmol/and cortisol - 56.91 nmol/l - primary adrenal insufficiency was confirmed and continuous treatment with hydrocortisone was started, gradually reducing the doses to maintenance doses. In case of a tendency to hyponatremia and hypotension, fludrocortisone was added to hydrocortisone. Renal function and electrolyte imbalance were fully restored, inflammatory indicators normalized. The patient tested for other autoimmune diseases - confirmed chronic autoimmune thyroiditis with euthyroidism. Anti-GAD and anti-IA2 were also positive, but there are currently no data for diabetes. The autoimmune polyglandular syndrome (APS-2) was diagnosed.
Conclusion
In untreated Addison's disease, stress such as trauma, infection, or illness can lead to an Addison's crisis. Immediate treatment with intravenous hydrocortisone is recommended for patients with suspected adrenal crisis without waiting for test results.
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EP1164

Adrenal fusion during renal transplantation: A challenging situation

Rania Dassoufi[1], Eleazar Nyogushima[2], Sana Rafi[2], Ghizlane El Mghari[2] & Nawal El Ansari[2]
[1]CHU Mohamed VI, Endocrinology, Marrakech, Morocco; [2]CHU Mohamed VI, Endocrinology, Morocco

Introduction
Adrenal-renal fusion is a rare entity wherein the capsule of the adrenal gland is fused to the kidney. Generally asymptomatic, it is only in pathological situations or in cases of adrenal or renal resection that this situation can cause problems. Adrenal transplantation has long been studied in rats solely to treat adrenal insufficiency, but no cases of accidental transplantation have been reported. Here, we report a case of adrenal-renal fusion making intraoperative dissection challenging, followed by a renal transplant including adrenal tissue.
Observation
We consulted a 17 years old and obese patient in the nephrology department at Day 1 post renal transplantation with a history of nephropathy for 1 and a half year undergoing haemodialysis at a rate of 2 sessions per week for chronic interstitial nephritis, c complicated by hypertension He received a renal transplant from his sister, complicated peroperatively by the fortuitous discovery of adrenal adhesion to the renal capsule, adrenal tissue was left on the kidney subsequently grafted to the recipient with anastomosis of the graft to the external iliac artery and external iliac vein. Post-operative follow-up was marked by isolated hyperglycemia at 3 g/dl, followed by normoglycemia at daily follow-up. He was put on immunosuppressive prednisolone in decreasing doses up to 50 mg/d, which he is currently taking.
Discussion
Transplantation of adrenal cells is similar to that of a small malignant tumor. Unless it achieves vascularization it will die or remain very small. It is imperative to use a source of a potent angiogenic factor such as FGF 3T3 secreting cells. Overall, in an intact human body, the accidental transplantation of adrenal tissue without preparation or growth factors seems to be doomed to apoptosis.

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EP1165

Modified classification of autoimmune adrenal insufficiency

Nurana Nuralieva, Marina Yukina & Ekaterina Troshina
Endocrinology Research Centre, Moscow, Russian Federation

Objectives
to modify the classification of autoimmune adrenal insufficiency (AAI).
Methods
$n = 8$ patients with early stages (potential and latent) of AAI were included (table 1).
Results
Based on the analysis of clinical and laboratory data of patients, a modified classification of AAI has been developed (table 2).
Conclusion
It is recommended to introduce a modified classification of AAI in clinical practice.

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EP1166

Simultaneous papillary and medullary thyroid carcinoma, primary hyperparathyroidism and ACTH-independent Cushing syndrome- an intriguing puzzle of endocrine disorders

Ana-Iolanda Badita[1], Simona Jercalau[1], Andrei Goldstein[1], Andreea Marcu[1], Oana Stanciulea[2], Anda Dumitrascu[1], Larisa Buduluca[1] & Corin Badiu[1]
[1]C.I. Parhon National Institute of Endocrinology, Bucuresti, Romania; [2]Fundeni Clinical Institute, Bucharest, Romania

Case presentation
A 67-year old diabetic and hypertensive female, with no significant family history, first underwent total thyroidectomy, with a histological and immunohistochemical result of both papillary thyroid carcinoma (PTC) T3Nx stage III and medullary thyroid carcinoma (MTC), with additional radioiodine treatment for PTC, showing excellent response to therapy at follow-ups (stimulated thyroglobulin <0.2 ng/ml, normal CEA and calcitonin). Almost 10 years later, the patient presented for the first time with elevated total serum calcium (12.5 mg/dl) and elevated PTH (82.2 pg/ml). A 99mTc-pertechnetat/99mTc-sestamibi scintigram was performed, showing a left superior parathyroid adenoma, for which she underwent parathyroidectomy, with constant normal PTH and total serum calcium after surgery. At that point, a thorough laboratory and genetic examination was performed. Pheochromocytoma was not confirmed. Screening for genetic mutations of the RET gene for exons 5, 8, 10, 11, 13, 14, 15 and 16 were all negative. Unfortunately, sequencing the entire RET coding region was not possible. During this extensive endocrine evaluation, an abnormal overnight 1 mg dexamethasone suppression test (13.4 mg/dl) raised the possibility of an associated Cushing syndrome. A low ACTH level (1.7 pg/ml) and an elevated midnight plasma cortisol (7.9 mg/dl) confirmed the ACTH-independent Cushing syndrome. The abdominal computed tomography (CT) showed bilateral macronodular adrenal hyperplasia. Adrenal vein sampling not being available at that time in Romania, we carried on with initial left adrenalectomy (being the largest of the two glands). At 6 months postoperative, the patient presented with persistent hypercortisolemia: ACTH = 14.9 pg/ml, basal plasma cortisol = 19.95 mg/dl, midnight plasma cortisol = 9.2 mg/dl, overnight 1 mg dexamethasone suppression test cortisol = 10 mg/dl. The patient had a second adrenalectomy and received prompt glucocorticoid (GC) and mineralocorticoid (MC) substitution. Interestingly, the patient's main complaint was persistent proximal muscle weakness, with persistent cushingoid features, persistent diabetes and hypertension. After gradual withdrawal of GC substitution, a high-dose Synacthen test confirmed residual endogenous glucocorticoid secretion (cortisol at $30' = 27$ mg/dl, $60' = 32$ mg/dl) with a normal 2×2 mg dexamethasone suppression test (0.95 mg/dl). The abdominal CT described an 8 mm nodule most likely a residue of the right adrenal gland.
Conclusion
Our case portrays an interesting association of ACTH-independent Cushing syndrome with normal endogenous cortisol secretion after bilateral adrenalectomy in a patient with prior PTC, MTC and primary hyperparathyroidism (a suspected MEN type 2A without genetic confirmation)- a constellation of rather rare endocrine disorders showcasing the importance of in-depth genetic studies.

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EP1167

Demographic, clinical, and paraclinical features of patients with adrenal incidentaloma

Mariam Mabrouk, Arige Abid, Oueslati Ibtissem, Elyes Kamoun, Faten Cherchir, Meriem Yazidi & Chihaoui Melika
RABTA Hospital, Endocrinology, Tunis, Tunisia

Introduction
Adrenal incidentalomas (AI) are adrenal masses detected on imaging performed for reasons other than suspected adrenal disease. It is important to categorize whether the mass is a functioning or non-functioning incidentalomas to determine the appropriate management and follow-up. The aim of this study was to assess demographic, clinical, and paraclinical features of patients with AI.

(Abstract EP1165) Table 1. Characteristics of patients

Characteristics	Patients							
	No1	No2	No3	No4	No5	No6	No7	No8
Sex (F/M)	F	M	F	M	M	F	F	F
Age, years	25	26	19	50	18	40	38	39
Antibodies to P450c21, U/ml (RI < 0,4)	2,940	92,670	0,604	71,976	12,858	55,623	23,604	35,508
ACTH, pg/ml (RI 7,2-63,3)	84	79	51	501	81	1077	101	21
Basal cortisol, nmol/l (RI 171-536)	402,8	477,7	576,4	157,7	482,3	342,7	420,4	560,7
Maximum cortisol during insulin tolerance test, nmol/l (RI ≥ 500)	481,6	509,4	-	141,4	497,2	350,3	690,4	-
Aldosterone, pmol/l (RI 69,8-1085,8)	121	74	207	73,4	237	350	112	732
Renin, IU/l (RI 2,8-39,9)	> 500	125	26	331	164	379	> 500	18
DHEA-S, mcmol/l	0,1*	1,6**	3,1*	3,0**	2,1**	0,7***	0,5*	3,2*
Stage of AAI	lAAI	lAAI	pAAI	lAAI	lAAI	lAAI	lAAI	pAAI

* RI 1,65-11** RI 1,2-13,4*** RI 0,26-6,68
Notes: F – female; M – male; P450c21 – 21-hydroxylase; ACTH – adrenocorticotropic hormone; DHEA-S – dehydroepiandrosterone sulfate; RI – reference interval; AAI – autoimmune adrenal insufficiency; l – latent; *P* – potential.

Table 2 Modified classification of AAI

Stages	AB to P450c21	ACTH	Cortisol basal	Cortisol during insulin tolerance test, nmol/l	R	A	D-S[1]	Clinics of AAI
pAAI	↑	N	N	≥ 500	N	N	N	-
lAAI								
-substage 1	↑	N/↑	N/↓ (but ≥ 140 nmol/l)	≥ 500	↑	N/↓	↓	±
- substage 2	↑	N/↑	N/↓ (but ≥ 140 nmol/l)	< 500	↑	N/↓	↓	±
mAAI	↑[2]/N[3]	↑↑	↓↓ (< 140 nmol/l)	< 500	↑↑[2]	N/↓	↓	+[2]

Notes: AAI – autoimmune adrenal insufficiency; AB – antibodies; P450c21 – 21-hydroxylase; ACTH – adrenocorticotropic hormone; R – renin; A – aldosterone; D-S – dehydroepiandrosterone sulfate; N – norm (within the laboratory reference interval); ↑ – increased; ↑↑ – significantly increased; ↓ – decreased; ↓↓ – significantly reduced; l – latent; *P* – potential; m – manifest.[1]
An additional diagnostic criterion. It is advisable to conduct the study only in women aged 18-40 years.[2]
At the onset of the disease.[3]
With a long course of the disease.

Methods
This was a monocentric retrospective study including 155 patients with adrenal incidentaloma (AI) followed up at the department of endocrinology of la Rabta university hospital in Tunis between 2015 and 2022. Clinical and paraclinical data were collected from patients medical files. Patients with missing data were excluded.
Results
There were 103 women and 52 men with a sex-ratio of 1.98. The mean age at the diagnosis was 52 + 12.7 years (range: 20-84). Past medical history included obesity (8.8%), hypertension (53.5%), diabetes (11.8%), dyslipidemia (5.3%), and urolithiasis (4.1%). AI was unilateral in 80.6% of cases (56.2% on the right) and bilateral in 11.6% of cases. The mean initial size at diagnosis was 21.4 ± 16.8 mm (range: 7 – 130). The AI size was ≥ 40 mm in 7% of cases. AI were homogeneous in 80% of case. The mean spontaneous density value was 9.5 HU (interquartile interval: -2 and 14). Endocrine investigation revealed that 47.7 % of patients had nonfunctional tumors, 35.5% had primary hyperaldosteronism, 11.6% had Cushing's syndrome, 4.5% had pheochromocytoma, and 0.6% had coexisting autonomous cortisol secretion and pheochromocytoma. Bilateral AI (17.6% vs 6.2%, $P=0.027$, Odds Ratio = 3.23, 95%-confidence interval: 1.09-9.58) and heterogeneous tumors (26% vs 8.6%, $P=0.004$, Odds Ratio: 1.73, 95% confidence interval: 1.27-2.36) were more frequently functional than unilateral and homogeneous ones.
Conclusions
Our results showed that AI were more frequent in women than in men. They were unilateral, homogeneous, measuring less than 40 mm, and functional in the majority of cases. It is therefore important to explore all adrenal incidentalomas for an appropriate management.

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EP1168

Testicular adrenal rests in a patient with congenital adrenal hyperplasia: a case report and literature review

Hind Ouakrim, Fatiha Ettalibi, Sana Rafi, Ghizlane El Mghari & Nawal El Mghari
Chu Mohamed Vi Marrakesh - Drh, Marrakech, Morocco

Introduction
Congenital adrenal hyperplasia (CAH) is a group of rare inherited autosomal recessive disorders, CAH is caused by a mutation in the CYP21A2 gene that leads to a deficiency of 21-hydroxylase (CYP21), due to CYP21A2 gene mutations. Testicular adrenal rest tumors (T-ARTs) is a rare kind of benign tumor in the testis, which occurs mainly secondary to congenital adrenal hyperplasia (CAH). We report a rare case of bilateral TART in a patient with CAH whose diagnosis was revealed by precocious puberty.
Case report
The 7-year-old patient was referred to early puberty. Clinical examination revealed advanced stature, and Tanner stage G5P5. Additionally, a heterogeneous mass in the left testicle was identified. The bone age was assessed as 17 years. Cortisol and ACTH levels were 3.02 µg/dl and 365.0 ng/l, respectively. Gonadotropin hormones (FSHus and LH) were suppressed, while testosterone was elevated at 9,74 ng/dl. Cytogenetic analysis revealed a 46XY karyotype. Testicular ultrasound showed increased size with heterogeneous echostructure, suggestive of intratesticular adrenal inclusions. A diagnosis of congenital adrenal hyperplasia complicated by early puberty with testicular adrenal inclusions was established. Treatment involved progressive administration of hydrocortisone up to 40 mg/day, followed by monitoring with a 17OHP level of 775.9 nmol/l. Subsequent testicular ultrasound revealed multiple nodular formations, measuring 32×20×38.6 mm on the right and 40×24.4×54 mm on the left, likely related to an adrenal testicular inclusion. The patient was then treated with dexamethasone at a dose of 1 mg/day.
Discussion
TARTs are a complication in males affected by congenital adrenal hyperplasia (CAH), boasting an average prevalence of 40%. They stand out as the primary cause of infertility among male CAH patients. TARTs manifest during childhood, their prevalence surges during puberty and adulthood. Distinguishing between TARTs and Leydig cell tumors proves challenging. TART occurrence in individuals without CAH is exceedingly rare. TARTs exhibit characteristics of both adrenal and testicular origins, suggesting a pluripotent cell type as their source. While ACTH emerges as a pivotal stimulating factor in TART development among CAH patients, additional unidentified factors contribute to this process.
Conclusion
Patients diagnosed with congenital adrenal hyperplasia should undergo routine scrotal ultrasound examinations from childhood. If testicular nodules are detected, the most likely diagnosis is TART, especially in prepubertal boys with bilateral involvement, poor compliance to replacement therapy, and suggestive echo-Doppler appearance. It is crucial to optimize replacement therapy and conduct regular ultrasound follow-ups to observe the regression of anomalies, confirming the diagnosis.

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EP1169

Congenital adrenal hyperplasia: Cardiometabolic and bone outcomes

Hamdi Frikha[1], Nesrine Dhieb[1], Hana Charfi[1], Dhoha Ben Salah[1], Mahdi Kamoun[1], Thouraya Kamoun[2], Mongia Hachicha[2], Mouna Mnif[1], Habib Sfar[3], mouna elleuch[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology; [2]Hedi Chaker University Hospital, Department of Pediatrics; [3]Tahar Sfar University Hospital, Department of Endocrinology

Introduction
Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder affecting adrenal steroid synthesis. Its treatment aims to achieve a balance between optimal glucocorticoid replacement and normal androgen levels. The long-term outcomes of this condition are poorly studied. The objective of this study is to evaluate the impact of CAH due to 21-hydroxylase deficiency on final height (FH), bone metabolism, and cardiometabolic risk in a Tunisian cohort.
Methods
A retrospective and descriptive bicentric study was conducted on patients with CAH followed at the endocrinology department of Hedi Chaker University Hospital in Sfax and the endocrinology department of Tahar Sfar University Hospital in Mahdia.
Results
Twenty-six patients (11 men and 15 women; mean age: 27.4 ± 8.2 years) were recruited. The mean FH was 159.5 ± 9.7 cm. Twenty-one patients (80.7%) had an FH below the target height. Ten patients (38.4%) had bone demineralization. Eight patients (30.7%) were obese. Lipid profile abnormalities and glucose metabolism disorders were detected in 10 (38.4%) and 5 (19.2%) patients, respectively. Seven patients (27%) had carbohydrate intolerance. Ambulatory blood pressure monitoring revealed abnormalities in 6 patients (23%). An increase in carotid intima-media thickness was observed in 14 patients (53.8%).
Conclusion
Patients with CAH are at risk of cardiometabolic and bone complications. The latter is attributed in various studies to iatrogenic hypercorticism. Regular follow-up, optimization of treatment, early lifestyle interventions, and evaluation of bone mineralization are necessary.

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EP1192

Case of amenorrhea in identical twin sisters. late-onset congenital adrenal hyperplasia (?)

Naia Lataria
Academician Bochorishvili Clinic, Endocrinology, Tbilisi, Georgia

Overview
Congenital adrenal hyperplasia is a group of autosomal recessive disorders. In the presented case we will evaluate milder form of the disease, also referred as, non-Classical''. Prevalence of CAH is 1-9/100000. In 90-95% of cases, CAH is caused by a mutation in the *CYP21A2* gene located on chromosome 6p21.3
Presented case
16-year-old girl came to our clinic with amenorrhea, she had her last menstrual cycle 1 year ago. No signs of hirsutism and/or acne. She had gained 10 kg since February. Her BMI was 26.4 kg/m^2. After evaluating, she had elevated insulin resistance index, vitamin D deficiency and elevated 17(OH) progesterone - 4.135 ng/ml. DHEAs, LH, FSH, Free Testosterone, Estradiol, Prolactin in normal range Metformin 1000 mg and Vitamin D3 4000 IU and 17(OH)progesterone measurement after ACTH stimulation for the verification of non-Classical congenital adrenal hyperplasia had been prescribed. She came again, in December, with her identical twin sister, both with amenorrhea. Sister N2 had normal weight. DHEAs, LH, FSH, Free Testosterone, Estradiol, Prolactin in normal range as well as in sister N1. 17(OH)progesterone was measured again in twin sisters. Sister N1, had 17(OH)Progesterone – 2.83 ng/ml, Sister N.2 had 17(OH)Progesterone - 2.78 ng/ml. In February 2023 ACTH stimulation test with Synacthen was performed: Sister N1: Cortisol basal – 711 nmol/l 17(OH) Progesterone T0 – 8.2 nmol/l Cortisol in 30 minutes – 978 nmol/l 17(OH)Progesterone T60 – 11.1 nmol/l Cortisol in 1 hour – 1131.38 nmol/l Sister N2: Cortisol basal – 583 nmol/l 17(OH)Progesterone T0 – 8.7 nmol/l Cortisol in 30 minutes – 878 nmol/l 17(OH)Progesterone T60 – 9.2 nmol/l Cortisol in 1 hour – 1017.70 nmol/l Prescription and recommendation: In sister N1 case, her test result is equivocal, CAH is not

excluded so urine steroid profile and genotyping was recommended. In sister N2 case, CAH was excluded. Oral contraceptives were prescribed for menstrual cycle management in both sisters.
Conclusion
It is important to evaluate NCCAH in all girls/women with menstrual abnormalities, hirsutism and acne for right diagnose and treatment of infertility.
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EP1199

Precocious puberty: a case report
Omaima Hammami[1], Ines Mezghani[1], Rim Marrakchi[1], Souhir Maalej[2], Faten Hajkacem[2], Mariem Boudaya[1], Kamel Jammoussi[1], Nabila Rekik[2], Mohamed Abid[2] & Mouna Turki[1]
[1]Hedi Chaker University Hospital, Biochemistry Departement, sfax, Tunisia; [2]Hedi Chaker University Hospital, Endocrinolgy Departement, sfax, Tunisia

Introduction
Precocious puberty is characterized by the onset of signs of puberty before the usual age and can be caused by various etiologies. Congenital adrenal hyperplasia represents a rare cause of precocious puberty. Our aim was to report a case of a child with precocious puberty.
Observation
A 4-year-old and 11 months patient, from a consanguineous marriage, hospitalized in the endocrinology department for precocious puberty. The clinical examination found a child in good general condition, a bone age of 13 years, a stature advancement of +1 standard deviations (SD) and the presence of a dysmorphic syndrome including a rounded forehead, an enlarged nose, almond-shaped eyes, micrognathism, retrognatism, slight hypotelorism, and bilateral ulna valgus. The hormonal assessment shows a high testosterone level of 3.25 nmol/l. The 17-OH progesterone was highly elevated (20 ng/ml), cortisol at 8 a.m: 51.3 ng/mL, FSH: 0.6 mIU/ml, LH is low, less than 0.1 mIU /ml, androstenedione was elevated to 0.11 ng/mL and SDHEA was increased to 7.58 µg/mL. The diagnosis of congenital adrenal hyperplasia linked to a 21 OH adrenal enzyme block was made, the genetic study is in progress and the patient received hydrocortisone at a reducing dose of 10 mg/m^2/day, divided into 2 taken.
Conclusion
congenital adrenal hyperplasia due to enzymatic block represents a complex clinical cause that requires a careful diagnostic and therapeutic approach. This disorder, although rare, can lead to early manifestations of puberty, posing significant challenges for healthcare professionals.
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EP1214

Adrenal insufficiency in allgrove syndrome:a case report
Hajar Azagouagh, Karimi Meryem, Nawal Moussaid, Rifai Kaoutar, Iraqi Hind & Mohamed Elhassan Gharbi
CHU IBN SINA, Endocrinology, Rabat

Introduction
Allgrove syndrome or triple A syndrome is a rare genetic disorder of autosomal recessive inheritance combining in its complete form: esophageal achalasia, alacrymia and adrenal insufficiency.
Observation
Patient aged 16, 3rd of 4 siblings from a consanguineous marriage, followed for allograve Sd with megaesophagus operated on in 2016, alacrymia with artificial tears and neurological impairment. As part of the follow-up of his pathology, an 8-hour cortisolaemia was performed, showing low cortisolaemia with high ACTH. The patient was started on hydrocortisone 30 mg and received several therapeutic education sessions. Genetic counseling of siblings was requested.
Discussion and conclusion
Allgrove syndrome is a rare disorder (97 published cases) of autosomal recessive inheritance, characterized by adrenal insufficiency with isolated glucocorticoid deficiency, achalasia, alacrymia, autonomic dysfunction and neurodegeneration. The gene responsible for the disease, located on chromosome 12, codes for the ALADIN protein (for alacrima-achalasia-adrenal insufficiency neurologic disorder). The exact role of this protein in Triple A syndrome is not yet known. The incidence of the condition is unknown and difficult to determine, due to the clinical variant of the disease and the infant mortality due to attacks of adrenal insufficiency, hence the importance of a careful anamnesis in search of a history of mortality in siblings. Allgrove affects both males and females, regardless of race (rational sex = 1). Achalasia and alacrymia are the first signs of the disease and may appear from birth, whereas adrenal insufficiency attacks may be discovered in adulthood, during the 2nd decade, or may never appear at all, which justifies regular monitoring and the importance of genetic counseling in siblings.
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EP1215

Addison's disease presented as a persistent hyperkaliemia in a patient with diabetic ketosis and autoimmune polyendocrine syndrome type 2 (APS-2). a case report and review of literature
Marjeta Kermaj, Dorina Ylli, Violeta Hoxha, Klodiana Poshi & Agron Ylli
[1]UHC "Mother Tereza", Endocrinology, Tirana, Albania

Introduction
APS-2 is the most common autoimmune polyendocrine syndrome. It is characterized by the presence of various endocrine-related diseases, such as autoimmune thyroid disease, type 1 diabetes mellitus, Addison's disease, primary hypogonadism, and, in rarer cases, hypoparathyroidism or hypopituitarism.
Case report
Our patient is a 38-year-old female with a medical history of type 1 diabetes mellitus (DMT1) for 13 years, Hashimoto's thyroiditis 2 years later (euthyroid under treatment with levothyroxine), and newly diagnosed Addison's disease. The patient presented to the emergency room with symptoms of diabetic ketosis, including vomiting and general body weakness. Additionally, the patient had noticed recently, darkening of the skin on her face and palms. The patient's initial assessment revealed elevated glycaemia and ketones in urine, confirming the diabetic ketosis diagnosis. However, what caught the attention of the medical team was the persistence of hyperkalaemia, despite following the appropriate treatment for diabetic ketosis. Further investigation, including laboratory tests, showed normal level of TSH and Ft4 but high levels of adrenocorticotropic hormone (ACTH) and low level of cortisolemia, confirmed the presence of Addison's disease. With the initiation of hydrocortisone treatment, the situation improved. A week later, the patient discharged the hospital in a good general health condition with diagnoses: Autoimmune poliglandular syndrome Type 2 (DMT1, Hashimoto's thyroiditis and Addison's disease) under hormone replacement therapy.
Conclusion
Addison's disease can present with hyperkalaemia due to adrenal insufficiency. Our case highlights the vital importance of recognizing and managing coexisting autoimmune endocrine disorders in patients with DMT1, as they can significantly impact a patient's clinical presentation and treatment approach.
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EP1223

Primary aldosteronism: clinical presentation and management about 2 cases
Ahmed Boukhalfa, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Mohamed VI University Hospital Center, Marrakech, Morocco, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Introduction
Primary aldosteronism (PA) is widely recognized as the most common form of secondary hypertension (1). PA, also known as Conn syndrome, is a group of pathological conditions associated with an aldosterone secretion inappropriate for sodium intake, that is relatively autonomous from renin–angiotensin system activity and potassium levels.
Clinical Case 1
Thirty two year-old patient, diagnosed since 11 months with arterial hypertension with peaks reaching 18 of systolic. The patient reported intermittent headaches and a recent weight gain of 7 kg. Clinically, we noted blood pressure at 15/8 cmhg, acanthosis nigricans and Buffalo hump. Biological tests revealed: normal kidney function, urinary methoxylate derivatives and urinary free cortisol were negative, Aldosterone:1318 pmol/l, Rénine: 6,3 mUI/l, Aldosterone to Rénine Ratio (ARR) very high at 209. Abdominal CT scan showed nodular left adrenal formation, well-limited rounding, < 10 of spontaneous density measuring 22*18 mm. The patient underwent left adrenalectomy, anatomopathological study was in favor of an adrenocortical adenoma. Evolution was marked by the normalization of blood pressure.

Clinical Case 2
Fifty six year-old patient, diagnosed since 1 year with arterial hypertension, wich despite triple antihypertensive therapy, remained poorly controlled. The patient reported fatigability with muscle cramps. Clinically, we noted high BP at 16/9 cmhg. Biological tests revealed: kidney faillure with 13 ml/mn of creatinine clearance, chronic hypokalemia, Aldosterone to Rénine Ratio (ARR) was superior than 70. Abdominal CT scan showed nodular left adrenal formation, measuring 25 mm. The patient underwent left adrenalectomy, anatomopathological study was in favor of an adrenocortical adenoma.
Discussion
Prevalence of PA varies from 6 to 18 %. While the majority of cases of PA are sporadic, four forms of autosomal-dominant inheritance have been described: familial hyperaldosteronism types I to IV. Severe or resistant hypertension, association with hypokalemia represent conditions which requires screening for PA. The Aldosterone -to-Renine Ratio has higher sensitivity than other measures. Antihypertensive drugs that can be maintained during exploration include alpha-blockers and calcium channel blockers ideally long-acting and non-dihydropyridine antagonists (2). Treatment of PA amis at preventing or correcting hypertension, hypokalemia and target organ damage. Spironolactone controls hypertension and hypokalemia and may prevent postoperatve hypoaldosteronism. Partial adrenalectomy and non-surgical ablation have no proven avantage over total adrenalectomy.
Conclusion
PA is one of the most frequent causes of secondary hypertension. Prevention requires screening for hypertensive patients, to enable specific medical or surgical management to avoid cardiovascular morbidity and mortality.
Key words primary aldosteronism, ARR, adenoma.

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Calcium and Bone

EP4

Involvement of age, obesity and genetic polymorphisms in the increment of 25(OH)D levels after 12-month treatment with calcifediol and cholecalciferol

Esteban Jódar[1,2], Paula Arranz-Gutiérrez[3] & Jose Luis Perez-Castrillon[4,5]
[1]Department of Endocrinology and Nutrition, Quirón Salud Madrid and Ruber Juan Bravo University Hospitals, Madrid, Spain; [2]Universidad Europea de Madrid, Madrid, Spain.; [3]Department of Research, Development and Innovation, FAES FARMA, Leioa, Bizkaia, Spain.; [4]Department of Internal Medicine, Hospital Universitario Río Hortega, Valladolid, Spain.; [5]School of Medicine, Universidad de Valladolid, Valladolid, Spain.

Introduction
Vitamin D deficiency is a prevalent condition worldwide. Low serum 25(OH)D levels are associated with several diseases, being age and obesity strongly related to hypovitaminosis D. In addition, several genetic variants have also been associated with lower and/or higher 25(OH)D levels.
Objective
We aimed to assess the potential influence of age, BMI, waist circumference and genetic variants on the efficacy of 12-month treatment with calcifediol compared to cholecalciferol in postmenopausal women with vitamin D deficiency. Genetic influence on 25(OH)D modulation was assessed studying 14 polymorphisms linked to VDR and vitamin D metabolism.
Methodology
This was a long-term, phase III-IV, double blind, randomized, controlled, multicenter clinical trial including postmenopausal women with basal 25(OH)D levels <20 ng/ml treated monthly with calcifediol (0.266 mg, $n=101$) or cholecalciferol (0.625 mg, $n=98$). Subgroup analyses were performed using ANOVA analysis if there was no baseline effect of the response variable; otherwise, ANCOVA analysis was used. In both cases, Weighted Least Squares (WLS) was considered if the assumptions of the model were not met. Polymorphisms were analyzed using a multivariate mixed model approach.
Results
Change in 25(OH)D levels from baseline to month 12 was significantly affected by BMI in patients treated with cholecalciferol (ANOVA $P=0.0177$; ANCOVA $P=0.0068$), whereas no significant differences were observed when treated with calcifediol ($P=0.4582$). Accordingly, abdominal circumference ≥ 80 cm produced lower 25(OH)D increments in cholecalciferol group (ANOVA $P=0.0259$; ANCOVA $P=0.0274$; WLS $P=0.0871$), but not in calcifediol group ($P=0.6899$). When results were analyzed among three different age subgroups (<65;65-74; >74 years), no differences in efficacy were observed for any of the treatments tested. Modulation of 25(OH)D levels according to genotype (PP population) shows certain association for *GC* and *VDR* in cholecalciferol group and for *CYP2R1* in calcifediol group. *CYP2R1*, that encodes 25-hydroxilase, shows that the less frequent allele of this polymorphism is linked to higher 25(OH)D levels in the calcifediol group. In the cholecalciferol group, the polymorphism rs7041 (*GC*) and rs2228570 (*VDR*) under recessive models shows a lower response due to its effect on the transporter protein and a lower affinity of the active metabolite on the receptor. These results suggest pharmacogenetic differences between calcifediol and cholecalciferol.
Conclusion
Increments on 25(OH)D levels after calcifediol treatment are independent of patients age and BMI, whereas cholecalciferol treatment shows a lower rise in 25(OH)D levels in obese patients. Pharmacogenetic differences between calcifediol and cholecalciferol were observed, although their clinical relevance remains unclear.
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EP8

Novel germline variant of CDC73 identified during screening for familial primary hyperparathyroidism

Andreea Muntean[1], Isabel Mazarico Altisent[1], Ismael Capel Flores[1], Laia Casamitjana Espuña[1], Alba Hernández Lázaro[1], Santiago Barcons Vilaplana[2], Xavier Guirao Garriga[2], Neus Baena Diez[3], Ana Romero Gregori[1], Berta Bella Burgos[4], Valeria Arsentales Montalva[1], Judith Jover Gornall[1] & Mercedes Rigla Cros[1]
[1]Endocrinology and Nutrition Department, Parc Taulí University Hospital, Institut d'Investigació i Innovació Parc Taulí (I3PT), Sabadell, Barcelona, Spain; [2]Surgery Department, Parc Taulí University Hospital, Institut d'Investigació i Innovació Parc Taulí (I3PT), Sabadell, Barcelona, Spain; [3]Genetic Department, Parc Taulí University Hospital, Institut d'Investigació i Innovació Parc Taulí (I3PT), Sabadell, Barcelona, Spain; [4]Pathology Department, Parc Taulí University Hospital, Institut d'Investigació i Innovació Parc Taulí (I3PT), Sabadell, Barcelona, Spain

Background
Hyperparathyroidism jaw-tumor syndrome (HPT-JT) is a rare and under-diagnosed cause of familial primary hyperparathyroidism (incidence $<$ 1/1000000). It is caused by a pathogenic variant in the *CDC73* (or *HRPT2*) gene that encodes parafibromin. Patients with HPT-JT have a 15–20% risk of developing parathyroid carcinoma. Other related conditions are jaw tumors in 30% of cases, kidney abnormalities in 15% of cases, and uterine tumors in 50% of cases.
Case report
A 21-year-old woman with bipolar disorder undergoing lithium treatment referred from psychiatry due to hypercalcemia. Primary hyperparathyroidism was diagnosed, with PTH 125 pg/ml, and Ca 11.3 mg/dl. Imaging tests located a lesion in the upper left parathyroid. Because the patient had a sister with two parathyroid adenomas, uterine polyps, and giant cell bone tumors, a genetic study (for suspicion of familial hyperparathyroidism) was conducted. The genetic study identified a heterozygous frameshift variant *CDC73* c.110del, p.(Lys37Argfs*72) , not previously described, classified as likely pathogenic. The patient underwent parathyroidectomy, and the pathology report defined the lesion as parathyroid adenoma. Additionally, the patient presented uterine polyps with benign characteristics, no malformations of the urinary system, and currently is awaiting a mandibular imaging study. A segregation study was performed, whereas genetic studies are pending for the remaining siblings and parents, as well as additional tests to identify conditions related to the mutation. Two siblings had primary hyperparathyroidism (diagnosed at 19 years in both cases) and underwent surgery. Pathology studies showed parathyroid adenoma in one case, and atypical parathyroid tumor in the other (this case presented with severe hypercalcemia and ECG abnormalities, which required admission into the Critical Care Unit); three siblings showed benign uterine polyps, and one sibling had giant cell bone tumors in the lower extremities. No urinary system malformations nor jaw tumors were identified so far in the family.
Conclusion
Performing a genetic screening for familial hyperparathyroidism and segregation studies in suspected cases lies in providing early diagnosis and treatment for parathyroid tumors, as well as identifying potential conditions associated with HPT-JT syndrome. These conditions may limit the functionality of patients and pose a life-threatening risk if not identified and treated promptly.
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EP26

Involvement of the vitamin D receptor gene in children with growth hormone deficiency

Mariana Ryznychuk[1,2] & Olena Bolshova[3]
[1]Bukovinian State Medical University, Department of Pediatrics and Medical Genetic, Chernivtsi; [2], Ukraine; [3]Institute of Endocrinology and Metabolism named after V.P. Commissioner of the National Academy of Sciences of Ukraine, Department of Pediatric Endocrine Pathology, Kiev, Ukraine

Introduction
Polymorphisms of genes involved in the growth process are an important cause of growth hormone deficiency (isolated form). Isolated growth hormone deficiency can be caused by genetic defects in about 10% of patients, in 34% of cases it is a consequence of familial pathology, and 4% are sporadic cases. The nuclear receptor for vitamin D mediates most of the biological functions of this vitamin. It belongs to the steroid hormone receptor family, the gene for which (vitamin D receptor — VDR) is locatedon chromosome 12q13.1.
Aim
To study the TaqI polymorphism of the VDR gene in children with GH-deficiency.
Material and methods
Determination of the TaqI polymorphism of the VDR gene (rs731236) was performed in 36 prepubertal GHD children by polymerase chain reaction followed by analysis of the length of the restriction fragments when detected by agarose gel electrophoresis.
Results
In the group of patients with GHD, the proportion of heterozygotes for T/C TaqI polymorphism of the VDR gene (rs731236) is 1.28 times higher than among healthy individuals. There were 0.68 and 0.90 times fewer patients carrying T/T and C/C genotypes than in the control group. The presence of a homozygous TT genotype increases the risk of developing GHD, but not significantly (odds ratio (OR) = 1.89, 95% confidence interval (CI) 0.66–5.39; $P = 0.23$), and the presence of a homozygous CC genotype is protective (OR = 0.75, 95% CI 0.17–3.22; $P = 0.70$). When analyzing alleles in patients with GHD, the following data were obtained: carriage of the T allele for the polymorphic loci TaqI rs731236 of the VDR gene is associated with the risk of GHD (OR = 1.24, 95% CI 0.65–2.36; $P = 0.52$) but not significantly. The ratio of allele (pT = 0.554, qC = 0.446) frequencies practically does not differ from1:1, which indicates the preservation of allele frequencies in the Ukrainian population.
Conclusions
A significant number of GHD children (55.56%) have heterozygous T/C genotype of TaqI polymorphism (rs731236) against the background of significantly lower levels of IGF-1 and stimulated GH in comparison with these indicators in children carrying homozygous C/C genotype. Hypovitaminosis D was detected in all patients with somatotropic insufficiency: deficiency - in children with homozygous T/T genotype (42.08 ± 15.70 nmol/l), and vitamin D deficiency - in carriers of heterozygous T/C genotype (56.24 ± 18.60 nmol/l) and homozygous C/C genotype (68.25 ± 16.87 nmol/l).

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EP29

The usefulness of 18F-choline PET/CT in patients with negative findings on 99mTc-sestamibi SPECT/CT in Locating Hyperfunctioning Parathyroid Glands in Primary Hyperparathyroidism

Ante Mandic[1], Ivana Kraljevic[2,3], Tanja Skoric Polovina[2], Karin Zibar Tomsic[2], Tina Dusek[2,3], Annemarie Balasko[2], Mirsala Solak[2] & Darko Kastelan[2,3]
[1]University Clinical Hospital Mostar, Department of Endocrinology, Mostar, Bosnia and Herzegovina; [2]University Hospital Centre Zagreb, Zagreb, Croatia; [3]School of Medicine, University of Zagreb, Zagreb, Croatia

Objective
This study aimed to investigate the diagnostic performance of ^{18}F-choline PET/CT in patients with negative or inconclusive results of ^{99m}Tc-sestamibi SPECT/CT in locating hyperfunctioning parathyroid tissue in primary hyperparathyroidism patients.
Methods
We conducted a retrospective study involving patients who were operated on due to primary hyperparathyroidism from April 2019 to March 2022. The analysis focused on patients undergoing ^{18}F-choline PET/CT scan due to previously negative or inconclusive findings on ^{99m}Tc-sestamibi SPECT/CT in order to localize a hyperfunctioning parathyroid gland(s). Pathohistological reports were used as a reference standard for the assessment of imaging results.
Results
The study included 29 patients (23 (79.3%) females), with a mean age of 56.3 years (range 25–74). Pathohistological analysis revealed 36 glands. The detection rate of ^{18}F-choline PET/CT in per lesion analysis was 88.9% (95% CI 70.8–97.7).
Conclusion
The results of our study showed the significant usefulness of ^{18}F-choline PET/CT in patients with negative or inconclusive results of ^{99m}Tc-sestamibi SPECT/CT in accurately locating hyperfunctioning parathyroid glands in primary hyperparathyroidism patients.

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EP32

Predictive factors of early postoperative hypocalcemia in patients with secondary hyperparathyroidism undergoing parathyroidectomy

Mezri Sameh[1], chaima zitouni[1], Wadii Thabet[2] & akkari khemaies[1]
[1]Principal Military Hospital, ENT, Tunis, Tunisia; [2]Taher Sfar Hospital, ENT, Mahdia, Tunisia

Introduction
Secondary hyperparathyroidism is the main disorder of mineral and bone metabolism associated with chronic kidney disease. This disorder is characterized by hypersecretion of parathyroid hormone (PTH). Given the high cost and unavailability of calcimimetics, surgery remains a good alternative. In the immediate postoperative period after parathyroidectomy, hypocalcemia is common and close monitoring is critical.
Objective
The aim of our work was to evaluate the surgical results of parathyroidectomy in terms of efficacy and postoperative hypocalcemia.
Methods
This is a retrospective study including 45 patients operated on in our department during the period from 2010 to 2023. The analytical study evaluated the predictive criteria of hypocalcemia after surgery.
Results
The mean age of our patients was 46 years with a sex ratio of 1.5. The mean preoperative PTH level was 2030 ng/l. The mean preoperative corrected serum calcium level was 2.4 mmol/. Twenty-five patients underwent subtotal parathyroidectomy (7/8). Fifteen patients had selective parathyroidectomy (3/4) and five of them underwent selective surgery. According to KDOQI 2003 criteria, the surgical success rate was 87%. The mean postoperative PTH level was 202 ng/l. Subtotal parathyroidectomy provided the best surgical success rates. In our study, 38 patients developed postoperative hypocalcemia. It was severe in 47% of cases. Among them, 13 patients developed Hungry Bone syndrome. Alkaline phosphatase level > 500 IU/l and preoperative hypocalcemia were respectively the main factors predicting postoperative hypocalcemia.
Conclusion
In our study, preoperative serum alkaline phosphatase and calcium concentrations were found to be predictors of postoperative hypocalcemia in patients with secondary hyperthyroidism who underwent parathyroidectomy. These variables may help clinicians identify patients undergoing hemodialysis who are at higher risk of hypocalcemia following parathyroid surgery and thus monitor them more closely during the postoperative period. Such high-risk patients may benefit from postoperative calcium and vitamin D supplementation.

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EP35

Primary hyperparathyroidism in pregnant women: experience of a specialized centre

Ekaterina Bibik[1], Anna Eremkina[1], Svetlana Vorotnikova[2] & Natalia Mokrysheva[3]
[1]Endocrinology Research Centre, Parathyroid pathology and mineral disorders, Moscow; [2]Endocrinology Research Centre, Endocrinopathies and pregnancy, Moscow; [3]Endocrinology Research Centre, Moscow

Background
Primary hyperparathyroidism (PHPT) during pregnancy is rare and often unrecognized. Most of these patients are asymptomatic or have nonspecific complaints but some of them can present with classical symptoms of PHPT and even with severe complications of pregnancy as preeclampsia, miscarriage, preterm labor etc. The incidence of maternal complications is approximately 67%, poor fetal outcomes, including stillbirth and intrauterine growth retardation

may reach 80%. Therefore, PHPT in pregnancy requires close monitoring of the multidisciplinary team.
Aim
We present a case series of PHPT in pregnancy.
Results
We managed 15 young women (median age 32 [28; 37] years), who were referred to our Centre at 21 [17; 24] weeks gestation (min 16, max 34) and only one in the early postpartum period. Two of them had *MEN1* mutation. The main laboratory features of PHPT were: iPTH 133.1 pg/ml [84.5; 232.7], albumin-adjusted serum calcium 2.87 mmol/l [2.74; 2.90], 24-h urinary calcium 10.8 mmol [6.3; 12.8]. The most common PHPT complication was nephrolithiasis (67%), among non-classical complications - hypertension (13%) and gestational diabetes (20%). 6 women received conservative treatment (group 1), because of mild disease ($n=3$) , patient's withdrawal ($n=1$) or high risks of preterm labor ($n=2$), and 9 people (group 2) underwent parathyroidectomy (PTE). The calcium and iPTH levels were comparable in both groups (for all $P>0.05$). A conservative management in all cases included low-calcium diet and oral rehydration. One patient from group 1 received cinacalcet 30 mg for 4 weeks before delivery and another one from group 2 for 2 weeks before PTE with a positive effect on serum calcium level in both cases. One patient underwent emergency C-section because of preeclampsia. In all cases a selective PTE was performed at 22 [18; 25] weeks followed by parathyroid adenoma confirmation. The total frequency of fetal/newborn complications was 50% in the group 1 and 22% in the group 2, among them hypocalcemia ($n=1$), congenital pneumonia ($n=2$), intrauterine fetal death in twins ($n=1$) were observed. In a single case (group 2) after successful PTE surgical abortion was carried out at 21 weeks gestation because congenital heart defect had been detected.
Conclusion
Surgical approach seems more beneficial for pregnant patients with symptomatic PHPT. PTE performed during the second trimester resulted in good outcomes. Mild forms of the disease can be managed conservatively with low-calcium diet and optimal oral hydration.

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EP53

Impact of bodycomposition on bone mineral density: beyond BMI

Sofia Lopes, Cátia Araújo, Mafalda Martins Ferreira, Luísa Ruas, Carla Baptista, patrícia oliveira, Dírcea Rodrigues & Isabel Paiva
Coimbra Hospital and Universitary Centre, Endocrinology, Diabetes and Metabolism, Coimbra, Portugal

Introduction
The interaction between obesity and bone metabolism is complex and not fully understood. Historically, higher body weight was considered to be protective against osteoporosis. This association has affected clinical practice: body mass index (BMI) is one of the variables included in Fracture Risk Assessment Tool (FRAX), where a higher BMI leads to a lower fracture risk. Despite this association between bone mineral density (BMD) and body weight, it is not clear whether it prevails for higher BMI values, or which components of body composition are responsible for this correlation. The aim of our study was to evaluate the impact of BMI and body composition on BMD in patients with obesity.
Methods
Cross-sectional study including patients with obesity from a tertiary hospital. To assess BMD, T-score value was used for postmenopausal women or men aged 50 or over; Z-score value for the remaining patients. Body composition was assessed by bioimpedance and DEXA.
Results
A total of 30 patients were included, 80% female, mean age of 45 ± 11 years. Mean BMI was 42.1 ± 5.9 kg/m^2 (70% in class III obesity). Mean fat mass percentage was 51.9 ± 10.6% and 47.8 ± 5.9%, as measured through bioimpedance and DEXA, respectively. There was no significant correlation between BMI and BMD ($P=0.251$). There was a negative correlation between total body BMD and body fat mass percentage assessed by bioimpedance ($r=$-0.423; $P=0.040$) and by DEXA ($r=$-0.730; $P=0.003$). Femoral neck BMD was negative and weakly correlated with body fat mass percentage assessed by DEXA ($r=$-0.455; $P=0.022$). Although there was no significant correlation between visceral adipose tissue and total body BMD ($P=0.097$), there was a negative and weak correlation between visceral adipose tissue index and femoral neck BMD ($r=$-0.448; $P=0.025$).
Conclusions
Our study challenges the belief that obesity is protective against osteoporosis, suggesting that increased fat mass should act as a red flag for the development of osteoporosis. The exact mechanism for the effects of obesity on bone health remains unclear. Several mechanisms have been proposed: accelerated senescence in stromal stem cells; increased inflammation (especially visceral adiposity, due to associated low-grade chronic systemic inflammation); replacement of osteoblasts by adipocytes in bone marrow; mutations in the obesity-associated genes leading to bone fragility. In our study, fat mass had a negative impact on femoral neck BMD, suggesting that body fat may selectively affect cortical rather than trabecular bone. The effects of fat mass on skeletal strength might be site dependent.

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EP70

Risk of osteoporotic fractures among patients with thyroid cancer: a nationwide population-based study

Eun Kyung Lee[1], Eu Jeong Ku[2], Won Sang Yoo[3], Yu Been Hwang[4], Subin Jang[4], Jooyoung Lee[4], Shinje Moon[5], Hwa Young Ahn[6] & Young Joo Park[7]
[1]National Cancer Center, Center for Thyroid Cancer, Department of Internal Medicine, Goyang; [2]Seoul National University Hospital Healthcare System Gangnam Center; [3]Dankook University College of Medicine; [4]Chung-Ang University College of Statistics; [5]Hallym University College of Medicine; [6]Chung-Ang University College of Medicine; [7]Seoul National University College of Medicine

Background
The association between thyroid cancer and skeletal outcomes has not been thoroughly investigated. We aimed to investigate the risk of osteoporotic fractures in patients with thyroid cancer compared with a matched control group.
Methods
This retrospective cohort study included 2,514 patients with thyroid cancer and 75,420 matched controls from the Korean National Health Insurance Service-National Sample Cohort (NHIS-NSC, 2006-2019). Rates of osteoporotic fractures were analysed and associations with levothyroxine dose were evaluated.
Results
Patients with thyroid cancer had a significantly lower risk of fracture compared with the control group (hazard ratio [HR] 0.81, 95% confidence interval [CI]: 0.69 to 0.94, $P=0.006$). The group diagnosed with thyroid cancer after the age of 50 (older cancer group) had a significantly lower risk of fractures compared with the control group (HR: 0.72, 95% CI: 0.6 to 0.85, $P<0.001$), especially for spine fractures (HR: 0.66, 95% CI: 0.51 to 0.85, $P=0.001$). The older cancer group started osteoporosis treatment earlier than the control group (65.5 ± 7.5 vs 67.3 ± 7.6 years, $P<0.001$). In addition, a lower dose of levothyroxine was associated with a lower risk of fracture.
Conclusions
In the actual clinical setting, the risk of fracture in women diagnosed with thyroid cancer after the age of 50 years was lower than in the control group, which is interpreted as a phenomenon caused by more proactive osteoporosis treatment in postmenopausal women with thyroid cancer.

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EP110

Young osteoporosis - factors affecting the course of T-score: a 3-year follow-up of the German register young osteoporosis

Ashley Macline Wandji[1], Clara Kühner[1], Veronika Koeppen-Ursic[2], Mandy Warda[3], Alexander Defèr[3], Marion Bogatsch-Gis[1], Katharina Pfeifer[1] & Vanadin Seifert-Klauss[1]
[1]Klinikum rechts der Isar der Technischen Universität München, Interdisziplinäres Osteoporosezentrum, Munich, Germany; [2]Klinikum Freising, Abteilung für Orthopädie und Unfallchirurgie, Freising, Germany; [3]DVO - Osteoporose Register, Dresden, Germany

Background
Osteoporosis is a disease usually associated with postmenopausal women and men over sixty. Little is known about the long-term course of early-onset osteoporosis and the factors affecting fracture risk and bone density(T-score).
Objectives
Factors that cause osteoporosis or aggravate its progression in younger patients are less studied than in older patients. Data are lacking on treatment choice, adherence and effectiveness. Our study group pursues this topic in the current follow-up of the Register Young Osteoporosis.
Methods
Women $\leq$50 yrs. and men $\leq$60 yrs. at the time of diagnosis who presented to our outpatient clinic, were recruited into the Register Young Osteoporosis, a sub-

register of the German Osteoporosis register in cooperation with the DVO (Dachverband Osteologie e.V). After written informed consent, information about bone mineral density (BMD), fractures, personal medical and family history were recorded in the register. For the follow-up, a questionnaire on the course of osteoporosis and its management (BMD, fractures, osteoporosis medication, risk factors) was sent to patients with records of at least 2 DXA-measurements. T-scores of participants who had been followed for at least 3 years were analyzed for change over time in relation to sex, medication use, fracture history, weight and (in women) menopause.

Results

72 (54,96%) out of 131 responded to the questionnaires, 46 (63,89%) women and 26 (36,11%) men. At the time of diagnosis, mean age was 35 ± 8 years in women and 47 ± 11 years in men. Vitamin D supplementation was associated with an increase in lumbar spine (LS) T-scores in both men ($P = 0{,}031$) and women ($P = 0{,}050$). 19/26 men received specific osteoporosis medication, they had lower baseline T-scores (LS:-3,1, total hip(TH):-2,0) than those who did not. 23/26 men had a positive fracture history. A significant improvement in LS T-scores ($P = 0{,}045$) was seen in men who received medication. Average baseline T-score in women with osteoporosis medication was LS:-2,8, TH:-2,0. 34/46 women had a positive fracture history. Those who received medication had lower T-scores (LS:-2,8, TH:-1,9) than fractured women who didńt. Premenopausal women (30/46) presented a higher increase in LS T-scores ($P = 0{,}041$), compared to postmenopausal women (16/46). Premenopausal women showed a significant increase in LS T-scores ($P = 0{,}015$). A significant decrease in TH T-scores ($P = 0{,}006$) was seen in underweight women (BMI < 18,5).

Conclusions

Vitamin D supplementation, osteoporosis medication, as well as fracture history, weight and (in women) menopause are influential in the management of young osteoporosis patients. Multicentre participation in the registry should be enhanced.

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EP116

Ectopic mediastinal parathyroid adenoma: Diagnostic and therapeutic difficulties across three cases

Gorgi Khaoula, Echchad Lamya, Cheibetta Zakaria, Rifai Kaoutar, Iraqi Hinde & Gharbi Mohamed El Hassan
Ibn Sina University Hospital, Endocrinology, Morocco

Introduction

Primary hyperparathyroidism (PHPT) represents a prevalent medical condition frequently characterized by asymptomatic manifestations. The etiology of PHPT is predominantly attributed to parathyroid adenomas, accounting for 85% of cases, with 10% demonstrating ectopic localization. The prevalence of asymptomatic presentation poses distinctive challenges in both diagnostic and therapeutic realms, necessitating a nuanced approach to effectively address the complexities associated with this pathology.

Observation

In a series of challenging cases, a 54-year-old female patient, previously treated twice for primary hyperparathyroidism (PHPT), underwent left upper parathyroidectomy and mediastinal ectopic parathyroid resection. A decade later, she reappeared with hypercalcemia, elevated PTH, low phosphoremia, and increased 24-hour calciuria. Despite normal ultrasound and cervicothoracic CT results, sestamibi scintigraphy revealed a mediastinal ectopic parathyroid focus. Another case involved a 59-year-old female with primary hyperparathyroidism who underwent parathyroidectomy for a left inferior polar parathyroid lesion. Despite persistent hypercalcemia, elevated PTH, and abnormal 24-hour calciuria, cervical ultrasound and cervicothoracic CT scans showed no abnormalities. However, sestamibi scintigraphy indicated anterior mediastinal ectopy. Additionally, a 68-year-old male patient, post-parathyroidectomy for primary ectopic posterior mediastinal hyperparathyroidism, presented with disrupted phosphocalcic balance. Despite inconclusive results from cervical ultrasound, cervicothoracic CT, and MIBI scintigraphy, a PET scan confirmed posterior mediastinal fixation. In all three cases, thorough investigations for other components of multiple endocrine neoplasia (NEM) yielded negative results, and our patients experienced positive outcomes following surgical resection of the ectopic focus. The anatomopathological study consistently favored the diagnosis of a mediastinal ectopic parathyroid adenoma, highlighting the diagnostic challenges and successful outcomes achieved through advanced imaging-guided interventions in recurrent hyperparathyroidism.

Discussion & Conclusion

The ectopic parathyroid adenoma is a an important cause of refreactory abd recurrent hyperparathyroidism. The mediastinal location of ectopic parathyroid tissue, though relatively rare in contrast to cervical localizations, present distinctive diagnostic and therapeutic challenges. Optimal management entails a meticulous imaging assessment, a pivotal prerequisite for determining precise anatomical localization. This intricate mapping is imperative for devising an exact therapeutic strategy tailored to the unique characteristics of this parathyroid adenoma manifestation.

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EP117

83 cases of primary hyperparathyroidism: insights and observations

Gorgi Khaoula[1], Errahali yassine[2], Tadaloui Abderahmane[2], Lamya Echchad[1], Rifai Kaoutar[1], Iraqi Hinde[1] & Gharbi Mohamed El Hassan[1]
[1]Ibn Sina University Hospital, Endocrinology, Rabat, Morocco; [2]Mohamed V Military training hospital, Endocrinology, rabat, Morocco

Introduction

Primary hyperparathyroidism (PHPT) is a common endocrine disease secondary to autonomous hypersecretion of parathyroid hormone (PTH) by one or more parathyroid glands. It is a predominantly female disease and most often asymptomatic. Its positive diagnosis is purely biological. Its curative treatment is surgical.

Patients & methods

This retrospective descriptive study encompasses 83 patients who were hospitalized and longitudinally monitored for primary hyperparathyroidism. The study was conducted at the Endocrinology Department of the Ibn Sina University Hospital of Rabat and the Endocrinology Department of the Mohamed V Military Training Hospital. The observational period spans seven years, from 2015 to 2022.

Results

The mean age of our patient cohort was 53.27 ± 16.862 years, with a predominant representation of females accounting for 90.4% of cases. Clinical presentations exhibited variability, notably characterized by osteoarticular manifestations in 65.6% of cases, urinary signs in 10.8%, and general signs in 36.1%. Primary hyperparathyroidism remained asymptomatic in 39.7% of cases. The average blood calcium level was 122.8 ± 21.4 mg/l, with normal levels observed in 9.6% of cases. Parathyroid hormone (PTH) was elevated in all cases, demonstrating a mean level of 261.7 ± 186.8 pg/ml. Cervical ultrasound, conducted in all patients, exhibited a sensitivity of 89.1%, while 64 patients underwent MIBI scintigraphy, achieving a sensitivity of 92%. Management of primary hyperparathyroidism revolves around addressing hypercalcemia, with surgical intervention implemented when indicated. Surgical treatment was undertaken in 79 patients, constituting 95.18% of cases. Anatomopathological examination revealed parathyroid adenoma as the predominant finding in 81.92% of cases. The anatomopathological study showed a parathyroid adenoma in 81.92% of cases.

Discussion & Conclusion

Our study substantiates the observed predominance of primary hyperparathyroidism in females. It emphasizes the significance of routinely assessing serum calcium levels, especially in women aged over 50, to enable early detection of PHPT at its asymptomatic phase. This proactive approach aims to prevent complications that pose risks to vital prognosis and mitigate the onset of renal and skeletal complications.

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EP118

Unusual presentation of parathyroid carcinoma

Ricardo Fonseca, Catarina Roque, Ana Sofia Osório & Sofia Castro Oliveira
Hospital Fernando Fonseca, Endocrinology, Amadora, Portugal

Background

Parathyroid carcinoma is a rare cause of primary hyperparathyroidism. There's an overlap between benign and malignant disease clinical presentation, but the presence of very high calcium levels (> 14 mg/dl), markedly raised levels of PTH, palpable neck mass or severe bone/kidney disease is more common in parathyroid carcinoma. We present a case of primary hyperparathyroidism due to a parathyroid carcinoma, with unusual presentation.

Case

A 75 years-old male was referred to the Endocrinology department to evaluate hypercalcemia, identified during the study of alithiasic acute pancreatitis. The patient had a previous history of pre-Diabetes, arterial hypertension and chronic kidney disease. During the previous hospitalization, a pancreatic mass and pelvis bone lesions were noticed in the abdominal CT. A FDG-PET was performed, with uptake

at both locations. There was a suspicion of pancreatic malignant disease, with bone metastasis, but the bone biopsy was compatible with brown tumors and the pancreatic mass biopsy was benign. Laboratory tests showed a calcium level at presentation of 12.9 mg/dl (8.8-10.2), with a phosphate of 2.4 mg/dl (2.5-4.5), PTH level of 357 pg/ml (normal range 15-65) and an estimated glomerular filtration rate of 38 ml/min/1.73 m^2. After vigorous hydration and intravenous Pamidronate, a reduction of calcium to basal levels of 10.6 – 11.4 mg/dl was noticed in the following months. Primary hyperparathyroidism was assumed, with bone disease (brown tumors at pelvis) and kidney disease (lithiasis and chronic kidney disease). Cervical ultrasonography and CT showed a mixed nodule with 34×24×22 mm at the inferior pole of right thyroid lobe, concordant with sestamibi scintigraphy result. The patient had selective parathyroidectomy with a low normal intraoperative PTH level. Postoperatively, the patient had a low normal calcium/hypocalcemia, corrected with calcitriol and oral calcium. Histology was malignant (parathyroid carcinoma). Two years after surgery, the patient has normal calcium and phosphate and a secondary hyperparathyroidism due chronic kidney disease (latest laboratory results: calcium 9.2, phosphate 3.2, PTH 75, glomerular filtration rate of 28 ml/min/1.73m^2) without signs of recurrence of the disease.

Discussion

Parathyroid carcinoma is a challenging entity, with various clinical presentations. In our case, calcium level at presentation (12.9 mg/dl), basal calcium after bisphosphonates (10.6-11.4) and PTH levels were not suspicious of malignant disease. However, the patient had severe target organ involvement – chronic kidney disease, lithiasis, brown pelvis tumors and acute pancreatitis – that are more frequent in malignant disease.

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EP150

Role of MEN1 mutation on postoperative outcomes in patients with Multiple Endocrine Neoplasia type 1-related primary hyperparathyroidism: a single center experience

Laura Pierotti1[1], Elena Pardi[1], Chiara Sardella[2], Simone Della Valentina[1], Anna Dal Lago[1], Paolo Piaggi[3], Maria Adelaide Caligo[4], Gabriele Materazzi[5] & Cetani Filomena[2]
[1]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University of Pisa, Unit of Endocrinology, Pisa, Italy; [3]University of Pisa, Department of Information Engineering, Pisa, Italy; [4]University of Pisa, Laboratory of Molecular Genetics, Pisa, Italy; [5]University of Pisa, Department of Surgical, Medical and Molecular Pathology and Critical Area, Pisa, Italy

Subtotal parathyroidectomy (PTX) is considered the surgery of choice for patients with MEN1, because it optimally balances the risk of recurrence/persistence against surgical complications. Notably, MEN1 patients negative at the genetic test (*MEN1*-negative) seem to exhibit distinct clinical characteristics compared to their mutated counterparts (*MEN1*-positive). Therefore, we hypothesized that these patients may also have a different surgical outcome. The objective of our retrospective study, conducted at our Endocrine Unit from January 1993 to January 2023, was to compare the rate of remission, persistence, and recurrence of primary hyperparathyroidism (PHPT) in *MEN1*-positive and *MEN1*-negative patients according to different surgical procedures. We evaluated 101 MEN1 patients undergoing PTX, including 80 *MEN1*-positive and 21 *MEN1*-negative patients. The diagnosis of MEN1 occurred in 29 (28.7%) cases post-surgery (69% in *MEN1*-positive and 31% in *MEN1*-negative patients). Patients underwent several types of surgery: total PTX ($n=4$), subtotal PTX ($n=48$), PTX with cervical exploration ($n=12$), simple PTX ($n=37$); none of the *MEN1*-negative group underwent total or subtotal PTX. No significant difference was observed between the two groups in terms of remission rate (38.8 % vs 50%, $P=0.37$), persistence (32.5% cs. 28.6% $P=0.9$) and recurrence (28.7% vs 23.8% $P=0.16$). The median time to remission and recurrence was 84 (41-120) and 72 (36-120) months in *MEN1*-positive and 36 (12-36) and 36 (12-24) months in *MEN1*-negative respectively. By excluding patients who underwent total and subtotal PTX, we found a significantly higher rate of remission in *MEN1*-negative compared to *MEN1*-positive patients (50 % vs 10.7 %, $P=0.007$). We found a significantly higher rate of recurrence in *MEN1*-positive than in *MEN1*-negative patients (54% vs 20% $P=0.01$). No difference was found in the persistence rate between the two groups (35.7% vs 30% $P=0.9$). When including only patients who had simple PTX we observed a significant higher remission in MEN1-negative compared to MEN1 positive patients (35.7% vs 0%; $P=0.0087$). No difference in term of the rate of persistence (41% vs 36% $P=0.7$) and recurrence (59% vs 28%; $P=0.09$) was found between the two groups. Thirteen patients (12.7%) ($n=11$ subtotal, $n=2$ total PTX), all belonging to *MEN1*-genetic positive patients, developed a chronic post-surgical hypoparathyroidism. Only one patient, belonging to MEN1-positive group, developed permanent laryngeal palsy. According to our results, MEN1-negative patients might benefit from bilateral cervical neck exploration with selective removal of the pathological glands. This surgery could present a good trade-off between risk of recurrence/persistence and surgical complications.

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EP162

Exploring complications associated with primary hyperparathyroidism: findings from an 83-case study

Gorgi Khaoula[1], Errahali Yassine[2], Lamya Echchad[1], Moktar Mohamed[1], Rifai Kaoutar[1], Iraqi Hinde[1] & Gharbi Mohamed El Hassan[1]
[1]Ibn Sina University Hospital, Endocrinology, Rabat, Morocco; [2]Mohamed V Military training hospital, Endocrinology, Rabat, Morocco

Introduction

Primary hyperparathyroidism (PHPT) is a common endocrinopathy caused by inappropriate PTH secretion by the parathyroid glands, which leads to alterations in phosphocalcic metabolism. The aim of our study is to determine the prevalence of complications of PHPT.

Materials and Methods

Retrospective descriptive study of 83 patients with primary hyperparathyroidism collected over a period of 07 years (between 2015 and 2022) in the endocrinology department at the Ibn Sina University Hospital of Rabat and in the endocrinology department of the Mohamed V training military hospital, Clinical and paraclinical parameters were collected from patient records.

Results

Our series encompasses 83 patients, with an average age of 53.27 years (range: 11-85), notably demonstrating a pronounced female predominance in 90.4% of cases. Functional manifestations were diverse, with 65.6% presenting with bone-related symptoms, 10.8% exhibiting urinary signs, 15.7% displaying digestive symptoms, 10.8% manifesting cardiovascular issues, and 6.5% experiencing neuropsychological and neuromuscular symptoms, along with a 6% incidence of QT interval shortening. Complications observed were widespread, with 48.2% exhibiting bone-related complications, encompassing fractures in 14.5% of cases and brown tumors in 9.6%. Bone densitometry, performed in 85.5% of cases, revealed osteoporosis in 33.7% and osteopenia in 20.5%. Additionally, digestive complications accounted for 4.8%, with two cases of pancreatitis, while renal complications were observed in 10% of cases. This comprehensive analysis provides a detailed overview of the clinical spectrum and complications associated with primary hyperparathyroidism in our patient cohort.

>Discussion & Conclusion

Primary hyperparathyroidism emerges as a disorder characterized by the inappropriate secretion of parathyroid hormone, consequently leading to hypercalcemia. Typically discovered incidentally due to elevated serum calcium levels or, less frequently, in the context of complications such as osteoporosis or, more rarely, digestive issues like pancreatitis. The clinical ramifications of PHPT are primarily associated with chronic hypercalcemia, hypercalciuria, or hyperparathormonemia. Within the skeletal system, excess parathyroid hormone fosters heightened bone resorption, suppressing osteoblastic activity while augmenting the osteoclast pool. This imbalance contributes to significant bone remodeling, reduced bone mineral density, and subsequently, the development of osteoporosis and bone fractures. In the renal system, there is an increase in tubular reabsorption of calcium and urinary excretion of phosphates, resulting in hypercalciuria. This elevated urinary calcium excretion can predispose individuals to episodes of renal lithiasis (20%) or, less commonly, nephrocalcinosis. The intricate interplay between parathyroid hormone, calcium metabolism, and renal function underscores the multifaceted clinical consequences of primary hyperparathyroidism.

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EP163

Features of vitamin D metabolism during normal pregnancy

Ilana Katsobashvili, Ekaterina Pigarova, Svetlana Vorotnikova, Ekaterina Bibik & Larisa Dzeranova
Endocrinology Research Center, Moskva, Russian Federation

Introduction

Vitamin D plays an important role in the regulation of the mother-placenta-fetus systemensuring normal growth, weight and development of the fetus, reducing the risks of gestational diabetes mellitus, eclampsia and preterm labor. There is insufficient data in the literature on the vitamin D metabolic pathways in pregnant women, and the available results require confirmation using more accurate methods of determination.

Objective
To study of vitamin D metabolism peculiarities in normal pregnancy in comparison with a control group of healthy female patients.
Methods
Two groups of patients participated in the study: group 1- pregnant patients ($n=20$) from 18 to 45 years of age with gestational age from week 9 to 13; group 2 - healthy female patients ($n=19$) who underwent blood sampling for vitamin D metabolites to determine total 25(OH)D by immunochemiluminescence assay and 25(OH)D3, 3-epi-25(OH)D3, 24,25(OH)2D3, 1,25(OH)2D3 by high-performance liquid chromatography with mass spectrometric detection (HPLC-MS/MS).
Results
In group 1, the following results were obtained: total 25(OH)D, 26.1 ng/ml [17.4; 37.3], 25(OH)D3, 25.6 ng/ml [17.4; 37.3], 3-epi-25(OH)D3, 1.8 ng/ml [1.1; 3.2], 1,25(OH)D3, 33.4 pg/ml [16.1; 46.0], 24,25(OH)D3, 0.8 ng/ml [0.4; 1.5]. In group 2: total 25(OH)D - 16.7 ng/ml [13.5; 27.2], 25(OH)D3 - 19.5 ng/ml [14.0; 27.0], 3-epi- 25(OH)D3 - 1.1 ng/ml [0.75; 1.47], 1,25(OH)D3 - 38.8 pg/ml [34.0; 46.4], 24,25(OH)D3 - 1.5 ng/ml [0.82; 2.69]. For the above parameters, statistically significantly higher levels in the pregnancy group were obtained for total 25(OH)D ($P=0.02$) and 3-epi-25(OH)D3 ($P=0.002$). The ratio of 1,25(OH)D3/25(OH)D3 metabolites, reflecting 1-alpha-hydroxylase activity, was 0.00132 ng/ml [0.00067; 0.00206] vs 0.0021 ng/ml [0.00153; 0.00264] ($P=0.02$); the 25(OH)D3/24,25(OH)D3 ratio reflecting 24-hydroxylase activity was 24.1 ng/ml [18.6; 60.7] vs 11.6 ng/ml [10.9; 17.6], $P=0,003$, and the 3-epi-25(OH) D3/25(OH)D3 ratio reflecting 3-epimerase activity, 0.08 ng/ml [0.07; 0.10] vs 0.05 ng/ml [0.05; 0.6], $P=0.0004$, for group 1 and group 2, respectively.
Conclusions
The data obtained indicate that in the first trimester of pregnancy the epimerization of vitamin D increases, which raises the levels of this metabolite in the blood. A decrease in activation and increase in deactivation of vitamin D in pregnant women was also observed, which reflects the ratios of metabolites that characterize these processes.

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EP173

The relationship between bone mineral density, vitamin d level and sleep quality in postmenopausal women with osteoporosis

Emir Avşar[1], Selda Celik[2], Hande Peynirci[3], Feride Taşkın Yılmaz[4] & Gülden Anataca[5]
[1]Yeditepe University, Faculty of Health Sciences, Department of Nursing, Turkey; [2]University of Health Sciences, Hamidiye Faculty of Nursing, Department of Internal Medicine Nursing, Turkey; [3]University of Health Sciences, Kanuni Sultan Suleyman Training and Research Hospital, Department of Endocrinology and Metabolic Diseases, Turkey; [4]Sakarya University of Applied Sciences, Faculty of Health Sciences, Department of Nursing, Turkey; [5]University of Health Sciences, Kanuni Sultan Suleyman Training and Research Hospital, Department of Diabetes Nursing, Turkey

Introduction
Osteoporosis is a skeletal disease characterized by decreased bone mineral density and destruction of the microarchitecture of bone structure. This study was conducted to determine the relationship between bone mineral density, vitamin D level and sleep quality in female patients with osteoporosis.
Material and Method
This descriptive correlational study included a total of 318 women diagnosed with osteoporosis. The data were collected using a patient identification form, including items for plasma vitamin D level and bone mineral density score obtained by DXA method, and the Pittsburgh Sleep Quality Index (PSQI). The data were analyzed using parametric and non-parametric tests according to whether they had normal distribution.
Results
The mean age of the women was 56.49 ± 5.68 years and their femoral neck T mean score, an indicator of bone mineral density, was -2.94 ± 0.31. Only 6.3% of the women had adequate vitamin D levels. In addition, according to their PSQI scores, 85.8% of the women had poor sleep quality. In the study, no significant difference was found between the women's bone mineral densities and vitamin D levels according to sleep quality ($P>0.05$). However, there was a weak negative correlation between the duration of osteoporosis and sleep quality ($P<0.05$).
Conclusion
The majority of the women diagnosed with osteoporosis had poor sleep quality. There was no association between vitamin D level, bone mineral density and sleep quality, but the duration of osteoporosis was negatively associated with sleep quality. Accordingly, it may be recommended to provide education and counseling to postmenopausal women diagnosed with osteoporosis on issues such as sunbathing, vitamin D and calcium preparation intake, weight control and non-pharmacological treatment approaches by making necessary individual-specific plans to improve sleep quality.

Keywords: Osteoporosis; bone mineral density, vitamin D; sleep quality.
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EP202

Romosozumab therapy after parathyroidectomy for osteoporosis caused by primary hyperaparathyroidism: two case reports

Saya Takebe, Yasufumi Seki, Kaoru Yamashita, Noriyoshi Takano, Kananko Bokuda, Daisuke Watanabe, Satoshi morimoto & Atsuhiro Ichihara
Tokyo Women's Medical University, Department of Endocrinology and Hypertension, Tokyo, Japan

Background
Primary hyperparathyroidism (PHPT) reduces bone mineral density (BMD), leading to secondary osteoporosis. While parathyroidectomy has been reported to increase BMD, the efficacy of medical therapy for PHPT-induced osteoporosis after parathyroidectomy remains uncertain. Herein, we report two PHPT cases with osteoporosis, where romosozumab, an anti-sclerostin monoclonal antibody, increased BMDs after parathyroidectomy.
Case 1
A 67-year-old woman was admitted to our department with mild hypercalcemia (10.2 mg/dl) and elevated PTH levels. She was diagnosed with osteoporosis at the age of 55 and had taken 0.75 μg eldecalcitol and 60 mg raloxifene for six months before admission. Serum calcium (reference, 8.5-9.9) and intact PTH (reference, 15-65) were 9.4 mg/dl and 110 pg/ml, respectively. Echography and ^{99m}Tc-sestamibi (MIBI) scintigraphy revealed a 9 mm-sized parathyroid gland behind the left lobe of the thyroid. Dual-energy X-ray absorptiometry (DXA) indicated reduced BMDs with T-scores of -4.0 in the lumbar spine and -5.4 in the 33% radius. She was diagnosed with PHPT and underwent parathyroidectomy. Raloxifene was replaced with 210 mg/month of subcutaneous romosozumab 5 years after the surgery. The 12-month romosozumab therapy increased T-scores from -5.6 to -2.1 in the lumber spine and from -5.6 to -5.4 in the 33% radius.
Case 2
A 64-year-old woman with a history of urolithiasis was admitted with mild hypercalcemia (11.0 mg/dl) and elevated PTH levels. She had taken 20 mg of bazedoxifene and 0.25 μg of alfacalcidol since her diagnosis of osteoporosis at the age of 60. Serum calcium and intact PTH levels after cessation of alfacalcidol were 10.3 mg/dl and 161 pg/ml, respectively. Echography and ^{99m}Tc-MIBI scintigraphy revealed a 20 mm-sized parathyroid gland below the right lower pole of the thyroid. DXA scans indicated reduced BMDs with T-scores of -4.1 in the lumbar spine and -4.9 in the 33% radius. She was diagnosed with PHPT and underwent parathyroidectomy, followed by a 12-month romosozumab therapy. The romosozumab treatment increased T-scores to -2.8 in the lumbar spine and -4.9 in the 33% radius.
Discussion
We present two cases of PHPT with osteoporosis, which demonstrated improved BMDs by romosozumab therapy after parathyroidectomy, especially in the lumbar spine. The absence of prior bisphosphonate treatment may enhance the effect of romosozumab on BMDs. Our cases suggest romosozumab as a potential postoperative therapy for PHPT-induced osteoporosis.

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EP241

9-year remission of severe primary hyperparathyroidism after high-dose cinacalcet treatment: case report

Michal Krcma
University Hospital, Diabetes & Endocrine unit, Pilsen, Czech Republic

Introduction
Parathyroid adenomas with marked hypercalcemia need in most of cases surgical treatment. Calcimimetic treatment is usually a bridging therapy to correct hypercalcemia (in combination with other approaches, e.q. bisphosphonates). We describe case of conservative treatment in a patient in whom surgical therapy was not possible due to severe acute pancreatitis and where a high dose of calcimimetics led to clinical, laboratory and graphic remission with the possibility of discontinuation of treatment.
Case report
A 64-year-old lady was admitted to our hospital for severe acute pancreatitis, triggered with hypercalcemia in primary hyperparathyroidism (iPTH 740 ng/l; Ca

3.4 mmol/l). Hypercalcemia was corrected with intravenous bisphosphonate and during very complicated and prolonged disease (from July to November) with impossibility of surgery it was necessary to proceed to treatment with high dose of cinacalcet (up to 180 mg three times a day). Initial graphic examinations (sonography, CT) showed a probable 10mm adenoma of the right lower parathyroid gland; in the acute condition we did not perform functional imaging. After resolution of pancreatitis, ^{99m}TC MIBI scintigraphy was performed, but the enlarged parathyroid gland (with same size) appeared to be inactive. We gradually reduced the dose of cinacalcet while controlling calcemia and managed to discontinue the treatment within 6 months. Further scintigraphy one month after discontinuation of treatment showed no accumulation of the isotope. In the next two years, calcemia and PTH levels remained normal. Further scintigraphy showed a reduction parathyroid adenoma to 5mm (corresponding sonographic finding) and physiological isotope accumulation. The patient remains under follow-up in our endocrinology outpatient clinic (also for secondary - post-pancreatic diabetes requiring insulin therapy) and over the next six years, she continues to have physiological calcium metabolism with adequate parathyroid hormone levels, need for D-vitamin replacement and osteopenia.

Discussion

A case report of parathyroid apoplexy followed by hypocalcemia as a consequence of cinacalcet administration is described in the literature. It is not clear whether our patient's case was a consequence of supramaximal treatment with cinacalcet or a result of a generally severe, months-long condition that could have led to ischemia of the adenoma. In any case, there was a remission of primary hyperparathyroidism lasting many years.

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EP255

An interesting case of co-existence of autosomal dominant hypocalcemia 1 with chronic myelogenous leukemia

Maria Eleni Chondrogianni[1,2], Ioannis Kyrou[3,4,5,6,7,8,9], Anna Papadopoulou[10], Aikaterini Kaperda[1], Panagiotis Diamantopoulos[11], Anna Angelousi[12], Harpal Randeva[3,4,5,6] & Eva Kassi[1,2]
[1]National and Kapodistrian University of Athens, Endocrine Unit, 1st Department of Propaupedic Internal Medicine, Laiko Hospital, Athens, Greece; [2]National and Kapodistrian University of Athens, Department of Biological Chemistry, Medical School, Athens, Greece; [3]University Hospital Coventry & Warwickshire, Warwickshire Institute for the Study of Diabetes, Endocrinology and Metabolism (WISDEM), Coventry, United Kingdom; [4]University Hospitals Coventry and Warwickshire NHS Trust, Institute for Cardiometabolic Medicine, Coventry, United Kingdom; [5]University of Warwick, Warwick Medical School, Coventry, United Kingdom; [6]Coventry University, Centre for Health & Life Sciences, Coventry, United Kingdom; [7]Aston University, Aston Medical School, College of Health and Life Sciences, Birmingham, United Kingdom; [8]University of Derby, College of Health, Psychology and Social Care, Derby, United Kingdom; [9]School of Food and Nutritional Sciences, Agricultural University of Athens, Department of Food Science and Human Nutrition, Laboratory of Dietetics and Quality of Life, Athens, Greece; [10]National and Kapodistrian University of Athens Medical School, 3rd Department of Pediatric, University General Hospital "Attikon", Athens, Greece; [11]National and Kapodistrian University of Athens, Unit of Endocrinology, 1st Department of Internal Medicine, Athens, Greece; [12]National and Kapodistrian University of Athens, 1st Department of Internal Medicine, Athens, Greece

Introduction

Autosomal dominant hypocalcemia (ADH) type 1 is a rare form of hypoparathyroidism, caused by heterozygous, inherited or de novo, activating mutations in the *CASR*. CASR is also expressed in the kidney and activating mutations lead to decreased calcium renal absorption. Activating mutations in the CasR, inhibits salt transport, leading to Bartteŕs syndrome (BS) type V which can co-exist with ADH1. Chronic myeloid leukemia (Cml) is characterized by the clonal hyperproliferation of immature blood cells. Recently, CaSR has been raised as a targetable factor in Aml progression, however, data on its role in Cml are scarce.

Clinical presentation

33-year-old man was referred to the outpatient for poorly controlled hypoparathyroidism along with hypomagnesemia, and mild hypokalemia and dehydration. His hypoparathyroidism was diagnosed on the second day of birth. The patient presented nephrolithiasis and basal ganglia calcification. In 2020, he was also diagnosed with Cml. He was treated with calcium carbonate, alfacalcidol, cholocalciferol, hydroclorothiazide. He also received dasatinib for the Cml. At the outpatient, rhPTH was initiated along with magnesium supplements leading to reduction of the alfacalcidol and calcium supplements and to a better control of hypocalcemia and hypercalciuria. NGS was performed and demonstrated a genetic change (c.2486A>G) in exon 7 of the *CaSR*. The patient had a heterozygous substitution of adenine (TAT) for guanine (TGT) at codon 829.

Discussion

This is the third case of the specific mutation. In one case, mild Bartter V syndrome was also co-exist. The clinical presentations and onset timing of BS phenotype differ according to the type of mutation. Moreover, BS phenotype can differ between patients who have the same *CaSR* mutation, deteriorating the loss of water and predisposing to hypokalemia to varying extent. Of interest, this is the second case presenting with ADH1 and Cml. In the first reported case, severe hypocalcemia was triggered by imatinib leading to the diagnosis of underlying ADH1. CaSR has been found to modulate intracellular levels of Ca2+ and consequently calcium-dependent protein kinases which coordinate several signaling pathways (i.e. P-ERK and b-catenin) which are crucial to Cml malignant transformation in the same manner as *BCR-ABL* does. Conclusively,1)in Cml patients treated with TKIs and presented with severe hypocalcemia, the possible existence of ADH1 may need to be investigated, 2) a potential role *CASR* activating mutations in the pathogenesis and progress of Cml merits investigation.

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EP261

Outcomes of parathyroidectomy in patients with primary hyperparathyroidism

Sameh Mezri[1], chaima zitouni[1], Wadii Thabet[2] & Khemaies Akkari[1]
[1]Principal Military Hospital, ENT, Tunis, Tunisia; [2]Taher Sfar Hospital, ENT, Tunis, Tunisia

Introduction

Hyperparathyroidism is the clinical and biological manifestation of excessive and inappropriate parathyroid hormone (PTH) production. It is the third most common endocrinopathy. It is often secondary to a single adenoma (80%). Occasionally, it may be a multi-glandular disease (15-18%). Treatment is surgical.

Objective

the aim is to evaluate therapeutic results after surgery for primary hyperparathyroidism.

Method

This is a retrospective study including 84 patients operated on for primary hyperparathyroidism in our department over a period from 2015 to 2023.

Results

The mean age of our patients was 49 years, with a clear female predominance. Patients presented osteoarticular signs in 60% of cases, renal signs in 29%, digestive signs in 15% and neuropsychic signs in 5%. Hyperparathyroidism was discovered incidentally on biology data in 32% of patients (27 cases). Mean calcemia was 2.8 mmol/l. Normocalcic forms were noted in 8.4% of cases. Malignant hypercalcemia was noted in 5.9% of cases. Hypovitaminosis D was found in 48% of cases. The mean PTH level was 411µg/l. Postoperatively, the rate of improvement in osteoarticular signs, renal signs, digestive signs and neuropsychic signs was 62%, 58%, 54% and 75% respectively. We noted normalization of PTH levels within 72 hours of surgery in 90.5% of cases. Failure was noted in 6 cases. This failure was related to incomplete surgery for a triple adenoma in 1 case, hyperplasia in 3 cases, glandular ectopy in 1 case and multiple endocrine neoplasia in 1 case.

Conclusion

Parathyroidectomy is the only curative treatment option available in primary hyperparathyroidism with high cure rates. This surgery can reduce symptoms and prevent further complications.

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EP288

Hyperparathyroidism: secondary to myeloma or concomitant association

Hind Ouakrim, neima hassan, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Chu Mohamed Vi Marrakesh - Drh, Marrakech, Morocco

Introduction

Hyperparathyroidism is a pathological condition characterized by the excessive secretion of parathyroid hormone (PTH), resulting from the hyperactivity of one

or more parathyroid glands. This condition can manifest as primary, secondary, or tertiary hyperparathyroidism. However, determining the primary or tertiary origin of hyperparathyroidism can pose challenges in certain complex situations. In this report, we present a clinical case where identifying the primary or tertiary origin of hyperparathyroidism remains intricate.
Case Report
A 50-year-old patient with a three-year history of multiple myeloma complicated by end-stage renal failure requiring hemodialysis was diagnosed with hyperparathyroidism during routine medical follow-up. Despite maintaining a normal phosphocalcic balance, the patient reported diffuse bone pain and a general decline in health, with no other associated symptoms observed during the clinical examination. Sestamibi-Tc99 scintigraphy revealed three focal retentions of MIBI-Tc99m: one behind the upper right pole measuring 5.7×4.6 mm, one behind the lower right pole measuring 5.9×4.3 mm, and one behind the lower left pole measuring 5.6×4.8 mm. These findings suggested the presence of pathological parathyroid tissues, without any identified ectopic focus. Subsequently, the patient was referred for subtotal parathyroidectomy.
Discussion
Multiple myeloma is a hematologic malignancy characterized by osteolytic bone destruction resulting from increased osteoclastic resorption without a corresponding increase in bone formation. This process contributes significantly to the morbidity and mortality in multiple myeloma patients, leading to symptoms such as bone pain, diffuse osteopenia, focal lytic lesions, pathologic fractures, spinal cord compression, and hypercalcemia. Kidney failure, a common complication of multiple myeloma, can give rise to secondary and tertiary hyperparathyroidism. While both multiple myeloma (MM) and primary hyperparathyroidism (PHPT) are common causes of hypercalcemia, the simultaneous occurrence of these two pathologic processes in a single patient is exceedingly rare. Literature suggests that monoclonal gammopathies are more prevalent in patients with PHPT than in the general population, highlighting the importance of screening for monoclonal gammopathy in patients with PHPT. In the presented case, the patient had a history of kidney failure secondary to MM and presented with hyperparathyroidism. Sestamibi scintigraphy revealed hyperplasia of the parathyroid glands, consistent with both tertiary and primary hyperparathyroidism.
Conclusion
In cases where the origin of hyperparathyroidism remains challenging to determine, particularly when associated with multiple myeloma, careful consideration and further investigation are warranted. The coexistence of primary hyperparathyroidism with multiple myeloma represents a rare presentation, emphasizing the need for a thorough examination and comprehensive assessment.
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EP309

Hypercalcemia caused by advanced chronic liver disease without malignancy: a rare entity
Nauman Jadoon
NHS Greater Glasgow & Clyde, Endocrinology, Glasgow, United Kingdom

Background and Aims
Hypercalcemia in patients with advanced chronic liver disease (CLD) without hepatic neoplasia is a rarely reported and poorly understood entity. CLD is usually associated with hypocalcaemia because of hypoalbuminemia. Hypercalcemia on the other hand is extremely rare and needs meticulous ruling out of other causes.
Methods
Here a case of 55-year-old male with hypercalcemia who had chronic liver disease in the absence of malignancy, is presented.
Results
A 55-year-old male who was admitted with jaundice, weight loss and hypercalcaemia. He had a calcium that peaked at 3.34 with a suppressed PTH (<0.4). Labs revealed worsening liver enzymes. Total bilirubin peaked around 9 days, at 149 umol/l, before starting to trend down. He had extensive evaluation of hypercalcemia. He had an urgent CTCAP to look for malignancy which found new diagnosis of liver cirrhosis with multi nodular liver and features of portal hypertension. Focal hepatic abnormality was difficult to exclude with the background of cirrhosis. He went onto have an MRI on which there were no discrete focal liver lesions although there was decompensation with ascites not seen on the first scan few days prior. His vitamin D was low, ruling out parathyroid adenoma or vitamin D toxicity. AFP and ACE levels were normal, as was TSH and T4, ruling out malignancy and hyperthyroidism as aetiology. Normal renal function ruled out renal aetiology for hypercalcemia. There was no evidence of granulomatous disease. He had raised IgG 21.2 but normal immunoglobulins. Serum electrophoresis and urine BJP were negative. No paraprotein detected, no urinary free light chains. After extensive work-up, no cause was found, and he was treated with IV fluids and given an IV infusion of bisphosphonate.
Conclusions
Hypercalcemia caused by advanced chronic liver disease in the absence of malignancy is a rare condition. It is a diagnosis of exclusion and responds well to bisphosphonate treatment, leading to resolution of hypercalcemia and prevention of further debility.
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EP330

Early puberty and abnormal bone health: a comprehensive review
Ashraf Soliman, Nada Alaaraj, Fawzia Alyafei, Noor Hamed & Shayma Mohamed
Hamad General Hospital, Pediatric Endocrinology, Doha, Qatar

Introduction
The relationship between early puberty and abnormal bone health has garnered significant research attention, with varying outcomes.
Objectives
This review systematically examines studies up to March 2023 to determine whether early puberty is associated with abnormal bone health, specifically low bone mineral density (BMD), osteopenia, and osteoporosis. We analyze and summarize research articles ($n=25$) to elucidate the potential link between early puberty and the occurrence of abnormal bone health, particularly low BMD, osteopenia, and osteoporosis.
Results
Peak Bone Mass and Pubertal Timing: Peak bone mass (PBM), a critical determinant of osteoporosis risk and fractures, shares similarities with pubertal timing in terms of physiological variability and genetic influence. Factors influencing pubertal timing also affect bone acquisition. Fetal and infancy exposure to nutrients like vitamin D, calcium, and protein influence both traits. The Gothenburg Osteoporosis and Obesity Determinants study shows a negative association between age at peak height velocity (PHV) and bone density in young adult men. Using National Health and Nutrition Examination Survey (NHANES) data, a study reveals that an age of menarche ≥ 16 years is associated with lower lumbar spine (LS) BMD, even after adjusting for confounding factors. This suggests that late menarche may increase the risk of lumbar osteoporotic fractures. A large study on Swedish men finds that late pubertal timing is associated with increased adult fracture risk. Age at peak height velocity (PHV) predicts fractures, independent of factors like birth weight, childhood BMI, and adult height. Girls with idiopathic central precocious puberty (CPP) show increased bone mineral density, but this advantage wanes when corrected for bone age. GnRH agonist treatment seems to have no detrimental effect on bone mineral density. Longitudinal studies on British participants suggest that male participants gain bone density faster than females. Late pubertal age is associated with persistently lower bone mineral density in both genders. Studies analyzing GnRH agonist treatment in children with CPP reveal mixed results. While some suggest a reversible reduction in bone mineral density during treatment, others find restoration of bone mass after cessation of therapy.
Conclusion
Overall, this review highlights the complex relationship between early puberty and abnormal bone health. While some studies indicate associations between early puberty and decreased bone health, others emphasize the potential for recovery post-treatment cessation. Further research is necessary to fully elucidate the impact of early puberty on bone health, especially in the context of preventative measures for osteoporosis and fractures.
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EP331

Denosumab therapy in diffuse sclerosing osteomyelitis – a case report
Mona Vahidi Rad, Samir Ahmed, Michael Whitaker & Aditi Kumar
Mayo Clinic, Endocrinology, diabetes and metabolism, Scottsdale, United States

Introduction
Diffuse sclerosing osteomyelitis (DSO) of the jaw is a chronic and rare condition that can present with recurrent and severe jaw pain and mandibular swelling. The treatment of this condition can often be quite challenging. We present a patient with mandibular DSO who had significant improvement in jaw pain with denosumab injections.
Clinical Case
A 23-year-old female presented with left mandible pain for 4 years. Her symptoms started after a blunt trauma to her jaw. Based on clinical features and

CT scan findings, she was diagnosed with chronic non-infectious osteomyelitis of the jaw. She was treated with oral appliances, trigger point injections, analgesics, anti-inflammatory medications, and oral steroids but only had minimal and temporary resolution in her pain. She was seen in endocrinology clinic and received denosumab which resulted in significant improvement and about 50% reducation in jaw pain. A second injection of denosumab was given 6 months later with continued improvement in her symptoms. Repeat imaging after denosumab injections revealed stable thickening and sclerotic signal changes in the body and angle of the left mandible corresponding to chronic osteomyelitis, without additional osseous abnormalities.

Discussion

There have been several medical and surgical options proposed to treat DSO. The typical medical treatment options include anti-inflammatory drugs, intravenous or oral antibiotics, corticosteroids, and analgesics for pain control. The medical treatment might often require several months and may not provide adequate pain control. There have been limited number of reports of using antiresorptive medications including bisphosphonates and denosumab to control pain and inflammatory activity in DSO. These antiresorptive treatments can potentially reduce pain and swelling via direct inhibition of the osteoclast activity that plays an important role in pathogenesis of DSO. Our patient with DSO experienced significant pain relief after denosumab injections. Given the potential risk of medication related osteonecrosis of the jaw (MRONJ) with antiresorptives, denosumab has the advantage of having a shorter half-life in bone compared with bisphosphonates thus decreasing the duration of risk for MRONJ.

Conclusion

Denosumab may be a promising treatment option for pain control in DSO. Additional studies are needed to further study the effects of denosumab and its roles in treatment of DSO.

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EP333

Bone mineral density in women with breast cancer receiving adjuvant aromatase inhibitors and anti-resorptive treatment – healthy living after breast cancer

Rasmus Jansen[1], Djordje Marina[1], Simone Diedrichsen Marstrand[1], Michael Andersson[2], August Nielsen[1], Kristian Buch Larsen[1] & Peter Schwarz[1,3]

[1]Department of Endocrinology and Metabolism, Rigshospitalet, Copenhagen, Denmark; [2]Department of Oncology, Centre for Cancer and Organ Diseases, Rigshospitalet, Copenhagen, Denmark; [3]Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Introduction

Aromatase inhibitors, such as Letrozole or Exemestane, are often used as adjuvant treatment for post-menopausal breast cancer. However, they are known to reduce bone mineral density (BMD). Furthermore, breast cancer patients often undergo chemotherapy with drugs associated to BMD loss by themselves. Therefore, patients treated for breast cancer are subject to a considerable risk of BMD loss, and to alleviate this the treatments are normally combined with an anti-resorptive agent such as zoledronic acid or denosumab. These drugs have proven effective at stopping BMD loss during breast cancer treatment in several trials. A current oncological protocol is to use adjuvant i.v. zoledronic acid 4 mg every 6 months for 4 years while patients undergo treatment with aromatase inhibitors. We have investigated a group of women with breast cancer undergoing this protocol regime in a regular, clinical setting with the aim of determining whether all-cause BMD loss can be halted and/or reversed in an average, unselected population of women with early post-menopausal breast cancer.

Methods

A prospective study of BMD changes in post-menopausal women with breast cancer undergoing adjuvant treatment with aromatase inhibitors and anti-resorptive treatment in a clinical setting. We are currently following this cohort of women from diagnosis to finalized aromatase inhibitor treatment, and data presented here represent an interim analysis after two years of aromatase inhibitor treatment.

Results

A total of 79 women with a mean age of 59.4 years ($\pm$6.0) was included. BMD was measured by DXA-scan at baseline, after 12 months and after 24 months. In this interim analysis we found that adjuvant antiresorptive treatment significantly increases BMD after 12 months in all sites; in lumbar spine from 0.920 to 0.975 g/cm^2 ($P<0.001$), in total hip from 0.828 to 0.851 g/cm^2 ($P=0.006$) and in femoral neck from 0.704 to 0.725 g/cm^2 ($P=0.005$). All three sites remained significantly increased compared to baseline after 24 months ($P<0.001$ at lumbar spine; $P=0.017$ at total hip; $P=0.045$ at femoral neck).

Conclusion

Adjuvant treatment with anti-resorptive drugs can, in a short time, significantly improve BMD in women treated for early breast cancer with chemotherapy and aromatase inhibitors, in normal clinical practice.

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EP334

Bone disorders in oncological patients treated with Immune-Checkpoint Inhibitors (ICIs)

Vasiliki Siampanopoulou[1], Anna Angelousi[1], George Lyrarakis[2], Athina Karampela[1], Petros Papalexis[1], Alexandros Lafioniatis[1], Chrysoula Mytareli[1], Elisavet Tasouli[1], Dimitrios Ziogas[2], Evanthia Kassi[3,4] & Helen Gogas[2]

[1]Unit of Endocrinology, First Department of Internal Medicine, Laiko General Hospital, National and Kapodistrian University of Athens, Athens, Greece; [2]First Department of Internal Medicine, Laiko General Hospital, National and Kapodistrian University of Athens, Athens, Greece; [3]Unit of Endocrinology, First Department of Propaedeutic and Internal Medicine, Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece; [4]Department of Biological Chemistry, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Background

The use of immune checkpoint inhibitors (ICIs) has been lately established as a promising and effective treatment in several solid malignancies. Endocrine-related adverse effects are common, however their effects on bone metabolism is unknown.

Methods

We retrospectively investigated the prevalence of bone-related complications in patients undergoing or completing treatment with ICIs. Epidemiological and clinical data from the medical files of 72 patients treated mainly for melanoma (90.2%) were recorded. Bone health metrics were determined by Dual Energy X-ray Absorptiometry (DEXA) scans and biochemical markers.

Results

In this study, a total of 72 patients were included, with a female to male ratio (54% vs 46%) and a mean age of 59.2 years for women and 64.8 years for men. Monotherapy with ICIs was administered in 48.6% of the cases, with nivolumab being the most common type (36.1%). Sequential and/or combination treatments were also administrated in 26.3% of the patients, including chemotherapy + ICI (9.8%), sequential ICIs (8.3%), Interferon A + ICI (4.1%) and Tyrosine Kinase Inhibitors (TKIs) + ICIs (4.1%). DEXA scans revealed normal bone density in 48.6% of the cases, osteopenia in 36.1% and osteoporosis in 15.2%. In all cases, bone density data were acquired in a mean time of 22.7 months post-ICI initiation. It should be noted that the patients with osteopenia or osteoporosis had no prior personal history of bone disease and did not receive any antiosteoporotic medication. No osteoporotic fractures were reported in any of our patients. Mean osteocalcin (BGP) levels in patients with osteoporosis and osteopenia were statistically significantly higher compared to those with normal DEXA [28 $\pm$ 11.6 ng/ml (p-value$=0.016$) and 22.8 $\pm$ 9.1 ng/ml (p-value$=0.013$) accordingly, vs 16.4 $\pm$ 9.8 ng/ml (p-value$=0.315$)].

Conclusions

Our findings suggest that bone health issues have a significant prevalence among oncological patients treated with ICI irrespective of the treatment schemes. Bone health is a parameter that should not be underestimated in oncological patients.

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EP335

Trabecular bone score and specific bone turnover markers in high-dose glucocorticoid therapy among individuals with graves' orbitopathy

Lukasz Gojny, Justyna Kuliczkowska-Płaksej, Aleksandra Jawiarczyk-Przybyłowska, Jowita Halupczok-Żyła & Marek Bolanowski

Wroclaw Medical University, Department of Endocrinology, Diabetes and Isotope Therapy, Wrocław, Poland

The Trabecular Bone Score (TBS) has recently been developed through the grayscale textural analysis of Dual-Energy X-ray Absorptiometry (DXA) images. Due to its capability to evaluate the microarchitectural texture of bone, TBS proves valuable in the assessment of bone quality. While the clinical relevance of TBS has been partially confirmed in relation to hormonal disorders, there is currently a lack of precise data regarding its application during specific phases of treatment for individuals with Graves' Orbitopathy (GO) undergoing high-dose glucocorticoid (GS) therapy. The objective of this investigation was to assess the utility of TBS testing and specific bone turnover markers at various stages of GO treatment. This evaluation aimed to identify their practical value in routine clinical practice. Between 2020 and 2023, the study focused on a cohort of 47 patients experiencing active moderate-to-severe GO who underwent treatment with intravenous methylprednisolone (MP). Within a subset of 29 patients treated from 2020 to 2022, the study evaluated the therapeutic effects on TBS, Lumbar Spine Bone Mineral Density (LS BMD), and Femoral Neck Bone Mineral Density (FN BMD). Another subgroup consisting of 42 patients treated during the

same period underwent an assessment of therapy impact on specific markers, including sclerostin (SCL), osteoprotegerin (OPG), osteocalcin (OC), and N-terminal telopeptide of type I collagen (NTX). BMS and TBS assessments were conducted immediately prior to the initiation of treatment and two months following the administration of the final dose of MP. Measurements of bone turnover markers were taken at the onset of treatment, preceding the sixth MP dose, subsequent to the 12th MP dose, and two months post the final MP dose. Within the cohort receiving treatment, statistically notable alterations in LS BMD and TBS were identified, showing a rise of 3% and 0.7%, respectively. Furthermore, within the subset of patients undergoing marker assessments, a decline in the average concentrations of SCL, OPG, NTX was noted, along with an increase in OC concentration. The findings from the conducted study indicate that BMD TBS exhibit comparable responses to high-dose corticosteroid therapy in individuals with thyroid orbitopathy. It has been verified that the use of MP in the treatment of thyroid orbitopathy leads to alterations in the rate of bone turnover. Given these observations, patients undergoing planned or ongoing MP therapy necessitate continual clinical assessment and enhanced diagnostic scrutiny to evaluate the risk of osteoporotic fractures and implement suitable preventive measures.

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EP338

Association between reduced physical activity and 10-years risk of fracture in postmenopausal women with osteopenia/osteoporosis

Aikaterini Andreadi[1,2], Alessandro Minasi[1], Ilenia D'Ippolito[1], Maria Romano[1], Valeria Ruotolo[1], Marco Meloni[1,2], Francesco Maria Iafrate[1], Flavio Pozzi[1], Alfonso Bellia[1,2] & Davide Lauro[1,2]
[1]Policlinico Tor Vergata Hospital, Unit of Endocrinology and Diabetology, Rome, Italy; [2]University of Rome Tor Vergata, Department of Systems Medicine, Section of Endocrinology and Metabolic Diseases, Rome, Italy

We conducted a cross-sectional analysis on a sample of postmenopausal women ($n=88$, aged 66 ± 5 years) attending the osteoporosis outpatient service of our University Hospital between September and October 2023. All patients underwent physical examination and Dual Energy X-ray Absorptiometry (GE HealthCare-Lunar) scans at lumbar spine and hip level. 10-years risk of major osteoporotic fracture was assessed with the FRAX® algorithm. Level of physical activity was assessed by the International Physical Activity Questionnaire (IPAQ) - Short Form, whereas adherence to Mediterranean diet was evaluated by the Medi-Lite score. Associations were tested using logistic regression analysis, with dichotomic variables entered as follows: 10-years fracture risk $>20\%$ vs $<20\%$; being overweight/obese (BMI ≥25) vs normal weight (BMI ≤25); low level of physical activity (IPAQ class 3) vs moderate/high level (IPAQ class 1 or 2); low adherence to Mediterranean diet (Medi-Lite score <6) vs moderate/high adherence (Medi-Lite score 7-18). The majority of women had osteopenia (47%) or osteoporosis (41%) according to relative T-Score reference range. None reported a history of fracture. More than 90% of the patients were on anti-resorptive therapy (bisphosphonates, denosumab) and/or vitamin D supplementation, as appropriate. Approximately one-third of the patients (27.3%) were overweight or obese according to BMI (≥25). BMI ≥25 was significantly associated with having a 10-years risk of fracture higher than 20%, irrespective of age and concomitant medications (OR 1.28; 1.11-2.72, $P=0.038$). Being physical inactive according to IPAQ was significantly associated with having a 10-years risk of fracture higher than 20%, irrespective of age, concomitant medications and class of BMI (OR 1.76; 1.22-3.01, $P=0.004$), whereas no significant association were seen between adherence to Mediterranean diet and 10-years risk of fracture (OR 1.12; 0.76-1.91, $P=0.42$). Low level of physical activity assessed with a standardized self-administered questionnaire (IPAQ) turns out to be significantly related with a 10-years major osteoporotic fracture risk higher than 20% in an unselected group of post-menopausal women with osteopenia/osteoporosis. This relationship may be independent of body weight and adherence to Mediterranean diet. Since assessment of physical activity is currently not included in the FRAX® algorithm, these preliminary results deserve to be confirmed/better addresses in a broader population of post-menopausal women.

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EP348

Pediatric case of autosomal dominant hypocalcaemia type 2 (ADH2) due to GNA11 gene mutation

Nada Akad[1,2], Maria Christina Ungureanu[1,2], Ana Tofan[3], Ioana Vasiliu[1,4] & Otilia-Andreea Tarcau[2]
[1]Universitatea de Medicină şi Farmacie "Grigore T. Popa" din Iaşi, Iaşi, Romania; [2]Saint Spiridon County Hospital, Iaşi, Romania; [3]Arcadia - Spitale şi Centre Medicale, Iaşi, Romania; [4]Saint Mary Emergency Children Hospital, Iaşi, Romania

Introduction
Autosomal Dominant Hypocalcemia (ADH) presents with low calcium and high phosphorus levels due to hypoparathyroidism. It is categorized into type 1, resulting from gain-of-function mutations in the calcium-sensing receptor (CASR), and type 2, caused by activating mutations in GNA11, a key mediator in CASR signaling. Our contribution involves reporting a rare case of pediatric ADH 2.
Case presentation
We present the case of a 9-year-old boy who first addressed the Department of Endocrinology Iasi to investigate short stature and low Body Mass Index (BMI) (Height at -2.89SD and BMI at - 4.46SD) and persistently low levels of calcium and PTH**.** In his medical background, we highlight the diagnosis of gut dysbiosis at the age of 6. It is important to mention that the older brother and the father experience chronic hypocalcemia, the father suffering from clinical manifestations of hypocalcemia. Hormonal and biochemical assessment eliminated the possibility of adrenal and thyroid dysfunction. Regarding somatotropic axis, the baseline values of GH and IGF1 were low with no adequate stimulation of GH when stimulated with arginine. Low IGF1 may be in the context of malnutrition, but this does not explain GH deficiency. HrGH treatment was initiated with height improving to -1.93SD in 18 months. Because of the alteration in phosphate-calcium balance, genetic testing was done. It was identified a heterozygous mutation of the GNA11 gene, c.178c>t (p.arg60cys), responsible for the development of ADH2. Treatment with calcitriol was underwent for 18 months. Calciuria begun to rise, and together with the elevated phosphates and the absence of symptoms lead to the therapeutic decision to stop calcitriol considering the risk of renal lithiasis and calcification of basal nuclei.
Discussion
The protein produced of GNA11 gene is the alfa subunit of G11 protein that functions alongside CASR in calcium regulation. The activating mutation of GNA11 is accountable of developing ADH2. Data from literature show that ADH2 is associated with a milder phenotype in terms of hypocalcemia and it is rarely associated with hypomagnesemia or hypercalciuria, possibly because CASR couples with proteins other than G11 in the kidney. ADH2 patients present more often short stature, implying that GNA11 plays a role in skeletal growth, and calcifications of the basal ganglia. The treatment is not recommended in asymptomatic patients.
Conclusion
Although genetic disorders are not a common cause of hypoparathyroidism, accurate diagnosis of the underlying genetic etiology is essential, affecting treatment goals, comorbidity screening, and family planning.

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EP369

Elevated parathyroid hormone is not enough to make the diagnosis

Yordan Vlahov[1], Boyana Trifonova[1], Ralitsa Mekova[1], Antoniya Nikolova[1], Radina Ivanova[2], Gabriela Mateva[3], Pavel Bochev[3] & Anna-Maria Borissova[1]
[1]University Hospital Sofiamed, Sofia, Bul, Clinic of Endocrinology, Sofia, Bulgaria; [2]Medical University, Sofia, Bulgaria, Department of Pathology, Sofia, Bulgaria; [3]Acibadem City Clinic UMBAL mladost, Clinic of nuclear medicine, Sofia, Bulgaria

PTH increases calcium uptake from bone, tubular calcium reabsorption and renal phosphate excretion, and by stimulating 1α-OH vitamin D hydroxylase in the kidney increases production of 1,25(OH)2D.
Aim
To differentiate and characterize the various diseases associated with an increase in PTH in the material of the Endocrinology Clinic, Sofiamed University Hospital for 3 years.
Material
167 patients with elevated PTH were examined, 145 (87.3%) women and 21 (12.7%) men, with an average age of 62.01 ± 12.73 years (36-85 years). Patients are divided into two groups: 1. with Primary Hyperparathyroidism (PHPT), n-77; 2. with Secondary Hyperparathyroidism (SHPT), consisting of three subgroups - 2.1. with vitamin D deficiency (n-31) 2.2. with CKD stage 3-4 (n-39); 2.3. with CKD stage 5 (n-20).
Methods
Standard biochemical and hormonal studies of the mineral exchange, neckultrasonography, Spect-CT and fine needle puncture biopsy in 23% (38/167) of the patients.

Results
The oldest were the patients with SHPT with CKD pre-dialysis, and the youngest were the CKD patients on chroniodialysis compared to the other groups, $P<0.001$. The serum calcium was significantly higher in patients with PHPT, $P<0.001$. The serum level of phosphorus was significantly lowest in patients with PHPT and significantly highest in patients with SHPT on chroniodialysis, $P<0.001$. The same group also had a significantly higher level of alkaline phosphatase compared to patients with PHPT, $P<0.001$. PTH was significantly higher in patients with SHPT on chroniodialysis, $P<0.001$, and patients with PHPT had a significantly higher level of PTH only against patients with vitamin D deficiency, $P<0.001$. In chronodialysis SHPT group, eGFR was significantly lowest vs the other groups, $P<0.001$. There is a significant direct inverse relationship between the levels of 25(OH)D and PTH in patients with SHPT with CKD pre-dialysis and vitamin D deficiency. There is no dependence of PTH on the level of 25(OH)D in the other two groups - with PHPT and with SHPT of chroniodialysis due to the non-participation of vitamin D in the pathogenesis of both diseases. A significant correlation of eGFR/PTH is present in patients with CKD pre-dialysis, and it is absent in patients with PHPT and group with vitamin D deficiency.
Conclusion
Hyperparathyroidism requires complex investigations carried out by a highly specialized team with sufficient experience for correct diagnostic and subsequent therapeutic assessment.

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EP395

Linear growth and response to GH therapy in short children with normal vs low IGF1 level and normal BMI at presentation

Ashraf Soliman, Fawzia Alyafei, Nada Alaaraj, Noor Hamed & Shayma Mohamed
Hamad General Hospital, Pediatric Endocrinology, Doha, Qatar

We conducted a longitudinal study on 95 children presented to pediatric clinic with short stature. Children were classified to low IGF1 (IGF1SDS <-1) ($n=25$) and normal IGF1 (IGF1SDS >-1) ($n=70$) and treated with human GH (0.03: 0.05 mg/kg/day) for 2 years. Anthropometrics data (HtSDS, difference from mid-parental height SDS (MPHSD), BMISDS, bone age and IGF1 level were studied for 2 years.
Results
At presentation, the age, bone age, HtSDS and Growth velocity (GV) did not differ significantly among the 2 groups. The peak GH response to provocation was lower in the low IGF1. Children with low IGF1 had lower BMI vs those with normal IGF1. GH stimulation using clonidine showed that 10/25 (40%) of patients with low IGF1 have GH deficiency (Peak <7) while 23/70 (32.8%) of patients with normal IGF1 had low peak GH to provocation (not significant). The IGF1/GH peak ratio was significantly higher in the normal IGF1 group vs the low IGF1 group (higher response of IGF1 for their peak level of GH). After an average of 2 years of GH therapy (0.03 -0.05 mg/kg/day), The IGF1 SDS increased significantly in both groups with higher levels in the normal IGF1 group. the HtSDS increased significantly in both groups ($P<0.01$) however, the increment was significantly higher in the Low IGF1 group (+1.2 SD) vs the normal IGF1 group (+0.74 SD).
Conclusion
Our data confirms good growth response to GH therapy and increment in IGF-1SDS in both low and normal IGF1 level with better growth response in the low IGF1 group.

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EP421

Tumour-induced osteomalacia secondary to a toe mesenchymal tumour – a case report

Charlotte Choo & Nikhel Sachdev
Singapore General Hospital, Endocrinology, Singapore, Singapore

Tumour-Induced Osteomalacia (TIO) is a rare paraneoplastic syndrome that is often underdiagnosed given its non-specific manifestations. A 64-year-old Chinese male presented with chest discomfort and generalized weakness. He was treated for symptomatic iron deficiency anaemia, with two units of blood transfusion given his low haemoglobin of 6.1 g/dl; no intravenous iron replacement was given. Concurrently, laboratory results revealed a low phosphate level of 0.4 mmol/l [reference range: 0.94-1.50 mmol/l], requiring aggressive intravenous and oral phosphate replacements. Past medical history was significant for atrial fibrillation, dilated cardiomyopathy with an ejection fraction of 37%, myositis on mycophenolate mofetil, and glucocorticoid-induced osteoporosis – presently on drug holiday after three years of alendronate. There was no previous history of hypophosphataemia. On subsequent follow-up, he remained persistently hypophosphataemic (0.34-0.4 mmol/l). He had no symptoms to suggest gastrointestinal losses. His calcium and renal function were normal at 2.15 mmol/l [reference range 2.09-2.46 mmol/l] and 32 pmol/l [reference range 37-75 pmol/l] respectively. iPTH was mildly elevated 9.6 mmol/l [reference range 1.30 – 7.60 pmol/l], possibly contributed by Vitamin D insufficiency (21 ng/ml). In light of persistent hypophosphataemia, 24-hour urinary phosphate studies were pursued. The fractional excretion of phosphate of 32.9%, and the ratio of tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) of 0.43 mmol/l for a corresponding low phosphate reading of 0.76 nmol/l suggested renal phosphate loss. He had no syndromic features and has no family history of abnormal phosphate metabolism or skeletal disorders. Examination did not reveal palpable lymph nodes or masses, and was otherwise systemically unremarkable. Fibroblast growth factor 23 (FGF-23) was elevated at 102 pg/ml [reference range ≤59 pg/ml]. 1,25-Dihydroxyvitamin D was normal. Following the suspicion for TIO; ^{68}Ga-DOTATATE PET/CT was performed with tracer-avidity localising to the left big toe. This was confirmed subsequently on magnetic resonance imaging as an ill-defined 1.2 x 0.5 x 1.2 cm^3 T1 w/T2w hypointense, heterogeneously enhancing lesion at the lateral aspect of the hallux proximal phalanx. He was given phosphate, colecalciferol and calcitriol replacements and eventually underwent excision of the left big toe soft tissue tumour. Histology yielded monomorphic ovoid tumour cells, consistent with a phosphaturic mesenchymal tumour. Post-operatively, serum phosphate normalized as did FGF-23 to 24 pg/ml. This patient's insidious presentation of muscle weakness was initially perceived to be from symptomatic anaemia. His persistent hypophosphataemia led to an eventual diagnosis of TIO, with no overt clinical findings, highlighting the challenges in the diagnosis of TIO.

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EP424

Body composition of the arms as an index of bone quality

Maria Eleni Chondrogianni[1,2], Ioannis Kyrou[3,4,5,6,7,8,9], Theodoros Androutsakos[10], Nektaria Papadopoulou-Marketou[2], Maria Panagaki[2], Despina Polichroniadi[11], Gregory Kaltsas[2], Harpal Randeva[3,4,6,7] & Eva Kassi[1,2]
[1]Medical School, National and Kapodistrian University of Athens, Department of Biological Chemistry, Athens, Greece; [2]Medical School, National and Kapodistrian University of Athens, Endocrine Unit, 1st Department of Propaupedic Internal Medicine, Athens, Greece; [3]University Hospitals Coventry and Warwickshire NHS Trust, Warwickshire Institute for the Study of Diabetes, Endocrinology and Metabolism (WISDEM),

(Abstract EP395) Anthropometric data and response to GH therapy in short children with low vs normal IGF1 level.

	Age 1	HTSD 1	BMISD 1	GV 1	Tanner stage 1	IGF1SD 1	Bone age 1	TSH 1	T4 1	Peak GH	IGF1/GH	MPHSD
IGFZ <-1	**9.59**	**-2.3**	**-0.9**	**5.28**	**1.28**	**-1.7**	**8.08**	**3.25**	**15.9**	**4.24**	**16.1**	**-0.8**
***n*=25**	**3.61**	**0.5**	**1.32**	**1.5**	**0.56**	**0.66**	**4.42**	**2.6**	**2.65**	**3.0**	**13.9**	**0.89**
IGFZ>-1	**9.97**	**-2.0**	**-0.26**	**5.6**	**1.64**	**0.25**	**8.98**	**2.5**	**15.9**	**6.6**	**52.74**	**-0.87**
***n*=70**	**3.21**	**1.08**	**1.31**	**2.53**	**0.79**	**0.93**	**3.84**	**1.47**	**2.27**	**4.35**	**29.19**	**0.93**

	Age 3	HTSD 3	BMISD 3	Tanner stage 3	IGF1SD 3	Bone age 3
IGFZ <-1	**11.50**	**-1.03**	**-0.33**	**3.75**	**1.20**	**13.00**
***n*=25**	**3.41**	**1.18**	**0.97**	**3.63**	**0.50**	**2.24**
IGFZ>-1	**11.55**	**-1.23**	**-0.32**	**3.00**	**2.46**	**10.40**
***n*=70**	**3.34**	**0.96**	**1.28**	**0.00**	**0.49**	**4.18**

Coventry, United Kingdom; [4]University Hospitals Coventry and Warwickshire NHS Trust, Institute for Cardiometabolic Medicine, Coventry, United Kingdom; [5]School of Food and Nutritional Sciences, Agricultural University of Athens, Department of Food Science and Human Nutrition, Athens, Greece; [6]University of Warwick, Warwick Medical School, Coventry, United Kingdom; [7]Coventry University, Centre for Health & Life Sciences, Coventry, United Kingdom; [8]Aston University, Aston Medical School, College of Health and Life Sciences, Birmingham, United Kingdom; [9]University of Derby, College of Health, Psychology and Social Care, Derby, United Kingdom; [10]Medical School, National and Kapodistrian University of Athens, Department of Pathophysiology, Athens, Greece; [11]Medical School, National and Kapodistrian University of Athens, Evgenidion Hospital, Athens, Greece

Introduction
Traditionally, obesity is thought to exert a positive impact on bone mineral density (BMD). However, the effect of adipose tissue on bone health is under investigation. Trabecular bone score (TBS) is a measure of bone texture, providing information on bone quality and microarchitecture, independently of BMD. Lower values of TBS indicate a worsening in bone quality and amplify fracture risk. Herein, we aimed to investigate the association of body composition and bone quality as evaluated by lumbar spine TBS.
Methods
We included 83 subjects (69 women and 14 men) with a mean age of 62.38years ± 10.48. There was no history of secondary osteoporosis, neither received anti-osteoporotic drugs. Body composition and lumbar spine TBS were evaluated by dual-energy X-ray absorptiometry (DXA). To determine the associations among the variables of interest linear regression analysis was performed (Stata Corp (2017)).
Results
Our analysis demonstrated that total fat mass is negatively associated with TBS ($P<0.01$). Moreover, total lean mass is positively correlated with TBS. Extending our analysis to examine the association of visceral adipose tissue (VAT) mass and arm fat mass with TBS, we demonstrated that VAT mass is negatively associated with TBS ($P<0.05$). Furthermore, we found that right and left arm fat mass, each one or combined, associated negatively with TBS ($P<0.05$), even after adjustment for age and weight. Each right and left arm lean mass or combined were positively associated with TBS reaching statistical significance ($P<0.1$).
Conclusions
Our study provide evidence that total fat and in specific VAT negatively impacts bone quality as it is estimated by TBS. It is known that VAT is the main source of proinflammatory adipocytokines provoking low grade inflammation that has potentially a negative impact on bone quality. We also showed for the first time that the body composition of the arms is correlated with the bone quality of lumbar spine, possibly underscoring the importance of the physical exercise of the upper part of the body in the bone quality of vertebrae.
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EP430

The effect of denosumab treatment on metabolic and inflammatory parameters in postmenopausal osteoporosis

Gizem Gok, Aysen Akalin & Goknur Yorulmaz
Eskisehir Osmangazi University, Meselik Campus, Endocrinology, Turkey

Denosumab is a monoclonal antibody against RANKL used in the treatment of postmenopausal osteoporosis. RANK/RANKL/OPG cycle is effective on both immune system and osteoporosis. Some RANK mutations are associated with hypogammaglobulinaemia. There are studies suggesting that the RANK/RANKL pathway may mediate the development of insulin resistance and hepatosteatosis. However, the clinical effects of denosumab on inflammation and immunity are not well known. In this study, we aimed to investigate the effects of denosumab treatment on metabolic and inflammatory parameters. In our study, 30 patients who were over 50 years of age, had been in menopause for at least one year, had a lumbar vertebra or hip T score of -2.5 or below in bone mineral density measurement, or had a history of fragility fracture, and were unable to use or did not respond to other treatments, who applied to the outpatient clinics or were followed up in the wards of our hospital between November 2021 and March 2023 were included. Patients received 60 mg subcutaneous denosumab and standard doses of calcium and vitamin supplementation (1g elemental calcium + 880IU vitamin D3). Complete blood count, neutrophil/lymphocyte ratio, erithrocyte sedimentation rate (ESR), CRP, fibrinogen, ferritin, procalcitonin, D-dimer, homocysteine, fasting blood glucose, insulin, HOMA-IR, LDL, HDL, triglyceride, lipoprotein (a), calcium, albumin, phosphorus, parathormone, alkaline phosphatase parameters were evaluated retrospectively before and 1 month after treatment. In our study, no significant difference was found between the metabolic parameters analysed before and after denosumab administration ($P>0.05$). A significant decrease was found in calcium ($P=0.003$), phosphorus ($P<0.001$) and albumin ($P=0.005$) levels. A statistically significant increase was found in parathormone levels ($P<0.001$). Leukocyte ($P=0,042$), neutrophil ($P=0,042$) and monocyte ($P=0,034$) values before and after denosumab treatment showed a significant decrease. In our study, it was found that short term denosumab treatment had no effect on metabolic parameters. But it has been shown that it may have an effect on immune system responses and inflammation by reducing nerutrophil and monocyte levels.
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EP432

Hyperparathyroidism in patients with acute fragility fractures

Anamarija Zrilic Vrkljan[1], Mirna Hrabar[1], Jelena Andric[1], Jelena Jaksic[2] & Vlatka Pandzic Jaksic[1]
[1]University hospital Dubrava, Department of Endocrinology, Diabetes, Metabolism and Clinical Pharmacology, Zagreb, Croatia; [2]School of Medicine, University od Zagreb

Background
An acute fragility fracture is considered a 'bone attack,' necessitating prompt treatment of osteoporosis. Standard clinical practice involves assessing the patient's clinical status, comorbidities, and secondary causes of osteoporosis, influencing the choice between osteoanabolic or antiresorptive therapy. Normocalcemic hyperparathyroidism is common among fragility fracture patients. While it is commonly associated with vitamin D deficiency and chronic kidney disease, this study aims to investigate other variables that may also influence parathyroid hormone (PTH) levels.
Methods
Within the Fracture Liaison Service, we retrospectively studied 249 consecutive patients aged 50 and above with no prior anti-osteoporotic therapy, hospitalized for acute fragility fractures (hip, vertebra, distal forearm, humerus, pelvis). Participants were categorized into two groups based on normal or high PTH levels, excluding those with typical primary hyperparathyroidism. We analyzed the prevalence of secondary causes of osteoporosis (vitamin D deficiency, chronic kidney disease, premature menopause, hyperthyroidism, malabsorption, monoclonal gammopathy, use of corticosteroids, aromatase inhibitors, and chemotherapy), as well as the presence of diabetes and malignancies. We also collected data on serum creatinine, albumin, calcium, phosphorus, 25-hydroxy vitamin D, leukocytes, and CRP, and calcium in urine samples.
Results
Among all participants, 91 (36.5%) had high PTH, and 158 (63.5%) had normal PTH levels. Patients with high PTH were older, less likely to receive vitamin D supplementation before the fracture, and showed a higher prevalence of aggregated secondary causes of osteoporosis and diabetes ($p\leq0.01$). Secondary causes of osteoporosis, excluding hyperparathyroidism and chronic kidney disease, were more common in the normal PTH group ($P<0.01$). No difference in malignant disease presence was observed between groups. The high PTH group had significantly higher creatinine but lower albumin, albumin-corrected calcium, phosphorus, urine calcium, and 25-hydroxy vitamin D ($P<0.05$). CRP at admission was also significantly higher in this group ($P=0.028$), while leukocyte count showed no difference. In the multiple regression model, PTH levels were independently predicted by higher creatinine, lower 25-hydroxy vitamin D, albumin-corrected serum calcium, urine calcium, and phosphorus. Diabetes, female gender, and advanced age entered as independent predictors of PTH too ($R2=0.37$).
Conclusion
Hyperparathyroidism often prevents or postpones timely osteoanabolic therapy after fragility fractures. It is essential to recognize bone metabolism markers beyond the conventional ones that impact elevated PTH levels and to intervene accordingly. The modest proportion of variance explained by standard laboratory and clinical parameters in our model suggests the presence of other unknown variables influencing PTH levels, emphasizing the need for further investigation.
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EP433

Differences of bone mineralization in individuals with klinefelter syndrome compared to hypogonadotropic hypogonadism under long-term testosterone replacement therapy

Roza Sabia[1], Nina Fischer[2], Felix Wüste[2], Gisa Ufer[2], Lena Rauschek[2], Martin Heni[2], Martin Wagner[2] & Burkhard Manfras[2]
[1]Ulm University Medical Center, Department of endocrinology diabetes and metabolic diseases, Ulm, Germany; [2], Ulm, Germany

Introduction
Klinefelter syndrome has been associated with decreased bone density most likely due to testosterone deficiency. Furthermore, a negative effect of long-lasting follicle-stimulating hormone (FSH) excess (starting from puberty) on trabecular bone has been suggested. Other endocrine mechanisms, such as global Leydig cell dysfunction, higher oestradiol levels, altered 25-OH vitamin D levels, and genetic aspects related to the supernumerary X chromosome might be involved. An increased risk for vertebral fractures has been reported as a complication of Klinefelter syndrome despite testosterone replacement therapy.
Objective
This study aimed to investigate bone health in a cohort of individuals with Klinefelter syndrome (KS) compared to patients with hypogonadotropic hypogonadism (HH) considering the influence of testosterone replacement therapy.
Methods
Ten individuals with known KS (23-78 years) and 15 individuals with HH (33-87 years) were submitted in regard to metabolic markers, bone density (BMD), bone formation markers (alkaline phosphatase and osteocalcin), a bone turnover marker (beta-crosslinks) and 25-OH vitamin D levels. BMD was measured by dual-energy X-ray absorptiometry (DXA) and expressed as T-scores. Nine of the KS individuals and 14 of the HH patients administered testosterone replacement therapy. Serum levels of testosterone, FSH, 25-OH vitamin D and bone markers were measured by commercial immunoassays in a routine clinical laboratory.
Results
All but one individual treated with exogenous testosterone had a bone mineral density within the normal range. Patients with KS had higher FSH concentrations ($P=0.0043$) but testosterone levels were comparable. The T-score of bone mineral density was found to be lower in lumbar spine than in the femoral neck in KS patients. In contrast, in HH individuals T-score of bone mineral density of lumbar spine was similar to T-scores of the femoral neck, demonstrating a difference in bone mineralization of the lumbar spine in KS vs HH ($P=0.04$). Bone formation biomarkers (alkaline phosphatase, osteocalcin) and the bone turnover biomarker were comparable between groups.
Conclusions
Despite comparable bone markers, we found significantly lower lumbar spine bone mineralization in patients with Klinefelter syndrome compared to hypogonadotropic hypogonadism under long-term testosterone replacement therapy. The underlying mechanism of this observation remains to be identified but may explain the previously reported increased risk of individuals with Klinefelter syndrome for vertebral fractures.

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EP435

A tertiary center experience on denosumab treatment

Alexandra Balasa[1], Andreea Manole[1], Ramona Dobre[1,2], Madalina Sorohan[1,2] & Catalina Poiana[1,2]
[1]National Institute of Endocrinology "C.I. Parhon", Bucharest, Romania; [2]University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania

Background
Osteoporosis is a chronic metabolic bone disease, highly prevalent in the elderly population, especially in postmenopausal women. Denosumab is a potent anti-resorptive drug, which can be used as an initial therapy or as an alternative therapy in the treatment of osteoporosis.
Objective
We aimed to analyze the characteristics of patients, the evolution of bone mass density (BMD) and trabecular bone score (TBS) and the factors associated with fragility fractures, all under treatment with Denosumab.
Methods
Between Nov 2013 and Nov 2023, 1375 patients were diagnosed with osteoporosis in our center, of which 184 patients received treatment with Denosumab and we had follow up for 81 patients, which included osteodensitometric (DXA scan) evaluation before and after the treatment with Denosumab and radiological vertebral fracture assessment.
Results
The patients had a mean age of 72 years, 98.8% women (97.5% postmenopausal), with an average BMI of 25.31 kg/m^2, 95% had an osteodensitometric score of osteoporosis and the median period of therapy with Denosumab was 3 years. The batch had an average lumbar spine T score of -3 DS and a TBS value of 1.235. Under Denosumab therapy, BMD increased at the level of all segments, the increase being statistically significant at the lumbar spine and the hip. Twenty-eight percent of patients presented secondary causes of osteoporosis: Hyperthyroidism (9.9%), diabetes 7.4%, hyperthyroidism (4.9%), acromegaly (2.5%), glucocorticoids therapy (2.5%), and hypogonadism (1.2%). We detected a history of old fragility fractures in 78% of the patients, the most common being vertebral fractures (48%). Before undergoing treatment with Denosumab 92% underwent treatment with bisphosphonates, 14.8% also with teriparatide and only 2% were treatment naive. Ten percent of patients suffered a fragility fracture during Denosumab therapy. We performed a comparative analysis of the group according to the occurrence of fragility fractures during Denosumab treatment and observed that patients with new fractures on therapy had significantly lower TBS at follow up and had a history of old hip fractures.
Conclusions
Fracture prevention is the main treatment goal in osteoporosis, as the fractures can be debilitating and can increase the likelihood of death. Denosumab has clear indications for osteoporotic patients and it is an effective treatment, that leads to substantial increases in bone mass. The potential for fractures to occur upon treatment, especially at patients with a history of old hip fractures and those who have lower TBS at follow-up, as seen in our study, requires close-up management.

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EP480

Maternal vitamin d supplementation during pregnancy and lactation: effects on maternal and infantile vitamin d status

Ashraf Soliman, Fawzia Alyafei, Nada Alaaraj, Noor Hamed, Shayma Mohamed & Maya Itani
Hamad General Hospital, Doha, Qatar

This review assessed recent literature (RCTs, longitudinal studies, meta-analyses) from the past decade via PubMed, Google Scholar, and Scopus to gauge the impact of prenatal and postnatal vitamin D (VD) supplementation on maternal and infantile vitamin D status.
Results
We analyzed 12 studies ($n=6253$ mothers). In a prospective interventional study involving 80 women who received two doses of VD injections (600,000 IU/ml each), 60% of women displayed unsatisfactory VD levels despite high-dose treatment. A randomized study of 180 women at 27 weeks' gestation explored different vitamin D supplementation strategies: a single oral dose of 200,000 IU VD, a daily supplement of 800 IU VD from 27 weeks until delivery, and a no-treatment group. Supplemented groups exhibited significantly higher 25-hydroxyvitamin D (25OHD) levels and lower secondary hyperparathyroidism instances. Cord blood 25OHD levels significantly increased with maternal supplementation. Maternal supplementation during lactation elevated infant serum 25OHD levels, with higher doses proving more effective in boosting infantile 25OHD. Maternal supplementation with 50 μg VD_3/d during gestation safeguarded 98% of unsupplemented breastfed infants from VDD (<30 nmol/l) for at least 8 weeks. In comparison, 10 or 25 μg VD/d protected only 57% and 84% of infants, respectively. Maternal VD supplementation dosages displayed nonlinear effects on maternal and infantile 25OHD concentrations. High doses (≥ 6000 IU/day) effectively rectified VDD in both mothers and infants. A maternal dose of 6400 IU/day surpassed the 400 and 2,400 IU doses in achieving VD sufficiency. A longitudinal study involving 6-month maternal supplementation with 6000 IU resulted in 96% of mothers attaining adequate serum 25(OH) D levels (≥ 50 nmol/l), compared to 52% for those on 600 IU ($P<0.0001$). Infants born to mothers on 600 IU, supplemented with 400 IU vitamin D3, displayed slightly higher serum 25OHD levels compared to those born to mothers on 6000 IU alone. Among Arab women randomized at 12-16 weeks' gestation, supplementation with 400, 2000, and 4000 IU/d VD3 demonstrated that higher maternal doses were more effective in increasing maternal and infant 25OHD levels. In another study, maternal supplementation with 4000 IU of vitamin D during lactation resulted in adequate serum vitamin D levels in $>90\%$ of infants.
Conclusion
For breast-fed infants, a recommended dose is 400 IU vitamin D3/day. Alternatively, maternal supplementation with 4000 to 6,400 IU vitamin D3/day during pregnancy and lactation can augment breast milk's vitamin D content, offering a practical choice.

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EP482

Distinctive features of primary hyperparathyroidism in multiple endocrine neoplasia type 2a: a series of five cases

Gorgi Khaoula[1], Echchad Lamya[1], Rifai Kaoutar[1], Iraqi Hinde[1] & Gharbi Mohamed El Hassan[2]
[1]Ibn Sina University Hospital, Rabat, Morocco; [2]Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Multiple endocrine neoplasia type 2A (MEN2A) is a rare genetic condition characterized by medullary thyroid cancer (MTC), often accompanied by primary hyperparathyroidism (PHPT) in 20% to 30% of cases which is usually detected while investigating other issues and is not commonly the initial indicator of the condition. This study aims to describe the specific features of primary hyperparathyroidism (PHPT) in MEN2A, providing insights into its distinct characteristics for a better understanding of this complex endocrine disorder.
Subjects and methods
This retrospective and descriptive study covers a period of seven years and focuses on the clinical data of five individuals with Multiple Endocrine Neoplasia Type 2A (NEM2A) due to genetic alterations in the RET gene. The study was conducted at the Department of Endocrinology, Diabetology, and Metabolic Diseases at Ibn Sina University Hospital of Rabat, Morocco.
Results
The average age at diagnosis of PHPT was 26.8 years. Renal lithiasis was observed in only one patient, and another presented with a fracture. The parathyroid hormone (PTH) level was notably elevated, measuring 182.2 pg/ml (normal range: 8-76), and the mean serum calcium level was 101.2 mg/l (normal range: 85-105). Parathyroid ultrasound revealed lesions in all patients, leading to surgical intervention in each case. The surgical approach involved the excision of one to three parathyroids.
Discussion & Conclusion
Our study elucidates the frequent manifestation of primary hyperparathyroidism (PHPT) in individuals diagnosed with Multiple Endocrine Neoplasia Type 2A (NEM2A). PHPT is commonly identified during lesion assessments, serving as an incidental rather than a primary diagnostic indicator. Noteworthy is the frequent observation of normocalcemic presentations, potentially attributed to prevalent vitamin D deficiencies in contemporary populations. The adoption of systematic screening protocols proves instrumental in achieving early detection, thus contributing to a more favorable prognosis and timely therapeutic interventions in the context of NEM2A-associated primary hyperparathyroidism.

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EP483

Assessment of vitamin d status in patients with primary hyperparathyroidism: implications for clinical management

Gorgi Khaoula[1], Errahali Yassine[2], Echchad Lamya[1], Rifai Kaoutar[1], Iraqi Hinde[1] & Gharbi Mohamed El Hassan[1]
[1]Ibn Sina University Hospital, Endocrinology, Rabat, Morocco; [2]Mohamed V Military training hospital, Endocrinology, Rabat, Morocco

Introduction
Primary hyperparathyroidism is frequently accompanied by low vitamin D levels. This study aims to assess the vitamin D status of patients diagnosed with primary hyperparathyroidism, with a focus on determining the prevalence of insufficient and deficient 25(OH) D levels in this patient population.
Patients and Methods
Conducted as a retrospective study over a 7-year period (2015-2022), our research was carried out at the endocrinology-diabetology department of CHU IBN SINA RABAT and the Mohamed V military hospital in Rabat. The study concentrated on patients hospitalized for primary hyperparathyroidism, analyzing their vitamin D levels.
Results
A total of 63 patients, with an average age of 55.8 years, were included in the study. Systematic measurement of vitamin D levels revealed a mean serum 25(OH)D level of 19.20 ng/ml. Notably, 18% of patients had vitamin D insufficiency, while 60.7% exhibited vitamin D deficiency. In patients with low vitamin D, the average serum calcium was 121.8 mg/l, and the mean parathyroid hormone (PTH) level was 261.7 ng/ml. Patients with insufficient vitamin D displayed higher PTH and blood calcium levels compared to those with normal vitamin D levels.
Discussion/Conclusion
Primary hyperparathyroidism is commonly associated with vitamin D deficiency, resulting in more pronounced bone damage and a significant elevation in blood calcium and parathyroid hormone levels. This study emphasizes the importance of vitamin D supplementation in individuals with primary hyperparathyroidism who have deficient or insufficient 25(OH)D levels.

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EP488

Hungry bone syndrome following parathyroidectomy for primary hyperparathyroidism treatment: a report on three cases

Gorgi Khaoula, Cheibetta Zakaria, Lamya Echchad, Rifai Kaoutar, Iraqi Hinde & Gharbi Mohamed El Hassan
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Hungry Bone Syndrome (HBS) is characterized by a profound and persistent state of hypocalcemia, typically observed following parathyroidectomy or thyroidectomy. This syndrome manifests in the postoperative period, and its occurrence is associated with extended exposure to elevated levels of parathyroid hormone (PTH) or thyrotoxicosis. This prolonged exposure results in heightened bone turnover rates, marked by a net loss of bone minerals through resorption. We report three cases of Hungry bone syndrome after parathyroidectomy for primary hyperparathyroidism.
Cases
Three patients, aged 46, 78, and 58, presented with altered general conditions, prompting a work-up revealing hypercalcemia (185 mg/l, 141 mg/l, and 140 mg/ml, respectively), hypophosphatemia (19 mg/l in all cases), and elevated parathyroid hormone levels indicative of hyperparathyroidism (4936 pg/ml, 392 pg/ml, and 420 pg/ml, respectively). Initial medical management included rehydration and intravenous bisphosphonates administration. Following localization workup confirming a parathyroid origin, parathyroidectomy was performed in each case, revealing parathyroid adenomas on anatomopathological examination. Post-operatively, all patients experienced prolonged hypocalcemia and hypophosphatemia with normal PTH levels, consistent with the diagnosis of Hungry Bone Syndrome (HBS). These cases underline the clinical challenges and postoperative complications associated with hyperparathyroidism and emphasize the importance of vigilant management in mitigating adverse outcomes.
Dicussion & Conclusion
Hungry Bone Syndrome (HBS), though infrequent, manifests as a severe and enduring condition characterized by profound hypocalcemia. The severity of hypocalcemia stems from a substantial escalation in calcium utilization by the skeletal system. This heightened demand is a consequence of the abrupt cessation of bone resorption, despite persistently elevated circulating parathyroid hormone (PTH) levels, leading to a rapid and pronounced shift towards increased bone formation. The therapeutic approach to HBS is focused on rectifying the substantial calcium deficit and reinstating normal bone turnover. This is achieved through the administration of high doses of calcium and active metabolites or analogues of vitamin D, aiming to restore the delicate balance of bone metabolism and alleviate the severe hypocalcemic state associated with this syndrome.

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EP496

Hypercalcemic crisis in pregnancy, a case report

Nour El Houda Bedrane & Khiter Chafika
Centre Hospitalier Intercommunal de Villeneuve-Saint-Georges, Lucie & Raymond Aubrac, Val de marne, Villeneuve-Saint-Georges, France

Introduction
Hypercalcemic crisis is a rare therapeutic emergency, but one that should not be overlooked, particularly during pregnancy, when it is associated with significant maternal-fetal morbidity. The most frequent etiology is PHPT, including during pregnancy.
Observation
We report the case of a 34-year-old patient with no particular pathological history, pregnant at 34 weeks of amenorrhea, who presented with acute cholecystitis. The blood test showed malignant hypercalcemia at 3.56 mmol/l, hypophosphatemia and elevated PTH at 30.7 pg/l (1.9-8.5). Good fetal vitality but IUGR. We started with hydration, and after discussion with the gynecologists, we decided not to start FUROSEMIDE because of the risk of placental hypo-perfusion and worsening of the IUGR. Cervical ultrasound revealed a 7 mm parathyroid adenoma. Given the relative contraindication to bisphosphonates and calcinomimetics, and after a collegial decision, we requested a F-choline PET scan, which was concordant with the ultrasound. We had a choice between either minimally invasive surgery under local anaesthetic and parahyroidectomy with acouhement at term, or Caesarean section, extraction of the baby and subsequent conventional parathyroid surgery. In the end, we opted for the first solution, given the baby's IUGR. methoxylated

derivatives of catecholamines are negative in the NEM2 hypothesis. Following the operation, blood calcium and PTH levels returned to normal.
Conclusion
Hypercalcemic crisis is rare, particularly during pregnancy, and is responsible for high maternal-fetal morbidity: miscarriage, IUGR. The etiological and therapeutic management during pregnancy is complex, and there are few recommendations. A multidisciplinary approach is required.

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EP497

Calcium- alkali syndrome: an endocrine complication in the management of hypoparathyroidism

Eleni Kouroglou[1], Efthymia Kallistrou[1], Stella Proikaki[1], Anastasia Dede[2], Sofia Dionysopoulou[1], Georgios Gavriiloglou[1], Dimitra Ragia[1], Vasiliki Tsiama[1], Konstantinos Belis[1], Ioannis Ilias[1] & Christos Savvidis[1]
[1]Hippocration General Hospital of Athens, Department of Endocrinology, Athens, Greece; [2]Chelsea and Westminster Hospital, London, United Kingdom

Background
Milk- alkali syndrome (MAS), characterized by the triad of hypercalcemia, metabolic alkalosis, and renal dysfunction, is increasingly recognized as a complication of calcium supplementation, particularly in the management of hypoparathyroidism. Some have proposed should be called calcium- alkali syndrome (CAS). We delineate two cases of CAS and provide a review of relevant literature, emphasizing the endocrine aspects of CAS.
Case Presentations
The first case details a 52-year-old male with iatrogenic hypoparathyroidism post-thyroidectomy, who developed marked hypercalcemia (corrected serum calcium: 13.1 mg/dl) and acute kidney injury (serum creatinine: 2.8 mg/dl) and alkalosis (pH: 7.52, $HCO3^-$: 33.5 mmol/l, PCO_2: 41mmHg). This was attributed to olmesartan/hydrochlorothiazide, alphacalcidol, calcium carbonate and cholecalciferol. Treatment included intravenous hydration and medication titration, leading to calcium level normalization. The second case involved an 83-year-old woman with a background of hypoparathyroidism, presenting with cognitive impairment and hypercalcemia (corrected serum calcium: 15.36 mg/dl) and acute kidney injury (serum creatinine: 2.6 mg/dl) and alkalosis (pH: 7.51, HCO3: 33.5 mmol/l, PCO_2: 42mmHg) secondary to alfacalcidol, irbesartan and calcium carbonate ingestion; renal function was also compromised. Intravenous fluid administration and medication dose adjustment led to clinical improvement; renal impairment remained.
Discussion
The pathophysiology of CAS is anchored in hypercalcemia-induced nephropathy, precipitated by excessive exogenous calcium intake. This initiates a cascade involving decreased glomerular filtration, enhanced renal calcium reabsorption. Volume depletion promotes tubular reabsorption of bicarbonate creating metabolic alkalosis which in turn decreases renal calcium excretion enhancing metabolic alkalosis. Clinical manifestations are varied, ranging from subacute neuromuscular symptoms to chronic renal insufficiency. Historically associated with antacid overuse, the contemporary landscape of CAS has shifted towards excessive calcium supplementation in the context of osteoporosis, post-surgical hypoparathyroidism, and specific demographics like postmenopausal women or those with renal insufficiency.
Conclusion
These cases highlight the importance of cautious calcium supplementation in hypoparathyroidism management. Endocrinologists and healthcare providers should maintain a high index of suspicion for CAS, especially in predisposed subjects, and advocate for regular serum calcium monitoring. Adjustments in calcium and vitamin D supplementation must be made judiciously to prevent the potentially serious complications of CAS, including irreversible renal damage.

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EP500

Diagnostic value of daily calciuria on a strict diet in patients with primary hyperparathyroidism

Michal Popow & Sebastian Szewczyk
Warsaw Medical University, Endocrinology, Warsaw

Diagnostic value of daily calciuria on a strict diet in patients with primary hyperparathyroidism. The most common cause of primary hyperparathyroidism is monoclonal hyperplasia of a single mutant cell. Most somatic mutations found in adenomas regulate the cell cycle by increasing the speed of cell division. This means that stimulating stimuli, such as negative calcium balance, increased phosphorus retention, disturbances of the calcitriol/VDR/FGF23/KLOTHO axis, or lack of inhibitory stimuli, such as estrogen deficiency, will favor the development of adenomas. One of the causes of stimulation of parathyroid cell division is chronic renal calcium loss. The aim of the study was to assess daily calciuria in a population of patients with hyperparathyroidism hospitalized at the Department of Endocrinology of the Medical University of Warsaw. Due to the predominant hyperabsorptive nature of hypercalciuria, two daily urine collections were performed in the studied patients on a standard diet and on a strict diet. The results were correlated with the assessment of the urinary system for nephrolithiasis and the level of vitamin D. The results showed significant differences in calcium excretion on a regular and strict diet in some patients, which was interpreted as the possibility of co-occurring mild tubulopathies. A negative calcium balance would promote increased proliferation of a clone of parathyroid cells whose cell cycle is disrupted by the presence of the somatic mutation.
Conclusion
Assessment of fasting 24-hour calciuria as an adjunct to routine 24-hour calciuria testing may help determine the cause of stimulation of a clone of cells with a somatic mutation predisposing to hyperparathyroidism

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EP501

Exacerbation of hypercalcaemia in primary hyperparathyroidism following immobilisation in the elderly

Timothy Green, Rhiannon Berkeley, Genevieve Tellier & Anthony Wilton
Bangor Hospital, Endocrinology, Bangor, United Kingdom

Primary hyperparathyroidism is a common cause of hypercalcaemia increasing in prevalence with age peaking in females at 70-90 years of age (492 cases/100,000 population) and in males above 80 years of age (264 cases/100,000 population). Immobilisation hypercalcaemia is regarded as an uncommon non-parathyroid hormone dependent cause of hypercalcaemia typically occurring in young patients with spinal cord injuries and neuromuscular disorders. It is of complex physical and molecular aetiology with increased osteoclast activity predominating over osteoblast activity resulting in bone loss and hypercalcaemia. When superimposed on primary hyperparathyroidism confusion as to the aetiology of the hypercalcaemia can occur.
Case studies
We describe the cases of two elderly females (92 years of age case 1 and 77 years of age case 2) with known 'asymptomatic' primary hyperparathyroidism. Both were independently living prior to hospitalisation with recent falls. Both had acute kidney injury and biochemical evidence of mild primary hyperparathyroidism. Following admission they were immobile due to the sustained soft tissue injuries and calcium levels significantly increased despite a fall in parathyroid hormone levels. Beta-cross laps were raised in both and case 1 had vitamin D deficiency. Both developed delirium prolonging their immobilisation. Case 1 was initially treated with cinacalcet which was ineffective. Treatment with intravenous pamidronate lowered calcium levels with a rise in PTH levels and resolution of delirium and acute kidney injury. Mobilisation maintained calcium at 'asymptomatic' pre-admission levels.
Discussion
Despite the high prevalence of the falls, immobilisation and hyperparathyroidism triad in the elderly there is a paucity of cases reporting hypercalcaemia. The commonest reported causes of hypercalcemia in the elderly being primary hyperparathyroidism and malignancy. Hypercalcaemia causes neurological, muscular and psychiatric symptoms in the elderly at a lower level than in younger patients which may contribute to falls. In the patients we describe it is possible that the hypercalcaemia contributed to the falls with consequent immobilisation and rapid rise in calcium resulting in delirium which delayed their rehabilitation.
Conclusion
1) Immobilisation should be considered in the differential diagnosis of hypercalcaemia in elderly patients particularly those with primary hyperparathyroidism. 2) 'Asymptomatic' primary hyperparathyroidism may have subtle neuromuscular and psychiatric effects contributing to falls risk. 3) The threshold for treatment of hypercalcaemia in the elderly should possibly be lower than in younger patients.

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EP515

Evaluation of bone status in obese women: about 48 cases

Salsabil Haouach[1], Mennani Fatima Ezzahra[2], Sana Rafi[3], Ghizlane El Mghari[3] & Nawal El Ansari[3]

[1]Rue Ibn Qodama, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakech, Morocco; [2]Amerchich, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco; [3]Marrakesh, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Introduction
Obesity has become a major health problem and a global epidemic, with a worldwide prevalence that has doubled over the last three decades. According to the WHO, obesity is defined as a body mass index of 30 kg/m2 or more The relationship between obesity and bone capital has been proven. A few years ago, it was thought that obesity had a protective effect on bone, a belief that influenced clinical practice. However, various pathogenic mechanisms, notably vitaminD deficiency through sequestration, may be responsible for bone loss in obese populations, increasing the risk of osteopenia, osteoporosis and fractures. The aim of our study is to determine bone status in obese population.
Materials and methods
Retrospective descriptive study conducted at the Department of Endocrinology, Diabetology and Metabolic Diseases, CHU MohamedVI, on 48 obese patients with BMI $\geq$ 30 kg/m^2
Results
We identified 48 patients with a BMI $\geq$ 30 kg/m^2. The mean age was: 46.18 years, with extremes ranging from 22 to 71 years. The main comorbidities found were: cardiovascular in 31.25% of cases, diabetes in 27.08% of cases, dyslipidemia in 14.58% of cases and osteoarthritis in 10.41% of cases. Blood calcium and phosphorus levels were normal in all patients Vitamin D deficiency in 72.91%of cases, secondary osteoporosis in 4.17%, osteopenia in 25% and normal bone mineral density in 70.83%. Fractures occurred in 4% of cases, and vitamin D supplementation was performed in patients with vitamin D deficiency. All patients with osteoporosis or fracture received anti-osteoporotic treatment
Discussion
The association between bone and adipose tissue is complex both tissues are metabolically very active, interacting via adipokines, estrogens and metabolic factors of bone origin. The data currently available, provided by numerous studies in obese subjects, seem to show that obesity can affect bone metabolism via several mechanisms. It can increase adipocyte differentiation and fat accumulation, while decreasing osteoblast differentiation and bone formation. It is associated with chronic inflammation through increased pro-inflammatory cytokines, which can promote osteoclast activity and bone resorption by modifying the receptor activator of NF-κB (RANK)/RANK ligand/osteoprotegerin pathway In addition, excessive leptin secretion and/or reduced adiponectin production by adipocytes can affect bone formation, while high fat consumption can interfere with intestinal calcium absorption and reduce calcium availability for bone formation
Conclusions
In fact the prevalence of bone loss and vitamin Ddeficiency are quite frequent in obese people as our study shows, with a non-negligible risk of fractures

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EP517

Management of acute hypocalcemia in a tertiary referral center in morocco

Nabil Skouta, Nassim Essabah Haraj, Siham El aziz & Asma Chadli
UHC Ibn Rochd, Casablanca, Morocco, Department of Endocrinology, Diabetology and Metabolic Diseases, Casablanca

Introduction
Hypocalcemia is one of the most common electrolyte disorders. It is defined by a total calcium level $<$2.12 mmol/l (85 mg/l). Acute hypocalcemia is considered as a medical emergency.
Objectives
To describe the epidemiological, clinical, and etiological profile of patients undergoing treatment for acute hypocalcemia, as well as the management.
Patients Et Methods
This is a retrospective study including 60 patients hospitalized in the Endocrinology and Diabetology Department of Ibn Rochd University Hospital in Casablanca for acute hypocalcemia from January 2020 to December 2023. Patients with renal insufficiency were excluded. Data were analyzed using IBM SPSS Statistics 27.0.
Results
The mean age was 40 years with a female predominance of 78%. The average duration of symptoms was 16 days. Patients experienced tetany episodes, with 33% showing QT interval prolongation on ECG. The mean corrected calcium level at admission was 59 mg/l. Etiologies included 72% post-surgical hypoparathyroidism, 22% autoimmune hypoparathyroidism, 5% pseudohypoparathyroidism, and 1% infiltrative hypoparathyroidism (hemochromatosis). Before hospitalization, 80% of patients were already on replacement therapy with poor therapeutic compliance. Patients received intravenous calcium infusion with a good clinical and biological response.
Conclusion
Acute hypocalcemia is a life-threatening emergency, requiring careful evaluation by clinicians for diagnosis and management. Patients with hypoparathyroidism should be educated about the vital necessity of replacement therapy.

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EP520

Vitamin d and reproduction in hereditary vitamin d resistant rickets. what we can learn from an *in vivo* model

Francesca Allosso, Lucia Digitale Selvaggio, Graziella Grande, Martina Errico, Claudia Di Ludovico, Raffaele Navarra & Daniela Pasquali
University of Campania L. Vanvitelli, Department of Advanced Medical and Surgical Sciences, Naples, Italy

Several studies suggest that vitamin D (VitD) has beneficial effects on male reproduction. Analysis of the correlation between VitD and sperm quality parameters demonstrated that it has a significant impact on sperm motility, partially suggesting a relationship between higher serum testosterone levels and VitD levels. In females, vitD deficiency is associated with adverse pregnancy outcomes and metabolic complications in PCOS. However, there is still no concrete evidence to support the use of VitD supplementation to improve the outcomes of patients with altered sperm parameters and hormonal disorders. Here we analyze reproductive hormonal function, fertility outcome, and sexual dysfunction in a rare disease, X-linked hypophosphatemic rickets (XLH), as an *in vivo* model for VitD resistance, in patients not on conventional therapy with calcitriol or phosphate salts. Nine patients with XLH were studied, 3 men and 6 women (mean age 36.89 $\pm$ 12.10). We evaluated: BMI, HOMA index, 25OHVitD, 17-β-estradiol, testosterone, FSH, LH, number of pregnancies with live births. All patients responded to questionnaires to identify sexual dysfunctions: FDSF (Female Sexual Distress Scale) and FSFI (Female Sexual Function Index) for female sexual dysfunctions and IIEF-5 (International Index of Erectile Function-5), SIEDY (Structured Interview on Erectile Dysfunction) and PEDT (Premature Ejaculation Diagnostic Tool) for erectile dysfunction and premature ejaculation. We found that the male population was obese (I degree) and with an increased HOMA index. All patients had low VitD levels, normal gonadotropin levels and only one patient had low testosterone levels but was father of two daughters. In the female population, only 1 patient was obese (II degree) and with an increased HOMA index. All had low levels of VitD, normal levels of estrogens and gonadotropins. The questionnaires used showed no sexual dysfunction, except for premature ejaculation in one patient. Three females had one or more spontaneous pregnancies; two males were fathers of their children. No patient had to undertake assisted reproductive techniques. Studies claim that VitD can positively affect fertility by influencing hormone levels and metabolic markers. Here we show an apparently normal hormonal profile, fertility and sexual health in our patients with XLH. The limited number of our sample does not allow us to reach solid conclusions. Further data are needed to evaluate the real role of VitD in the reproductive process.

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EP522

Long-term complications of chronic hypoparathyroidism

Malak Iggar, Haraj Nassim Essabah, El Aziz Siham & Chadli Asma
CHU Ibn Rochd, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
Chronic hypoparathyroidism and its treatment are associated with an increased risk of complications that can impact the patient's quality of life.
Objectives
To describe the epidemiological, clinical, etiological profile, and long-term complications of patients with chronic hypoparathyroidism.
Patients and methods
A retrospective descriptive study over a 4-year period involving 66 patients with chronic hypoparathyroidism at the Department of Endocrinology and Metabolic Diseases of Ibn Rochd University Hospital.
Results
Of the 66 included patients, 48 had post-surgical hypoparathyroidism, 15 non-surgical, and 3 had pseudohypoparathyroidism. The average age was 41.2 years with a female predominance in 80.3% of cases. The average disease duration was

5.8 years. Regarding complications of chronic hypoparathyroidism, 24.2% of patients had nail and hair disorders, 15% had bilateral cataracts, and 13.6% experienced generalized seizure episodes. Brain imaging was performed in 42% of patients, with Fahr's syndrome observed in 21.2% of cases, with no observed link between seizures and Fahr's syndrome. Kidney stones were observed in 22.7% of patients. 93.9% of patients presented signs of hypocalcemia requiring hospitalization, and 6% manifested a hypercalcemia crisis requiring intensive care and dialysis in one patient.
Conclusion
Patients with chronic hypoparathyroidism frequently develop complications, including ectopic calcifications. Therefore, there is a need to increase screening for long-term complications in accordance with guidelines.

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EP526

Cardiovascular risk in primary hyperparathyroidism

Ikram Karabila[1], Khawla Rhouzali[1], Soumiya Berrabeh[1], Rania El Amel[1], Yousra Laalaoua[1], lamiae zarraa[1], Siham Rouf[2] & Hanane Latrech[2]
[1]Endocrinology-Diabetology and Nutrition Department CHU Mohamed VI Oujda, Faculty of Medicine and Pharmacy, Mohammed First University Oujda, Morocco; [2]Endocrinology-Diabetology and Nutrition Department CHU Mohamed VI Oujda, Faculty of Medicine and Pharmacy, Mohammed First University Oujda, Morocco, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy, Mohammed First University Oujda, Morocco

Introduction
Primary hyperparathyroidism (PHPT) is characterized by parathyroid hormone (PTH)-dependent hypercalcemia. It is associated with numerous complications, including an increased risk of cardiovascular disease. The aim of our study is to assess the cardiovascular risk of patients with PHPT.
Methods
We conducted a retrospective descriptive study, including 51 patients hospitalized in the department of endocrinology-diabetology and nutrition for the management of PHPT. Clinical and paraclinical data were collected from medical records and analyzed using the SPSS-V21 software. The Framigham Risk Score (FRS) was used to assess the cardiovascular risk of our patients. It estimates the risk of the occurrence of cardiovascular disease in 10 years. Patients are considered at high risk if the FRS is equal to or higher than 20%, at moderate risk if it ranges from 10 to 19%, and at low risk if the FRS is less than 10%.
Results
Our population consisted of 40 women and 11 men, with a mean age of 55.5 ± 13 years. Type 2 diabetes, hypertension, and dyslipidemia were found in 20.8%, 33.3%, and 41.3%, respectively. Only 2.2% were smokers, and there was no history of cardiopathy among our patients. The majority of cases had moderate cardiovascular risk (44.4%), followed by low risk (33.1%) and high risk (24.4%). The mean FRS in our patients was 14.4 ± 8, and it was significantly correlated to calcemia and PTH1-84 levels ($P = 0.028$, $P = 0.029$).
Conclusion
Cardiovascular risk appears to be correlated with calcemia and PTH1-84 levels in PHPT. Consequently, an assessment of the effect of PHPT treatment on the improvement of cardiovascular risk is necessary in order to improve the quality of life and life expectancy.

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EP528

Primary hyperparathyroidism revealed by hypercalcemia crisis

Malak Iggar, Haraj Nassim Essabah, El Aziz Siham & Chadli Asma
CHU Ibn Rochd, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
Hypercalcemia crisis constitutes a metabolic emergency associated with high mortality. Occasionally, it can be the mode of revelation of primary hyperparathyroidism.
Objectives
To analyze the clinical characteristics of patients presenting with hypercalcemia crisis revealing primary hyperparathyroidism. And to describe the complications and evolution of the disease.
Patients and methods
Retrospective descriptive study of 32 cases of primary hyperparathyroidism collected at the Department of Endocrinology and Metabolic Diseases of Ibn Rochd University Hospital over a 4-year period from January 2020 to December 2023. We included 9 cases of hypercalcemia crisis revealing primary hyperparathyroidism.
Results
In our series, there was a female predominance (5 women/4 men) with an average age of 40.7 years (10–78). The mean value of serum calcium was 154.7 mg/l (140-184), and PTH was 1270 pg/ml (117–2500). The discovery of hypercalcemia crisis was either incidental in 3 patients or associated with symptoms such as bone pain in 3 patients, renal colic in one patient, and vomiting in a patient who was 24 weeks pregnant. The topographic diagnosis was established by MIBI scintigraphy in 6 patients, cervical MRI in 2 patients, and ultrasound in one patient. The average size of the nodules was 23 mm. Among the bone complications, 4 patients experienced fractures (patella, tibia, and humerus), bone densitometry revealed osteoporosis in 7 patients, renal ultrasound identified kidney stones in 4 patients, one patient developed a cardiac arrhythmia, and one patient presented with pancreatitis. The treatment included reanimation measures for all patients with dialysis for some, followed by parathyroid surgery in 8 patients, with one patient refusing surgery. The histological examination revealed 7 parathyroid adenomas and 1 carcinoma. In the postoperative period, 3 patients experienced hypocalcemia.
Conclusion
Hypercalcemia crisis is an unusual mode of primary hyperparathyroidism revelation, indicative of a longstanding form with delayed diagnosis. Its management must be rapid and effective as the prognosis is at stake.

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EP544

The effects of obesity on bone mineral density in women with Ehlers–Danlos syndrome

Podstawka Jakub[1], Emilia Babula[1], Poprawa Iga[1], Żuk-Łapan Aleksandra[1], Julia Latocha[1], Zuzanna Szymańska[1], Domański Jan[1], Bernadetta Kaluza[1] & Edward Franek[1,2]
[1]National Medical Institute of the Ministry of the Interior and Administration in Warsaw, Warszawa, Poland; [2]Mossakowski Medical Research Centre Polish Academy of Sciences, Department of Human Epigenetics, Warszawa, Poland

Background
Ehlers–Danlos syndrome is a group of genetic diseases characterized by alterations in connective tissue structure, which may lead to increased bone mass loss and predispose to osteopenia and osteoporosis. The effect of obesity on bone mass loss is inconclusive. The purpose of this study was to assess the relationship between obesity and bone mineral density (BMD) in women with Ehlers–Danlos syndrome.
Material and methods
The study involved a prospective assessment of 30 female patients, aged 20–53 years, with hypermobile or classical Ehlers–Danlos syndrome. All patients underwent calcium and phosphorus metabolism testing, BMD scans of the femoral neck and lumbar spine, and had their body mass index (BMI) calculated as the body weight [kg]/(height [m])^2. The patients were divided into two subgroups: those without obesity (BMI <30 kg/m^2) (group 1, $n = 21$) and those with obesity (BMI >30 kg/m^2) (group 2, $n = 9$).
Results
Groups 1 and 2 showed no significant differences in terms of bone turnover markers, such as bone-specific alkaline phosphatase (9.37 ± 2.76 µg/l vs 9.9 ± 2.6 µg/l, $P = 0.54$), beta-crossLaps (CTX 0.421 ± 0.19 ng/ml vs 0.31 ± 0.13 ng/ml, $P = 0.1$), and osteocalcin (22.3 ± 7.57 ng/ml vs 16.5 ± 5.3 ng/ml, $P = 0.06$), as well as femoral neck BMD (0.92 ± 0.11 vs 0.97 ± 0.16, $P = 0.49$); however, differed significantly in terms of lumbar spine BMD (0.91 ± 0.11 vs 1.06 ± 0.11, $P = 0.007$). The study showed no significant correlation between the BMI and femoral neck BMD (r_s 0.15, $P = 0.44$), bone-specific alkaline phosphatase (r_s 0.27, $P = 0.15$), CTX (r_s -0.12, $P = 0.54$), and osteocalcin (r_s -0.18, $P = 0.34$); however, there was a significant correlation between BMI and lumbar spine BMD (r_s 0.48, $P = 0.007$).
Conclusions
The study showed a statistically significant, positive correlation between BMI and lumbar spine BMD; however, no such correlation was observed between BMI and either bone turnover markers or femoral neck BMD, which indicates a complex nature of the effects of obesity on BMD, also in patients with Ehlers–Danlos syndrome.

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EP545

Vitamin D deficiency in patients with Ehlers–Danlos syndrome

Poprawa Iga[1,2], Babula Emilia[1,2], Żuk-Łapan Aleksandra[1,2], Podstawka Jakub[1,2], Julia Latocha[1,2], Zuzanna Szymańska[1,2], Domański Jan[1,2], Bernadetta Kaluza[1,2] & Franek Edward[1,2,3]
[1]National Medical Institute of the Ministry of the Interior and Administration, Department of Internal Medicine, Endocrinology and Diabetology, Warsaw, Poland; [2]National Medical Institute of the Ministry of the Interior and Administration, Students Scientific Group of the Medical University of Warsaw at the Department of Internal Medicine, Endocrinology and Diabetology, Warsaw, Poland; [3]Mossakowski Medical Research Centre Polish Academy of Sciences, Warsaw, Poland, Department of Human Epigenetics, Warsaw, Poland

Background
Ehlers–Danlos syndrome encompasses a group of genetic conditions characterized by alterations in connective tissue structure, with the consequent increased risk of developing osteopenia, osteoporosis, and incurring fractures. Maintaining vitamin D levels within normal limits is known to play an important role in preventing these complications, which seems to be particularly important in patients with Ehlers–Danlos syndrome. The purpose of this study was to assess serum 25-hydroxyvitamin D, or 25(OH)D, levels in women with Ehlers–Danlos syndrome.
Material and methods
The study involved a prospective assessment of 30 female patients, aged 20–53 years, with hypermobile or classical Ehlers–Danlos syndrome. All patients underwent calcium and phosphorus metabolism testing and bone mineral density (BMD) scans of the femoral neck and lumbar spine. The patients were divided into two groups: those with vitamin D deficiency, defined as serum 25(OH)D levels of $<$ 30 ng/ml (group 1, $n=18$) and those with normal ($>$ 30 ng/ml) 25(OH)D levels (group 2, $n=12$).
Results
Eighteen patients (60%) showed vitamin 25(OH)D deficiency, with three of those (16.7%) showing secondary hyperparathyroidism. Study groups 1 and 2 showed no significant differences in terms of serum levels of calcium (2.4 ± 0.09 mmol/l vs 2.39 ± 0.07 mmol/l, $P=0.88$), phosphorus (3.51 ± 0.7 mg/dl vs 3.42 ± 0.51 mg/dl, $P=0.86$), bone-specific alkaline phosphatase (10.36 ± 3.06 µg/l vs 8.28 ± 1.31 µg/l, $P=0.007$), beta-CrossLaps (0.39 ± 0.19 ng/ml vs 0.39 ± 0.17 ng/ml, $P=0.69$), or osteocalcin (20.14 ± 8 ng/ml vs 21.23 ± 6.67 ng/ml, $P=0.46$), femoral neck BMD (0.95 ± 0.12 g/cm^2 vs 0.92 ± 0.13 g/cm^2, $P=0.57$), or lumbar spine BMD (0.12 ± 0.16 g/cm^2 vs 0.13 ± 0.11 g/cm^2, $P=0.14$).
Conclusions
Sixty percent of patients with Ehlers–Danlos syndrome showed vitamin 25(OH)D deficiency. Parameters of calcium–phosphorus metabolism in these patients were not significantly different from those in patients with normal serum vitamin 25(OH)D levels.

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EP589

Primary hyperparathyroidism imaging

Sameh Mezri[1], Chaima Zitouni[1], Wadii Thabet[2] & Khemaies Akkari[1]
[1]Principal Military Hospital, ENT, Tunis, Tunisia; [2]Taher Sfar Hospital, Mahdia, Tunisia

Introduction
Hyperparathyroidism is the third most common endocrinopathy. Minimally invasive surgery using a unilateral approach is now increasingly common. In such cases, preoperative localization of the lesion by imaging is essential. Among the techniques available, ultrasound and scintigraphy play a predominant role.
Objective
our aim is to evaluate the diagnostic contribution of ultrasound and parathyroid scintigraphy in localizing the pathological gland(s) in primary hyperparathyroidism.
Methods
This is a retrospective study including 84 patients treated for primary hyperthyroidism in our department over a period from 2015 to 2023.
Results
Ultrasound and parathyroid scintigraphy were performed in all cases. CT or MRI scans were performed in 5 cases. The sensitivity of ultrasound, scintigraphy and combined ultrasound-scintigraphy was 51%, 68% and 80% respectively. The specificity of ultrasound, scintigraphy and combined ultrasound-scintigraphy was 96%, 97% and 98% respectively. The sensitivity of these examinations was lower in the case of multi-glandular or ectopic involvement, or in the case of lesions $<$ 2 cm.
Conclusion
Coupled use of cervical ultrasound and scintigraphy enables reliable preoperative location of pathological glands.

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EP590

Severe biphasic disorder of calcium homeostasis in a patient with rhabdomyolysis: Case report

entela Puca[1,2], Edmond Puca[3] & Dorina Ylli[4]
[1]Western Balkan University, Internal Medicine, tirana, Albania; [2]Western Balkans University, Tirana, Albania; [3]Mother Teresa Hospital, infectious Disease, Tiranë, Albania; [4]Mother Teresa Hospital, endocrinology, Tiranë, Albania

Management of calcium disorders can be a real challenge during the different stages of acute kidney injury complicating rhabdomyolysis.
Aim
The aim of this presentation is to present a clinical case diagnosed with rhabdomyolysis, which was complicated by severe hypocalcemia during the acute phase and later on during the recovery phase with hypercalcemia.
Case presentation
We present a female patient, 57 years old, who presented to the hospital with profound weakness and difficulty in breathing. Physical examination upon admission showed normal consciousness, body temperature of 37 °C, blood pressure of 110/70 mmHg, heart rate of 98/min, and oxygen saturation 90-92%. Her initial Creatine kinase (CK) was 5852 U/l (26-192). Creatinine was 0.9 mg/dl and ionized calcium was 0.71 nmol/l (1.13-1.32) total calcium was 8.59 mg/dl (8.8-10.2), PTH 204 pg/ml (15-65), 25OHD3 24.4 ng/ml (25-80) and phosphor 7.9 mg/dl (2.5-4.5) and myoglobinuria $>$500 ug/ml $<$30. She was hospitalized because she told us that some years before she suffered a similar situation. During the clinical course in hospital, the patient was transferred to intensive care unit because she was complicated with multiple organ failure: acute kidney injury with a rapid increase in serum creatinine 8.06 mg/dl). During the oliguric phase the calcium reached the lowest level: total calcium 5.04 mg/dl and ionized calcium 0.65 mmol/l, CK was $>$ 174608. She had some hemodialysis sessions and was discharged from hospital on day 13. During her recovery as her renal function was improving she developed progressive severe hypercalcemia with a peak calcium level 17.5 mg/dl and ionized calcium 2,15 mmol/l. Renal replacement therapy was restarted to correct hypercalcaemia. On day 30 her calcium level was normal 9.24. The patient had an excellent outcome 1 week following her discharge, calcium levels remained within normal range.
Conclusions
This case report showed us that rhabdomyolysis may present initially with severe hypocalcemia and followed by hypercalcemia. In most of the cases, these situations are self-limited and do not require specific measures other than monitoring and rehydration, but may require more intensive treatment when it becomes severe and symptomatic. Clinicians must take into account this kinetic of calcium in order to prevent the complications of hypo and or hypercalcemia.

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EP591

Study of vitamin D status with SARS-CoV-2 infection

Jihene Ben Abdallah[1], Chaima Boughzala[1], Sawssen Mrad[1], Yosra Hasni[2], Hamza Elfekih[2], Oumayma Zarrouk[2], Mohamed Ilehi Aiachi[3], Naoufel Chbili[3], Bassem Charfeddine[1] & Selima Ferchichi[1]
[1]University Hospital of Farhat Hached, Biochemistry laboratory, sousse; [2]University Hospital of Farhat Hached, Endocrinology departement, sousse; [3]university hospital of sahloul, Emergency Medical Assistance Service 03, sousse

Introduction
COVID-19 is a potentially serious disease with a high case fatality. At present no specific drug has been shown to be effective and safe in treating it. Recently, evidence suggests that higher levels of vitamin D protect against this infection. However, published studies on this subject are limited. The aim of this work was to investigate an association between hypovitaminosis D and SARS-CoV-2 infection.
Methods
This was an analytical cross-sectional study over a period from 1 December 2020 to 07 January 2021 including patients suspected of COVID-19. They had undergone a PCR test and a vitamin D assay. The "Wondfo" SARS-CoV-2 real-time RT-PCR assay was used to detect coronavirus nucleic acid.

Vitamin D status was assessed by measuring 25(OH)D using the direct competitive immunoassay technique with chemiluminescence revelation on Cobas e601. 25(OH)D deficiency was defined as a level below 10 ng/ml, insufficiency was defined as values between 10-30 ng/ml and a result above 30 ng/ml was considered optimal.
Results
Two hundred and thirty-five patients suspected of having COVID-19 were included, with a median age of 35 years and a sex ratio of 0.71. The RT-PCR test was positive in 49.4%. The prevalence of vitamin D deficiency was 79.9% in non-diseased subjects and 81.9% in diseased subjects, with mean vitamin D concentrations of 21.5 ng/ml and 21.8 ng/ml, respectively. There was no significant difference in vitamin D levels between coronavirus-affected and nonaffected subjects ($P = 0.857$).
Discussion
Our preliminary results, which do not support a potential link between vitamin D levels and infectious risk, are in line with the literature. However, contrasting results were reported in two Israeli and US studies, providing strong evidence of an association between lower 25(OH)D levels and an increased risk of COVID-19.
Conclusion
The design of large-scale studies will be required to assess the relationship between vitamin D and COVID-19 and generate more robust conclusions.

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EP604

Primary hyperparathyroidism and acute pancreatitis: about three cases

Gorgi Khaoula, Lamya Echchad, Rifai Kaoutar, Iraqi Hinde & Gharbi Mohamed El Hassan
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Primary hyperparathyroidism (PPH) may be complicated by pancreatitis. The association of primary hyperparathyroidism with pancreatitis is rare, We report the case of three patients presenting with hyperparathyroidism revealed by acute pancreatitis.
Observation
A 78-year-old female patient with no previous history of pancreatitis presented to the emergency department with abdominal pain and bilious vomiting. An abdominal CT scan was ordered, revealing pancreatitis stage C. A etiological investigation revealed a profile of primary hyperparathyroidism with PTH at 397 pg/ml, hypercalcemia at 147 mg/l and hypophosphatemia at 19 mg/l. Patient aged 60, with no particular history, admitted for management of primary hyperparathyroidism, during his hospitalization he presented with epigastric pain associated with vomiting, a workup was ordered in favor of very high lipasemia and an abdominal CT scan was also ordered in favor of stage A pancreatitis. A 56-year-old patient with chronic kidney disease presented with an acute digestive complaint of abdominal pain and vomiting, associated with diffuse bone pain. A workup was ordered, and found to be consistent with primary hyperparathyroidism. Localization workup confirmed parathyroid localization in our 3 patients, and parathyroidectomy was performed with good evolution.
Discussion/conclusion
The association between HPTP and pancreatitis is rare, however, the pathophysiology of this association is still poorly understood. The relationship between HPTP1 and pancreatitis is controversial to date, although most publications and experimental data in favor of a direct or indirect causal role for hypercalcemia via activation of pancreatic proteases. The degree of hypercalcemia may play an important role in this association. Calcium levels should be measured in all patients with acute pancreatitis.

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EP617

Hypercalcemia in locally advanced laryngeal cancer: an etiology to consider and a case report

Houas Jihene[1], Heyfa Belhadj-Miled[1], Monia Ghammam[1], Ben arfi Tayssir[1], Malika El Omri[1], Abir Meherzi[1], Mouna Bellakhdhar[1], El Ghali Wassim[2], Yosra Hasni El Abed[3], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT department, Sousse, Tunisia; [2], Department of Anaesthesia, Sousse, Tunisia; [3], departement of endocrinology, Sousse, Tunisia

Introduction
Although Primary hyperparathyroidism is the most common cause of hypercalcemia in the general population, it is a less frequent cause of hypercalcemia among patients with cancer. It is estimated that approximately 80% of the hypercalcemia in cancer is mediated by humoral hypercalcemia of malignancy resulting from elevated parathyroid hormone-related peptide (PTHrp), while almost 20% is the result of local osteolytic hypercalcemia. The aim of this work is to present a clinical case of head and neck cancer associated with hypercalcemia and the etiological and therapeutic management.
Observation
This concerns a 75-year-old man, known to have diabetes and a history of alcohol and tobacco use, who was admitted to our ENT department for the management of laryngeal dyspnea overlaid on chronic hoarseness that the patient had neglected. Upon examination: A poorly defined, hard, midline cervical mass was observed, adjacent to the thyroid cartilage, with skin infiltration. Clinically suspicious cervical lymph nodes were present. CT scan revealed an extensive tumoral process of the larynx invading the three levels, classified as T4aN2. Direct laryngoscopy with biopsy confirmed the diagnosis of laryngeal squamous cell carcinoma. Additionally, asymptomatic hypercalcemia of 2.8 mmol/l was incidentally discovered during the pre-surgical biological assessment. Parathyroid hormone (PTH) was measured at 123 ng/l, and parathyroid scintigraphy returned negative. The patient underwent an extended total laryngectomy with total thyroidectomy and central and bilateral lateral neck dissection. Postoperatively, calcium and PTH levels normalized. The final histopathological examination confirmed the cancer diagnosis and identified a 2 cm parathyroid adenoma.
Conclusion
Although primary hyperparathyroidism is a less common cause of hypercalcemia in malignancy, it nonetheless should not be overlooked and an elevated calcium concentration cannot always be attributed to a known malignancy.

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EP619

Acute pancreatitis revealing hyperparathyroidism: an unusual presentation: three case reports and literature review

Hind Ouakrim, Eleazar Nyogushima, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Chu Mohamed Vi Marrakesh - Drh, Marrakech, Morocco

Introduction
Primary hyperparathyroidism(PHPT) is a prevalent endocrine disorder characterized by hypercalcemia due to the overproduction of parathyroid hormone(PTH) from one or more parathyroid glands. While PHPT is typically diagnosed incidentally through routine laboratory testing due to asymptomatic hypercalcemia, acute pancreatitis as the initial symptom is a rare occurrence. This article presents three cases where acute pancreatitis served as the first manifestation ofPHPT.
Case reports
A 69-year-old patient was with an acute digestive presentation of transfixing epigastric pain and bilious vomiting, revealing pancreatitis classified as Balthazar stage D. The etiological assessment revealed primary hyperparathyroidism. Scintigraphy with SestamibiTc99m identified 2 focal retention areas in the MIBI-Tc99m. The patient received rehydration followed by bisphosphonate infusion and underwent successful surgical intervention. A 35-year-old patient was admitted for an acute digestive presentation, revealing pancreatitis classified as stage B. The etiological assessment showed hypercalcemia at 132 mg/l with hypophosphatemia at 19 mg/l. PTH was elevated at 985 pg/ml. Cervical ultrasound revealed a hyper-vascularized right retro-thyroid formation. SestamibiTc99m scintigraphy revealed a focus below the lower right thyroid pole. The patient underwent an adrenalectomy, with pathological examination confirming a parathyroid adenoma. A 28-year-old patient was admitted for epigastric pain, nausea. Lipase levels were elevated, and a CT scan revealed pancreatitis stage C. Primary hyperparathyroidism was diagnosed in the etiological assessment, with a PTH level of 3111 pg/ml, hypercalcemia of 136 mg/l, and hypophosphatemia of 22 mg/l. Sestamibi scintigraphy revealed three focal retention areas in the MIBI-Tc99m. The patient underwent a 7/8 parathyroidectomy with total thyroidectomy. Histological examination indicated parathyroid carcinoma, and unfortunately, the patient's condition became fatal after the development of multiple metastases.
Discussion
Hypercalcemia is a rare cause of acute pancreatitis, even more so if secondary to primaryhyperparathyroidism, with a prevalence varying from 1.5% to 5%. The association between hyperparathyroidism and acute pancreatitis has been debated, with three proposed mechanisms supporting this connection. These mechanisms involve hypercalcemia triggering trypsinogen conversion, calcium accumulation obstructing pancreatic ducts, and elevated calcium levels combined with genetic mutations increasing pancreatitis risk in PHPT patients. Patients with PHPT exhibit

a higher pancreatitis rate than those without, and given the high morbidity and mortality associated with acute pancreatitis, immediate treatment is crucial. The primary focus should be on managing pancreatitis initially. Once pancreatitis subsides, parathyroidectomy becomes imperative as it is the sole treatment for symptomatic PHPT. This comprehensive approach aims to address both acute pancreatitis and the underlying primary hyperparathyroidism to optimize patient outcomes.

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EP620

Primary hyperparathyroidism caused by an ectopic thymic parathyroid adenoma: A Case Report

Amal Ourdi[1], Houda Ennaifer[1], Françoise Latil Plat[1], Amina Bounaga[1], Arnaud Pforr[2] & Guillaume Granier[3]
[1]Avignon, endocrinology, Avignon, France; [2]Avignon, thoracic surgery, Avignon, France; [3]Avignon, anathomopathology, Avignon, France

Introduction
Primary hyperparathyroidism, is a common endocrine disorder, but rarely related to ectopic parathyroid. Often asymptomatic, it presents a problem of localization and hence therapeutic management. We report a rare case of an ectopic thymic parathyroid adenoma.
Description
We report a case of 62-year-old women, with a history of recurrent urinary infection due to pyelocalcic lithiasis, whose etiological investigation revealed the presence of hypercalcemia. Clinically, she had polydipsia, muscle cramps and tingling of the extremities. The diagnosis was primary hyperparathyroidism (hypercalcemia 3.51 mmol/l, hypophosphatemia 0.45 mmol/l and elevated PTH 1041 ng/ml). Cervical ultrasound was normal. Parathyroid scintigraphy showed the presence of an anterior mediastinal hypermetabolic mass in the thymic lodge with a heterogeneous cystic component. CT scan showed a solid cystic mass of the anterosuperior mediastinum region, measuring 46×37×55 mm. Genetic testing was performed, and excluded genetic forms of hyperparathyroidism. Correction of hypercalcemia was based on rehydration and cincalcet hydrochloride. Thymectomy was performed by video-thoracoscopy. Anatomopathological examination concluded to an intra-thymic parathyroid adenoma. Post-operatory calcemia was normal, and PTH decreased to 84.9 ng/ml. The 3 months CT scan was normal.
Discussion
Parathyroid glands and the thymus had a common embryological origin, which explains the thymic ectopy of the parathyroid. It's a rare entity, whose prevalence is about 16% in patients with primary hyperaldosteronism[1]. The diagnosis can be evoked by persistent disorders of phosphocalcic metabolism. Cervical ultrasound and scintigraphy are first line imaging. Imaging remains an essential step in management, providing accurate cervical and mediastinal mapping enabling the surgeon to perform a targeted surgical excision, avoiding white surgical explorations. Minimally invasive radio-guided surgery, assisted with PTH measurement, improves surgical outcomes.
Reference
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EP625

Acute necrotising pancreatitis in Primary Hyperparathyroidism

Keerthi Madhurya Kethireddi[1] & Maria Luiza Silveira[2]
[1]Worthing Hospital, Endocrinology and Diabetes, Worthing, United Kingdom; [2]Worthing Hopsital, Endocrinology and Diabetes, Worthing, United Kingdom

Introduction
Acute Necrotising Pancreatitis caused by Hypercalcemia secondary to Primary hyperparathyroidism is a rare condition[1]. The prevalence of acute pancreatitis in patients with PHPT is estimated between 1.5% and 7%[2]. We report a case of male patient with severe necrotising pancreatitis associated with hypercalcemia secondary to primary hyperparathyroidism.
Case Report
A 55-year-old man presented with sudden episode of severe abdominal pain to emergency department. He had a CT abdomen that showed the extensive necrotising pancreatitis. He was diagnosed with primary hyperparathyroidism 6 months ago, when he initially presented with polyuria, polydipsia, painful joints, back ache. He has no significant past medical history and not on any regular medications. He is a non-smoker and drinks alcohol socially. His blood analysis showed adjusted calcium 3.16 mmol/l, phosphate 0.79 mmol/parathormone –17.9 pmol/l, egfr-49 ml/min. He was managed conservatively with free fluids and analgesia. His stay was complicated by worsening abdominal pain and required critical care admission. His management included sliding scale insulin, patient-controlled analgesia and Naso jejunostomy feeding. His repeat imaging showed pancreatic pseudocyst for which surgical intervention was performed. Cinacalcet was commenced. Sestamibi imaging of parathyroid showed mild tracer uptake in all four parathyroid glands suggesting multi gland hyperplasia.4D CT imaging showed a nodule below the inferior pole of left lobe of thyroid gland could potentially a parathyroid adenoma. His case was discussed in Parathyroid multidisciplinary team meeting, and plan is for surgery. Interim, he had a cardiac arrest due to massive Myocardial infarction and was revived. Currently he is managing well on cinacalcet 90 mg twice daily which was gently up titrated, waiting for surgery.
Conclusion
This case illustrates primary hyperparathyroidism as one of the causes for acute necrotising pancreatitis, which can be fatal.
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EP636

Crosstalk between neurovegetative control, bone status and physical exercise: clinical use of a unitary autonomic nervous system index in postmenopausal women with osteoporosis

Luca Giovanelli[1], Vittoria Favero[1], Mara Malacarne[1], Sabrina Corbetta[2,3] & Daniela Lucini[1,4]
[1]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy; [2]University of Milan, Department of Biomedical, Surgical and Dental Sciences, Milan, Italy; [3]Istituto Auxologico Italiano, IRCCS, Unit for Bone Metabolism Diseases and Diabetes, Department of Endocrine and Metabolic Diseases, Milan, Italy; [4]Istituto Auxologico Italiano, IRCCS, Exercise Medicine Unit, Milan, Italy

Background
In the multifarious etiopathogenesis of skeletal fragility, an intriguing novel element is the possible existence of a crosstalk between autonomic nervous system (ANS) function and bone health. Indeed, sympathetic overactivity might stimulate osteoclastogenesis and inhibit osteoblastic proliferation, whereas opposite effects would be exerted by a prevalent parasympathetic activation. Autonomic Nervous System Index (ANSI) is a percent ranked (0–100) unitary proxy of cardiac autonomic regulation (CAR), derived from the autoregressive spectral analysis of heart rate variability by combining the three most informative indexes. It is a simple and non-invasive method for evaluating ANS function, being by design free of age and gender bias. Notably, this index has also proved to highlight neurovegetative improvements induced by therapeutic strategies such as aerobic endurance exercise. In this respect, physical activity itself is well-known to play a key part in reducing (re)fracture risk.
Aim
To investigate CAR as well as the effects of a structured and personalized exercise program on CAR, skeletal turnover, bone mass and body composition, in postmenopausal women affected with osteopenia/osteoporosis.
Methods
17 osteopenic/osteoporotic women aged between 50 and 70, referred to the Exercise Medicine Clinic of Istituto Auxologico IRCCS, were enrolled. Several evaluations, including bone turnover markers, CAR (by means of ANSI), body composition, and lifestyle (with ad hoc questionnaires) were performed, and a structured and personalized exercise program was prescribed.
Preliminary results and future perspectives
At the baseline assessment, bone turnover biomarkers were significantly impaired in comparison with reference populations from other studies. High variability in the ANSI score (32.5-79.5%) was observed. It will be interesting to explore CAR in a wider sample, as well as the effects of a customized exercise program both on bone metabolism and ANS function (as evaluated by non-invasive techniques), and their potential mutual correlation/interaction.

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EP638

Evaluation of Irisin levels in a group of young patients with Cerebral Palsy compared with healthy matched controls

Federica Saponaro[1], Giuseppina Sgandurra[2], Elena Beani[2], Paola Paolicelli[2], Elena Brunori[2], Francesca Tinelli[2], Silvia Filogna[2], Giovanni Cioni[2], Grazia Chiellini[1], Beatrice Polini[1], Caterina Ricardi[1], Patrizia Pignataro[3], Silvia Colucci[3], Manuela Dicarlo[4], Roberta Zerlotin[4], Graziana Colaianni[4], Pasquale Comberiati[5], Gianpiero Baroncelli[5], Agnese Gamborino[1], Alessandro Saba[1] & Maria Grano[4]
[1]Biochemistry Unit, Department of Surgical, Medical and Molecular Pathology and Critical Care, Pisa, Italy; [2]Stella Maris IRCCS, Calambrone, Italy; [3]University of Bari, Department of Translational Biomedicine and Neuroscience, Bari, Italy; [4]University of Bari, Department of Precision and Regenerative Medicine and Ionian Area, Bari, Italy; [5]University of Pisa

Introduction
Cerebral palsy (CP) is the most common chronic disability in childhood, burden by motor, sensation, cognition, feeding and communication impairment. A serious concern in children with CP is bone/muscle health deterioration, which negatively impacts the already reduced quality of life (QoL). Irisin is a myokine secreted by contracting muscle, which mediates beneficial effects on several targets, including brain. The aim of this pilot study was to evaluate serum levels of irisin in children with PC compared to healthy matched controls, to understand if irisin could be considered a biomarker of disability.
Methods
$n=39$ consecutive young patients (aged 3-18) with CP were enrolled at Fondazione IRCCS Stella Maris (Pisa) between 2021 and 2023 and $n=40$ healthy children matched for age and gender, were enrolled in the same period at Paediatric Unit, University of Pisa. Serum samples were collected in all of them, stocked at -80°C at Biochemistry Laboratory, University of Pisa and sent to University of Bari for Irisin serum levels measurement.
Results
Serum levels of Irisin were statistically significantly lower in the CP group compared with healthy matched controls or Crl (10.8 ± 2.4 vs 12.5 ± 3.2 ng/ml, $P=0.01$) and this difference was even greater when considering subjects with irisin levels under the median value (CP 8.7 ± 0.9 vs Crl 9.9 ± 1.3 ng/ml, $P=0.001$). In the CP group there was not difference in irisin levels between females ($n=12$) and males ($n=27$) (11.1 ± 3.1 vs 10.6 ± 3.2 ng/ml, $P=0.9$). Younger patients (aged <11 years) showed the higher difference in irisin levels between CP and Crl subjects ($P=0.004$).
Conclusions
Irisin is a myokine, with potential protective effects on CNS. We observed for the first time that irisin is markedly decreased in young patients with CP compared with controls, suggesting a potential role as biomarker of disability. Moreover, further analysis will correlate irisin levels with clinical, biochemical, and morphological markers of muscle-bone health in these patients, to understand the role of irisin as marker or as therapeutical target.

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EP640

Influence of muscle function on bone status in patients with hypophosphatasia

Victoria Contreras Bolivar[1,2,3], María Del Carmen Andreo-Lopez[1], Enrique Moratalla-Aranda[2,4], Trinidad González-Cejudo[2,5], Luis Martínez-Heredia[2], Francisco Andújar-Vera[2,3,6], Cristina García-Fontana[1,2,3], Beatriz García-Fontana[1,2,3] & Manuel Muñoz-Torres[1,2,3,7]
[1]Endocrinology and Nutrition Unit, Hospital Universitario Clínico San Cecilio, Granada, Spain; [2]Institute of Biosanitary Research of Granada (ibs.GRANADA); [3]CIBER on Frailty and Healthy Ageing (CIBERFES), Instituto de Salud Carlos III, Granada, Spain; [4]Nuclear Medicine Unit, Hospital Universitario Clínico San Cecilio, Granada; [5]Clinical Analysis Unit, Hospital Universitario Clínico San Cecilio, Granada, Spain; [6]Andalusian Institute for Research in Data Science and Computational Intelligence, Granada, Granada, Spain; [7]Department of Medicine, University of Granada, Granada, Spain

Introduction
Hypophosphatasia (HPP) is characterised by a deficiency of non-tissue-specific alkaline phosphatase. This results in abnormal mineralisation of bone tissue which predisposes to fragility fractures. Moreover, an affected muscle compartment could favour the risk of fracture. The aim was to evaluate the relationship between the bone and muscle compartment.
Material and Methods
Cross-sectional study in adults with PPH. Demographic (age, sex), analytical (alkaline phosphatase-FA-) and clinical variables were collected (fractures, muscle strength measured with Jamar dynamometer in kilograms (kg) -cut-off point: <p10 of Spanish population-, muscle mass of the rectus femoris of the quadriceps with ultrasound -Sonosite S-Nerve®- and bone mineral density with dual energy X-ray absorptiometry expressed according to T and Z-score. Statistical analysis was performed with IBM SPSS v.25.
Results
Thirty-three subjects were studied, 55% women, mean age: 49 ± 18 years and mean AF: 29 ± 11. Fifty-one per cent had affected family members. 52% had at least one bone fracture and 67% had dental pathology. Low muscle strength was detected in 24%. The mean rectus femoris quadriceps muscle thickness was 1.4 ± 0.7 and its mean area, 4.4 ± 2. 22.2% (4) of the women suffered from osteopenia and 27.8% (5) from osteoporosis (OP). Of the males, 26.7% (4) had osteopenia and none had OP. Muscle strength was positively correlated with Y-axis or thickness ($r=0.42$, $P=0.02$), with muscle area ($r=0.4$, $P=0.02$), with T-score in femoral neck ($r=0.48$, $P=0.01$) and in lumbar spine ($r=0.66$, $P=0.00$). A positive correlation was even found with FA values ($r=0.48$, $P=0.008$).
Conclusions
Hand dynamometry is associated with body composition and bone parameters, and is a useful parameter for assessing muscle status in PPH patients. Therefore, given the high prevalence of fractures in PPH patients, it could be useful to enhance the muscle compartment.

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EP641

Management of maxillary osteitis fibrosa cystica in a patient with secondary hyperparathyroidism: a report of a case

Amel Elkorbi, Nawres Bouaziz, Mahdi Ferjaoui, Rachida Bouatay, Naourez Kolsi, Harrathi Khaled & Jamel Koubaa
مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction
Brown tumor of bone, also called osteitis fibrosa cystica is a rare non-neoplastic lesion resulting from abnormal bone metabolism in hyperparathyroidism (HPT). Facial involvement is exceptional and, when present, usually involves the mandible, but is rare in the maxilla. These lesions can simulate a malignancy on clinical examination and routine radiographs. We aim through this case to present clinical and therapeutic particularities of a maxillary located brown tumor secondary to a HPT in a young woman.
Case report
A 36-year-old female presented to our department complaining about a 6 months history of an asymptomatic, expansive mass in the right side of the face causing facial disfigurement. She had a 6-year history of hemodialysis dependent anuric renal failure of undetermined cause. The physical examination showed a bilaterally enlarged jaw, more to the right associated with facial asymmetry and deletion of the right nasolabial fold. The oral examination revealed a hardened, expansive exuberant lesion in the right palate, causing multiple diastemas in maxillary teeth and transverse and anterior expansion of the maxilla, extending from anterior region to posterior right side. This expansive lesion measured 5 cm* 3 cm. The overlying mucosa was intact. Laboratory work up showed elevated creatinine, urea and parathormone (PTH) level of 1237 pg/dl, total serum calcium level was normal. Scintigraphy showed hyperfixation in the four parathyroid gland. Facial computer tomography found an expansive well limited lesion on the left maxilla associated with a thinning of the bony cortex sized 44x54x34 millimeters. A generalized demineralization of the facial bones was noted. Fine needle aspiration cytology of the maxillary mass showed a giant cell lesion. The patient underwent subtotal parathyroidectomy associated to a partial hemi-maxillectomy using the Caldwell-Luc approach. The post-operative course was unremarkable. The oral diet was restored on the second postoperative day. Histological sections confirmed the diagnosis of a brown cell tumor associated with parathyroid hyperplasia. Post-operative PTH levels decreased towards normal values and the patient benefited from an obturator prothesis. Four years after the surgery, no noticeable bone changes were observed in the patient.
Discussion/Conclusion
The bony complications of HPT have declined over a period of time, due to early diagnosis and multidisciplinary follow-up. Appropriate management of hyperparathyroidism is the the primary treatment of brown tumors; however, in the case of larger growing lesions or those causing incapacity, surgical management should be considered.
Disclosure of interest: none declared

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EP704

Hyperparathyroidism and the kidney: the culprit or the victim

Hind Ouakrim, Mennani Fatimaeezzahra, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Chu Mohamed Vi Marrakesh - Drh, Marrakech, Morocco

Introduction
Hyperparathyroidism is a condition marked by an overproduction of parathyroid hormone (PTH) due to excessive activity in one or more parathyroid glands. It is a prevalent disorder that may manifest as primary, secondary, or tertiary. In this report, we present three clinical cases highlighting intricate scenarios where determining the primary or tertiary origin of hyperparathyroidism proves challenging.
Case reports
A 33-year-old female with end-stage renal failure was diagnosed with hyperparathyroidism during her medical follow-up. Symptoms were associated with severe headaches and bilateral vision loss. An MRI revealed a pathological mass compressing the optic chiasm. Laboratory evaluation showed an elevated prolactin level, leading to the diagnosis of both hyperparathyroidism and prolactinoma. A 60-year-old female, under treatment for renal insufficiency due to multiple kidney stones, developed hypercalcemia with hyperparathyroidism. A MIBI scintigraphy revealed hyperactive uptake in a parathyroid gland in the left basal lower region. Parathyroidectomy was performed, revealing hyperplasia of the parathyroid gland. However, despite the intervention, persistent hyperparathyroidism was observed. A subsequent MIBIscintigraphy revealed an enlarged parathyroid gland on the right side. Parathyroidectomy was performed Patient, 63, with a 20-year history of nephropathy and end-stage renal failure, presented with progressive BAV, diplopia, hypoacusis, bone pain, and renal colic. Brain MRI showed a locally infiltrating lesion in the sphenoethmoidal complex. Nasal biopsy suggested a reparative granuloma. Cervical ultrasound revealed a multinodular goiter and a left parathyroid nodule. Hyperparathyroidism was confirmed. The patient underwent a left parathyroidectomy.
Discussion and conclusion
These three clinical cases present diagnostic and therapeutic challenges due to uncertainty regarding the primary or tertiary origin of hyperparathyroidism. In first case, the concurrent presence of a prolactinoma complicates the situation, making it difficult to determine whether the association between the prolactinoma and hyperparathyroidism is coincidental or part of multiple endocrine neoplasia type 1(MEN1). This uncertainty is further heightened by the inability to confirm the primary origin of hyperparathyroidism. Insecond case, despite the identification and surgical removal of a hyperplastic parathyroid gland, persistent hyperparathyroidism is observed, raising questions about possible primary or tertiary hyperparathyroidism related to parathyroid hyperplasia. In the third case, the diagnosis of hyperparathyroidism was established after the appearance of brown tumors in the context of chronic nephropathy with multi-lithiasic kidneys, complicating the clinical situation and highlighting the difficulty in distinguishing between primary and tertiary hyperparathyroidism. A multidisciplinary approach involving endocrinologists, nephrologists, and surgeons is essential for a comprehensive evaluation and optimal management of these patients.

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EP749

Is autoimmune thyroiditis in females with Ehlers–Danlos syndrome associated with lower bone density?

Emilia Babula, Poprawa Iga, Żuk-Łapan Aleksandra, Podstawka Jakub, Julia Latocha, Zuzanna Szymańska, Domański Jan, Bernadetta Kaluza & Edward Franek
National Medical Institute of the Ministry of the Interior and Administration in Warsaw, Department of Internal Medicine, Endocrinology and Diabetology, Warszawa, Poland

Background
Collagen, whose biosynthesis is regulated by thyroid hormones, is the most abundant connective tissue protein. Ehlers–Danlos syndrome alters collagen structure, which may affect bone mineral density (BMD). The purpose of this study was to assess the effect of autoimmune thyroiditis on BMD in females with Ehlers–Danlos syndrome.
Material and methods
The study involved a prospective assessment of 30 female patients, aged 20–53 years, with either hypermobile or classical Ehlers–Danlos syndrome. All patients underwent thyroid function tests, calcium and phosphorus metabolism tests, and BMD scans of the femoral neck and lumbar spine. Patients were divided into two groups: those with no autoimmune thyroiditis (group 1, $n=24$) and those with autoimmune thyroiditis (group 2, $n=6$).
Results
Study groups 1 and 2 showed no significant differences in terms of hypothyroidism ($n=4$ (16.7%) vs $n=2$ (33.3%), $P=0.39$), thyroid-stimulating hormone (TSH) levels (2.06 $\pm$1.16 µIU/ml vs 2.35$\pm$2.16 µIU/ml, $P=0.59$), free triiodothyronine levels (3.43$\pm$0.64 pg/ml vs 3.19$\pm$0.72 pg/ml, $P=0.42$), or free thyroxine levels (1.35$\pm$0.25 ng/dl vs 1.34$\pm$0.12 ng/dl, $P=0.44$), respectively. Moreover, no significant differences were noted in bone turnover markers, such as bone-specific alkaline phosphatase (9.89$\pm$2.88 µg/l vs 8.1$\pm$0.81 µg/l, $P=0.19$), beta-crossLaps (0.411$\pm$0.19 ng/ml vs 0.3$\pm$0.15 ng/ml, $P=0.2$), and osteocalcin (21.32$\pm$7.82 ng/ml vs 17.62$\pm$4.76 ng/ml, $P=0.34$), or in the BMD of the femoral neck (0.93$\pm$0.12 vs 0.96$\pm$0.15, $P=0.59$) or lumbar spine (0.95$\pm$0.12 vs 0.94$\pm$0.17, $P=0.98$). Furthermore, no significant correlation was observed between the levels of TSH, anti-thyroperoxidase autoantibodies, or anti-thyroglobulin antibodies on one hand and femoral neck BMD on the other (r_s 0.09, $P=0.61$; r_s 0.1, $P=0.59$; and r_s -0.03, $P=0.89$, respectively) or between any of those three markers and lumbar BMD (r_s 0.11, $P=0.56$; r_s 0.02, $P=0.93$; and r_s -0.03, $P=0.84$).
Conclusions
This study showed no relationship between autoimmune thyroiditis, bone turnover markers, and the BMD of either the femoral neck or the lumbar spine in women with Ehlers–Danlos syndrome.

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EP750

Can tenascin - X be a marker of bone turnover in patients with Ehlers-Danlos syndrome?

Aleksandra Żuk - Łapan, Babula Emilia, Poprawa Iga, Podstawka Jakub, Julia Latocha, Zuzanna Szymańska, Domański Jan, Zagozda Małgorzata, Wilk Juliusz, Korcz Tomasz, Cicha-Brzezińska Małgorzata, Bernadetta Kaluza & Edward Franek
National Medical Institute of the Ministry of the Interior and Administration in Warsaw, Warszawa, Poland

Background
The alterations in collagen synthesis and connective tissue structure that occur in Ehlers–Danlos syndrome translate to an increased risk of bone mass loss and development of osteopenia and osteoporosis, which may be evaluated with bone turnover biomarkers. Some subtypes of Ehlers–Danlos syndrome are associated with structural alterations in the extracellular matrix glycoprotein tenascin-X. The purpose of this study was to assess the relationship between tenascin-X and both bone turnover markers and bone mineral density (BMD) in patients with Ehlers–Danlos syndrome.
Material and methods
This study involved a prospective evaluation of 30 female patients, aged 20–53 years, with hypermobile or classical Ehlers–Danlos syndrome. All patients underwent tests of their tenascin-X levels, calcium and phosphorus metabolism parameters, and BMD scans of the femoral neck and lumbar spine.
Results
The study showed no significant correlation between tenascin-X levels on one hand and femoral neck BMD (r_s 0.13, $P=0.49$), lumbar spine BMD (r_s 0.17, $P=0.36$), alkaline phosphatase levels (r_s 0.18, $P=0.33$), beta-crossLaps levels (r_s 0.11, $P=0.56$), or osteocalcin levels (r_s -0.08, $P=0.66$). Univariate logistic regression showed no statistically significant effect of tenascin-X levels on the development of osteoporosis (OR 0.48, 95% CI 0–1.32, $P=0.99$).
Conclusions
Tenascin-X does not show significant correlation with either bone turnover markers or BMD in females with Ehlers–Danlos syndrome.

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EP773

A Case of Seizure Revealing Fahr's Syndrome with Primary Hypoparathyroidism

Hemmat El Haddad, Heba Murad, Nehal Hamdy, Rokaya Abdel Aziz, Heba Moustafa, Randa Salam, Mohamed magdy, Fady Nagi & Ahmed Atef
Cairo University, Internal medicine, endocrinology, Cairo, Egypt

Introduction
Fahr's disease, is a rare neurological disorder characterized by abnormal calcified deposits in the basal ganglia with a prevalence of $<1/1\ 000\ 000$
Case report
A 15-year-old male presented with focal seizures in right upper and lower limbs that progressed to generalized tonic clonic seizure and status epilepticus. No

history of head trauma, central nervous system infection, stroke, hypertension, diabetes, or autoimmune disease No family history of epilepsy He had recurrent episodes of focal seizures since the age of 10. EEG showed epileptiform waves, antiepileptic drug were started The patient was admitted to ICU with status epilepticus sedated on midazolam infusion, intubated and mechanically ventilated Pulse: 90/min, Bp: 100/70, RR: 18/min, Temperature: 37c (Hb) 13.4 g/dl, white blood cell count (WBC) 17.4 u/l; platelet 300 u/l, glucose 111 mg/dl (AST) 108 U/l; (ALT) 38 U/l U/l, creatinine 1.3 mg/dl; potassium 3.5 mmol/l; calcium 3.3 mg/dl; phosphorus 6.3 mg/dl; magnesium, 2.2 mg/dl (1.9–3.1 mg/dl); parathormone (PTH) 2.1 pg/dl (15–65 pg/dl); 25-OH vitamin D3 14.4 ng/ml (8.0–51.9 ng/ml); ANCA negative CT brain showed extensive bilateral cerebral calcification The patient received, calcium IV infusion (rate 0.5 mg/kg/h) for 24 h, antiepileptics (Levetiracetam 500 mg twice daily. Discharged on, oral medication started. Calcium Carbonate 600 mg 3 times daily oral Cholecalciferol) one bottle weekly Upon discharge calcium: 6.2 mg/dl, with no recurrent convulsions
Conclusion
We report a case of Fahr's syndrome with hypoparathyroidism in a patient with seizures as the main symptom. suspected by symmetrical and abnormal cerebral calcification

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EP775

Brown Tumor in a Normocalcemic Patient with Primary Hyperparathyroidism - A Case Report

Rokaya Abdel Aziz, Randa Salam & Walid Hassan
Cairo University, Internal medicine, endocrinology, Cairo, Egypt

Introduction
Brown tumor is a rare expansile osteolytic lesions benign bone lesion that arises as a direct result of parathyroid hormone on bony tissue in some patients with hyperparathyroidism. The reported prevalence of the brown tumour is 0.1% Brown tumor as the only and initial symptom of normocalcemic primary hyperparathyroidism is a rare clinical entity. Here, we present a case with multiple brown tumors in a young normocalcemic woman as a sequele of primary hyperparathyroidism mimicking bone metastases
Case report
44 year old female diabetic, hypertensive and hypothyroid presented by painless swelling over the lumbo-sacral region gradually increased in size not related to trauma. PAN-CT: large infiltrative heterogenous soft tissue mass at the sacrum (19.8×19.5×12.3 cm) serum calcium, phosphate and alkaline phosphatase, PTH were normal. Biopsy taken showed: numerous osteoclast-like multinucleated giant cells follow up of the mass size was advised every 3 – 6 months The patient developed anemic manifestation (Hb= 5 g/dl), for which She received blood transfusion 3 times and referred to our hospital for further assessment
Examination
She was depressed, BP:170/80, pulse:103 /mint, Temp: 37 C, pallor, Bilateral lower limb edema A mass felt occupying right iliac, suprapubic, left iliac fossae, large oval Lumbo-sacral swelling 19×10 cm, normal neurological examination HB 7.6 g/dl, MCV 90 fl, Platelet 351 U/l, TLC 6.4 U/l, creatinine 1.39 mg/dl, calcium 9 mg/dl, phosphrous 4.3 mg/dl, PTH 199.7 pg/ml (10-55) Abdominal and pelivc sonar showed, pelvi- abdominal mass with multiple cystic areas (23.3×15 cm) Kidneys: Bilateral Moderate Back pressure with bilateral Hydroureter 19×11 cm. 99 mTc Sestamibi parathyroid scan showed intense radiotracer uptake in the left upper neck (parathyroid adenoma), uptake in the sacrum (?brown tumor) Surgical removal of sacral mass was not applicable Left parathyroidectomy was done biopsy reported parathyroid adenoma Follow up after 3 years: normal serum PTH level, marked decrease in mass size (6.2×5.2×3.3 cm)
Conclusions
Brown tumors are extremely rare in normocalcemic primary hyperparathyroidism, accurate diagnosis enables the proper treatment

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EP776

Hypophosphatemic Rickets a clinical case report

Miriam Cozar, Rossana Manzanares Cordova & Manuel Martín López
Hospital Juan Ramón Jiménez, Endocrinology, Huelva, Spain

Background
Hypophosphatemic rickets, mostly of the X-linked dominant form caused by pathogenic variants of the PHEX gene, poses therapeutic challenges with consequences for growth and bone development and portends a high risk of fractions and poor bone healing, dental problems and nephrolithiasis/nephrocalcinosis (1). Children with hypophosphatemic rickets present poor growth, deformities of weight-bearing limbs such as genu varum or valgus, a 'rachitic rosary' involving the costochondral junctions, or enlargement of wrist, knees, or ankles among other symptoms. Family history may lead to detection of genetic forms prior to demonstration of rickets. (2)
Case report
14-year-old woman, referred from pediatrics due to growth retardation since early childhood. Family history of mother with pathological short stature of unstudied origin. Analyzes show persistently low phosphorus with low 25 OH vitamin D and elevated alkaline phosphatase, normal IGF1 and IGFP3. Karyotype 46XX. Bone age delayed 2 and a half years for chronological age. On physical examination, discrete genu varus, with short stature of 143 cms (-2.87 SD). Given the suspicion of hypophosphatemic rickets, a genetic study is requested: The patient is a heterozygous carrier of the variant c.1843A>C (p.Thr615Pro) in the PHEX gene, which is later confirmed in her mother. Currently undergoing treatment with oral phosphorus and cholecalciferol, she remains asymptomatic, with normalization of analytical parameters and with good clinical evolution.
Conclusions
Hypophosphatemic rickets/osteomalacia represent a set of rare disorders with many genetic and acquired causes and potential in long-term complications for children and adults, and diminishing physical function and quality of life. Conventional treatment with phosphate supplements and pharmacologic doses of active vitamin D may require the addition of growth hormone and calcimimetics. New biological therapeutics, including FGF23 targeting monoclonal antibodies or recombinant receptor blockers, are being developed and becoming available. Lastly, identification of genetic mutations associated with hypophosphatemia syndromes has contributed to our understanding of the pathogenesis and potential treatment of hypercalciuria, nephrocalcinosis, and renal stones disease.

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EP780

Exploring the Uncharted Territory: Abacavir in HIV Treatment Unveils Rare Side Effect - A Focus on Hypophosphatemia

Abhishek Vyas & Asad Ali
King's Mill Hospital, United Kingdom

This case report highlights an unusual side effect of hypophosphatemia linked to Abacavir; a medication commonly used in the treatment of HIV. A 36-year-old male patient was referred to the endocrine team due to persistent hypophosphatemia while receiving Abacavir for his HIV management. Extensive investigations, including assessments of calcium levels Urea and Electrolytes, parathyroid hormone (PTH), Vitamin D, serum magnesium, and serum cortisol and fibroblast growth factor 23 (FGF23), yielded normal results. Following these findings, the case was discussed in an endocrine multidisciplinary team (MDT) meeting, leading to a consensus that the hypophosphatemia was likely associated with Abacavir use. This report aims to contribute to the existing body of evidence regarding this uncommon side effect. By presenting this case, we seek to raise awareness among healthcare professionals about the potential for hypophosphatemia in individuals undergoing Abacavir treatment for HIV. The involvement of various experts in the MDT discussion adds weight to the conclusion that the observed hypophosphatemia is likely attributed to Abacavir. This case report underscores the importance of considering medication-induced complications in patients with persistent hypophosphatemia, even when routine investigations produce normal results. By sharing this clinical observation, we hope to contribute valuable information to the medical community, fostering a better understanding of potential side effects associated with Abacavir and aiding in the optimization of patient care.

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EP782

Klinefelter Syndrome and Primary hyperparathyroidism—just a coincidence?

Cristina Ene
"Doctor Victor Babes" Foundation, Bucharest, Romania

Background
Two prevalent and underdiagnosed endocrine disorders are primary hyperparathyroidism and Klinefelter syndrome. The main cause of primary hyperparathyroidism is parathyroid adenoma. Less commonly multiple parathyroid hyperplasia have been described with or without genetic mutations. Klinefelter

syndrome could also be seen as a genetic disorder, being a chromosomal condition.
Methods
We report an uncommon association, without any family history, between Klinefelter syndrome and primary hyperaparathyroidism caused by the affection of two parathyroid glands.
Case report
The patient is a 50 year-old man, previosly diagnsticated with Klinefelter syndrome. He was referred by the urologist because of the suggestive clinical profile. The hypergonadotropic hypogonadism was confirmed as a Klinefelter syndrome by the cartiotip analysis. At the time of diagnosis, he also had a normocalcemic hyperparathyroidism in the presence of a vitamin D deficiency. Dual-energy X-ray absorptiometry (DXA) was normal. The patient receveid testosteron replacement. There was no need for fertility assessment. 1000 IU per day were used to treat the vitamin D3 deficit. After the diagnosis, the calcium levels started to rise above normal two years later. By now, the neck ultrasound had revealed a small right hyperechoic thyroid nodule and hypoechoic images with a polar doppler signal in the lower half, posterior to the left and right thyroid lobes, indicating parathyroid adenomas or hyperplasia. Technetium 99m-MBI-SPECT confirmed bilateral enhanced radionuclide accumulation at inferior parathyroid glands. DXA reveals a small decrease in bone mineral density only in the 1/3 distal part of the radius (osteopenia). The level of metanephrines/normetanephrines and calcitonin were normal. The patient was proposed to surgery, but due to the epidemiological context of COVID-19, survaillance was the choice. For now, the level of calcium is still above the normal level, with a normal level of phosphorous and vitamin D and normal renal function. No renal stones or progressive demineralization in the DXA study were observed. Ultrasound showed a growing left parathyroid nodule and a stationary right one. The thyroid nodule is also stationary. Surgery is scheduled to be done. Genetic testing is to be performed.
Conclusion
There hasn't been any evidence of a pathological or genetic connection between the two endocrine disorders. Our patient is scheduled for genetic testing – MEN syndrome and familial hyperparathyroidism must be ruled out in this instance, due to the enlargement of two parathyroid glands. Monitoring these rare occurrences is nevertheless essential to identify more abnormalities in the future.
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EP786

Milk alkali syndrome secondary to over counter Antacids
Kalyani Nagarajah[1] & Marc Lyndon Evans[2]
[1]Swansea, Department of Endocrinology and diabetes, Swansea, United Kingdom; [2]University Hospital Llandough, Department of Endocrinology and diabetes, Cardiff, United Kingdom

Introduction
Milk – alkali syndrome is a rare and distinctive disorder caused by ingestion of large amounts of calcium and absorbable alkali resulting in hypercalcemia. It is characterized by a triad of hypercalcemia, metabolic alkalosis and renal failure. It was first described in 1920s, as it was mainly caused by administration of milk and bicarbonate for treatment of peptic ulcers. Since the usage of new treatment modalities for peptic ulcer disease, the incidences of milk alkali syndrome have decreased.
Case report
Here we present a 59 years old female patient, who presented to Emergency department for a fall and Syncopal episode. Our patient had few days history of increasing thirst, polyuria and diffuse abdominal discomfort. This prior to her syncopal episode, which lasted for few minutes with quick recovery. She had a past medical history of Endometriosis, Type 2 diabetes mellitus, epilepsy and ex-IVDU user with hep B in remission. She was suffering with frequent episodes of heart burns and self-treated this with over counter Rennie tablets. She had been taking almost 100 Rennie tablets per day and this over few weeks. On admission our patient was found to be confused and dehydrated. she had an adjusted calcium level of 4.55, Phosphate levels of 0.85, Suppressed PTH levels and acute kidney injury. Her Vitamin D levels on admission was 34 with urea of 16.9 and creatinine of 334. She had ECG changes related to the severe hypercalcemia. CT head performed for her syncopal episode did not report any abnormalities. Bence jones proteins, electrophoresis and ACE levels were within normal range. A CT Thorax, Abdomen and Pelvis was reported a 25 mm exophytic low density lesion over the upper pole of the right kidney. Following this an ultrasound was performed and this resulted in simple cyst as the lesion found on the upper pole of the kidney. Her Calcium levels responded well to aggressive Intravenous fluid resuscitations. Her latest calcium levels and renal function are within normal range and she was also imitated on vitamin D therapy.
Conclusion
We would like to emphasise the importance of considering over counter antacids treatment as iatrogenic cause of hypercalcemia, especially severe hypercalcemia like our patients. As mentioned above milk Alkali syndrome is rare nowadays, given new treatment modalities for indigestion and peptic ulcers.
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EP796

Severe Hypercalcemia After Parathyroidectomy: When the Unexpected Happens
Tânia Carvalho, Gustavo Rodrigues, Bárbara Filipa Araújo, Joana Saraiva, Mara Ventura, Sofia Gouveia, Dírcea Rodrigues & Isabel Paiva
Centro Hospitalar e Universitário de Coimbra, Serviço de Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal

Introduction
Severe hypercalcemia is defined as a total serum calcium level >14 mg/dl or ionized calcium >10 mg/dl . The most common causes are primary hyperparathyroidism (PHPT) and neoplasms (90% of cases). Vitamin D intoxication is an extremely rare cause.
Case Report
A 56-year-old man presented to the emergency department with vomiting, generalized weakness and complaints of imbalance over one week. Upon physical examination, he displayed confusion, trunk and limb ataxia and abolished osteotendinous reflexes. He had history of multiple endocrine neoplasia (MEN) 1 and PHPT with a hypercaptant left inferior parathyroid on scintigraphy. Six weeks before admission, he underwent parathyroidectomy of the inferior glands (histology: hyperplasia). Postoperatively, calcium and parathyroid hormone (PTH) declined, reaching levels of 6.0 mg/dl for calcium and 0.3 pg/ml for PTH. His 25(OH)vitamin D level was 22 ng/ml. Supplementation was adjusted, and he was discharged with a regimen of Calcium Carbonate + Colecalciferol 1500 mg + 400IU, 2 tablets every 8 hours, and Calcitriol 0.25µg, 1 tablet every 6 hours. Upon admission, the patient's total serum calcium was exceptionally elevated at 23.8 mg/dl, with albumin measuring 4.4 g/dl, creatinine at 4.35 mg/dl (baseline 1.62), PTH <0.5 pg/ml, and 25(OH)vitamin D at 42 ng/ml. Phosphate and magnesium levels were within normal ranges. The therapeutic approach encompassed intensive fluid therapy, furosemide administration, calcitonin and zoledronic acid. Subsequently, the patient's serum calcium exhibited a gradual reduction, reaching 7.9 mg/dl by the 10th day of hospitalization. At this time, the patient reported that he had been taking not one but four calcitriol tablets every 6 hours due to a misunderstanding of the prescription, supporting the hypothesis of 1,25(OH)vitamin D intoxication. Oral supplementation was re-initiated. Serum calcium continued to decrease, reaching 6.6 mg/dl on the 13th day of hospitalization, which required intravenous calcium and adjustments to oral supplementation. Upon discharge, there was an improvement in renal function (creatinine 2.06 mg/dl), and serum calcium was stabilized at 8.4 mg/dl with a regimen of Calcium Carbonate + Colecalciferol 1500 mg + 400IU $2+2+1+2$ tablets and Alfacalcidol 1 mg $1+1$ tablet.
Conclusion
The possibility of vitamin D intoxication should be considered in the presence of hypercalcemia, decreased PTH, and no suspicion of malignancy. The patient was taking 4 mg of calcitriol daily, a dose much higher than recommended for hypoparathyroidism treatment (0.5–1.0 µg/day). This case reminds us of the need to regularly monitor calcium levels in patients with post-surgical hypoparathyroidism and ensure that patients understand the proposed therapeutic regimen.
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EP799

Burnett's Syndrome – A Modern Presentation
Mohammad Jeeyavudeen & Ganesh Arunagirinathan
Metabolic Unit, Western General Hospital, Edinburgh, United Kingdom

Introduction
Milk-Alkali Syndrome (MAS), also known as Burnett's syndrome, is a triad of hypercalcemia, acute kidney injury and metabolic alkalosis, traditionally associated with excessive intake of milk and absorbable alkali. With changes in dietary supplements and medical prescriptions, its re-presentation in modern clinical practice has evolved making it the third common cause for hypercalcemia. This abstract presents a unique case of MAS resulting from relatively supraphysiological doses of calcium supplements in a patient with a low body mass index (BMI).
Case presentation
A woman in her early 60s presented with symptoms including confusion, constipation, excessive thirst, and tiredness. She has chronic excessive alcohol

intake, self-neglect, and poor oral nutritional intake. Three years prior to this admission, following low-velocity falls resulting in fractures, she was started on calcium and vitamin D supplementation containing 500 mg of calcium carbonate and 400 IU of cholecalciferol. Given her extremely low BMI of 10.59 kg/m^2, she was supplemented with Fortisip which contains additional calcium. On examination, she appeared severely emaciated with dry mucous membranes and signs of dehydration. Laboratory findings indicated a significantly low parathyroid hormone (PTH) level, elevated albumin corrected calcium, low magnesium and phosphate levels, and normal 25-hydroxy vitamin D. Her serum bicarbonate was extremely elevated. A full-body CT scan showed multiple bladder calculi with no evidence of underlying malignancy.

Discussion

The patient's medical history and acute presentation led to the diagnosis of MAS, primarily due to her high intake of calcium carbonate relative to her body weight, as evidenced by her metabolic alkalosis despite acute kidney injury. Upon discontinuation of calcium supplements, her PTH rose to 33.1 pmol/l, while calcium levels dropped to 2.16 mmol/l. MAS is classified into three types based on symptom duration and organ dysfunction: acute MAS or toxemic form, subacute form or Cope's syndrome, and chronic form or Burnett's syndrome. This case emphasizes the importance of individualized patient care, especially in managing dietary supplements, and highlights the potential risks of excessive calcium intake in patients with low BMI. It also stresses the need for vigilant monitoring of calcium and PTH levels to prevent recurrent hypercalciuria and kidney stone formation.

	Patient's value	Normal range
Adjusted calcium	4.38	2.2- 2.6 mmol/l
Phosphate	0.61	0.8-1.4 mmol/l
Magnesium	0.45	0.7-1.0 mmo/l
Bicarbonate	34	22-30 mmol/l
PTH	1.6	1.6-6.9 pmol/l
25-Hydroxy Vitamin D3	86	50-170 nmol/l
Estimated Glomerular Filtration Rate	59	
Myeloma and coeliac screen	Negative	

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EP800

Severe bone disease: Unusual mode of revelation of primary hyperparathyroidism in young A case Report

Meryam Alahyane, Sana Rafi, Salma El Hilali, Ghizlane El Mghari & Nawal El Ansari
Mohammed VI university hospital of Marrakesh, Department of Endocrinology, Diabetes, Metabolic diseases and Nutrition, MARRAKESH, Morocco

Background

Primary hyperparathyroidism (PHPT) is a systemic disease caused by lesions of the parathyroid gland, such as parathyroid adenoma, parathyroid hyperplasia, and parathyroid carcinoma. Bone disease is an important complication of hyperparathyroidism. We herein report a rare case of severe bone disease caused by primary hyperparathyroidism.

Case report

A 33-year-old female patient presented with a history of right lower limb pathological fracture, that restricted her mobility. The fracture was first treated surgically, without any medical follow-up. 5 years later, she presented in Emergency department with a severe anemia requiring a blood transfusion. Meanwhile laboratory data showed a hypercalcemia of 129 mg/l with an elevated serum Parathormone (PTH)of 744.3 pg/ml and vitamin D deficiency. Thyroid and multiple endocrine neoplasia (MEN) assessment were normal. X-ray examination showed Multiple osteolytic brown bone tumors disseminated throughout the skeleton. The CT scan demonstrated heterogeneous nodular formation located in the postero-inferior pole of the left thyroid lobe with a mediastinal extension measuring 26×25×47 mm. The patient was finally diagnosed with PHPT. She was prepared pre operatively with isotonic salin hydratation to manage hypercalcemia and vitamin D supplementation to avoid hungry bone syndrom. The patient underwent a surgical excision of the left inferior parathyroid. The surgical exploration of the remaining parathyroid glands was normal. The patient was discharged in good clinical condition. Total serum calcium and parathormone were within the reference range on the second day after surgery. Anatomopathological study in still in progress.

Discussion

PHPT leads to an excessive synthesis and secretion of PTH which causes an enhancement of osteoclasts' effects and causes Therefore calcium and phosphore in bones to be dissolved into the blood, resulting in hypercalcemia and hyperphosphatemia. Most patients with PHPT are asymptomatic. Very few may present with skeletal system manifestations such as bone pain, osteoporosis and pathological fracture; they may also develop brown tumors and osteitis fibrosa cystica. Most patients are first diagnosed in the department of orthopedics, resulting in a high rate of delayed treatment or misdiagnosis which can lead to further aggravation of pathological bone damage. Once confirmed, timely resection of the diseased parathyroid glands is considered to be the preferred method for the treatment of PHPT with severe bone disease, rather than treatment of the skeletal system disease only. After surgery PTH and other relevant indicators gradually return to normal levels, and new bone tissue gradually grows within and resolves the skeletal lesions.

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EP820

Predictive factors of postoperative hypocalcemia in primary hyperparathyroidism

Sameh Mezri[1], Chaima Zitouni[1], Wadii Thabet[2] & Khemaies Akkari[1]
[1]Principal Military Hospital, Tunis, Tunisia; [2]Taher Sfar Hospital, Mahdia, Tunisia

Introduction

hyperparathyroidism is an endocrinopathy affecting calcium metabolism. Its curative treatment is surgical. Postoperative hypocalcemia is one of the main risks of this surgery.

Objective

The aim of this study is to identify predictive factors of postoperative hypocalcemia after surgery for primary hyperparathyroidism.

Method

This is a retrospective study including 84 patients operated on for pimary hyperparathyroidism in our department over a period from 2015 to 2023. We performed a statistical study in order to identify predictive factors of postoperative hypocalcemia.

Results

Early hypocalcemia (<4 days from surgery) was noted in 18 cases. It was related to hypoparathyroidism in 2 cases and to Hungry bone syndrome in 3 cases. Hypocalcemia was severe, leading to tetany in 3 cases. Predictive factors of early postoperative hypocalcemia were: the nature of the approach (unilateral or bilateral), association with a thyroid surgery, preoperative vitamin D deficiency and postoperative hypoparathyroidism (after 24 hours). Predictors of prolonged hypocalcemia (> 2 months) were: preoperative vitamin D deficiency, removal of a healthy gland in addition to the adenoma, preoperative malignant hypercalcemia, advanced bone disease, postoperative hypoparathyroidism and bulky adenomas.

Conclusion

Postoperative hypocalcemia is conditioned by certain clinical and biological factors. Demonstrating the involvement of these factors allows selecting at-risk patients in order to act on these parameters preoperatively, and to ensure stricter monitoring of the at-risk population postoperatively.

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EP823

Surgery of primary hyperparathyroidism

Sameh Mezri[1], Chaima Zitouni[1], Wadii Thabet[2] & Khemaies Akkari[1]
[1]Principal Military Hospital, ENT, Tunis, Tunisia; [2]Taher Sfar Hospital, Mahdia, Tunisia

Introduction

Primary hyperthyroidism relates to the thyroid gland producing large amounts of hormone due to either uncontrolled growth of hormone-producing functional tissue. This condition needs to be treated surgically in order to prevent complications.

Objective

The aim of this study is to describe the surgical treatment of primary hyperparathyroidism.

Method

This is a retrospective study of 84 patients operated on for pimary hyperparathyroidism in our department over a period from 2015 to 2023.

Results

The mean age of our patients was 49 years, with a clear female predominance. Cervical ultrasound and parathyroid scintigraphy were performed in all cases. CT or MRI scans were performed in 5 cases. The approach was bilateral in 29% of cases, and unilateral in 71%. Among the patients operated on, a single gland was removed in 78 cases: an adenoma in 77 patients, and a hyperplasia in 1 case. Two glands were removed in 6 patients: a healthy gland with an adenoma in 2 cases, a

hyperplasia of both glands in 2 patients, and a double adenoma in 2 patients. Thyroid surgery was performed in 42.8% of cases. Postoperatively, dysphonia associated with unilateral recurrent paralysis was noted in 2 cases. Early hypocalcemia was noted in 18 cases. It was related to hypoparathyroidism in 2 cases and to Hungry bone syndrome in 3. Hypocalcemia was severe, leading to generalized tetany in 3 cases. We noted normalization of PTH levels within 72 hours of surgery in 90.5% of cases. Failure was noted in 6 cases, related to incomplete surgery for triple adenoma in 1 case, hyperplasia in 3 cases, glandular ectopy in 1 case and multiple endocrine neoplasia in 1 case.
Conclusion
Surgery of primary hyperparathyroidism leads to good therapeutic results. However, there is a risk of failure. It may be related to multiple adenoma, glandular ectopy or hyperplasia of several glands.

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EP844

Case Report- An Atypical Case of Familial Hypocalciuric Hypercalcemia: A Novel missense mutation in the CASR Gene?

Taqiyeddine Louifi[1], Jana Perpetue[2] & Hajer Zayet[2]
[1]Nord Franche-Comte Hospital (HNFC), Department of Endocrinology and Diabetes, Trevenans, France; [2]Nord Franche-Comte Hospital (HNFC), Trevenans, France

Back Ground
Familial hypocalciuric hypercalcemia (FHH) is a benin cause of hypercalcemia that is characterized by autosomal dominant inheritence with high penetrance. In most cases, FHH results from inactivating mutations in the CaSR, the phenotypic aspect is a mild to moderate hypercalcemia, inappropriately normal or high PTH levels and relative hypocalciuria.
Case report
We describe an atypical case of a 46 years old man who had clinical finding compatible with FHH but with unusual description: asymptomatic severe hypercalcemia up to 3.02 mmol/l, high PTH level up to 166 ng/l and a very low 24 hours calciuria: calcium-to-creatinine-clearance ratio 0.0013. First Genetic analysis revealed an unknown missense variant CASR gene sequence: c.1682G>A (p.Cys561Tyr).
Discussion
Severe hypercalcemia is unusual with FHH type 1, we describe an atypical presentation of FHH. To our knowledge, this CASR sequence variation has not previously reported in the literature. Nevertheless, this is still a provisional result, it will be completed and confirmed by a second genetic analysis on a PAXgene blood DNA Tube.
Conclusion
This CASR mutation will probably represent a novel pathogenic sequence variation causing a type 1 FHH with severe hypercalcemia.

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EP849

Assesement of the quality of life among patients followed for chronic hypoparathyroidism

Nabil Skouta, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
UHC Ibn Rochd, Casablanca, Morocco, Department of Endocrinology, Diabetology and Metabolic Diseases, Casablanca

Introduction
Hypoparathyroidism refers to a set of clinical and biological manifestations that occur when parathormone secretion is insufficient. Individuals enduring persistent hypoparathyroidism encounter various symptoms and face enduring complications that may jeopardize their overall well-being."
Objectives
The objective of our study is to assess the quality of life (QOL) of patients followed for hypoparathyroidism receiving conventional treatment.
Patients Et Methods
This is a descriptive cross-sectional study involving 39 patients followed in the endocrinology outpatient clinic at Ibn Rochd University Hospital in Casablanca from January 2023 to November 2023. The impact on QOL was assessed using the SF-36 score. Data were analyzed using IBM SPSS Statistics 27.0.
Results
Our study included 39 patients with an average age of 41 years, with a female predominance of 80%. The etiologies of hypoparathyroidism were as follows: 74% post-surgical hypoparathyroidism, 20% autoimmune hypoparathyroidism, and 5% pseudo-hypoparathyroidism. The scores were on average 47% for physical limitation, 33% for psychological limitation, 43% for energy, 60% for mental health, 75% for social activity, 45% for pain, and 54% for general health.
Conclusion
This study suggests an impairment of the quality of life in multiple domains in patients with chronic hypoparathyroidism. It is necessary to improve medical treatment and management for these patients.

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EP859

Milk-alkali syndrome in primary hypoparathyroidism: a case report

José Vicente Rocha[1], Mariana Silva de Sousa[2], Mariana de Griné Severino[1], Yolanda de Sá Pereira[2], Tiago Santos[2] & Ana Gomes[2]
[1]ULS Santa Maria, Endocrinology, Diabetes and Metabolism, Lisbon, Portugal; [2]ULS Santa Maria, Internal Medicine, Lisbon, Portugal

Introduction
Hypoparathyroidism treatment is aimed to achieve a serum calcium at the lower limit of normal providing symptom resolution and preventing complications such as urolithiasis and renal impairment. Milk-alkali syndrome (MAS) incidence has been gradually rising associated with the increase of calcium carbonate and vitamin D supplementation. The classic triad is characterized by metabolic alkalosis, hypercalcemia and renal failure.
Case report
A 34-year-old male with DiGeorge syndrome was referred to the Endocrinology clinic due to primary hypoparathyroidism. Previous personal history was relevant for Evans syndrome under Eltrombopag treatment, epilepsy and schizophrenia. He was treated with a calcium carbonate/cholecalciferol association (1500 mg + 400 UI) and calcitriol 0.25 mg with daily doses being titrated to 9000 mg of calcium carbonate and 1.25 mg of calcitriol daily in order to achieve a serum calcium of 8-8.4 mg/dl and a normal serum phosphorus. At a scheduled revaluation, the patient presented with hypercalcemia (serum calcium of 13.9 mg/dl), acute renal failure (serum creatinine of 2.72 mg/dl), and metabolic alkalosis (pH of 7.52, pCO2 46.3 mmHg and HCO3 29.2 mmol/l). The patient denied anti-inflammatory medication, nausea and vomiting, fever, respiratory or gastrointestinal symptoms. Hypoparathyroidism treatment was stopped and the patient was admitted to the hospital. Intravenous fluid replacement was started with a slow gradual renal function recovery and calcium normalization. Malignant hypercalcemia was excluded with whole body CT scan, PTHrP measurement and serum PSA. Angiotensin converting enzyme and serum immunofixation were normal. Patient denied frequent consumption of antacids or canned or preserved foods but admitted to daily consumption of calcium enriched milk. MAS diagnosis was assumed. Calcium carbonate and calcitriol were restarted at lower dosages, and dietary counselling was made. Patient maintained desired calcium levels with 4500 mg of calcium carbonate 1 mg of calcitriol.
Conclusion
This case highlights that MAS is a possible complication of hypoparathyroidism treatment. Calcium and vitamin D supplementation should be tailored to individual patients and a closer monitoring may be needed in patients under higher daily doses.

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EP863

Lameness revealing primary hyperparathyroidism jaw-tumor syndrome (HPT-JT)!

Marwa El Arem[1], Taieb Ach[2], Asma Ben Abdelkarim[2], Amel Maaroufi[2], Molka Chadli Chaieb[2] & Koussay Ach[2]
[1]Hospital Fatouma Bourguiba, Endocrinology; [2]Farhat Hached University Hospital Sousse, Endocrinology

Introduction
Primary hyperparathyroidism JawTumor Syndrome is a rare genetic disorder characterized by the synchronous or metachronous occurrence of primary hyperparathyroidism and an ossifying fibroma of the maxilla and/or mandible, associated with an increased risk of parathyroid carcinoma.
Observation
We report the case of a 30-year-old young woman who consulted for a limp in walking,6 months after having been operated for a juvenile ossifying fibroma of the mandible. Standard X-ray showed multiple giant lacunar images at the level of the two iliac bones and the right femur, evoking brown tumours. A phosphocalcic assessment was requested showing a malignant hypercalcemia at 4.3 mmol/l,

hypophosphatemia at 0.4 mmol/l, PTH = 1360 pg/ml, PAL = 900 IU/l, creatinine = 85 µmol/l. Dual energy X-ray (DXA) showed osteoporosis at the neck of hip and 1/3 proximal of the radius. Cervical ultrasound and the SPECT-CT scintigraphy with 99m Tc-MIBI showed a 2.5×15 mm hypoechoic left subthyroidal formation with regular contours and hypervascularisation, no thyroid nodule, and no cervical adenopathies. The clinical picture was strongly suggestive of primary hyperparathyroidism in the context of jaw tumour syndrome. The abdomino- pelvic ultrasound was also performed, which showed no associated uterine polyps or tumours, nor renal tumors. The patient underwent a left inferior parathyroidectomy which was atypical in appearance. The histological examination revealed a parathyroid adenoma with no evidence of malignancy.

Conclusion

Primary hyperparathyroidism jaw -tumor syndrome is an entity that should be known given the association with malignant and atypical forms of parathyroid tumors of non-endocrine tumors that should be sought.

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EP864

Non-traumatic fractures in the elderly do not omit primary hyperparathyroidism

Abdelkader Yahi, Longo Redoune, Benabdellatif Katia, Lachekham Aicha, Haffaf Lounes, Amokrane Affaf, Boumesbah A, Addab Fahd, Rannai A, Ould-Kablia Samia & Bensalah Meriem
Algeria, Endocrinology, Bir Mourad Rais

Background

The presentation of primary hyperparathyroidism has changed radically over 30 years. Indeed, currently, asymptomatic forms which represented around a quarter are now estimated at 80% of cases.

Case description

We report the case of a 57-year-old women, postmenopausal for 10 years, who presented following a fall from height with a triple pathological fracture (the left humeral head and the two upper ends of the femurs). Surgical treatment was indicated but rejected in the face of severe osteoporosis (Tscore a -6.3 at the cortical bone level). The pre-therapeutic assessment of bisphosphonates revealed severe hypercalcemia (> 3 mmol/l). The diagnosis of primary hyperparathyroidism was confirmed with a PTH level > 5000 pg/ml on a left parathyroid macroadenoma, mixed solido-cystic with a long axis of 44 mm. Morphological exploration revealed multiple brown tumors, and multiple bilateral renal micro- and macro-lithiasis with right hydronephrosis. The patient underwent a successful parathyroid adenectomy (post-operative PTH had PTH at 11 pg/ml). The histological study is in favor of benignity.

Discussion

The revelation of primary hyperparathyroidism by a fracture is rare. Brown tumors can be completely asymptomatic, manifest as bone pain or even pathological fractures. Histologically they correspond to an area of osteoclastic hyper-resorption containing hypervascular inflammatory connective tissue, giant cells, and hemosiderin deposits. The classic sites of involvement are the facial bones, ribs, pelvis, femur, other long bones and rarely the vertebrae. Primary hyperparathyroidism is most often related to a benign parathyroid adenoma. However, the existence of a polymorphic and more pronounced symptomatology due to severe hypercalcemia, with bone and renal manifestations; as well as other digestive, cardiovascular and psychological signs, should point towards parathyroid carcinoma

Conclusion

Serious skeletal manifestations of primary hyperparathyroidism (fibrocystic osteitis, brown tumors, pathological fractures) are rare. Any medical practitioner must consider the diagnosis of primary hyperparathyroidism at the stage of bone pain before complications set in.

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EP868

Simpson Golabi Behmel Syndrome: a new case and review of the literature

El Jadi Hamza[1], Moumen Amal[2] & Gaouzi Ahmed[3]
[1]Oued Eddahab Military Hospital, Endocrinology, Agadir, Morocco; [2]Moulay Ismail Military Hospital, Endocrinology, Meknes, Morocco; [3]Rabat Children's Hospital, Faculty of Medicine and pharmacy- Rabat, Mohamed 5 University, Pediatric Endocrinology Department, Rabat, Morocco

Summary

Simpson Golabi Behmel Syndrome (SGBS) is a rare syndrome characterized clinically by multiple congenital anomalies, pre and postnatal overgrowth, characteristic craniofacial anomalies, macrocephaly, and organomegaly associated with abnormalities of the skeletal system. The spectrum of signs and symptoms associated with SGBS is wide, ranging from very mild to fatal forms, especially in affected men. We report a rare case of a child affected by SGBS type 1, emphasizing the clinical, paraclinical, therapeutic and monitoring modalities of this possibly serious syndrome. A 12-year-old child from a non-consanguineous marriage consulted for tallness, mental retardation and school difficulties. The clinical examination finds a stature advance: his weight is 43 kg (+1 Standard Deviation (SD)) and his height is 168 cm (between +2 and +3 SD) with macrocephaly, facial dysmorphism made up of hypertelorism, an erased nasal root with a nasal saddle, a macrostomy with a thin upper lip, an everted lower lip with the presence of dental caries (figure 1). Furthermore, the patient presents with supernumerary breasts (figure 2), left post-axial polydactyly (image 3) and cryptorchidism. The skeletal assessment reveals rib synostosis. Ophthalmological, cardiovascular and abdominal examinations were normal. The biological and hormonal dosages are unremarkable. The genetic study suggested the diagnosis of SGBS type 1. The molecular study of the GPC3 gene showed that he carries a de novo nonsense mutation (c.271C>T: p.Gln91X), because his mother does not carry this mutation. SGBS is a rare syndrome. The spectrum of signs and symptoms associated with SGBS is broad, varying from very mild forms in carrier females to infantile lethal forms in affected males. A percentage of affected males die in the newborn period, some of them probably due to heart defects. Carrier females and people with milder cases often live into adulthood. Because of the varying degrees of manifestations and severity associated with the condition, prediction of prognosis and life expectancy most likely varies on an individual basis. Intellectual disability must be carefully evaluated due to the majority of patients have normal intelligence, and do not have the coarse facial and difficulties in speech as we expected for classical SGBS. Our observation reports a new case of SGBS type 1. Despite its rarity, this syndrome requires early and, above all, multidisciplinary management in order to take care of all potential complications in time.

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EP869

Morphofunctional assessment in patients with hypophosphatasia: usefulness of muscle ultrasound in the diagnosis of sarcopenia

María Del Carmen Andreo-Lopez[1], Victoria Contreras Bolivar[1,2,3], Enrique Moratalla-Aranda[2,4], Trinidad González-Cejudo[2,5], Luis Martínez-Heredia[2], Francisco Andújar-Vera[2,6,7], Cristina García-Fontana[1,2,3], Beatriz García-Fontana[1,2,3] & Manuel Muñoz-Torres[1,2,3,8]
[1]Endocrinology and Nutrition Unit, Hospital Universitario Clínico San Cecilio, Granada, Spain; [2]Institute of Biosanitary Research of Granada (ibs.GRANADA), Granada, Granada, Spain; [3]CIBER on Frailty and Healthy Ageing (CIBERFES), Instituto de Salud Carlos III, Spain; [4]Nuclear Medicine Unit, Hospital Universitario Clínico San Cecilio, Granada, Spain; [5]Clinical Analysis Unit, Hospital Universitario Clínico San Cecilio, Granada, Spain; [6]Andalusian Institute for Research in Data Science and Computational Intelligence, Granada, Spain; [7]Department of Computer Science and Artificial Intelligence, Granada, Spain; [8]Department of Medicine, University of Granada, Granada, Spain

Introduction

Hypophosphatasia (HPP) presents with defective bone mineralisation secondary to a deficit of non-tissue-specific alkaline phosphatase, increasing the risk of bone fracture. Sarcopenia may increase this risk. Therefore, rapid diagnosis with accessible and cost-effective tools such as ultrasound could be useful in clinical practice. The aim was to assess the correlation of ultrasound with another validated muscle mass assessment technique.

Material and Methods

Cross-sectional study in adults with PPH. Demographic (age, sex), analytical (alkaline phosphatase-AP) and clinical variables were collected (fractures, muscle strength measured with Jamar dynamometer in kilograms (kg) -cut-off point: <p10 of Spanish population-, rectus femoris quadriceps muscle mass with ultrasound -Sonosite S-Nerve®-, fat-free mass (FFM) in kg, fat mass and bone mineral density (according to T and Z-score) by dual-energy X-ray absorptiometry (DXA). Statistical analysis was performed with IBM SPSS v.25.

Results

Thirty-three subjects were studied, 55% women aged 49 ± 18 years and mean FA: 29 ± 11. 52% had at least one bone fracture and 67% had dental pathology. Low muscle strength was detected in 24% (62.5% men). Mean Y-axis was 1.4 ± 0.7, mean circumference 9 ± 2 and mean area 4.4 ± 2. Mean FFM was 46.5 ± 13.5. Muscle strength was positively correlated with Y-axis ($r = 0.42$, $P = 0.02$), with

muscle area ($r=0.4$, $P=0.02$), with T-score in femoral neck ($r=0.48$, $P=0.01$) and in lumbar spine ($r=0.66$, $P<0.001$). Pressor strength in women was associated with BMI and FFM ($P=0.004$). It also showed a tendency to be associated with ultrasound muscle circumference ($P=0.09$). Muscle area correlated positively with FFM ($r=0.52$, $P=0.01$) and negatively with fat ($r=-0.37$ $P=0.03$).

Conclusions

Ultrasound assessment was associated with body composition and muscle function parameters. Given its accessibility, ultrasound is a useful tool to assess muscle in PPH patients, allowing an early approach to reduce the risk of osteosarcopenia.

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EP921

Corticosteroid-associated osteonecrosis of the femoral head in young adolescents post-COVID 19 era - Two case reports

Andreea Anne-Marie Stefan[1,2], Burcea Iulia-Florentina[1,2], Dobre Ramona[1,2] & Catalina Poiana[1,2]

[1]C.I Parhon National Institute of Endocrinology, Pituitary and Neuroendocrinology Department, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania

Background

Avascular necrosis of the femoral head (AVNFH) is a disorder caused mainly by chronic glucocorticoid use. Systemic corticosteroid (CS) therapy was widely used in patients with mild or moderate SARS-CoV 2 infection despite lack of clinical benefits. However, emerging evidence suggests that COVID-19 infection can cause long-term effects, affecting different body systems, known as 'long COVID-19'[1]. One such sequela is AVNFH, although the link between AVNFH and SARS-CoV 2 infection has not been fully documented. We describe two cases of AVNFH following COVID-19 infection who received high-doses of CS.

Case study

The first case is that of a 17-year-old female patient, with history of non-Hodgkin lymphoma (NHL) stage III, treated with intensive chemotherapy, according to a specific protocol, which included dexamethasone (an approximate dose of 120 mg prednisone equivalent per day). Six months later, she received Prednisone, 50 mg/day for fourteen days for moderate COVID-19 infection. After three months, she was referred to our hospital with severe bilateral hip joint pain. Magnetic resonance imaging (MRI) of the hip showed AVNFH: on the right, stage IV and on the left, stage III according to FICAT and ARLET classification. The patient received one intravenous (iv) ibandronate injection, but the treatment was discontinued at the indication of her paediatric oncologist. Bilateral total hip arthroplasty was planned. The second case is that of a 16-year-old female patient with history of myasthenia gravis for which she received Prednisone, 45 mg/day, initiated in January 2022. Three months later, she developed severe SARS-CoV 2 infection, so the dose of Prednisone was increased at 50 mg/day. She was referred to our clinic after three months, presenting cushingoid phenotype and severe thoracic back pain caused by vertebral compression fracture at T4 and T8 level. She underwent progressive dose reduction of CS until cessation and was treated with iv ibandronate. One year later, after a mild COVID-19 infection, she experienced severe bilateral hip joint pain. MRI of the hip revealed bilateral AVNFH (right> left), stage II-III according (FICAT and ARLET classification). Treatment with iv bisphosphonate was continued and hyperbaric oxygen therapy was performed.

Conclusions

AVNFH in patients surviving COVID-19 could be considered a multifactorial problem and additional research is needed to establish a risk stratification and long-term follow-up protocol for these patients in order to properly diagnose and treat them.

Reference

1. Davis HE *et al*: Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol. 2023 Mar;21(3):133–46.

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EP922

Anti-osteoporosis therapy after discontinuation of menopausal hormone therapy: a systematic review

Panagiotis Anagnostis[1], Efstathiios Divaris[1], Julia Bosdou[2], Symeon Tournis[3], Konstantinos Stathopoulos[4] & Dimitrios Goulis[1]

[1]Aristotle University of Thessaloniki, Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Thessaloniki, Greece; [2]Aristotle University of Thessaloniki, Unit for Human Reproduction, 1st Department of Obstetrics and Gynecology, Thessaloniki, Greece; [3]National and Kapodistrian University of Athens, Laboratory for the Research of Musculoskeletal System 'Th. Garofalidis', School of Medicine, Athens, Greece; [4]National and Kapodistrian University of Athens, School of Medicine, Post Graduate Course on Bone Metabolic Diseases, Athens, Greece

Objective

Menopausal hormone therapy (MHT) is efficacious in reducing the risk of vertebral, non-vertebral and hip fractures, irrespective of age, falls risk or baseline FRAX probability. However, the optimal sequential anti-osteoporotic treatment after MHT discontinuation has not yet been designated. This systematic review aimed to obtain the best evidence regarding the effect of antiresorptive or osteoanabolic treatment on bone mineral density (BMD) and/or fracture risk following MHT.

Methods

A comprehensive search was conducted in PubMed, Scopus and Cochrane databases up to October 31, 2023. Randomized-controlled trials (RCTs) and observational studies conducted in postmenopausal women were included.

Results

After the exclusion of duplicates, 717 studies were identified. Two were eligible for qualitative analysis, one RCT and one retrospective cohort study. The RCT showed that alendronate 10 mg/day for 12 months further increased lumbar spine (LS) BMD by 2.3% following MHT, whereas a mean loss of 3.2% was observed in the placebo group (mean difference: +5.5% between groups). Regarding femoral neck (FN), alendronate maintained BMD, whereas it decreased by 1.4% in the placebo group ($n=144$). Alendronate also decreased bone anabolic and resorption markers by 47% and 36%, respectively. In the retrospective study ($n=34$), raloxifene 60 mg/day increased both LS and FN BMD at 12 months by 3% and 2.9%, respectively. A limitation of this study was the lack of a placebo group. No fractures were reported.

Conclusions

Anti-resorptive therapy with either a bisphosphonate (i.e., alendronate) or raloxifene could be considered a sequential anti-osteoporosis therapy after MHT withdrawal, since they have shown in studies to further increase BMD. However, no safe conclusions can be drawn from the existing literature.

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EP983

Superficial phlebitis: mode of revelation or complication of primary hyperparathyroidism: about 2 cases

Malak Riznat

Mohamed V Military training hospital, Rabat

Introduction

Superficial phlebitis is a clinical manifestation found in many pathologies, often unexplored or mistaken for simple venitis. It should be noted that it may be part of the thromboembolic complications of primary hyperparathyroidism, or an unusual mode of revelation. We describe 2 clinical situations which illustrate this symptom discovered in two different contexts

Observation 1

60-year-old patient admitted for investigation of symptomatic primary hyperparathyroidism revealed in a context of microlithiasis complicated by acute pyelonephritis with associated osteoarticular repercussions. During her hospitalization, the patient presented with painful edema of the limb, and ultrasound revealed venitis with thrombosis of the cephalic vein of the forearm. She was put on anticoagulant therapy for one month.

Observation 2

26-year-old patient admitted to the endocrinology department for management of hyperparathyroidism with the following biological criteria: PTH: 5 times normal Hypercalcemia 120 mg/ and hypophosphatemia and hypercalciuria 430 mg/24 h. This is an asymptomatic hyperparathyroidism with no complications, for which the phosphocalcic work-up was performed mainly when superficial venous thrombophlebitis of the ESV occurred.

Discussion and conclusion

Primary hyperparathyroidism is an increasingly frequent pathology, the diagnosis of which may be delayed by a clinical picture that may be suggestive of non-specific clinical signs. Thromboembolic manifestations have been reported as part of the complications of primary hyperparathyroidism, and can also constitute an unexpected mode of revelation, ranging from simple superficial phlebitis to deep vein thrombosis, with the risk of progression to pulmonary embolism, which can be life-threatening. A phosphocalcic assessment should be carried out in any patient presenting a clinical thromboembolic picture.

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EP984

Recurrent hyperparathyroidism after total parathyroidectomy with autotransplantation in a patient with long-term hemodialysis

Cristina Serban, Nicoleta Baculescu & Catalina Poiana
C.I. Parhon National Institute of Endocrinology

Background
Recurrenthyperparathyroidism following total parathyroidectomy with auto-transplantation in patients with end-stage renal disease who are on hemodialysis is not an uncommon condition and can be due to hyperplastic autografted tissue, remnant parathyroid tissues in the neck or in the presence of ectopic and/or supernumerary parathyroid glands.
Case report
We report the case of a 66-year-old patient with a history of chronic kidney disease on hemodialysis since 2012, surgical hypothyroidism (she underwent total thyroidectomy in 2017 for non-toxic multinodular goiter) and tertiary hyperparathyroidism for which she underwent total parathyroidectomy with autograft transplantation into the left sternocleidomastoid muscle in 2017, who referred to our clinic with a progressive swelling on the left side of the neck over the last few months. The clinical examination was unremarkable except for a soft, non-tender, mobile left-sided cervical mass of approximately 3×1.5 cm. Biochemical evaluation revealed normal corrected serum calcium (9.3 mg/dl, $n=8.5$-10.2) and serum phosphorus (3.6 mg/dl, $n=2.5$-4.5) levels and the intact PTH level was significantly increased (915.3 pg/ml, $n=15$-65) demonstrating secondary hyperparathyroidism. The bone turnover markers were elevated: crosslaps = 2.8 ng/ml ($n=0.33$-0.78), osteocalci$n$ = 463.6 ng/ml ($n=15$-46); alkaline phosphatase was 119 IU/l ($n=38$-105) and serum 25 OHD was 17.9 ng/ml ($n=20$-100). Her thyroid function revealed subclinical hypothyroidism; ATPO, ATG and calcitonin were within normal ranges. Neck ultrasound showed a hypoechoic nodular mass of 2.85/1.48 cm in the left thyroidectomy bed. Fine needle aspiration of the neck mass was performed; the level of PTH in the aspiration needle wash-out fluid was over 5000 pg/ml. We recommended treatment with Paricalcitol at a dose of 5 mg three times a week during hemodialysis sessions. Cinacalcet was not available as a therapeutic option. A three months follow-up revealed an iPTH level of 1515 pg/ml.
Conclusions
We presented a patient with end-stage renal disease and secondary hyperparathyroidism at 6 years after the total parathyroidectomy with autograft transplantation for tertiary hyperparathyroidism. Considering the refractory hyperparathyroidism on the pharmacological treatment available in this case, surgical reintervention to remove the hyperfunctioning parathyroid tissue is necessary.

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EP1003

Case report - congenital ichthyosis and hypoparathyroidism with hypocalcemic seizures in a teenager

Alexandra Mirica[1], Maria Lavinia Popa[1], Adriana Diaconeasa[1], Diana Monica Preda[1] & Diana Loreta Paun[2]
[1]Grigore Alexandrescu Emergency Clinical Hospital for Children, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania

Introduction
Congenital ichthyoses are a group of inherited keratinization disorders that pose a challenge in terms of diagnosis, treatment, and clinical associations with other pathologies. The association with vitamin D deficiency and possible bone changes is cited, but the exact mechanism of occurrence of endocrine pathologies is not described.
Case report
We report the case of a 16-year-old teenage boy known to have congenital ichthyosis, having been under the care of a dermatologist since birth. He was recently admitted to our clinic for hypocalcemic seizures, without a detectable etiology, with good response to calcium supplementation. On clinical examination, the adolescent had a normal waist and weight, being in Tanner stage 4 development. At the first endocrine evaluation we detected a total calcemia of 6 mg/dl, with low PTH values, slightly increased phosphorus, mild vitamin D deficiency, and normal albuminemia, glucose, renal and liver function values. In addition, evaluation of thyroid, adrenal, testicular and pituitary hormone axes showed normal values. Neurological and ophthalmological evaluation did not identify pathological changes, but cerebral CT showed the presence of intracerebral calcifications. In the face of a diagnosis of hypoparathyroidism the evolution was favourable on optimal treatment with oral calcium together with active vitamin D.
Conclusion
Hypoparathyroidism may be associated with congenital ichthyosis but further studies are needed to establish the exact etiopathogenic mechanisms.

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EP1008

Primary hyperparathyroidism in familial multiple endocrine neoplasia type 1- Case Report

Ana Tofan[1], Letitia Leustean[2,3], Cristina Preda[2,3], Gina Neculaes[3], Nada Akad[3] & Maria- Christina Ungureanu[2,3]
[1]Arcadia Hospital, Medical Departament, Iasi, Romania; [2]University of Medicine and Pharmacy –Gr.T. Popa, Endocrinology, Iasi, Romania; [3]St. Spiridon Hospital, Endocrinology, Iasi, Romania

Recurrent hypercalcemia after successful parathyroidectomy has been reported to be higher than previously thought. Most cases are transient and often associated with other factors, with only a minority requiring treatment. Multidisciplinary diagnosis is necessary to prevent persistence and recurrence. A 55-year-old female patient with a history of surgical removal of a right parathyroid adenoma four years prior, lost from follow-up, was referred to our clinic for persistent asthenia, weight loss and stool modification. Recent familial history with two sons operated for primary hyperparathyroidism. The biological assessment revealed a recurrence of primary hyperparathyroidism, renal failure (creatinine clearance 27 mg/dl), persistent anemia with high levels of Ca19-9 and Chromogranine A, and normal adrenal and pituitary hormonal profile. Abdominal CT scan pointed out bilateral adrenal adenoma, left renal lithiasis, obstructive pelvic calculus and grade IV left hydronephrosis. An exploration of the upper and lower digestive tubes was performed by endo and colonoscopy, revealing an active ulcer and chronic gastroduodenitis. In addition, a Scintigraphy with Tektrotyde (573.7 MBq) highlighted a small nodular hepatic lesion with a Krenning 2 score. The Tc99 Sestamibi imaging confirmed hot uptake lesions in the superior and inferior left parathyroid regions and a slight uptake in the right parathyroid region. With confirmatory imaging findings and presenting symptoms, our patient was clinically diagnosed with MEN 1 syndrome and underwent surgical and medical management in the urology and surgical department. Genetic findings and confirmation of MEN 1 syndrome in her eldest son reinforced our clinical suspicion.
Conclusion
Multiple endocrine neoplasia (MEN1) is a rare, inherited multi-tumor syndrome, often underdiagnosed, affecting neuroendocrine and non-endocrine tissues. Its aspects are highly variable, with no genotype-phenotype correlation. In our patient, MEN1 syndrome was revealed at an advanced age by recurrent primary hyperparathyroidism (parathyroid hyperplasia), non-functional adrenal bilateral lesions and neuroendocrine hepatic tumour. Long-term follow-up of serum calcium should be considered in patients after successful parathyroidectomy.

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EP1048

A bibliometric approach to scientific production on familialhypophosphatemic rickets in scopus (2000-2022)

Frank Hernández García[1,2], Helena Gil Peña[3], Julían Rodríguez Suárez[4], José López García[5], Patricia Oro Carbajosa[5], Rocío Fuente Pérez[6] & Ibraín Corrales Reyes[7]
[1]University of Oviedo - El Cristo Campus, Medicine, Oviedo, Spain; [2]Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Paediatrics Research Group, Oviedo, Spain; [3]Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain; [4]Central University Hospital of Asturias, Oviedo, Spain; [5]University of Oviedo - El Cristo Campus, Oviedo, Spain; [6]Fundación Jiménez Diaz, Madrid, Spain; [7], Florida, United States

Background
Hypophosphatemic rickets are disabling conditions that negatively impact physical functioning, activities of daily living, mental health, social life, and leisure activities. The most common cause of Hypophosphatemic rickets is genetic factors, such as X-linked hypophosphatemia. The evaluation of the scientific application of familial hypophosphatemic rickets aids in understanding the research landscape, identifying opportunities for improvement, and promoting significant advancements in the understanding and treatment of this medical condition.
Methods
An observational, descriptive, and cross-sectional study was conducted through a bibliometric analysis of the scientific output of the Familial Hypophosphatemic

Rickets published in journals indexed in Scopus during 2020-2022. To retrieve the publications, Scopus was accessed on April 4, 2023, and an advanced search was performed using a filter by title, abstract and key words, source (journals), publication year, and type of article (article and review). The search terms used were extracted from the PubMed Medical Subject Headings (MeSH) related to the disease included in the MeSH catalog. Additionally, an analysis of co-occurrence between countries and keywords was carried out with VOSviewer software.
Results
This study identified 1,269 articles on hypophosphatemic rickets (938 articles and 331 reviews). In total, 39,548 citations were received, with an H index of 95. The majority of the articles (76.9%) were published in high-impact journals (Q1 and Q2 journals). Scientific production has shown a growing trend in recent years. The countries with the highest scientific production are the U.S, Japan, and the United Kingdom, considering that middle- and low-income countries contribute less to international scientific production.
Conclusions
Scientific production has shown sustained growth in recent years. The U.S solidifies itself as the country leading scientific production on hypophosphatemic rickets.
Keywords: bibliometrics, familial hypophosphatemic rickets**,** rickets, FGF23 protein, PHEX protein, X-linked hypophosphatemic rickets, burosumab.
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EP1052

Severe osteoporosis in a patient with primary adrenal insufficiency and hypothyroidism: is there an association?
Davis Ogeto, Muhammad Tahir Chohan & Kamal Abouglila
University Hospital of North Durham, United Kingdom

Introduction
Osteoporosis can be associated with Cushing syndrome or hyperthyroidism but is an unusual finding in a patient with primary adrenal insufficiency (with physiological dose of steroid replacement) and concurrent autoimmune hypothyroidism without any other secondary causes of osteoporosis. We present a case of severe osteoporosis in a postmenopausal female in whom we could not establish a verifiable cause.
Case
A 60-year-old postmenopausal woman, previously fit and well and no past medical history of significance, not on any regular medications, initially diagnosed with autoimmune hypothyroidism but levothyroxine replacement resulted in further worsening of her symptoms mainly tiredness, lightheadedness and dizziness which prompted further screening of autoimmune adrenal insufficiency and physiological doses of hydrocortisone and fludrocortisone were initiated resulting in complete resolution of her symptoms remaining clinically well for the following 6-7 months. Beacuse of ongoing back pain and normal MRI lumbosacral spine, we did bone densitometry scan revealing severe osteoporosis with total hip T score of -3.5, lumbar spine -4.5 and femoral neck -2.9. There was no history of eating disorder, malabsorption or premature ovarian failure. She was not on any medications to cause severe osteoporosis except physiological doses of steroids (hydrocortisone 10 mg a.m., 5 mg lunchtime and 5 mg teatime). She was a non-smoker, no alcohol excess and no family history of osteoporosis or fragile fractures. All her secondary workup for osteoporosis were normal including renal functions, liver functions, bone profile, vitamin D, pituitary profile and coeliac screen. Osteoporosis was treated with weekly bisphosphonate resulting in improvement in her bone densitometry scan.
Conclusion
- Autoimmune adrenal insufficiency and autoimmune hypothyroidism can coexist as part of autoimmune polyendocrinopathy but it is extremely important to replace steroids first as patient can clinically deteriorate and levothyroxine replacement before steroids can lead to Addisonian crisis.
- It is well established that Cushing syndrome or hyperthyroidism can lead to osteoporosis but it remains unclear if there is any association of adrenal insufficiency and hypothyroidism with osteoporosis.

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EP1061

Intoxication with vitamin D as the cause of severe hypercalcaemia
Martina Jambrović & Marina Gradišer
County Hospital Čakovec, Department of Internal medicine, Čakovec

A 71-year-old man presented to the emergency department with dyspnoea and general weakness. He had a history of stable COPD, coronary artery disease, abdominal aneurysm surgery, and prostate cancer. One month ago, he had survived a SARS-CoV-2 infection. His somatic status was normal, blood pressure was 115/65 mmHg, heart rate was 63/min, he was afebrile 36.6 °C with the exception of SpO2 which was 83%. His initial laboratory results showed severe hypercalcaemia (Ca 3.52 mmol/l), other electrolytes were normal. Due to partial respiratory failure and severe hypercalcaemia, he was admitted to the Department of Internal Medicine. Further laboratory results showed a low PTH level (0.5 pmol/l, reference range 1.3 - 9.3 pmol/l) and a high vitamin D level (> 375 nmol/l). The patient and his family denied misuse of vitamin D supplements. Paraneoplastic hypercalcaemia was suspected, but imaging (US of the neck, CT of the thorax, abdomen and pelvis X-rays revealed no possible substrate). Tumour markers were normal and electrophoresis and immunoelectrophoresis of serum proteins were not suggestive of multiple myeloma. There was also no lymphadenopathy suggestive of lymphoma. At this point in the investigation, we suspected a granulomatous disease and additional sensitive immunological tests were carried out. Hypercalcemia was treated with crystalloid solutions and intravenous zoledronic acid, which led to an improvement in the hypercalcaemia (Ca 3.43 mmol/l – 3.18 mmol/l). At the next outpatient follow-up after discharge from hospital, the serum calcium level decreased accordingly (Ca 2.72- 2.66 mmol/l, iCa++ 1.31- 1.22 mmol/l). The patient admitted that he had been taking vitamin D supplements since overcoming SARS-CoV-2, two capsules of 20000 IJ twice a day.
Conclusion
The hypercalcaemia in this patient is a consequence of continued vitamin D therapy after treatment of the SARS-CoV-2 infection. More frequent monitoring and patient education on the use of supplements is required.

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EP1082

Autoimmune diseases and DiGeorge Syndrom: a case report
Samir Mkaouer, Nadia Khessairi, Elyes Kamoun, Meriem Yazidi, Oueslati ibtissem, Fatma Chaker & chihaoui melika
La Rabta university hospital, Endocrinology department, tunis, Tunisia

Introduction
DiGeorge syndrome (DGS) is mainly characterized by congenital heart defects, dysmorphic features, hopolasia of the thymus and parathyroid glands and immunodeficiency. Approximately 10% of patients with DGS have autoimmune disease[1].
Observation
This is a 21-year-old patient, diagnosed with DGS at the age of 14 year old. The diagnosis was suspected on the association of characteristic facial, hypoparathyroidism and a congenital heart defect (a right aortic arch with an aberrant retro-esophageal left subclavian artery). It was confirmed by a genetic study detecting a microdeletion of the T-box transcription factor TBX1. The patient was well balanced on low-dose Alphacalcidol. During follow-up, the patient developed an inaugural diabetic ketosis with Hb1Ac at 12%. The autoimmune type 1 diabetes was confirmed by positive GAD antibodies (>2000 IU/ml). We noted also autoimmune thyroiditis with high anti thyroperoxydase levels (>1000 IU/ml) with normal TSH Level. Antibodies caeliac disease were negative.
Discussion
DGS increases the risk of autoimmunity 10-fold compared with the general population. This may be explained by thymic hypoplasia and the inability of T lymphocytes to recognize peripheral antigens. Thyroid autoimmunity was associated with DGS in 22% of cases[2]. Anti-pancreatic autoimmunity appears to be less frequent and only 3 cases of type 1 diabetes have been published.
Conclusion
The association of autoimmune diseases with DGS remains underestimated and poorly studied. This prompts us to look for them in cases of clinical suspicion and to establish screening recommendations.
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EP1083

Unusual hypocalcemia in the context of neoplastic disease
Hind Ouakrim, Zineb Ait si ali, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Chu Mohamed Vi Marrakesh - Drh, Marrakech, Morocco

Introduction
While hypercalcemia is extensively studied in cancer patients, the occurrence of hypocalcemia is not as commonly reported. The unique aspect of this case lies in severe hypocalcemia against the background of a malignant tumor of the cervix, a condition often associated with hypercalcemia.
Case report
A 66-year-old patient, diabetic for 13 years with insulin therapy, is being treated for poorly differentiated squamous cell carcinoma of the cervix for the past 4 years. She underwent an extensive hysterectomy, lymph node dissection, followed by radiotherapy with chemotherapy. Five days after the last chemotherapy session, the patient experienced paresthesias and tingling in the face and upper and lower limbs, along with muscle cramps and a tetanic episodes. Faced with this clinical presentation, she was referred to our department. Upon clinical examination, the patient was stable, and Chvostek's sign was positive. The investigation revealed corrected hypocalcemia at 68 mg/l with a phosphorus level of 40 mg/l and a Vitamin D deficiency of 11.6 ng/ml. The PTH level was normal at 39.2 pg/ml. Renal and hepatic function tests were normal. The patient was placed on calcium and vitamin D supplementation, leading to significant improvement.
Discussion
While hypercalcemia is a well-recognized paraneoplastic syndrome, hypocalcemia remains a rare event in neoplastic diseases. Several factors may contribute to the development of hypocalcemia in cancer patients, including Chemotherapeutic agents, commonly used in cancer treatment, may contribute to hypocalcemia, as well as bisphosphonates frequently employed for bone metastases. Proton pump inhibitors, widely used in cancer patients, may decrease calcium absorption directly or through hypomagnesemia. Tumor lysis syndrome, common in hematological malignancies, can also occur in solid tumors, leading to acute renal failure and metabolic alterations, including hypocalcemia. Osteoblastic bone metastases can cause hypocalcemia through the avid capture of calcium, known as "hungry bone syndrome." Other causes include radiotherapy, infections, renal failure, and malnutrition.
Conclusion
Understanding the multifactorial nature of hypocalcemia development is crucial for appropriate diagnosis and management in cancer patients.

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EP1087

Primary hyperparathyroidism and autoimmune disorder: coealiac disease

Ghita Khamel, Lamyae Echchad, Ikram Amira, Hind Iraqi, Kaoutar Rifai & Mohamed Hassan Gharbi
chu ibn sina, chu ibn sina, rabat

Theassociation of primary hyperparathyroidism with autoimmune diseases is described very rarely in the literature so far. There are only few cases of immune-mediated hyperparathyroidism, associated with anti-calcium- sensing receptor autoantibodies, Recent epidemiological studies have shown that coeliac disease is more common than previously thought, with prevalence approaching 1%.
Observation
A 47-year-old woman was diagnosed as having coeliac disease revealed by weight loss and asthenia Laboratory showed a hypovitaminosis D with elevated PTH level, suggestive at first of secondary hyperparathyroidism. transglutaminase antibodies, Antinuclear antibodies were positive with elevated liver enzymes in favor of autoimmune hepatitis In addition, the patient presented with intermittent low-back pain; a phosphocalcic test was again ordered, showing hypercalcemia at 122 mg/ and osteoporosis on bone densitometry. Cervical ultrasound and mibi scintigraphy revealed a left retro-thyroidal formation in favour of a parathyroid adenoma; the patient was referred for surgery.
Discussion
In patients with primary hyperparathyroidism, there is a higher prevalence of autoimmune disease than in the general population. Primary hyperparathyroidism may present with nonspecific features, many of which are shared with coeliac disease, including fatigue, poor appetite and depression. that may compound the clinical diagnosis. There is a time lag of 1–5 years between diagnoses, because the low-normal vitamin D level was taken to be compensatory secondary hyperparathyroidism. The authors emphasised the need to look for intestinal malabsorption in the case of normocalcaemic hyperparathyroidism. The association of primary hyperparathyroidism with coeliac disease has both diagnostic and therapeutic implications. Hyperplasia of the parathyroid glands is the predominant morphological feature in tertiary hyperparathyroidism which implies that the adenoma in our case arose sporadically rather than as a result of chronic stimulation However, detecting a reduced expression of calcium-sensing receptor protein could also help to confirm the sporadic occurrence of adenoma in association with coeliac disease
Conclusion
Carrying out a screen for coeliac disease in patients with confirmed primary hyperparathyroidism and a control group may strengthen the evidence for an association. Further studies will be required to establish the link.

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EP1129

Lithium Induced Endocrinopathy; A reversible Entity

Asad Ali
King's Mill Hospital, Mansfield, United Kingdom

In the presented case, an 85-year-old female patient with bipolar disorder exhibited significant endocrine complications, including hyperparathyroidism and diabetes insipidus, which were strongly associated with long-term lithium therapy. The resolution of these complications following the discontinuation of lithium and the transition to an alternative mood stabilizer underscores several important clinical implications. Firstly, this case highlights the need for vigilant monitoring of elderly patients undergoing lithium therapy. Lithium-induced endocrine disturbances, although relatively uncommon, can manifest insidiously and have the potential to substantially impact the patient's quality of life and overall health. Secondly, the observed reversibility of hyperparathyroidism and diabetes insipidus upon discontinuation of lithium underscores the importance of early intervention. Furthermore, the case highlights the significance of individualizing treatment plans for elderly patients with bipolar disorder. In this population, where comorbidities are prevalent and overall health is a paramount concern, clinicians should carefully weigh the benefits of lithium therapy against the potential risks, particularly those related to endocrine function. In conclusion, this case report sheds light on the reversible nature of lithium-induced hyperparathyroidism and diabetes insipidus in an elderly patient with bipolar disorder. It underscores the importance of vigilant monitoring, early recognition, and individualized treatment strategies to optimize the care of bipolar disorder patients, especially in older individuals, where preserving overall health becomes increasingly crucial. While lithium remains a valuable tool in the management of bipolar disorder, its potential adverse effects should be carefully considered, and alternative mood stabilizers explored when deemed appropriate for the patient's well-being.

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EP1130

Primary hyperparathyroidism caused by an ectopic thymic parathyroid adenoma: A Case Report

Amal ourdi[1], Houda Ennaifer[1], Françoise Plat Latil[1], Amina Bounaga[1], Arnaud Pforr[2] & Guillaume Granier[3]
[1]Avignon, endocrinology, Avignon, France; [2]Avignon, thoracic surgery, Avignon, France; [3]Avignon, anathomopathology, Avignon, France

Introduction
Primary hyperparathyroidism, is a common endocrine disorder, but rarely related to ectopic parathyroid. Often asymptomatic, it presents a problem of localization and hence therapeutic management. We report a rare case of an ectopic thymic parathyroid adenoma.
Description
We report a case of 62-year-old women, with a history of recurrent urinary infection due to pyelocalcic lithiasis, whose etiological investigation revealed the presence of hypercalcemia. Clinically, she had polydipsia, muscle cramps and tingling of the extremities. The diagnosis of primary hyperparathyroidism was retained: hypercalcemia at 3.51 mmol/l, hypophosphatemia (0.45 mmol/l) and elevated PTH at 1041 pg/ml. Cervical ultrasound was normal. Parathyroid scintigraphy showed the presence of an anterior mediastinal hypermetabolic mass in the thymic lodge with a heterogeneous cystic component. CT scan showed a solid cystic mass of the anterosuperior mediastinum region, measuring 46×37×55 mm. Genetic testing was performed, and excluded genetic forms of hyperparathyroidism. Correction of hypercalcemia was based on rehydration and cincalcet hydrochloride. Thymectomy was performed by video-thoracoscopy. Anatomopathological examination concluded to an intra-thymic parathyroid adenoma. Post-operatory calcemia was normal, and PTH decreased to 84.9 pg/ml. The 3 months CT scan was normal.
Discussion
Parathyroid glands and the thymus had a common embryological origin, which explains the thymic ectopy of the parathyroid. It's a rare entity, whose prevalence is about 16% in patients with primary hyperparathyroidism[1]. Imaging

investigation remains an essential step in management, providing accurate cervical and mediastinal mapping enabling the surgeon to perform a targeted surgical excision, avoiding white surgical explorations. Minimally invasive radio-guided surgery, assisted with PTH measurement, improves surgical outcomes.

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EP1173

Secondary hyperparathyroidism after total en bloc gastrectomy due to Non-Hodgkin's lymphoma

Bratu Gratiela[1,2], Vlad Radulescu[1], Cristina Stancu[1] & Corin Badiu[1,3]
[1]National Institute of Endocrinology, Endocrinology IV, Bucuresti; [2]Parhon Hospital Bucharest, Bucureşti; [3]Carol Davila University of Medicine and Pharmacy, Endocrinology, Bucuresti

Introduction
Primary hyperparathyroidism is a condition in which one or more parathyroid glands have a pathological secretion of parathyroid hormone due to their abnormal function. Secondary hyperparathyroidism has normal parathyroid glands, but an abnormal secretion of PTH because of an underlying condition that influence their activity. It is important to differentiate between primary and secondary hyperparathyroidism because of the different treatment.
Methods
Review of the patient's record and the relevant literature.
Case report
A 68 year old woman, with personal antecedents of non-Hodgkin's lymphoma suffered a total en bloc gastrectomy with caudal splenopancreatectomy, left adrenalectomy and cholecystectomy; was admitted to the hospital with recently diagnosed hyperparathyroidism and hypocalcemia most probably due to malabsorption. The patient also associates type II diabetes, postmenopausal osteoporosis and renal failure stage IIIa. The patient complains of paresthesia in all four limbs. Physical examination revealed height of 165 cm, weight of 83 kg (gained 10 kg in the last year), BMI of 30.40 kg/m^2, excess of fat tissue with central disposition, moist and warm skin, blood pressure was 110/70 mmHg, heart rate was 65 beats/minute, normal thyroid dimensions. No signs of hypocalcemie were noticed. Blood tests showed elevated blood glucose, normal thyroid function, slightly low serum calcium (Ca = 7.6 mg/dl, normal value 8.4-10.2 mg/dl), elevated parathyroid hormone (PTH = 1158 pg/ml, normal value $<$65 pg/ml) and a deficit of 25-OH vitamin D (25-OH vit D = 8.1 ng/ml, normal value 20-100 ng/ml). The complete blood count, hepatic and renal tests results were normal. A computer tomograph was performed and it revealed no tumoral rest or recurrence near the eso-jejunal anastomosis.
Results
Considering all of the above, we concluded that the pacient had secondary hyperparathyroidism due to malabsorption after total en bloc gastrectomy. We initiated supplementation oral treatment with vitamin D spray 4000UI/day and calcium 40 mg/day. The evolution was favorable, with a decrease of PTH value from 1158 pg/ml to 153.2 pg/ml and vitamin D from 8.1 ng/ml to 22.8 ng/ml after 1 year of treatment.
Conclusions
This case report highlights the importance of determining the etiology of the hyperparathyroidism. This is because the treatment for primary hyperparathyroidism in most cases is surgical (parathyroidectomy), while in the case of a secondary parathyroidism, the treatment consists mostly of supplementation with calcium and vitamin D.

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EP1221

Hungry bone syndrome following parathyroidectomy - a case report

Milena Lackovic[1], Bojan Joksimovic[1], Vladimir Samardzic[1], Marija Sinik[1], Martina Tomasovic[1], Milos Marinkovic[1], Sonja Zafirovic[2], Esma R. Isenovic[2], Milan Obradovic[2], Emina Sudar-Milovanovic[2] & Zoran Gluvic[1]
[1]Zemun Clinical Hospital, Dept. of Endocrinology, Belgrade, Serbia, [2]"VINČA" Institute of Nuclear Sciences – National Institute of the Republic of Serbia, Department of Radiobiology and Molecular Genetics, Belgrade

One of the main causes of protracted, severe hypocalcemia after parathyroidectomy is hungry bone syndrome (HBS). We report the case of a 40-year-old man who was first admitted to the Endocrinology department of Zemun Clinical Hospital (ZCH) in order to perform a workup for hypercalcemia. Further laboratory and imaging diagnostics indicated that a giant parathyroid adenoma, measuring approximately 6 cm in size, was the cause of the hypercalcaemia. An endocrine surgeon at the Clinical Centre of Serbia performed a lower left parathyroidectomy and a left thyroid lobectomy due to intraoperative detection of suspicious thyroid nodule. Patient was readmitted to ZCH shortly after surgery, exhibiting hypocalcaemia symptoms and signs. He began receiving intense parenteral and oral calcium and vitamin D substitution, which he continued after his discharge. The histology examination of the removed lower parathyroid gland and left thyroid lobe pointed to an atypical parathyroid adenoma and micropapillary cancer. His findings from tests at follow-up revealed low normal serum calcium levels, elevated PTH, and decreased vitamin D. Patient is additionally being prepared for another thyroid surgery. Despite being rare, the risk of developing HBS following a parathyroidectomy should not be ignored, especially in the presence of several preoperative predictors (e.g. giant parathyroid adenoma, higher preoperative PTH, calcium or alkaline phosphatase levels, etc.). Treatment for HBS must be individualized for each patient and could require an extended period of time.

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Diabetes, Obesity, Metabolism and Nutrition

EP1

A rare cause of type B insulin resistance presenting after delivery

Alexandra Giannou[1], Evangelia-Ntaniella Dimopoulou[1], Paraskevi-Maria Bougiouka[1], Katerina Saltiki[2], Stavroula Paschou[2] & Vasiliki Vasileiou[1]
[1]Endocrinology Department and Diabetological Centre, Alexandra General Hospital, Athens, Greece; [2]Endocrine Unit, Department of Clinical Therapeutics, National and Kapodistrian University, Athens, Greece

Introduction
Type B insulin resistance is an extremely rare disease with unknown incidence. It is caused by autoantibodies, mostly IgG, against the insulin receptor that in low titres act as partial agonists. This can cause symptoms that include both hypoglycemia and hyperglycemia. It mostly affects middle-aged African-American women and the proposed treatment approaches include plasmapheresis, cyclosporine or cyclophosphamide, steroids and rituximab.
Case Report
We present a case of a 30-year-old Caucasian woman who referred to our outpatient department due to amenorrhea, worsening of pre-existing hirsutism, polyurea and weight loss, 8 months after giving birth. Medical history included Raynaud Syndrome, Polycystic Ovary Syndrome (PCOS) and newly diagnosed Systemic Lupus Erythematosus (SLE) on treatment with prednisolone. Clinical examination revealed severe hirsutism (Ferryman-Gallway score 24) and profound acanthosis nigricans. Her BMI was 19,2 kg/m^2. The paraclinical investigation showed deranged glucose metabolism with fasting hypoglycemia (65 mg/dl) and postprandial hyperglycemia ($>$200 mg/dl) with concomitant hyperinsulinemia (insulin 1201 μIU/ml) during OGTT and increased HbA1C (9.3%). Also, hyperandrogenemia with increased testosterone 575 ng/dl (5-52), and $\Delta 4\alpha$ 12.3 ng/dl (0.3-3.3). DHEAS,17OHPRG, SHBG were within normal limits and low titres of triglycerides were recorded. Immune panel revealed high IgG [2069 mg/dl (700-1600)], ANA and anti-RNP titres, and low C3 [46 g/l (90-180)] and C4[5 g/l (10- 40)]. Imaging was uneventful except from polycystic ovaries. Due to her medical history including a recent diagnosis of SLE and the affected glycemic control (hypoglycemia and hyperglycemia), the diagnosis of insulin resistance type B was proposed. Positive antibodies against the insulin receptor confirmed it (immunoprecipitation assay). Therapeutic approach consisted of dietary modifications, dapagliflozin and the immunoregulatory agent rituximab, an anti-CD 20 antibody, combined with pulses of steroids. Patient responded well with remission of hirsutism and an excellent glycemic control. Menstruation was restored. She remains stable until now.
Conclusion
Type B insulin resistance is an extremely rare disease with non-standardized treatment. Its clinical course can be confusing and the mortality rates remain high. Our patient benefited greatly from treatment with rituximab and steroids, and her current health status suggests that this approach may benefit more patients that fit similar characteristics.

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EP2

Identification of two novel LMNA variants causing familial partial lipodystrophy

Caterina Pelosini[1], Silvia Magno[2], Giovanni Ceccarini[2], Melania Paoli[1], Francesca Menconi[3], Donatella Gilio[2], Lavinia Palladino[2], Maria Rita Sessa[1] & Ferruccio Santini[2]
[1]Chemistry and Endocrinology Laboratory, University Hospital of Pisa, Italy; [2]Obesity and Lipodystrophy Center, Endocrinology Unit, University Hospital of Pisa, Italy; [3]Endocrinology Unit, University Hospital of Pisa, Italy

The predominant subtype of familial partial lipodystrophy (FPLD) is a rare autosomal dominant disease occurring in Arginine 482 codon of *LMNA* gene (FPLD subtype 2, also known as Dunnigan-type lipodystrophy). FPLD may also occur in patients harboring mutations in different exons of *LMNA*. We herein describe two unrelated patients referred to our Center for the suspicion of partial lipodystrophy and carrying two novel heterozygous *LMNA* variants. The first one is a 20-year-old woman who exhibited at physical examination an abnormal distribution of subcutaneous adipose tissue, characterized by the accumulation of fat in the neck and lipoatrophy in the lower limbs. Acanthosis nigricans was evident in the patient's groin and armpits. Her body mass index was 27.3 kg/m^2. Biochemical blood tests showed combined hyperlipidemia (triglycerides 494 mg/dl; total-cholesterol 246 mg/dl; HDL-cholesterol 45 mg/dl; LDL-cholesterol 135 mg/dl). The oral glucose tolerance test revealed severe insulin resistance (fasting 36 mUI/ml; two-hours 386 mUI/l) and the abdominal ultrasound showed hepatic steatosis. Plasma leptin and high molecular weight adiponectin levels were 23.9 mg/l and 1.9 mg/ml, respectively. She was found to carry a novel heterozygous p.Asn195Tyr *LMNA* variant in exon 3. The second case, is a 45 years old woman with a history of PCOS and insulin resistance from adolescence, at physical examination she showed an accumulation of fat in the neck and lipoatrophy in the upper and lower limbs resembling the fat distribution pattern of FPLD2. Her body mass index was 23.1 kg/m^2. Biochemical blood tests showed increased triglycerides levels (260 mg/dl). The abdominal ultrasound demonstrated hepatic steatosis. Plasma leptin and high molecular weight adiponectin levels were 4.8 mg/l and 1.5 mg/ml, respectively. Genetic testing revealed a novel heterozygous p.Ser239Arg *LMNA* variant located in exon 4. Notably, in silico analysis indicated a predicted damaging role for both aminoacid substitutions. In conclusion, we identified two novel missense variants in the *lamin* gene associated with familial partial lipodystrophy (FPLD). These previously unrecognized variants in subjects presenting with partial lipodystrophy underscore the considerable phenotypic heterogeneity in *LMNA* pathogenic mutations and emphasizes the necessity of additional research to unravel their physiopathological relevance and therapeutic implications.

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EP3

Atherosclerotic cardiovascular disease and its risk factors in type 2 diabetes in egypt: insights from PACT-MEA study and implications for interventions

Samir Assaad-Khalil[1], Atef Bassyouni[2], Dalia Toaima[3], Hanan Sotouhy Gawish[4], Hesham El Hefnawy[5], Magdy Helmy Megallaa[1], Manal Abushady[6], Nabil ElKafrawy[7], Salwa Seddik Hosny[8] & Tarek Mohamed Massoud[3]
[1]Faculty of Medicine, Alexandria University, Department of Internal Medicine, Alexandria, Egypt; [2]National Institute of Diabetes and Endocrinology, Department of Internal Medicine, Cairo, Egypt; [3]Novo Nordisk Egypt, Clinical, Medical, and Regulatory Department, Cairo, Egypt; [4]Mansoura University, Department of Endocrinology, Mansoura, Egypt; [5]National Institute of Diabetes and Endocrinology, Department of Endocrinology, Cairo, Egypt; [6]Ain Shams University, Department of Internal Medicine and Endocrinology, Cairo, Egypt; [7]Faculty of Medicine, Menoufia University, Department of Internal Medicine, Unit of Endocrinology & Diabetes, Menoufia, Egypt; [8]Ain Shams University, Endocrinology Unit, Cairo, Egypt

Background
Atherosclerotic cardiovascular disease (ASCVD) is a major complication to type 2 diabetes (T2D), in terms of both severity and prevalence rates. The Prevalence and clinical management of the Atherosclerotic Cardiovascular Diseases in patients with Type 2 Diabetes across Middle East and Africa countries (PACT-MEA) is a multinational study that aimed to investigate the prevalence of both established ASCVD and the risk for ASCVD in people with T2D as well as its clinical management in seven countries in the Middle East and Africa. Herein, we report the results for Egypt.

Methods
This is an observational, multicenter, cross-sectional study that involved medical charts review of adults with T2D for >180 days. Data was collected from eight secondary care centers across Egypt during a single scheduled visit in the period between July and August 2022. Complete medical history, demographics, laboratory, and pharmacotherapy data were collected to determine their ASCVD risk status and report on their clinical management. ASCVD was defined as the presence of coronary, cerebrovascular, or peripheral artery disease. High risk of ASCVD was defined according to risk criteria as per the European Society of Cardiology (ESC) 2021 guidelines.[1]

Results
A total of 550 adults with T2D were enrolled by the end of the study period. The mean (standard deviation [SD]) age was 54.5 (10.5) years, with a mean T2D duration of 9.3 (7.5) years and a mean HbA1c of 8.3% (2.1). Prevalence of established ASCVD was 19.6% (95% confidence interval [CI]; 16.5, 23.2) with a prevalence of 15.1% for coronary artery disease, 3.1% for cerebrovascular disease, and 2.9% for peripheral artery disease. In people without established ASCVD, prevalence of high ASCVD risk was estimated at 85.5% (95% CI: 81.9, 88.5). The weighted distribution of cardiovascular risk categories according to the 2021 ESC guidelines revealed that 27 % were classified as very high risk, 72.1% as high risk and only 0.9% as moderate Risk. Only 20% were receiving sodium glucose cotransporter 2 inhibitors, and 3% were receiving glucagon like peptide-1 analogues.

Conclusion
Egyptian adults with T2D present high prevalence of both established ASCVD and high risk/very high risk of ASCVD; a status that is accompanied by a lack of implementation of the guideline-recommended pharmacotherapy approaches and life-style modifications. Consequently, nation-wide initiatives to address the highlighted gaps in T2D management in Egypt are highly recommended.

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EP5

4-year setmelanotide weight outcomes of patients with POMC and LEPR deficiency obesity

Wendy Chung[1], James Swain[2], Peter Kühnen[3], Martin Wabitsch[4], Erica van den Akker[5], Jill Garrison[6], Guojun Yuan[6], Jesús Argente[7], Karine Clément[8] & Sadaf Farooqi[9]
[1]Division of Molecular Genetics, Department of Pediatrics, Columbia University, New York, United States; [2]Honor Health Research Institute, Scottsdale, United States; [3]Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin und Humboldt-Universität zu Berlin, Institute for Experimental Pediatric Endocrinology, Berlin, Germany; [4]Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics and Adolescent Medicine, University of Ulm, Ulm, Germany; [5]Division of Pediatric Endocrinology, Department of Pediatrics, Sophia Children's Hospital and Obesity Center CGG, Erasmus University Medical Center, Rotterdam, Netherlands; [6]Rhythm Pharmaceuticals, Inc., Boston, United States; [7]Department of Pediatrics and Pediatric Endocrinology, Universidad Autónoma de Madrid, University Hospital Niño Jesús, CIBER 'Fisiopatología de la obesidad y nutrición' (CIBEROBN), Instituto de Salud Carlos II; IMDEA Food Institute, Madrid, Spain; [8]Assistance Publique Hôpitaux de Paris, Nutrition Department, Pitié-Salpêtrière Hospital; Sorbonne University, Inserm, Nutrition and Obesity, Systemic Approaches (NutriOmique) Research Group, Paris, France; [9]Wellcome-MRC Institute of Metabolic Science and NIHR Cambridge Biomedical Research Centre, University of Cambridge, Cambridge, United Kingdom

Background
Patients with proopiomelanocortin (POMC; including variants in *POMC* or *PCSK1*) or leptin receptor (LEPR) deficiency due to biallelic gene variants have impaired melanocortin-4 receptor signaling that leads to hyperphagia and early-onset, severe obesity. Setmelanotide treatment in this population improved weight-related measures and hunger severity and was well tolerated. Reported here are long-term extension (LTE) outcomes after 4 years of setmelanotide treatment.

Methods
Patients with POMC or LEPR deficiency who achieved clinical benefit and acceptable safety in a prior trial of setmelanotide could enroll in the LTE (NTC03651765) and continue setmelanotide for ≥5 years or transition to a commercial product or other clinical trials. This analysis reports weight outcomes and adverse events at 4 years of setmelanotide treatment for patients who achieved a clinically meaningful, age-appropriate, 1-year index trial weight response defined as either ≥10% weight reduction (age ≥18 years at baseline) or reduction of ≥5 percentage points in percent of the 95th percentile for BMI (%BMI$_{95}$; age <18 years at baseline).

Results
A total of 24 patients entered the LTE with clinically meaningful weight response; 12 patients had 4 years of measurements and were included in this analysis. Of the 12 patients excluded, 3 pediatric patients transitioned to adulthood between the index trial and this analysis, 5 transitioned to commercial therapy, and 4 discontinued treatment. Compared with index trial baseline, the mean (SD) change in body weight was −32.6 kg (36.7) for patients aged ≥18 years ($n=8$) and −42.7 (22.44) percentage points in $\%BMI_{95}$ for patients aged <18 years ($n=4$). No new safety signals were observed between the index trial and the LTE.
Conclusions
Continuous setmelanotide treatment in patients with POMC or LEPR deficiency is supported by sustained meaningful benefit in weight-related measures with no new safety signals at 4 years of treatment in this population.

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EP6

Outcomes of gestational diabetes in native and non-native women – a three-year national study

Ana Quítalo[1], Francisca Leitão[1], Ricardo Capitão[1], Maria Manuel Costa[1], Sara Franco[1], Maria Carlos Cordeiro[1], Luísa Raimundo[1] & Grupo de Estudo Diabetes e Gravidez[2]
[1]Hospital Garcia de Orta, Almada, Portugal; [2]Sociedade Portuguesa De Diabetologia, Lisboa, Portugal

Introduction
In the last years, we have seen a high migration rate of people to Portugal. Not much is known about diet and lifestyle habits in some of these migrant women with gestational diabetes mellitus (GDM). On the other hand, communication can be a barrier and health care access may be more limited. For this reason, it is important to investigate whether there are differences in outcomes between these two populations, in order to question the need to change our clinical approach at national level.
Aims
To compare maternal and neonatal adverse outcomes of GDM between pregnant women born in a foreign country and those born in Portugal.
Methods
The prevalence of GDM complications was evaluated in a cohort of 5874 native women compared with 1414 non-native women, resident in Portugal along years 2020–2022 (total $n=7288$), delivering 7349 live births. For this purpose, the database of the SPD diabetes and pregnancy group was used. The variables were analysed using T test and Chi square test in SPSS®.
Results
Non-native women had higher glycated haemoglobin values in the third trimester (5.5% vs 5.2%; $P<0.001$) and needed more insulin therapy (17% vs 14.5; $P=0.028$), with no significant differences in age (15–52 years) and pre pregnancy weight. Migrants with GDM were diagnosed later (19 vs 18 weeks, $P=0.01$) and burdened by a higher rate of abortion (0.9% vs 0.4%; $P=0.018$), non-spontaneous labour (61% vs 58%; $P=0.023$) and caesarean sections (40.7% vs 36.5%; $P=0.012$). Their new-borns were significantly larger for gestational age (GA) (16.4% vs 12.6%; $P<0.001$) and they had less small for GA babies (8.7% vs 10.4%; $P<0.001$). However, these differences did not impact neonatal morbidity.
Conclusion
GDM in non-native women seem to be worse managed, with this population showing higher abortion and caesarean delivery rates, and heavier babies. These results bring us to question the reasons for these differences and highlights the eventual need to adjust our approach with these women, given their heterogeneity.

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EP10

The diagnosis and treatment of lipodystrophy: the experience of a portuguese tertiary centre

Renata Barbosa, Guilherme Assunção, Miguel Saraiva, Lia Ferreira, Rui Carvalho & Liliana Fonseca
Centro Hospitalar Universitário de Santo António, Endocrinology, Porto, Portugal

Introduction
This study presents four clinical cases of lipodystrophies, which are a group of rare and heterogeneous diseases characterized by the decrease or lack of adipose tissue (AT) accompanied by metabolic complications.
Clinical cases
1) 59-year-old woman with partial familial lipodystrophy, type 7 (OMIM #606721): Diagnosis of suspected type 1 diabetes (DM) at 28 (treated with insulin with poor control), class 1 obesity and hypertriglyceridemia. Objectively, absence of AT in the lower limbs, central obesity and accumulation of AT in the face and neck. Currently medicated with pioglitazone 15 mg, metformin/dapagliflozin 1000/5 mg twice daily, semaglutide 1 mg/weekly, atorvastatin 40 mg and ezetimibe 10 mg. HbA1c=7.2% and triglycerides(Tg)=134 mg/dl. 2) 27-year-old man with congenital generalized lipodystrophy - Berardinelli-Seip Syndrome: Generalized loss of AT in the 1st year of life. Comorbidities include DM diagnosis at 10, hypertriglyceridemia, hypoleptinemia (leptin<0.7 ng/ml), cirrhosis with portal hypertension, hypertrophic cardiomyopathy and hidradenitis suppurativa. Genetic study (GS) revealed a homozygous mutation in BSCL2. The patient is currently on metformin/empagliflozin 1000/5 mg twice daily, pioglitazone 30 mg and semaglutide 1 mg/weekly. HbA1c=6.0% and Tg=150 mg/dl. Metreleptin treatment was initiated in January 2024. 3) 19-year-old woman with acquired generalized lipodystrophy - Lawrence Syndrome: Clinical onset at 3 years. Comorbidities include Hashimoto's thyroiditis, autoimmune hepatitis (AIH) with advanced fibrosis, autoimmune gastritis, hypertriglyceridemia, hypoleptinemia (leptin<0.05 ng/ml) and DM (diagnosed at 13 – treated with metformin, prandial and basal insulin). GS negative for AGPAT2, BSCL2, LMNA and PPARG. Positive anti-perilipin 1 antibodies. Metreleptin started in 2019, with improvements in hypertriglyceridemia and hepatosplenomegaly as well as remission of DM (HbA1c=5.1%). 4) 22-year-old woman with partial lipodystrophy: Central adiposity and absence of AT in the limbs identified at age 3. Comorbidities include AIH, neurodegenerative brain iron accumulation with congenital ataxia, insulin resistance (insulin=58 μU/ml; RR 2.6-24.9) and hypertriglyceridemia controlled with lifestyle measures (Tg=175 mg/dl). GS negative for AGPAT2 and LMNA - currently under evaluation in a medical genetic consultation.
Conclusion
Lipodystrophies exhibit diverse phenotypes, emphasizing the crucial role of physical examination in evaluating AT distribution. Early diagnosis allows a more appropriate treatment of both lipodystrophies and their metabolic complications.

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EP11

Diabetes mellitus due to reduced insulin secretion and exocrine pancreatic dysfunction in a patient with a mutation in the carboxyl-ester lipase gene outside the VNTR region

Vasiliki Venetsanaki[1], Vasiliki Daraki[1], Amalia Sertedaki[2], Anny Mertzanian[2], Evangelia Pissadaki[1], Rodanthi Vamvoukaki[1], Grigoria Betsi[1], Maria Sfakiotaki[1], Christina Kanaka-Gantenbein[2] & Paraskevi Xekouki[1]
[1]University General Hospital of Heraklion, Department of Endocrinology Diabetes and Metabolic Diseases, Crete, Greece; [2]Children's Hospital Agia Sophia, Division of Endocrinology, Diabetes and Metabolism, Center for Rare Pediatric Endocrine Diseases, First Department of Pediatrics, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Introduction
Mutations in the variable number of tandem repeats (VNTR) region of the carboxyl-ester lipase (CEL) gene can cause a very rare type of maturity-onset diabetes of the young (MODY 8) characterized by insulinopenic diabetes mellitus (DM) in early adulthood and slowly progressive exocrine pancreatic dysfunction. We present the unusual case of a patient with heterozygosity in a variant of *CEL* outside the VNTR region suffering from DM, dyslipidemia and exocrine pancreatic dysfunction.
Case-report
A 68-year-old patient was referred to the endocrinology outpatient clinic for evaluation of paroxysmal hypertension. She reported gait and balance disorders, abdominal discomfort and steatorrhea following fatty meals since early adulthood that had significantly deteriorated in the past year. She had a history of gestational diabetes and was eventually diagnosed with DM at the age of 53, treated with metformin. She also had dyslipidemia, Hashimoto's thyroiditis, osteoporosis, localized scleroderma and a frontotemporal cavernous hemangioma. Clinical evaluation revealed impaired sense of balance and low-normal BMI. Computed Tomography of the abdomen revealed mesenteric lipodystrophy and bilateral adrenal hyperplasia. Biochemical investigation excluded hypersecretion of adrenal hormones. She also had elevated lipid levels and fasting blood glucose (104 mg/dl) with low insulin(1.6 μUI/ml) and low-normal c-peptide levels (1.22 ng/ml). Her HbA1c was 5.7%. Clinical and biochemical findings were suggestive of MODY, therefore genetic testing was performed, which revealed

heterozygosity in the *CEL*gene variant c.1341C>A, p.Tyr447Ter. The patient was treated with pancreatic enzymes (pancreatin) with significant improvement of her gastrointestinal and neurological symptoms.
Discussion
CEL is mainly expressed in pancreatic acinar cells and lactating mammary glands. Mutations in the VNTR region of the *CEL* gene, have been associated with early pancreatic atrophy due to pancreatic fibrosis, lipomatosis or pancreatic cyst formation and progressive exocrine insufficiency as well as adulthood-onset DM. Mutations outside VNTR regions of *CEL* gene have been associated with dyslipidemias but evidence on insulinopenic DM is scarce. Our patient had a mutation outside of the VNTR region and developed both insulinopenic DM and exocrine pancreatic insufficiency. We hypothesize that our patient's symptoms were associated with fat-soluble vitamin malabsorption which is corroborated by the significant improvement of her symptoms after dietary modifications and pancretin substitution.
Conclusion
Patients with heterozygous mutations outside the VNTR region of the *CEL* gene should be investigated for DM and exocrine pancreatic dysfunction and be treated accordingly.

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EP12

A complex phenotype with partial lipodystrophy due to mutations in HIST1H1E and OTOGL genes

Leonardo Bighetti[1], Martina Romanisio[1], Simona Mellone[2], Denise Vurchio[2], Edoardo Mollero[1], Tommaso Daffara[1], Giovanni Ceccarini[3], Caterina Pelosini[3], Gianluca Aimaretti[1], Mara Giordano[2] & Flavia Prodam[1]
[1]Endocrinology Unit and Department of Health Sciences, Università del Piemonte Orientale, Novara, Italy; [2]Laboratory of Genetics, SCDU Biochimica Clinica, Ospedale Maggiore della Carità, Novara, Italy; [3]Obesity and Lipodystrophy Center, Endocrinology Unit, University Hospital of Pisa, Pisa, Italy

Here we report a case of an adult patient (44y/o) followed for type-2 diabetes since he was 15 years, hypercholesterolemia treated with PCSK9 inhibitors and hypertension. At physical examination he presented: progeroid features, prominent forehead, hypertelorism, short palpebral fissures, broad nasal bridge, baldness, and hypotricosis. He was also affected by hearing loss with a jarring voice and lost teeth in early age. He showed developmental delay and ID, mild atrial septal defect, mild osteoporosis and a monolateral low testis volume, with subclinical hypergonadotroph hypogonadism. Diabetes was in control with metformin, and DPPIV-i, liver steatosis was in follow-up. The BMI was normal and subcutaneous fat was underrepresented in limbs, but increased in the abdomen. Since the abnormal distribution of fat and metabolic alterations at a young age, we suspected a progeroid lipodystrophy syndrome. Leptin (1.9 mg/l) was undetectable and the genes known to cause classical lypodistrophy syndromes were wild type as well as CGH-array. A whole genome sequencing (WES) of the proband and his parents was thus performed revealing a *de novo* pathogenic frameshift variant in *HIST1H1E* (MIM*142220), p.Ser150fs, c.447dupC, encoding the H1.4 histone protein. This protein is a member of the H1 histone family that acts as a structural component of the chromatin controlling DNA condensation, gene expression and DNA replication/repair. Mutations in these class of genes perturb cellular process resulting in cellular senescence and have been correlated to alteration of genome methylation. Truncating mutations in *HIST1H1E* are characteristic of the Rahman Syndrome (MIM#61743), a recently recognized developmental disorder characterized by mild to severe ID, a distinctive facial gestalt, variable somatic overgrowth which may manifest in early infancy, but not in adults, that often display decreasing height percentile over time, and an aging appearance. The WGS analysis also revealed a pathogenic variant in the *LDLR* gene explaining hypercholesterolemia and in *OTOGL* responsible for neurosensorial hearing loss. This case represented a complex phenotype that had remained for a long time without a clinical diagnosis and that reached it on the basis of the results obtained throught WGS with three genes explaining most of his phenotypic characteristics. It is remarkable that the patient also manifested lipodystrophy, characterized by a progressive metabolic impairment secondary to adipose tissue dysfunction, that might be explained by the pleiotropic effect of the *HIST1H1E* mutation. Trascriptomic analysis on the PBMC of proband and parents has been performed and is ongoing to detect molecular signaling specific of each mutation.

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EP16

Five years post sleeve gastrectomy do patients experience olfactory changes

Faten Mahjoub, Abir El Amri, Nadia Ben Amor, Ramla Mizouri, Saida Boumefteh & Jamoussi Henda
Institut De Nutrition, Tunis, Tunisia

Introduction
Post-operative modification of the sense of smell has been suggested as contributing to the reduction in energy intake and weight loss achieved following bariatric surgery. The aim of our study was to determine the prevalence of smell changes and their impact on weight loss five years after sleeve gastrectomy.
Methods
This was a descriptive longitudinal study conducted at the obesity research unit of the National Institute of Nutrition in Tunis involving 30 obese patients who had undergone sleeve-gastrectomy with medical follow-up of at least 5 years. Changes in the sense of smell were assessed using the Tichansky "Taste and smell" questionnaire.
Results
The mean age of our patients was 43 $\pm$ 9.5 years. The average duration of obesity was 26.4 $\pm$ 7.71 years, with extremes varying from 15 to 40 years. Average weight decreased from 133.04 $\pm$18.36 kg to 94.63 $\pm$ 19.81 kg after 5 years, corresponding to an average weight reduction of 28.8% ($P<10^{-3}$). The excess weight loss was 48.48 $\pm$ 22.72%. Mean body mass index decreased from 52.61 $\pm$ 10.07 kg/m^2 to 38.04 $\pm$ 9.26 kg/m^2 after 5 years, a reduction of 27.69% ($P<10^{-3}$). The majority of our patients (63%) reported a change in appetite after sleeve gastrectomy. This change was better than expected in 53% of patients. A change in the sense of smell 5 years after sleeve-gastrectomy was noted in 53% of patients and consisted of either an improvement (62%) or a different smell (38%). No patient had a total loss of smell. The majority of our patients (80%) confirmed that the olfactory component of food is important for food intake. According to twenty patients, the smell of food has a direct impact on food intake and weight loss. Two-thirds of the patients expected a better change in smell than that obtained after sleeve gastrectomy. Patients who had a change in their sense of smell had the greatest loss of excess weight at 2 years ($P=0.04$) and 5 years ($P=0.001$).
Conclusions
Following sleeve gastrectomy, circulating gut hormone levels are markedly altered and these changes are suggested to contribute to post-operative olfactory changes. Gut hormones are present in saliva and their cognate receptors are found on taste buds and olfactory neurons Hence, it is plausible that gut hormones mediate olfactory changes following bariatric surgery through weight-independent mechanisms.

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EP17

Glucose 'the cruel puppet master'. hyperglycaemia induced chorea with hypoglycaemia precipitated recurrence

Pablo Martinez Perez & Jana Bujanova
Southampton University Hospital NHS Foundation Trust, Department of Diabetes and Endocrinology, Southampton, United Kingdom

Introduction
Diabetic striatopathy is a rare neurological complication of diabetes presenting in most cases with an acute/subacute hemichorea associated with contralateral putamen T1 hyperintensity on MRI. It is associated with significant hyperglycaemia, high HbA1c and osmolality. It resolves within few days to 10 months in 74% of cases. Recurrence is seen in 13% of cases, mostly within the first two months. Hypoglycaemia induced chorea is extremely rare.
Case report
68-year-old male with a history of transient ischaemic attack and well controlled type 2 diabetes on oral therapies was admitted with fall and long lie. He was swaying when stood, had shuffling gait and his speech was difficult to understand. On admission had significant hyperglycaemia (33.6 mmol/l), raised osmolality (311 mosmol/kg) and dramatic HbA1c increase to 181 mmol/mol from 58 mmol/mol five months previously, likely precipitated by metabolic sequalae of severe Covid illness a year prior. He was described as 'restless, grabbing at things, picking at clothes' and was noted to have involuntary movements progressing to severe generalised and orofacial choreoathetosis. Interestingly, he was not distressed by these movements and appeared unaware. Brain MRI showed high T1 signal the putamina bilaterally and excluded a stroke. Thyroid, autoimmune, paraneoplastic and infection screen were negative. Diagnosis of hyperglycaemia induced chorea was made. Glucose control was achieved with a variable insulin infusion and basal insulin. His choreoathetosis worsened initially after

achievement of euglycemia preventing patient's ability to glucose monitor and insulin self-administer, but improved with stable glucose control allowing discharge 12 days after admission. He was readmitted 16 days later with chorea recurrence, this time in association with hypoglycaemia (glucose 2.7 mmol/l). He was discharged 6 days later and remained symptom free 2.5 years later.

Discussion

Diabetic striatopathy should be considered in a differential diagnosis of choreoathetosis of an acute or subacute onset together with a stroke, bleed, autoimmune disease, paraneoplastic syndrome, cocaine and HIV. Our case highlights several unique aspects including occurrence in a middle-aged Caucasian male, deterioration of symptoms after initial glucose normalisation, bilateral symptoms, bilateral putamina radiological changes and a recurrence precipitated by hypoglycaemia, which is to our knowledge very rare. Proposed mechanisms of hyperglycaemia induced choreoathetosis include an induction of mild ischaemia in the putamen via osmotic shift induced hypoperfusion leading to anaerobic metabolism and gamma-aminobutyric acid (GABA) depletion. Hypoglycaemia probably induces cell oedema and hypoperfusion and utilisation of GABA and acetylcysteine as alternative sources of energy.

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EP18

Exploring the relationship between trimethylamine N-Oxide levels, kidney function, and diabetes

Karina Levina[1], Sabīne Upmale-Engela[1], Melita Ozola[2] & Ilze Konrade[1]
[1]Rīga Stradiņs University, Rīga, Latvia; [2]Latvijas Organiskās Sintēzes institūts (Latvian Institute of Organic Synthesis), Rīga, Latvia

Since 2011 trimethylamine N-oxide (TMAO) has been established as a cardiovascular risk biomarker in various patient populations. Previous studies have shown the association of TMAO levels with insulin resistance and diabetes. Additionally, a higher risk of cardiovascular events has been observed in patients with type 2 diabetes and higher levels of TMAO. However, the direct link between TMAO levels and kidney function in patients with diabetes is still unclear. Our objective was to investigate the association between the level of TMAO and the degree of renal damage in patients with diabetes mellitus. Patients with type 1 diabetes (T1D) and type 2 diabetes (T2D) were involved in the study. Since the level of TMAO depends greatly on the composition of the diet, patients were instructed to refrain from eating fish and other seafood for two days before blood draw to avoid artificially high levels of TMAO. Blood sampling was performed in a fasted state to analyze biochemical markers: glucose, C-peptide, HbA1c, ALT, CRO, Urea, cystatin-C, creatinine, GFR, NGAL. Quantification of TMAO concentrations in plasma samples was performed by UPLC/MS/MS analysis. The data are presented as mean ± SEM. A total of 66 diabetes patients were subjected for testing: patients with T1D ($n=16$, 24%) and with T2D ($n=50$, 76%). The mean BMI of the patients was 30.8 ± 0.94 kg/m^2. Of 66 patients, 29 (44%) were male and 37 (56%) were female. The mean age of the patients was 57.6 years, ranging from 19 to 84 years. The average concentration of TMAO in plasma of the patients was 8.05 ± 1.36 μmol/l (min. 0.56 μmol/l; max. 66.34 μmol/l). Interestingly, HbA1c, fasting glucose, C-peptide levels, showed no correlation with TMAO level in plasma. Additionally, TMAO concentrations did not depend on the type of diabetes mellitus or the age of the patient. Meanwhile, markers of kidney glomerular function, creatinine, cystatin-C, GFR, showed a weaker correlation with TMAO levels ($R^2=0.292$, $R^2=0.279$, $R^2=0.223$, respectively, $P<0.0001$) than Urea ($R^2=0.4155$, $P<0.0001$), however a strong correlation was found with renal tubular damage marker NGAL ($R^2=0.6228$, $P<0.0001$) and TMAO. Based on data collected in the clinical setting, we observed a noticeable relationship between kidney tubular damage and plasma TMAO in patients with diabetes. As kidney injury in diabetic patients typically occurs due to mixed pathophysiological mechanisms, additional testing in preclinical models should be employed to confirm the hypothesis that impaired kidney glomerular and tubular function are the initial driving factors of TMAO accumulation.

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EP19

GLP-1 receptor agonists neuroprotective effect in type 2 diabetic patients is independent on glycemic control

Anna Simanenkova[1,2], Oksana Fuks[1], Natalya Timkina[1,2], Irina Matsueva[1], Tatiana Karonova[1,2] & Elena Grineva[1]
[1]Almazov National Medical Research Centre, Saint-Petersburg; [2]Pavlov First Saint-Petersburg State medical University, Saint-Petersburg

Background and aim

Acute and chronic brain dyscirculation comprise one of the main reasons of death and disability in type 2 diabetes. Glucose-lowering drugs of glucagon-like peptide-1 receptor agonists (GLP-1RA) group have proved to decrease myocardial infarction and stroke incidence, nevertheless their influence on chronic brain damage in not fully studied. Taking into account existing guidelines recommending treatment with GLP-1RA even for patients with satisfactory glycemic control, our aim was to study the influence of semaglutide in type 2 diabetic patients with target glycated hemoglobin (HbA1c) level on cognitive function and circulating neuronal damage markers.

Materials and methods

Type 2 diabetic patients aged 45-75 with target HbA1c (6.7[6.6;6.9]%) on metformin monotherapy were randomly divided into two groups: 'MET' ($n=28$) – those who continued metformin monotherapy, and 'SEMA' ($n=35$) – patients who were co-administered semaglutide (Rybelsus, Novo Nordisk) for 6 months. Additionally, 'Control' ($n=30$) group was formed – healthy volunteers comparable by age and gender. In all groups the levels of HbA1c, neuron-specific enolase (NSE), neurofilament light chains (NLC) were determined initially, cognitive assessment was performed by MOCA and MMSE scores. In 'SEMA' group these parameters were also evaluated 3 and 6 months after.

Results

Baseline NSE level in diabetic patients was higher than in healthy volunteers despite satisfactory glycemic control (3.60 [3.19;3.78] ng/ml in 'MET' and 3.78 [3.05;4.32] ng/ml in 'SEMA' groups and 2.76 [2.28;3.30] ng/ml in 'Control' group). Similarly baseline NLC concentration was high in both 'MET' and 'SEMA' groups than in 'Control' one (4.95 [3.30;5.56] ng/ml, 5.25 [3.75;5.56] and 4.10 [3.27;5.30]ng/ml, respectively). HbA1c decreased in 'SEMA' group, though not significantly, remaining in the target range. NSE concentration decreased in 'SEMA' group in 3 months (2.95 [2.42;3.4] ng/ml) and remained normal in 6 months (2.93 [2.58; 3.33] ng/ml). NLC also decreased in 'SEMA' group in 3 months (4.25 [3.13;8.50] ng/ml and even more prominently in 6 months (3.50 [1.69;5.88] ng/ml). Patients in 'MET' and 'SEMA' groups had cognitive impairment, resulting in the decreased points by both MOCA and MMSE scales. SEMA administration led to cognitive 4improvement – by 6th month of therapy MOCA scores in 'SEMA' group was 27.5 [25.75;29.75] (the normal value is 26 and more) and MMSE scores was 29.0 [27.5;29.5] (the normal value is 28-30). We found negative correlation between NLC level and MOCA, MMSE scores ($r=-0.512$, $p=0.005$ и $r=-0.703$, $p=0.000$, respectively).

Conclusions

DM, even with satisfactory glycemic control, has a negative impact on the brain, which is manifested by neuronal damage markers increase and cognitive dysfunction. Semaglutide can be neuroprotective in diabetic chronic brain damage independently on glycemic control.

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EP20

Assessment of basal and stimulated C-peptide in patients with type 1 diabetes mellitus on the administration of tolerogenic dendritic cells

Tatsiana Mokhort[1], Volha Shyshko[2], Alena Mokhort[3], Andrei Hancharou[4], Natalia Antonevich[4], Yana Minich[4], Volha Lazovtseva[1], Alena Dashkevich[5] & Elena Shishko[3]
[1]Belarusian State Medical University, Minsk, Belarus; [2]Minsk City Clinical Endocrinological Center, Minsk, Belarus; [3]Belarusian State Medical University, Endocrinology, Minsk, Belarus; [4]The Institute of Biophysics and Cell Engineering of National Academy of Sciences of Belarus, Minsk, Belarus; [5]10th City Clinical Hospital, Minsk, Belarus

Introduction

Preserving of C-peptide secretion in type 1 diabetes mellitus (DM1) is an important goal in treatment, as it provides the possibility of optimal compensation. We initiated a study (ClinicalTrials.gov 26.01.2022, NCT05207995) to assess the potential effect of Tolerant Dendritic Cells (tolDC) on the newly diagnosed DM1.

Methods

Evaluation of stimulated C-peptide against the background of a standard breakfast (carbohydrate content of 50g) was carried out twice (before tol-DC therapy) ($n=14$) and 3 months after completion of therapy ($n=9$). The test was performed with fasting glycemia in the range of 3.8 - 9.0 mmol/l, short-acting insulin was not administered before breakfast. The test was carried out for 2 hours with the determination of the level of C-peptide at 0, 30, 60, 90 and 120 minutes. The levels of C-peptide after food stimulation were studied with the calculation of AUC (area under curve). All patients ($n=16$) had their basal C-peptide levels determined twice. Determination of the level of C-peptide is carried out by the method of chemiluminescent enzyme immunoassay on the analyzer Cobas E411 by Roche Diagnostics (Germany).

Results
The median (Me, Q1; Q3) basal C-peptide level before therapy was 0.74 (0.71; 0.77) ng/ml, which met the requirements for inclusion in the study. Data obtained 3 months after completion of the study indicate that C-peptide secretion remained at 0.87 (0.68, 1.06) ng/ml. The AUC value before administration of tolDC was 409 ± 202.5 ng/ml×2 h. After therapy, AUC was 385.6 ± 145.5 ng/ml×2 h; no significant differences with the AUC level before tolDC therapy were detected ($P = 0.18$).
Conclusion
Our results indicate the potential effectiveness of the method for correcting carbohydrate metabolism in patients with type 1 diabetes using tolDC. Short-term use of Tolerogenic Dendritic Cells is accompanied by preservation of C-peptide secretion, which is a prognostically favorable factor in the course of DM1.
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EP22

Assessment of nutrition knowledge levels in tunisian children
Ben Othman Rym, Amorri Amani, Salma Abadlia, Ben Zina Baya, Ben Mansour Nadia, Kasraoui Sabeh, Gamoudi Amel & Jamoussi Henda
National Institute of Nutrition and Food Technology, Nutrition A, tunis

Introduction
The global prevalence of childhood obesity has surged to alarming levels, presenting a critical health issue. In order to promote a healthy lifestyle, evaluating the nutritional knowledge of children becomes imperative. We conducted our study aiming to assess the levels of dietary awareness in a sample of Tunisian children aged 9 to 11 years.
Methods
We conducted a multicenter cross-sectional study from December 2021 to June 2022, at the National Center for School and University Medicine in Tunis and five randomly selected nurseries in Ariana governorate. The study involved 315 children aged from 9 to 11 years. We evaluated participants' nutritional knowledge using an Arabic version of the validated French nutritional questionnaire QuesCA 9-11. The maximum score is 9/9. We developed the Arabic version following established translation and questionnaire validation guidelines.
Results
The participants' mean age was 9.9 ± 1 years. A slight male predominance was observed (55%). The majority of children (81%) had a normal weight, while 8% were classified as obese, and 6% were underweight. The average score on the questionnaire was 5.8 ± 0.6/9. Sixty percent of participants achieved a fair score (i.e. score ranging between 4 and 6/9). Approximately, one-third (31%) obtained a good score (i.e. score ≥ 7/9). Remarkably, 2.2% of the sample answered all items correctly, achieving the maximum score of 9/9, reflecting a strong nutritional knowledge. A minority (9%) received a poor score (i.e. score ≤ 3/9). Notably, one child among the 315 included had a score of 0/9. Furthermore, the items related to the theme of proteins, fruits and vegetables, and beverages were the easiest to answer. On average, 86% of responses to these items were correct. In contrast, the item related to the theme of starchy foods was the most challenging, with only 31.4% of correct responses.
Conclusion
Our results underscore the importance of targeted interventions to enhance nutritional education. This knowledge can serve as a foundation for developing strategies aimed at promoting healthier lifestyles and preventing childhood obesity in the Tunisian context.
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EP23

3-year setmelanotide weight outcomes in patients with bardet-biedl syndrome and obesity
Jack Yanovski[1], Gabriel Ángel Martos-Moreno[2], Sonali Malhotra[3], Guojun Yuan[4], Wendy Chung[5], Hélène Dollfus[6] & Karine Clément[7]
[1]Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, United States; [2]Universidad Autónoma de Madrid, University Hospital Niño Jesús, CIBER 'Fisiopatología de la obesidad y nutrición' (CIBEROBN), Instituto de Salud Carlos III, Department of Pediatrics and Pediatric Endocrinology, Madrid, Spain; [3]Rhythm Pharmaceuticals, Inc.; Harvard Medical School; Massachussetts General Hospital, Boston, United States; [4]Rhythm Pharmaceuticals, Inc., Boston, United States; [5]Columbia University, Division of Molecular Genetics, Department of Pediatrics, New York, United States; [6]Hôpitaux Universitaires de Strasbourg, CARGO and Department of Medical Genetics, Institut de Génétique Médicale d'Alsace, Université de Strasbourg; [7]Assistance Publique Hôpitaux de Paris, Nutrition Department, Pitié-Salpêtrière Hospital; Sorbonne Université, Inserm, NutriOmics Research Unit, Paris, France

Background
Bardet-Biedl Syndrome (BBS) is a rare genetic disease in which impaired melanocortin-4 receptor (MC4R) signaling leads to hyperphagia and obesity. In an index Phase 3 trial, broad clinical benefit was observed in patients with BBS based on improvement or stabilization in ≥1 measure of weight, hunger, or quality of life with 1 year of treatment with the MC4R agonist setmelanotide. Reported here are long-term extension (LTE) weight outcomes after 3 years of setmelanotide.
Methods
Patients with BBS who achieved clinical benefit and tolerability in a prior trial of setmelanotide could enroll in the LTE (NCT03651765) and continue treatment for ≥5 years or transition to commercial product or other clinical trials. This analysis reports age-appropriate weight-related outcomes and adverse events for 3 years of setmelanotide treatment in patients who achieved clinically meaningful response at 1 year of index trial, defined as ≥10% weight reduction (age ≥18 years at baseline) or reduction of ≥5 percentage points in the percent of the BMI 95th percentile (%BMI_{95}; age <18 years at baseline).
Results
Of 32 patients who entered the LTE with clinically meaningful age-appropriate weight responses, 21 patients with 3-year measurements were included in the analysis. Eleven patients were excluded as 1 pediatric patient transitioned to adulthood before this analysis, 5 had <3 years of treatment, 2 transitioned to commercial therapy, and 3 discontinued treatment. Mean (SD) index trial baseline for body weight was 129.8 (21.3) kg in patients aged ≥18 years ($n = 10$) and 148.7 (36.1) percentage points for %BMI_{95} in patients aged <18 years ($n = 22$); change at Year 3 was −22.0 (18.1) kg ($n = 8$) and −19.4 (19.4) percentage points ($n = 13$), respectively. No new safety signals were observed in the LTE.
Conclusions
Sustained meaningful benefit in weight-related measures at 3 years of treatment with no new safety signals supports continuous treatment with setmelanotide in patients with BBS.
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EP24

New therapeutic opportunities shared by obesity, type 2 diabetes and rheumatoid arthritis
Valentina Gavazova[1,1] & Sylvia Pashkunova
Military Medical Academy, Sofia, Bulgaria

Obesity and diabetes mellitus type 2 are proinflammatory states associated with increased disease severity in rheumatoid arthritis (RA). Weight loss is associated with improved disease activity in rheumatoid arthritis (RA). Furthermore science experiments demonstrated weight-independent anti-inflammatory and immunomodulatory effects of GLP-1 receptor agonists. Moreover, *in vitro* studies found anti-inflammatory effects of GLP-1 receptor agonists in fibroblast-like synoviocytes (FLS) from patients with RA. FLS are the main cell population in synovium. They can secrete pro-inflammatory cytokines like interleukin-6, interact with immune-related cells, and subsequently cause inflamed joints. These anti-inflammatory and immunomodulatory effects of GLP-1 receptor agonists in RA are associated with inhibition of the activation of proinflammatory signaling pathways like NF-kB, improvement of mitochondrial dysfunction induced by TNF- α, prevention of NOX-4 expression and oxidative stress, reduction of the expression of proinflammatory mediators like IL-6 and IL-1β, reduction of the expression of matrix metalloproteinases. The objective of this study was to determine whether treatment with GLP-1 receptor agonists is associated with improved disease activity in certain forms of inflammatory arthritis such as rheumatoid arthritis.
Methods
To estimate the role of GLP-1 receptor agonists in RA, we observed 30 patients (27 women and 3 men) with obesity, diabetes mellitus type 2 and RA treated with GLP-1 receptor agonist between 1 May 2023 and 1 January 2024. They are still receiving this medication. In this period observed patients did not take any disease-modifying anti-rheumatic drugs, steroids or biologic agents. The patients had morning stiffness in more than one joint, swelling in more than one joint and pain in fingers. In addition to symptoms we focused on measuring C-reactive protein (CRP) levels and erythrocyte sedimentation rate as inflammatory markers.

They were elevated before starting the applications of GLP-1 receptor agonists.
Results
For 6 months of treatment in the observed group we found out 10% weight reduction, improvement of patient's morning stiffnes and swelling and relieved pain in fingers. Furthermore the CRP levels and erythrocyte sedimentation rate were decreased after 6 months of treatment with GLP-1 receptor agonists.
Conclusions
These results suggest that GLP-receptor agonist could improve disease activity in RA associated with weight loss. Moreover GLP-1 receptor agonists have potential weight-independent anti-inflammatory effects. Their role as an adjunct in patients with rheumatoid arthritis, obesity and diabetes is understudied, require future research. The limitations of our study are low countability of patient group, short follow-up period, and lack of control group.

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EP25

Impact of setmelanotide on metabolic syndrome risk in patients with bardet-biedl syndrome

Andrea M. Haqq[1], Christine Poitou-Bernert[2], Wendy Chung[3], Anoop Iqbal[4], Elizabeth Forsythe[5], Sonali Malhotra[6], Nicolas Touchot[7], Karine Clément[2] & Jesús Argente[8]
[1]Division of Pediatric Endocrinology, University of Alberta, Edmonton, AB, Canada, Edmonton, Canada; [2]Nutrition Department, Assistance Publique Hôpitaux de Paris, Pitié-Salpêtrière Hospital; Sorbonne University, Inserm, Nutrition and Obesity, Systemic Approaches (NutriOmique) Research Group, Paris, France; [3]Division of Molecular Genetics, Department of Pediatrics, Columbia University, New York, United States; [4]Department of Clinical Research, Marshfield Clinic Research Institute, Marshfield, United States; [5]Clinical Genetics Department, Guys and St. Thomas' Hospitals, London, and National Bardet-Biedl Syndrome Clinics, Great Ormond Street Hospital, London, United Kingdom; [6]Rhythm Pharmaceuticals, Inc.; Massachusetts General Hospital; Harvard Medical School, Boston, United States; [7]Rhythm Pharmaceuticals, Inc., Boston, United States; [8]Department of Pediatrics and Pediatric Endocrinology, Universidad Autónoma de Madrid, University Hospital Niño Jesús, CIBER 'Fisiopatología de la obesidad y nutrición' (CIBEROBN), Instituto de Salud Carlos III; IMDEA Food Institute, Madrid, Spain

Background
Patients with Bardet-Biedl syndrome (BBS), a rare syndrome associated with obesity and hyperphagia, commonly manifest traits of metabolic syndrome, including abdominal obesity, impaired fasting glucose, low high-density lipoprotein cholesterol, hypertriglyceridemia, and hypertension. Setmelanotide treatment results in significant improvement in weight, hunger, and quality of life in these patients and may improve measures associated with metabolic syndrome development. We evaluated the metabolic syndrome Z score based on body mass index (MetS-Z-BMI), a measure of long-term risk for developing cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM). Each 1.0-point increase in MetS-Z-BMI increases the odds of future CVD and T2DM by 9.8 and 2.7, respectively, when assessed in children and by 2.4 and 2.8, respectively, when assessed in adults.
Methods
Data from a Phase 3 trial of patients with BBS (NCT03746522) were used to calculate MetS-Z-BMI score after 1 year of setmelanotide. Patients who achieved a meaningful response of $\geq$10% weight loss (if $\geq$18 years old) or $\geq$0.3-point BMI Z score reduction (if $<$18 years old) were compared with patients who did not meet those thresholds.
Results
Of 32 patients with BBS enrolled, 22 were evaluable (59% female, 10-44 years old). Setmelanotide was associated with reduced mean (SD) MetS-Z-BMI score after 52 weeks in patients with a meaningful weight response ($n=16$; -0.54 [0.56]). Patients not meeting weight thresholds ($n=6$) had an increase in MetS-Z-BMI ($+0.17$ ([0.50]; between-group difference, -0.71, $P=0.129$). MetS-Z-BMI change was generally comparable between females and males.
Conclusions
In addition to reduced hyperphagia and improved quality of life with setmelanotide, meaningful reductions in weight-related outcomes are associated with decreases in MetS-Z-BMI score in patients with BBS. These data suggest that early treatment initiation may lead to reduction in future risk of T2DM and CVD development.

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EP28

The relationship between continuous glucose monitoring metrics, circadian rhythms, and the presence of albuminuria in insulin-using patients with type 2 diabetes

Da Young Lee[1], Jung-Been Lee[2], Inha Jung[1], So Young Park[1], Ji Hee Yu[1], Ji A Seo[1], Heon-Jeong Lee[3] & Nan Hee Kim[1]
[1]Korea University Ansan Hospital, Ansan-si, Korea, Rep. of South; [2]Sun Moon University, Asan Campus, Asan-si, Korea, Rep. of South; [3]Korea University Anam Hospital, Seoul, Korea, Rep. of South

Background
We aimed to explore the relationship between continuous glucose monitoring (CGM)-derived indicators and the presence of albuminuria taking circadian features into consideration concurrently in Insulin-using patients with type 2 diabetes.
Methods
We analyzed data from 129 insulin-treated type 2 diabetes patients in Korea University Ansan Hospital. Over 10 days, we collected time-series data using Dexcom G6, Fitbit, and food diaries, along with cardiometabolic parameters. For CGM metrics, we computed daily time percentages within 70–180 mg/dl ($TIR^{70\text{-}180}$) and above 250 mg/dl ($TAR^{>250}$), standard deviation (SD), and coefficient of variation (CV). Cosinor analysis on Fitbit heart rate data yielded circadian rhythm indices, including amplitude and midline statistics of rhythm (MESOR). The amplitude represents the strength of the rhythm, whereas MESOR reflects mean heart rate. Logistic regression, adjusting for various factors, assessed albuminuria presence (urine albumin-creatinine ratio $\geq$30 mg/g). Factors included age, sex, BMI, eGFR, HbA1c, diabetes duration, systolic BP, daily step count, carbohydrate percentage, amplitude, and MESOR.
Results
Individuals with albuminuria were found to be older, with higher BP and HbA1c levels, a longer duration of diabetes, and lower amplitude compared to those without albuminuria. In logistic analysis, high HbA1c, systolic BP, and MESOR, and a low amplitude of among covariates were associated with a higher risk of albuminuria. Among the CGM-derived metrics, a low $TIR^{70\text{-}180}$ and a high $TAR^{>250}$ were significantly linked to the presence of albuminuria, even after adjustment for metabolic parameters and circadian features. In case of SD and CV, absence of significance was found.
Conclusions
We illustrated that a disrupted circadian feature, represented by a low amplitude or high MESOR, was associated with the presence of albuminuria. Considering this significance, $TIR^{70\text{-}180}$ and $TAR^{>250}$ are linked to the presence of microalbuminuria.

Table 1. Features associated with the presence of albuminuria

Clinical and circadian features	Odds ratio (95% CI)[a]
Age(years)	1(0.93–1.06)
Sex, men	0.61(0.24–1.54)
BMI(kg/m^2)	0.98(0.87–1.11)
eGFR	0.98(0.96–1.0)
HbA1c(%)	1.86(1.24–2.78)
Duration of diabetes(years)	1.06(1–1.14)
Systolic BP(mmHg)	1.06(1.03–1.10)
Ln(Daily step count)	1.22(0.61–2.46)
Percentage of carbohydrate	1.02(0.96–1.08)
Amplitude	0.81(0.68–0.96)
MESOR	1.06(1.01–1.11)
CGM metrics	**Odds ratio(95% CI)[b]**
$TIR^{70\text{–}180}$	0.97(0.94–0.99)
$LnTAR^{>250}$	1.49(1.01–1.07)
SD	1.03(0.99–1.07)
CV	0.98(0.90–1.07)

[a] All 11 variables were included as covariates in the logistic regression analysis.[b] Age, sex, BMI, eGFR, Hemoglobin A1c, duration of diabetes, systolic BP, daily step count, percentage of carbohydrate, amplitude, and MESOR were adjusted for each logistic regression analysis.

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EP30

Difference between HbA1c and GMI

Javier Gómez Pino, Viyey Kishore Doulatram Gamgaram, Luis Ignacio Navas Vela, Mariana Jesús Gomes Porras & Monica Tomé García
Hospital Regional Universitario, Endocrinology and Nutrition

Introduction
Evidence suggests that, for the same mean glucose level, protein glycation may be different and that this may have an impact on the occurrence of complications. We

currently have GMI that estimates mean glucose measured with the FreeStyle Libre 2 and HbA1c determined in the laboratory.
Objectives
To analyse the proportion of "rapid glycaemic" patients in our clinical setting (HbA1c-GMI > 0.5) and to assess the prevalence of microvascular complications (retinopathy, nephropathy, and neuropathy) in these patients and compare with the rest of the sample.
Methods
Cross-sectional descriptive observational study in people with type 1 diabetes mellitus followed up in the Diabetes Unit of the Axarquia Hospital carrying the FreeStyle Libre 2 system. Variables collected: age, sex, presence of microvascular complications, GMI and HbA1c.
Results
291 patients were included, mean age 42.9 ±14.8 years, 40% female, time of evolution 20.4 ± 13 years. Prevalence of microvascular complications 36.3% (9.8% nephropathy, 32.4% retinopathy and 12.9% neuropathy). Mean IGM 7.4 ±0.941% and mean HbA1c 7.70±1.17%. HbA1c-GMI difference: 0.170± 0.708. Proportion of rapid glycators: 26.1%. A significantly higher prevalence of microvascular complications was found (47.4 vs 34 <% with *P* 0.038), with statistically significant difference in retinopathy (44 vs 29.3% with *P* 0.020), neuropathy (21.1 vs 10.2% with *P* 0.016). The difference in nephropathy was not statistically significant (14.5 vs 8.8% with *P* 0.165).
Conclusions
The proportion of rapid glycators in our sample is high (26.1%). Rapid glycators in our sample have a higher prevalence of microvascular complications (retinopathy and diabetic neuropathy).

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EP31

Cellular immunity in type 1 diabetes: insights from comparative analysis with type 2 diabetes and healthy individuals by flow cytometry

Elena Zakharova, Anna Goncharenko, Ivan Golodnikov, Margarita Samsonova, Nadezhda Rusyaeva, Marina Shestakova & Marina Loginova
Endocrinology Research Centre, Moskva, Russian Federation

Goal
Type 1 diabetes (T1D) development involves intricate interactions between pancreatic β-cells and immune cells. Our study analyzed cellular immunity parameters in adult T1D patients' blood to identify factors influencing disease progression in comparison with healthy donors and type 2 diabetes (T2D) patients.
Methods
Three groups were studied - healthy volunteers ($n=13$), T1D patients ($n=10$), and T2D patients ($n=13$). Analysis included autoantibody measurement and flow cytometry (BD LSRFortessa) of peripheral blood.
Results
Analysis of the main populations of T cells ($CD3^+$-cells), B-cells ($CD19^+$-cells) and NK cells ($CD3^-CD19^-$-cells) did not reveal significant differences between the values in healthy donors and patients with T1D and T2D (Table 1). However, $CD3^+CD8^+$ T-cells and Immune Regulatory Index differed between healthy donors and T2D patients. In T1D, $CD3^-CD19^-CD8^-CD38^+$ NK-cells decreased compared to controls and T2D, with a negative correlation to insulin autoantibodies. On the other hand, there is a trend towards an increase in the quantity of $CD3^-CD19^-CD8^+CD38^+$ NK-cells compared to the control group (Table 1). Effector NK-cells ($CD3^-CD19^-CD16^{++}CD56^+$) decreased in T1D, while T2D had increased NK-cells with weak CD56 expression (Table 1). Correlation analysis did not reveal a connection between $CD3^-CD19^-CD8^-CD38^+$ NK-cells of the three studied groups and the levels of autoantibodies to GAD, islet cells, and tyrosine phosphatase (Table 1).
Conclusion
T2D shows reduced cytotoxic T-cells, while NK-cells play a crucial role in T1D. $CD8^-CD38^+$ NK-cells reduction in T1D correlates with insulin autoantibodies. Functional activity differences in NK-cells between early and long-term treatment stages may exist in T1D and T2D patients.
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Table 1. Comparison of cellular immunity parameters in patients with T1D, T2D and healthy volunteers.

Cellular parameters	Healthy	T1D	T2D	1vs2	1vs3	2vs3
$CD3^+$T-cells	73,2 70,6-79,3	76,1 69,7-80,8	73,4 65,7-80,4	–	–	–
$CD3^+CD4^+$ Th	45,5 40,8-52,1	47,9 46,6-54,5	49,9 44,5-55,8	–	–	–
$CD3^+CD8^+$ CTL	27,6 21,7-31,3	24,2 17,2-31,4	20,5 15,0-26,4	–	* $P=0,0441$	–
$CD4^+/CD8^+$	1,7 1,3-2,1	2,1 1,6-3,0	2,2 1,9-3,6	–	* $P=0,0281$	–
$CD3^+CD4^+CD8^+$	1,2 0,6-2,3	1,2 0,8-2,4	1,4 0,9-2,0	–	–	–
$CD3^-CD4^-CD8^-$	5,4 3,8-8,4	4,6 3,2-6,0	3,3 2,2-5,5	–	* $P=0,0387$	–
$CD3^-CD19^+$ B-cells	10,0 8,5-11,3	9,9 7,4-12,3	11,3 9,9-13,8	–	–	–
$CD3^-CD19^-$NK-cells	14,8 8,6-18,4	13,2 9,0-16,9	14,4 7,0-22,4	–	–	–
$CD3^-CD19^-CD8^-CD38^+$ NK-cells	49,2 47,7-63,2	38,1 30,6-45,4	50,6 42,4-59,1	* $P=0,0214$	–	* $P=0,0121$
$CD3^-CD19^-CD8^+CD38^+$ NK-cells	36,7 21,1-47,0	44,3 38,9-56,9	40,1 34,5-46,6	– $P=0,0647$	–	–
$CD3^-CD19^-CD56^+$ $CD16^{++}$ NK-cells	80,8 70,1-83,7	69,8 57,8-77,9	83,1 72,9-89,8	* $P=0,0343$		* $P=0,0044$
$CD3^-CD19^-CD56^+$ $CD16^-$ NK-cells	0,3 0,2-0,5	0,6 0,2-0,9	0,3 0,1-0,3	–	–	* $P=0,0351$
$CD3^-CD19^-CD56^{++}CD16^{++}$NK-cells	0,3 0,3-0,8	0,6 0,2-2,0	0,2 0,08-0,5	–	–	– $P=0,0862$

EP33

Glycemic variability assessed by continuous glucose monitoring system in insulin-treated diabetic patients on hemodialysis

Rihab Yamoun[1], Abdesslem Haifa[1], Aguerbi Sahar[2], Bornaz Emna[1], Boukhayatia Fatma[1], Ounaissa Kamilia[1], Ben Ayed Tasnim[2], Fattoum Safa[2,3], Bdrouchi Samara[2], Ben Hamida Fethi[2], Chargui Soumaya[2], Amrouche Chiraz[1] & Abderrahim Ezzeddine[2]
[1]National Institute of Nutrition and Food Technology, Department of Nutritional Diseases (D), Tunis, Tunisia; [2]Charles Nicolle Hospital, Internal Medicine department, Tunis, Tunisia; [3], Tunisia

Introduction
Glycemic control in diabetic patients undergoing hemodialysis is difficult to achieve because of the high glycemic variability in this population. The aim of our study was to assess the glycemic profile, using the continuous glucose monitoring system 'CGMS', in a group of insulin-treated diabetic patients on hemodialysis.
Methods
We conducted a descriptive, evaluative, longitudinal study involving insulin-treated diabetic patients undergoing hemodialysis. It was bi-centric in the National Institute of Nutrition and the Nephrology Department of Charles Nicolle Hospital between 2021 and 2022. We used a 7-day CGMS (Medtronic; Guardian 3) to monitor glucose levels including the dialysis days (HD) and the following inter-dialytic periods ('free' day [FD]).
Results
CGM data were available for 30 subjects (19 male) with a mean age of 57±15.5 years and mean diabetes duration of 21.4±6.9 years. The mean glucose management index (GMI) which provides an estimated glycated hemoglobin (A1c) level was 8.1±1.2%. The mean interstitial blood glucose was 210.7±50.5 mg/dl, with no significant difference between FD and HD (213.9±59.9 mg/dl vs. 217.6±52.4 mg/dl, $p=$NS). The mean coefficient of variation (CV) was 35± 8.7%. It was lower during FD (27.6±9.7% vs. 30.2±9.9%) with no significant difference ($p=$NS). However, the mean amplitude of glucose excursions (MAGE) and the standard deviation (SD) were significantly higher during the dialysis day than FD (93.7±35.8 mg/dl vs. 111.4±39.1 mg/dl, $P=0.01$ and 49.5±28.8 mg/dl vs. 62.4±18.8 mg/dl, $P=0.04$, respectively).
Conclusion
In this population of diabetic patients with end stage kidney disease undergoing hemodialysis, glycemic profile was shown differently between the HD and the FD. Therefore, the use of a CGMS to monitor glycemic control could improve the management of insulin therapy in these patients.

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EP34

Night eating syndrome improvement after 3 months of liraglutide administration in obese diabetic 2 patients

Fedir Laniush, Alina Urbanovych & Khrystyna Moskva
Danylo Halytsky Lviv National Medical University, Endocrinology, L'viv

Background and aims
Night eating syndrome (NES) is one of the most common eating disorder in patients with obesity and diabetes type 2 (DT2). It may affect the management and outcome of DT2. Liraglutide is used for obesity and DT2 management. It controls glucose metabolism, suppresses hunger, and causes weight loss. Leptin is a hormone produced by adipose tissue after food intake in order to promote satiety and maintain fat storage. Our aim was to evaluate how liraglutide affects leptin levels after 3 months of administration in obese patients with NES and DT2.
Materials and methods
82 individuals (mean age – 61.3 ± 7.4 years; BMI - 33.7 ± 3.2 kg/m^2; history of diabetes < 5 years) with DT2 and obesity were recruited into the study. After completing Night Eating Questionnaire, 17 individuals (20,7%) were screened positive for NES. 1st study group ($n = 8$) with NES started therapy with metformin and liraglutide 1,8 mg daily. 2nd study group ($n = 9$) used metformin and SGLT2-inhibitors for DT2 management. Leptin levels were measured twice: at the start of the study and after 3 months of liraglutide administration.
Results
The initial level of leptin in the 1st study group decreased from 11.02 ± 5.2 ng/ml to 6.6 ± 3.7 ng/ml ($P < 0.05$); they also demonstarted greater weight loss and reduction in the number of night eating episodes. In the 2nd study group leptin levels also reduced (12.3 ± 6.4 ng/ml to 11.4 ± 5.7 ng/ml), but not significantly ($P > 0.05$); number of night eating episodes did not change.
Conclusion
Liraglutide provides multifunctional positive effects on individuals with obesity and DT2. Owing to suppression of hunger center in hypothalamus and promoting satiety, liraglutide improves NES by reducing number of night eating episodes. Leptin level changes reflect body weight loss as well as renovation of sensitivity in hypothalamus to peripheral appetite-controlling peptides and reducing of leptin resistance.

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EP37

Microvascular changes using OCT Angiography in diabetic eyes without clinical evidence of retinopathy

Rekik Mona[1], Kammoun Sonda[1], Jallouli Aida[1], Nabila Rekik Majdoub[2] & Trigui Amira[1]
[1]Habib Bourguiba Hospital, Department of ophthalmology; [2]Hedi Chaker Hospital, Department of endocrinology

Introduction
Diabetic retinopathy (DR) is a common microvascular complication of diabetes mellitus, leading to visual impairment among individuals of working age. Optical coherence tomography angiography (OCTA) has been developed to visualize the retinal microvasculature and choriocapillaris based on the motion contrast of circulating blood cells.
Purpose
To investigate the qualitative microvascular changes in retinal vascular plexuses and choriocapillaris (CC) in patients with type 2 diabetes mellitus (DM2) without DR using swept-source optical coherence tomography angiography (SS-OCTA). hanges in retinal vascular plexuses and choriocapillaris in patients with type 2 diabetes mellitus (DM2) without diabetic retinopathy (DR)
Methods
An OCTA (DRI OCT Triton; Topcon Corp, Japan) system was used to collect 3 × 3-mm macular scans from diabetic patients without clinical evidence of diabetic retinopathy. We conducted a descriptive qualitative analysis of foveal and extrafoveal microcirculation at the level of the superficial (SCP), the deep (DCP) retinal capillary plexus and the choriocapillaris (CC) to identify microvascular changes in diabetic eyes without clinically detectable retinopathy.
Results
Thirty eyes from 15 diabetic patients without clinical evidence of retinopathy were analyzed. Microaneurysms seen in OCTA but not in fundus examination were found in 4 eyes. The presence of breaks in the perifoveal anastomotic circle is observed at the level of the SCP in 10 eyes. Within the DCP, there are vascular dilations in 8 eyes with an enlargement of the anastomotic circle in 10 eyes, which appears larger compared to its size in the SCP. Areas of hypo-perfusion are noted as hypo-signal zones within the CC in 8 eyes.
Conclusion
DM2 patients without DR have SCP, DCP and CC qualitative impairment. These study highlight that OCT A can identify preclinical microvascular abnormalities preceding the onset of clinically detectable DR, serving as potential biomarkers for the early detection of DR.

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EP38

Relations of C-reactive protein to post-glucose load glucose in patients with prediabetes and coronary artery disease

Valentina Tankovic[1,1], Sinisa Stankovic[1], Snjezana Popovic Pejicic[1], Gabrijela Malesevic[1], Aleksandra Markovic[1] & Djuro P. Macut[2]
[1]Faculty, of medicine, University of Banja Luka, Internal Medicine, Banja Luka; [2]University of Belgrade - Faculty of Medicine, Internal Medicine, Beograd, Serbia

Introduction
The association between CRP and prediabetes has not been sufficiently investigated. The aim of the study was to determine the association of prediabetes with subclinical inflammation, as well as to examine the correlation of sensitive CRP (hsCRP) with fasting glycemia and 2 h glycemia during exercise during the OGTT test.
Methods
The study included 106 patients with angiographically diagnosed coronary artery disease, who, based on the oral glucose tolerance test (OGTT), were classified into a group with type 2 diabetes (T2D, $n = 34$), a group with impaired glycemia and glucose intolerance (IFG/IGT, $n = 38$) and a group with normal glucose tolerance (NGT, $n = 34$). The control group consisted of subjects with normal glucose tolerance and no coronary disease ($n = 100$), individually matched by age and body mass index (BMI) with coronary patients included in the study. The circulating level of lipids, insulin, hsCRP, the albumin level in the morning urine sample, and the insulin resistance index HOMA were determined in all of them.
Results
The level of hsCRP was elevated in the group of coronary patients with diabetes ($P < 0.05$), as well as in the group of patients with prediabetes ($P < 0.05$), compared to the control group. hsCRP values were not significantly different in coronary patients, regardless of glycemic status ($P > 0.05$). A significant correlation of hsCRP with glycemia in 120 min OGTT test was found. ($P < 0.05$), independent of existing obesity.
Conclusion
Chronic subclinical inflammation, detected by an elevated level of C-reactive protein, is more strongly associated with post load glycemia than with fasting glycemia. Prediabetes leads to an increase in markers of subclinical inflammation, which is associated with increased cardiovascular risk.
Key words: C-reactive protein, hyperglycemia, prediabetes, coronary disease

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EP39

Self-perception of hypoglycemia symptoms in adolescents with type 1 diabetes

Meryem Chakir, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy-University Hassan II-Casablanca-Morocco, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Hypoglycemia is a common complication of diabetes in cases of perfect glycemic balance, leading to a deterioration in the quality of life for diabetic patients. Early perception of hypoglycemia symptoms can improve the health status of diabetic adolescents.
Objective
The aim of our study is to evaluate the self-perception of hypoglycemia symptoms in adolescents with type 1 diabetes.
Materials and Methods
A prospective study conducted at the Endocrinology-Diabetology Department of Ibn Rochd University Hospital in Casablanca, involving adolescents with type 1 diabetes, based on the Clarke score. Data analysis was performed using SPSS.
Results
Sixty-seven patients were included in the study, of which 62.7% were female. The mean age was 16.5 years. The average duration of diabetes was 4.9 years. The mean body mass index was 21.1 kg/m^2. The average HbA1c was 9.3%. All patients were on a basal-bolus regimen, predominantly using analog insulins at a rate of 59.7%. The frequency of hypoglycemia was 86.5%, with an average of 2 episodes per week. Hypoglycemic episodes mostly occurred in the afternoon. Normal hypoglycemia

perception was noted in only 38% of patients. Self-perception of hypoglycemia symptoms was associated with the duration of diabetes ($P=0.01$)
Conclusion
Our study shows that the perception of hypoglycemia symptoms was normal in adolescents with longer-standing diabetes. Training patients to better perceive the signals their bodies send them represents a new perspective for therapeutic education.
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EP42

Percutaneous radiological gastrostomy in our hospital: the key to improving nutritional status without complications
Maria Jose Vallejo Herrera, Veronica Vallejo Herrera & Maria Carmen Bautista Recio
Hospital Regional Málaga, Malaga

Background
Percutaneous radiological gastrostomy (PRG) is one of the techniques of choice for long-term enteral nutrition. Although safe and technically simple, it has been associated with relative morbidity and mortality.
Objective
We analyzed the results of the PRG insertion techniques with respect to morbidity and mortality, associated complications during the hospital stay, as well as nutritional results.
Methods
A cohort of 30 patients scheduled for PRG insertion from 08/2022 to 01/2023 was retrospectively evaluated. In 30 hospitalized patients, gastrostomy placement was scheduled during hospitalization in 30% (10 patients) and on an outpatient basis in 70% (20 patients). The mortality rate at one month was 16% (5 patients).
Results
We analyzed 30 PRGs in patients with a mean age of 60 (25-79) years in the referred period. 74% men and 26% women. The referral services for its implementation were Neurosurgery/Neurology, ENT, Maxillofacial and Endocrinology and other minority services. The underlying pathologies that indicated PRG were mainly neoplastic head and neck cancer, neurological diseases due to cerebrovascular disease and dementia, and patients with irreversible neurological lesions after multiple trauma. The average hospital stay of these patients was 53 days after admission. A 16F or 14F PRG tube was placed in most patients. There were no post-procedural complications, except for one case of transient paralytic ileus.
- The nutrition formulas prior to carrying out PRG corresponded to hyperprotein polymeric formulas. hypercaloric in all cases. The same nutritional formula was usually maintained at hospital discharge.
- The administration of enteral nutrition by PRG was in continuous perfusion during admission with transition to gravity upon discharge in the majority of cases. In prolonged admissions, after verifying good tolerance, the condition was changed to severity.
- The patients had an average BMI of 23. During the follow-up in the Nutrition consultations, 64% of the patients increased their BMI by an average of 2-4 and the remaining 26% maintained their initial BMI, with 16% (5 patients) loss of follow-up due to death.

Conclusion
The insertion of hospital PRG is a safe technique for long-term enteral nutrition, from which cancer patients or patients with neurological pathology mainly benefit, achieving maintenance or improvement of nutritional status in practically all patients through hyperprotein/hypercaloric formulas. cases, with a low rate of morbidity and mortality and associated complications.
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EP43

Autoimmune hypoglycemia: a rare case of Hirata's disease
Evangelia-Ntaniella Dimopoulou[1], Paraskevi-Maria Bougiouka[1], Alexandra Giannou[1], Stavroula Paschou[2] & Vasiliki Vasileiou[1]
[1]Alexandra General Hospital, Athens, Greece; [2]Endocrine Unit, Department of Clinical Therapeutics, National and Kapodistrian University, Athens, Greece

Introduction
Insulin autoimmune syndrome (Hirata's disease) is a rare cause of hypoglycemia in Caucasians, with an estimated prevalence of 0,017 cases per 100.000 in general population. It is characterized by mostly postprandial hypoglycemia and the presence of autoantibodies against insulin. Treatment options include dietary modifications, glucocorticoids, azathioprine, rituximab and plasmapheresis.
Case report
A 72-year-old woman with no medical history of Diabetes Mellitus (HbA1c 5,6%) presented to our outpatient department reporting episodes of hypoglycemia (glu 40-60 mg/dl) since 2 months, the majority of which postprandially, accompanied by early post-meal hyperglycemia (glu 250-300 mg/dl). She presented an OGTT with glucose values compatible with DM (glu 0': 104, glu 60': 311, glu 120': 256 mg/dl), concurrently with extremely high insulin values (ins 0': 181, ins 60': 1474, ins 120': 5340 mIU/l). Such a combination raised the suspicion that insulin could not act properly. Prolonged OGTT was performed and hypoglycemia was recorded at 220' (glu 33), while both insulin and C-peptide levels where profoundly increased (ins 220': 169 μIU/ml, C-pept 220': 11,3 ng/ml) simultaneously. After excluding some common causes of hypoglycemia (adrenal insufficiency, medications, alcohol abuse, malignancy), we proceeded with measurement of her insulin autoantibodies (anti-IAA), which turned out positive (>20 IU/ml – normal values <2,4). Our diagnosis was Hirata's disease. Our patient's medical history was free of exposure to susceptible drugs or recent infection. Treatment with methylprednisolone 15 mg daily was started and within a month her hypoglycemic episodes were significantly reduced. Two months later her antibody titre was within normal range (2 IU/ml), and remained within normal limits (1 IU/ml) at follow-up measurement 4 months later, even after treatment discontinuation. She reports no hypoglycemic episodes.
Conclusion
Despite the rarity of this condition, Hirata's disease is important to be considered early in the differential diagnosis of hypoglycemia. This case report aims to raise awareness of this clinical condition to the physicians, since a high titre of insulin autoantibodies would help avoid costly and complicated examinations.
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Exceptional observation of congenital hyperinsulinism with variable phenotypic expression
Hana Charfi, Dhoha Ben Salah, Yassmine Abdelkafi, Nesrine Dhieb, Mouna Elleuch, Fatma Mnif, Nadia Charfi, Mouna Mnif, Mohamed Abid & Nabila Rekik Majdoub
Hedi Chaker Hospital, Sfax, Tunisia

Introduction
Congenital hyperinsulinism (CHI) is a rare disease with an incidence of 1 in 30,000. It is the most common cause of persistent neonatal hypoglycemia, primarily due to inhibitory mutations in genes encoding the ATP-sensitive potassium channel in pancreatic beta cells, with ABCC8 (SUR1) and KCNJ11 (Kir6.2) mutations being the most frequent. In this context, we report a highly unusual case in terms of phenotypic and evolutionary aspects.
Clinical Case
A 17-year-old female presented with severe organic hypoglycemia related to endogenous CHI diagnosed since neonatal age. She had been treated with Diazoxide since childhood, but experienced recurrent hypoglycemia and therapeutic escape. The diagnosis of focal CHI was established based on pancreatic MRI and endoscopic ultrasound findings revealing hyperplasia in the pancreatic tail. A caudal pancreatectomy was performed, paradoxically leading to severe and persistent hyperglycemia reaching 8 g/l for 20 hours, accompanied by a significant decrease in insulin levels during its kinetic evaluation, dropping from 400 μIU/ml to 25 μIU/ml (concurrent blood glucose at 3 g/l). Subsequent postoperative evolution showed a gradual spontaneous normalization of blood glucose to 1 g/l, followed by the recurrence of hypoglycemia with a rise in insulin levels. Histopathological data confirmed the diffuse nature of pancreatic hyperplasia, indicating the need for total pancreatectomy. Molecular analysis of candidate genes involved in CHI was negative for ABCC8 and KCNJ11 genes. However, involvement of a molecular anomaly in the enzymatic chain of insulin secretion process was considered.
Conclusion
CHI, seemingly a straightforward entity, exhibits a highly complex etiopathogenesis, making the correlation between phenotypic and genotypic expression challenging. High-throughput sequencing techniques have provided insights into insulin secretion signaling pathways, but the involvement of environmental factors opens up a new research avenue, highlighting the Gene-Environment interrelation.
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EP46

Long term use of closed-loop systems in patients with type 1 diabetes and risk of hypoglycemia

Beatriz Torres Torres[1,2], Paloma Pérez López[1,2], Ainhoa Alcelai Uribeecheverría[2], Pablo Fernández Velasco[1,2], Jaime González Gutiérrez[1,2], Lucía Estévez Asensio[1,2], Esther Delgado García[1,2], Emilia Gómez Hoyos[1,2], Gonzalo Díaz Soto[1,2] & Daniel De Luis Román[1,2]
[1]Hospital Clínico Valladolid, Endocrinology, Valladolid, Spain; [2]Facultad de Ciencias de la Salud, IEN, Valladolid, Spain

Background and Aim
Data support the use of hybrid closed-loop systems, because of it positive impact in the management of patients with type 1 diabetes (T1D). The aim was to evaluate the impact of an hybrid closed-loop system in patients with T1D at high risk of hypoglycemia.
Methods
Retrospective study of patients with T1D controlled in a Endocrinology department older than 17 years old, who were carriers of an Insulin Pump (MiniMed™640G) and Flash Glucose Monitoring System. They switched to a MiniMed™780G Hybrid closed-loop system (Medtronic), at least two years before the study. At baseline, patients had a Coefficient of Variation(CV) $>$ 36% and/or a Time below 70 mg/dl (TBR)greater than or equal to 4%. Data of Time in Range (TIR), Time above 180 mg/dl (TAR), TBR, CV and Glucose Management Indicator(GMI) were collected at baseline and 3 months and 2 two years after change.
Results
18 patients were included. The age was 33.5 (28-43) years old, the evolution of their T1D was on 18.6 (15-24) years and 56% were women.
10 patients (55%) had an TIR $>$70% at baseline, compared to 100% of patients at both 3 and 24 months ($P<0.001$)
Conclusions
The use of hybrid closed-loop systems, in our series, has shown an increase in TBR due to a decrease in TAR, TBR and CV. Improvement in glycometric parameters was observed at 3 months and it was maintained after 2 years of follow-up.

Table 1. Summary of data outcome

	TIR	TBR	TAR	CV	GMI
Baseline	68,5% (56.7-76.0)	5% (3,5-7)	20% (16-29)	38.2 (33.7-41.5)	6.6% (6.5-7)
3 months	86.3% (80.0-89.0)	3% (2-4)	11% (7-16)	31.3% (27.8-34)	6.4% (6.4-6.6)
24 months	83.1% (80-87.5)	2% (1-4)	14% (9.5-18.5)	30.3% (28-33.1)	6.6% (6.4-6.8)
p	<0.001	<0.01	<0.001	<0.001	ns

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EP47

Mody-3 diabetes: is there a place for GLP-1 receptor agonists use?

Valentim Lopes, Patrícia Brito, Rita Ribeiro & Adriana Lages
ULS de Braga, Endocrinology, Braga, Portugal

Introduction
Maturity-onset diabetes of the young (MODY) represents 1 to 2% of all cases of diabetes. MODY-3 is the most prevalent subtype and is characterized by a high sensitivity to sulfonylurea (SU) therapy. To date, we have scarce evidence about the efficacy of other therapies in this population, namely GLP-1 receptor agonists (GLP-1ra).
Objective
Evaluate the metabolic impact of GLP-1ra use in MODY-3 patients.
Methods
Retrospective descriptive study including patients with genetically confirmed MODY-3 followed at the Endocrinology Department of a tertiary referral centre. Data were analysed using SPSS v.27. Results were considered significant if $P <$ 0.05.
Results
From a total of 53 patients with genetically confirmed MODY diagnosis followed at our centre, we selected 16 patients with MODY-3 for the final analysis (30.2%). We divided the patients in two groups: patients treated with GLP-1ra - group 1 – ($n = 9$, 56%) and patients not treated with – group 2 ($n = 7$, 44%). 12 (75%) of the patients of the total sample were female, with a median age at diagnosis of 23 (Q1 19 – Q3 26.5) and 18 (Q1 18 – Q3 24) years and a median disease duration of 29 (Q1 12.5 – Q3 36.5) and 17 (Q1 14 – Q3 27) years, respectively for the group 1 and 2. Patients of the group 1 (vs patients of the group 2) presented more weight loss – -7 ([-10.5]-[-4.5]) vs 0 ([-3]-2) kg, $P = 0.011$ – and a higher C-peptide/serum glucose ratio - 1.1 (0.7-2.4) vs 0.4 (0.3-0.5) ng/ml:mg/dl, $P = 0.006$. We did not find statistically significant differences between the two groups regarding total daily dosage of SU and insulin, frequency of usage of other pharmacological classes (namely metformin and SGLT-2 inhibitors), HbA1c and prevalence of micro and macrovascular complications.
Conclusion
Patients treated with GLP-1ra (group 1) presented a significantly higher weight loss and evidence of preservation of residual endogenous pancreatic secretion of insulin, highlighting the potential benefit of this pharmacological class in patients with MODY-3 diabetes mellitus.

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EP52

Evaluation of nutritional knowledge in Tunisian adolescents

Ben Othman Rym, Amorri Amani, Salma Abadlia, Ben Zina Baya, Ben Mansour Nadia, Kasraoui Sabeh, Gamoudi Amel & Jamoussi Henda
National Institute of Nutrition and Food Technology, Nutrition A, tunis

Introduction
The inequity in energy balance is the most common cause of obesity throughout adolescence. Thus, evaluating nutritional knowledge is crucial for effective planning of targeted preventive interventions, by identifying specific areas that require improvement. Our study was undertaken in order to assess the levels of dietary awareness in a sample of Tunisian adolescents aged 12 to 15 years.
Methods
It was a multicenter cross-sectional study including 315 adolescents aged from 12 to 15 years. Our study was conducted at the National Center for School and University Medicine in Tunis and five randomly selected nurseries in Ariana governorate from December 2021 to June 2022. Participants' nutritional knowledge was evaluated using an Arabic version of the validated French nutritional questionnaire QuesCA 12-15 with a maximum score of 9/9. We developed the Arabic version following established translation and questionnaire validation guidelines.
Results
The average age of adolescents was 13.1 ± 1 years. The sex ratio was 1.15. Three-quarts of the sample (76%) had a normal weight, 13% were obese and 9% were underweight. The mean score on the questionnaire was 5.814 ± 0.4/9. The majority of participants (79%) obtained a fair score (i.e. score ranging between 4 and 6/9). None of the participants answered all items correctly. Nevertheless, thirteen percent achieved a good score (i.e. score $\geq$ 7/9) indicating a robust understanding of nutrition. On the other hand, 8% received a poor score (i.e. score $\leq$ 3/9). Worth noting, one child had a score of 0/9. Moreover, correct responses exceeded 75% for items related to the themes of breakfast, beverages, proteins, fruits and vegetables, and sweets. In contrast, items related to themes of balanced diet, starchy foods, calcium-rich foods, and fats had correct response rates below 25%.
Conclusion
These insights provide a foundation for developing tailored interventions to enhance dietary awareness and combat the rising challenges of obesity among Tunisian adolescents.

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EP54

Indices of carbohydrate metabolism in patients during the acute period of covid-19

Umida Mirzaeva
Tashkent Pediatric medical institute, Endocrinology, Tashkent, Uzbekistan

Introduction
The World Health Organization has recognized a new coronavirus infection as a pandemic[1]. As of early October 2020, the number of infected people worldwide amounted to more than 37 million[2]. According to WHO data, the structure of morbidity of new coronavirus infection is dominated by elderly people and patients with comorbidities, among which the most frequent are diseases of the cardiovascular system, diabetes mellitus (DM), obesity, chronic lung diseases, and oncologic pathology[3].
Objective
To determine the indices of carbohydrate metabolism in patients with COVID-19 in the acute phase of the disease.

Materials and methods
The object of research were 31 patients in the acute period of coronavirus infection caused by COVID-19. The age of the patients ranged from 32 to 80 years. Of these, there were 13 (41.9%) males and 18 (58.1%) females. All patients underwent standard clinical and anamnestic examinations: anthropometric, hemodynamic, laboratory examination included general and biochemical blood analysis, liver function indices, coagulogram, lipid spectrum parameters, fasting glycemia, HbA1c, fasting insulin levels, with HOMA-IR index determination, urea, creatinine with calculation of SCF and CRP.
Results of the study
Carbohydrate metabolism disorder in the form of increased fasting glucose level was revealed in 6 (19,4%) patients, mainly older than 50 years old with concomitant arterial hypertension, excessive body weight and obesity. In 4 patients with type 2 DM in anamnesis the duration of the disease was on average 6.8 ± 1.7 years. In the majority of patients fasting glucose level was within the range of normal values (mean 4.4 ± 0.7 mmol/l). HbA1c above the reference interval was observed in 32.3% of patients. When analyzing insulin resistance indices, increased insulin level was noted in 22.6% of cases, HOMA IR ≥ 2.7 was found in 35.5% of patients, mostly with coronavirus infection of moderate severity.
Conclusions
Thus, the presence of impaired carbohydrate metabolism is associated with a more severe course of coronavirus infection. At the time of admission, the group with a moderate course of coronavirus infection had more co-morbidities than patients in the group with a mild course.
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EP55

The impact of diet on rheumatoid arthritis disease activity
Rym Ben Othman[1], Khaoula Zouaoui[2], Maryam Naifar[1], Ramla Mizouri[1], Ikhlas Trabelsi[1], Olfa Berriche[1] & Henda Jamoussi[1]
[1]national institute of nutrition; [2]La Rabta, Tunis, Tunisia

Introduction
Rheumatoid arthritis (RA) is a chronic autoimmune disease that may cause nutritional impairment. The aim of the present study was to assess differences in nutritional status and Mediterranean diet (MD) adherence among patients with rheumatoid arthritis (RA), according to disease activity.
Methods
A comparative cross-sectional study, conducted among patients consulting the rheumatology department of La Rabta University hospital for RA. To assess disease activity and adherence to Mediterranean diet, we opted for the subjective disease activity score28 (DAS28) and MedDietScore. The dietary survey data were subsequently analyzed using the NUTRILOG software.
Results
This study included 52 patients. Patients were subdivided into 2 groups: G1 includes 35 patients with low activity RA and G2 with very active RA according to DAS28. The median age was 56.26 ± 13.12 years. The mean Body Mass Index (BMI) was 28.84 kg/m^2 in G1 vs 28.20 kg/m^2 in G2 ($P=0.74$) and 52.9% of patients in G2 were obese (BMI ≥ 30 kg/m^2) Vs 48,6%; $P=0,76$. waist circumference was higher in G2 with no statistically significant association; $P=0,86$. the two groups ($P=0.22$). The eating pattern of G2 patients was more regular than that of patients in G1, with a P-value of 0.7. The frequency of consumption of certain foods such as Walnuts, Rapeseed Oil, Soybean Oil, Fish, Cinnamon, Garlic, Ginger, Sesame, and Turmeric did not differ significantly between the two groups. Patients in G1 adhered more to the Mediterranean diet without significant difference (7.26 vs 7.18; $P=0.88$). The calorie surplus was higher for patients in the low-activity PR group (404 kcal vs 52.09 kcal; $P=0.55$). Spontaneous macronutrient intake did not differ significantly between the two groups. Only the percentage of daily intake of polyunsaturated fatty acids (PUFA) was significantly higher in G2 ($P=0.03$). Regarding micronutrient and fiber intake, only the sodium intake was significantly higher in patients from G1 (6059,31 mg vs 4604,59 mg; P-value$= 0,01$.
Conclusion
Specialized nutritional management should be instituted in patients with RA to avoid disruption of their nutritional status.
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EP56

Weight reduction in patients with hypothalamic obesity treated with setmelanotide for 12 months
Christian L. Roth[1], Ashley Shoemaker[2], Michael Gottschalk[3], Jennifer Miller[4], Guojun Yuan[5], Sonali Malhotra[6], Cecilia Scimia[5] & M. Jennifer Abuzzahab[7]
[1]Seattle Children's Research Institute; Division of Endocrinology, Department of Pediatrics, University of Washington, Seattle, Seattle, United States; [2]Ian Burr Division of Endocrinology and Diabetes, Vanderbilt University Medical Center, Nashville, United States; [3]Pediatric Endocrinology, University of California San Diego/Rady Children's Hospital, San Diego, United States; [4]Pediatric Endocrinology, Department of Pediatrics, College of Medicine, University of Florida, Gainesville, United States; [5]Rhythm Pharmaceuticals, Inc., Boston, United States; [6]Rhythm Pharmaceuticals, Inc.; Harvard Medical School; Massachussetts General Hospital, Boston, United States; [7]Pediatric Endocrinology and Diabetes, Children's Minnesota, Saint Paul, United States

Background
Hypothalamic obesity (HO) is an acquired form of severe obesity characterized by rapid and excessive weight gain resulting from insult to the hypothalamus—primarily caused by tumor invasion, resection, or radiotherapy—that can impair melanocortin-4 receptor (MC4R) pathway signaling. Treatment with setmelanotide, an MC4R agonist, resulted in weight and hunger reduction at 16 weeks in a Phase 2 trial of patients with HO. Here, we report changes in weight-related parameters after 12 months of setmelanotide treatment in patients with HO who entered a long-term extension (LTE) trial.
Methods
The Phase 2, multicenter, open-label study (NCT04725240) was a 16-week trial in patients aged ≥ 6 to ≤ 40 years with a clinical diagnosis of HO. Patients who demonstrated adequate safety and meaningful clinical benefit were eligible to enroll in the LTE trial (NCT03651765). Mean (standard deviation [SD]) percent change in body mass index (BMI) for all patients and mean (SD) change in percent of the 95th BMI percentile (%BMI$_{95}$) for children (aged <18 years) from index trial baseline to Month 12 of setmelanotide treatment were assessed.
Results
Of 14 patients who entered the LTE, 12 (86%) received ≥ 12 months of setmelanotide at the time of analysis. One adult who experienced nausea discontinued study drug at 7 months and 1 child who had been lost to follow-up reconsented and reentered the LTE but did not have 12-month data. At Month 12, the mean (SD) percent BMI change from baseline was -24.9% (13.0%) across all patients ($n=12$) and in children ($n=11$), the mean (SD) change in %BMI$_{95}$ was -39.5 (19.4) percentage points. No new safety signals were identified.
Conclusions
In a heterogeneous population of patients with HO secondary to treatment of hypothalamic tumors, 12 months of setmelanotide treatment was associated with sustained meaningful BMI improvement with no new safety signals.
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Impact of setmelanotide on metabolic syndrome risk in patients with POMC and LEPR deficiency
Martin Wabitsch[1], Wendy Chung[2], Peter Kühnen[3], James Swain[4], Jill Garrison[5], Nicolas Touchot[5], Jesús Argente[6] & Karine Clément[7]
[1]Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics and Adolescent Medicine, University of Ulm, Ulm, Germany; [2]Division of Molecular Genetics, Department of Pediatrics, Columbia University, New York, United States; [3]Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin und Humboldt-Universität zu Berlin, Institute for Experimental Pediatric Endocrinology, Berlin, Germany; [4]Honor Health Research Institute, Scottsdale, United States; [5]Rhythm Pharmaceuticals, Inc., Boston, United States; [6]Department of Pediatrics and Pediatric Endocrinology, Universidad Autónoma de Madrid, University Hospital Niño Jesús, CIBER 'Fisiopatología de la obesidad y nutrición' (CIBEROBN), Instituto de Salud Carlos III; IMDEA Food Institute, Madrid, Spain; [7]Assistance Publique Hôpitaux de Paris, Nutrition Department, Pitié-Salpêtrière Hospital; Sorbonne University, Inserm, Nutrition and Obesity, Systemic Approaches (NutriOmique) Research Group, Paris, France

Background
Proopiomelanocortin (POMC; including biallelic variants in *PCSK1*) and leptin receptor (LEPR) deficiency are associated with hyperphagia and early-onset,

severe obesity. Treatment with the melanocortin-4 receptor agonist setmelanotide for 1 year results in significant and sustained improvements in weight (POMC, −25.6%; LEPR, −12.5%), hunger, and quality of life. We used the metabolic syndrome Z score based on body mass index (MetS-Z-BMI) to assess the effect of setmelanotide treatment on long-term risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM). Each 1.0-point increase in MetS-Z-BMI increases the odds of future CVD and T2DM by 9.8 and 2.7, respectively, when assessed in children and by 2.4 and 2.8, respectively, when assessed in adults.
Methods
Parameters from Phase 3 trials of patients with POMC (NCT02896192) or LEPR (NCT03287960) deficiency were used to calculate MetS-Z-BMI score change after 1 year of setmelanotide. Long-term clinical responders to setmelanotide were defined as achieving ≥10% weight loss (if ≥18 years old) or ≥0.3-point BMI Z score reduction (if <18 years old) after 1 year.
Results
Eighteen patients (56% female, 11-36 years old) were evaluated. A decrease in mean (SD) MetS-Z-BMI was observed in clinical responders after 1 year of setmelanotide ($n=14$; −1.31 [0.84]). Nonresponders ($n=4$) achieved minimal decrease in MetS-Z-BMI (−0.17 [0.23]; difference between groups, −1.13, $P=0.0187$). Responders with POMC ($n=9$) and LEPR deficiency ($n=5$) had changes in MetS-Z-BMI of −1.63 (0.84) and −0.72 (0.48), respectively. MetS-Z-BMI change was similar in female and male responders.
Conclusions
Clinical response to setmelanotide led to decreases in MetS-Z-BMI in patients with POMC and LEPR deficiency associated with reduced risk of developing CVD and T2DM in other populations. These data suggest that early initiation of setmelanotide may reduce future risk of T2DM and CVD.

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Fibroblast growth factor 21 in health and diseases

Hassan Heshmati[1] & Haitham Abu-Lebdeh[2]
[1]Endocrinology Metabolism Consulting, LLC, Hassan Heshmati and Valerie Shaw Endocrine Research, Anthem, AZ, United States; [2]Mayo Clinic, Division of Endocrinology, Diabetes, Metabolism and Nutrition, Rochester, MN, United States

Introduction
Fibroblast growth factor 21 (FGF21), a 181 amino acid peptide hormone predominantly produced by the liver, is a member of the endocrine FGF subfamily. It is involved in multiple physiological regulations and plays an important role in several pathological conditions. This literature analysis provides an update on the relevance of FGF21 in health and diseases.
Methods
A systematic search of literature was conducted using the search terms fibroblast growth factor 21, health, diseases, role, and analog.
Results
FGF21 is a stress hormone with various functions. It is involved in the regulation of energy expenditure and metabolism of lipids and glucose by acting on the adipose tissue and central nervous system. In normal subjects, serum FGF21 levels increase gradually with aging. There is an increase in FGF21 secretion under stressful conditions (e.g., fasting status, protein restriction, exercise, several metabolic disorders, kidney diseases, cardiovascular diseases, and sepsis). The increased serum FGF21 levels observed in metabolic disorders (e.g., obesity, nonalcoholic fatty liver disease 'NAFLD', and type 2 diabetes) and other conditions (e.g., kidney failure, heart failure, and sepsis) can be associated with a state of FGF21 resistance that is related in part to the presence of high circulating levels of fibroblast activation protein, a protease that inactivates FGF21. In contrast, low serum FGF21 levels have been reported in anorexia nervosa. Serum FGF21 level has the potential to be used as a biomarker in several metabolic disorders (e.g., NAFLD and type 2 diabetes) and other conditions (e.g., heart failure). In view of the multiple FGF21 functions related to energy expenditure and metabolism of lipids and glucose, long-acting FGF21 analogs (e.g., LY2405319, PF-05231023, pegozafermin, AKR-001, and LLF580) have been used in clinical trials for the treatment of various conditions such as obesity, NAFLD, dyslipidemia, and type 2 diabetes. The results of these trials show that FGF21 analogs can reduce body weight, liver fat, circulating lipids, and fasting insulin/insulin resistance. Thus far, these analogs are considered safe and well tolerated.
Conclusions
FGF21 is a peptide hormone synthesized predominantly by the liver and involved in the maintenance of metabolic homeostasis. FGF21 plays an important role in multiple pathological conditions. Serum FGF21 levels are increased in several diseases in a setting of FGF21 resistance. Although FGF21-based therapy appears to be an attractive approach to treat metabolic disorders, additional clinical studies are necessary before practical recommendations can be made for the use of FGF21 analogs.

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Evaluating the impact of a moderately low-calorie ketogenic diet on mafld in patients with obesity: the role of magnetic resonance imaging

Maria Chiara Massari[1], Davide Masi[1], Elena Colonnello[1], Filippo Biagi[1], Marta Zerunian[2], Benedetta Masci[2], Flaminia Ferri[3], Monica Mischitelli[3], Carla Lubrano[1], Stefania Mariani[1], Andrea Laghi[2], Stefano Ginanni Corradini[3], Lucio Gnessi[1], Damiano Caruso[2] & Mikiko Watanabe[1]
[1]Sapienza University of Rome, Department of Experimental Medicine and Endocrinology, Sapienza University of Rome, Rome 00161, Italy; [2]Department of Surgical and Medical Sciences and Translational Medicine, Sapienza University of Rome - Sant'Andrea University Hospital, Via di Grottarossa, 1035-1039, 00189 Rome, Italy; [3]Division of Gastroenterology, Department of Clinical Medicine, Sapienza University of Rome, Rome 00161, Italy

Introduction
Metabolically associated fatty liver disease (MAFLD), prevalent in the Western world and a leading cause of liver transplantation among U.S. women, ranges from intra-hepatocyte lipid accumulation to cirrhosis. Fibrosis severity is crucial for prognosis, correlating with risks of advanced cirrhosis, portal hypertension, and hepatocellular carcinoma. 5-10% weight loss is associated with improvement of liver steatosis, but achieving >10% weight loss is usually necessary to improve NASH. Ketogenic diets, regardless of calorie intake, seem effective in treating steatosis, but there is very little evidence on their impact on liver fibrosis. The objective of this study is to evaluate the effect of a moderately low calorie, high-fat ketogenic diet (HFKD) on liver health in patients with MAFLD.
Methods
This prospective, pilot study involved patients with a confirmed MAFLD diagnosis through Magnetic Resonance Imaging (MRE) and Proton Density Fat Fraction (PDFF). Inclusion criteria included age over 18, and BMI ≥ 30 kg/m^2, while exclusion criteria included decompensated liver failure, pregnancy/lactation, type 1 diabetes mellitus, chronic renal disease, alcoholism, hepatotropic viral infection. The primary outcome was reduction of liver steatosis, while secondary outcomes focused on safety, improvements in liver fibrosis, metabolic profile, and body composition. The patients underwent a moderately hypocaloric HFKD for 90 days and Magnetic Resonance Imaging (MRE) was employed to evaluate steatosis (PDFF %) and stiffness (kPa). Baseline and post-intervention assessments included anthropometric measurements, biochemical analysis, and body composition evaluation (DEXA).
Results
Seven patients with MAFLD (mean age 61.3 ± 8.14 years and mean BMI 38.84 ± 6.62 kg/m^2) were included. Following the dietary intervention, weight loss (-8.14 kg, $P=0.03$) and a decrease in mean BMI (-2.92 kg/m^2, $P=0.02$) and fat mass percentage (-3.57%, $P=0.02$) were reported. As expected given the small calorie deficit, none had >10% weight loss, allowing for better evaluation of the impact of macronutrient composition beyond calorie deficit/weight loss *per se*. MRE revealed a significant reduction in steatosis (PDFF -6.16%, $P=0.03$). Although no statistical reduction in liver fibrosis was observed overall likely due to the small sample size, three out of seven patients exhibited clinically relevant stiffness decrease. Notably, two patients achieved complete resolution of NASH, while another, despite remaining cirrhotic, demonstrated significant improvement. Safety parameters were unchanged.
Conclusion
Despite modest weight loss, preliminary data indicate a role for HFKD in managing MAFLD, not only in mitigating steatosis but potentially in more advanced stages characterized by liver fibrosis. MRE emerges as a sensitive tool for assessing MAFLD changes over time.

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EP60

The effects of multi-strain probiotics in patients with obesity and metabolic syndrome

Ivaylo Bogomilov[1], Vesela MIhneva[2] & Branimira Mihaylova[3]
[1]Medical University Of Sofia, Sofia, Bulgaria, Pharmacology and toxicology, Sofia, Bulgaria; [2]Military Medical Academy Sofia, Pharmacology and toxicology, Sofia, Bulgaria; [3]Medical University Of Sofia, Sofia, Bulgaria, Sofia, Bulgaria

Introduction
Obesity and metabolic syndrome (MS) to which it can lead are diseases that have become very important in recent decades. Understanding the complex mechanisms leading to the development of obesity and metabolic syndrome would give us the answers on how to properly manage these important socially significant diseases. The criteria for metabolic syndrome in recent years have changed a little bit, but invariably they include - visceral type of obesity - measured by waist circumference, arterial hypertension, dyslipidemia - characterized by low levels of HDL-cholesterol and increased levels of triglycerides, diabetes mellitus (DM) type 2 or impaired fasting glycemia. However, insulin resistance is both a consequence of obesity and one of the causes of the development of metabolic syndrome. In recent years, different groups of medications have proven their effect on insulin resistance and are used in the treatment of obesity and metabolic syndrome. Recent studies have shown that the gut microbiome is also extremely important in the development of insulin resistance and may be one of the keys to treating MS and obesity.
Methods
Forty patients with obesity, MS and HOMA-index above 5 were tracked during the study. The patients were given a probiotic - 2.5×10^9 cfu/g of Ecologic®Barrier (multi-strain probiotics) and a standard diet for 6 months. After 6 months, we followed the value of fasting blood sugar, fasting insulin and HOMA index.
Results
In all patients using probiotics, there was a decrease in the levels of fasting insulin, as well as in the levels of fasting glucose, respectively the levels of the HOMA-index, and this reached statistically significant values $P<0.05$. In thirty of the patients, there was a decrease in body weight of 5 ± 1 kg.
Conclusion
Usage of specialized probiotics and regulation of the gut microbiome may lead to improvement in metabolic parameters in MS and obesity. Extensive studies on the impact of probiotics on components of MS and obesity are needed to fully understand their effect in the treatment of these diseases.

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EP61

The influence of metabolic and hormonal changes in the treatment of obesity

Vesela Mihneva[1], Ivaylo Bogomilov[2] & Tzvetelina Totomirova[1]
[1]Military Medical Academy Sofia, Endocrinology and metabolic diseases, Sofia, Bulgaria; [2]Medical University Of Sofia, Sofia, Bulgaria, Pharmacology and toxicology, Sofia, Bulgaria

Introduction
Obesity is a chronic relapsing disease that has acquired pandemic dimensions in recent years. Obesity is not just a disease that is associated with an increase in body weight, but a condition that leads to a complete change in the hormonal status of patients.
Methods
In the Clinic of "Endocrinology and Metabolic Diseases" of the Military Medical Academy - Sofia, we tracked 100 people with obesity with a BMI over 30 kg/m2 for 6 months. Patients were divided into 5 different groups depending on the therapy they received-with metformin, with liraglutide up to 3 mg, semaglutide up to 2.4 mg, treatment with specialized probiotics or only on a standard diet. We monitored the values of thyroid hormones - TSH, fT4 fT3; levels of TAT, MAT; total testosterone in men and women, fasting insulin levels, fasting glucose levels and insulin and glucose levels during oral glucose tolerance test (OGTT), before the start of treatment and 6 months later.
Results
We found statistically significant changes ($P<0.05$) in the hormone levels - in patients who reduced more than 5% of body weight regardless of the therapeutic approach-a decrease in TSH levels was found, in patients with subclinical hypothyroidism at the beginning of the follow-up, without levothyroxine replacement therapy and increased total testosterone levels in men with baseline low total testosterone. In patients with a reduction of more than 10% of body weight, a decrease in fasting insulin levels was found, as well as in fasting glucose levels and glucose levels at 120 min of the performed OGTT compared to the values at the beginning of the follow-up.
Conclusion
The reduction of body weight and the treatment of obesity leads to an improvement in the general hormonal status of patients, independently of the therapeutic approach, but in correlation with the percentage of reduced body weight.

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EP62

Association study of obesity susceptibility gene polymorphisms in relation to 5 tunisian families

Hamdi Frikha[1], Hana Charfi[1], Yassmine Abdelkafi[1], Khouloud Boujelben[1], Dhoha Ben Salah[1], Faten Haj Kacem Akid[1], Nadia Charfi[1], Fatma Mnif[1], Mouna Mnif[1], Faiza Fakhfakh[2], Mouna Elleuch[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology; [2]University of Sfax, Laboratory of Molecular and Functional Genetics, Tunisia

Introduction
Obesity, in its common form, exhibits extreme genetic heterogeneity, and its mode of transmission remains unknown. To investigate the impact of the genetic component, we conducted an association study between polymorphisms of functional and positional candidate genes: Leptin and its receptor gene (LEP, LEPR), Melanocortin 4 Receptor (MC4R), FTO gene: Fat mass and associated obesity, and Pro-opiomelanocortin gene (POMC); with obesity and associated phenotypes (anthropometric and metabolic parameters, insulin levels, leptin levels, Homeostatic Model Assessment of Insulin Resistance HOMA-IR).
Materials and Methods
Our study included 50 patients from 5 Tunisian families affected by obesity and 52 controls from the Tunisian population. Genotyping of candidate gene single nucleotide polymorphisms (SNPs) was performed using PCR-RFLP and automatic sequencing. The association study was conducted using the Family-Based Association Test (FBAT).
Results
Statistical analysis of the genotyping results for different polymorphisms of the LEP gene showed that the SNPs (H1328084 A>G and +19 G>A), located in the 5' region of the gene, are associated with hyperleptinemia. In silico analyses demonstrated that these two polymorphisms could affect potential binding sites for certain transcription factors (c-Myb for A19G and NF-1 for H1328084) and consequently could play an important role in the regulation of plasma leptin levels. Regarding the LEPR gene, we found that the G allele of the c.A668G (Q223R) polymorphism is significantly associated with hyperinsulinemia and hyperleptinemia. Our results also showed that the RsaI variant of the POMC gene is associated with anthropometric parameters, plasma cholesterol levels, and blood pressure. Additionally, an association was detected with diastolic blood pressure and the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) for another 3'UTR polymorphism of the POMC gene (C8246T). Finally, no significant association was detected for the MC4R and FTO genes.
Discussion and Conclusion
The study of the genetic variability of the candidate genes in 5 Tunisian families confirms the association between the two functional leptin gene polymorphisms (H1328084 A/G and A19G) and the Q223R polymorphism of the leptin receptor gene LEPR with hormonal parameters. Only the C8246T polymorphism of the POMC gene seems to be associated with insulin resistance. A larger sample size study and inclusion of sporadic cases could better establish the impact of various genetic variants, particularly the MC4R and FTO genes.

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EP63

Difference in impact of flash glucose monitoring in patients with type 1 diabetes mellitus and pancreatogenic diabetes

Ana Ortolá Buigues[1], Carla Valles Valverde[2], Emilia Gómez Hoyos[1], Rebeca Jiménez Sahagún[1], Juan José López Gómez[1], Beatriz Torres Torres[1], Esther Delgado García[1], Gonzalo Díaz Soto[1], Beatriz Ramos Bachiller[1] & Daniel de Luis Román[1]
[1]Hospital Clínico Universitario Valladolid; [2]Facultad de Medicina. Universidad de Valladolid

Introduction
Diabetes mellitus secondary to exocrine pancreas diseases (pancreatogenic DM) is a heterogeneous type of DM that usually requires treatment with multiple doses of insulin (MDI), like type 1 DM (DM1). Our objective was to evaluate the difference in the impact of Flash glucose monitoring (FGM) on glycemic control in pancreatogenic DM and DM1.
Methods
Prospective, observational study in Spanish hospital. We included the first patients with DM1 who started FGM from June 2019 to April 2020 and patients

with pancretogenic DM from January 2021 to June 2023, all on treatment with MDI. Patient data collected included demographic, clinical, anthropometric variables, as well as etiology, duration and treatment of DM. In addition, blood glucose control variables from the Abbott FreeStyle Libre the first 14 days and at 3 months were recorded: glucose management indicator (GMI), coefficient of variation (CV), percentage of time in range (TIR) (70-180 mg/dl), and hypoglycaemic events in 14 days.
Results
86 patients with DM1 vs 26 patients with pancreatogenic DM were included. Of DM1 61.6% were male vs 50% in pancreatogenic DM ($P=0.291$). Their age was 37.4 (SD 13.0) vs 59.7 (SD 16.4) years ($P<0.001$). DM duration was 18.1 (SD 11.3) vs 8.8 (SD 6.8) years ($P<0.001$). Total insulin dose/kg/day at the first visit was 0.62 (SD 0.20) vs 0.52 (SD 0.29) IU/kg/day ($P=0.045$). Of the pancreatogenic DM, 53.8% were secondary to pancreatectomy (26.9% total and 26.9% partial), and 30.8% due to chronic pancreatitis. In the first 2 weeks of FGM, there were no significant differences in the number of scans, TIR or GMI, in the two types of DM. There was a significant higher CV in DM1 patients [41.3 (SD 7.4) vs 31.7 (SD 5.7) $P<0.001$] and hypoglycemia events [13.5 (SD 9.1) vs 2.5 (SD 2.9) $P<0.001$] and their duration [95.7 (SD 44.9) vs 56.8 (SD 56.3) min, $P<0.001$]. At 3 months, there were only improvements in DM1 glucometry in decrease of hypoglycemia events [10.7 (SD 6.7) vs 13.5 (SD 9.1) $P=0.001$], with no changes in pancreatogenic DM. Regarding treatment, there was no change at 3 months in DM1, while in pancreatogenic DM an increase in bolus insulin use was observed [13.9 (SD 9.5) vs 11.0 (SD 7.1) IU/day, $P=0.009$], with no change in basal insulin.
Conclusion
Pancreatogenic DM patients have lower risk of hypoglycemia than DM1 patients, and the decrease in hypoglycemia events described in DM1s with GMF is not observed in them.

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EP64

Progressive hyperparathyroidism post simultaneous pancreas-kidney transplantation in a long-term type 1 diabetes mellitus remission patient

Alexandra Zueva[1,2]
[1]Endocrinology Research Center, Moscow, Russian Federation; [2]The University of Sheffield, Sheffield, United Kingdom

Background
Simultaneous pancreas-kidney transplantation is an effective intervention for selected patients with insulin-dependent diabetes and end-stage chronic kidney disease (CKD), offering freedom from dialysis, insulin injections, and daily blood glucose monitoring. However, limited data exists on the impact of CKD complications on patient survival post-transplantation.
Case Presentation
A 58-year-old woman with Type 1 Diabetes (T1D) diagnosed in 1987 at the age of 22, end-stage CKD diagnosed in 2006, who underwent simultaneous pancreas-kidney transplantation in 2014, presented to our clinic for an annual check-up. It was known from her medical history that the patient had developed multiple diabetic complications such as diabetic kidney disease, diabetic retinopathy, and diabetes-related foot disease as a result of poor early glycemic control. Additionally, severe osteoporosis has developed since 2010 due to secondary hyperparathyroidism (HPT), treated with denosumab and cinacalcet. In 2022, she was diagnosed with tertiary HPT based on ultrasound signs of parathyroid glands hyperplasia, a decrease of bone mineral density (BMD), and multiple vertebral fractures on X-ray, although surgical intervention was not pursued, and alfacalcidol was added. A primary laboratory survey performed in our clinic showed HbA1c at 6.4%, C-peptide at 1.95 ng/ml, and normoglycemia without insulin. Under this treatment, creatinine clearance measured 49 mL/min, PTH and corrected total serum calcium remained within the normal range. While both transplants function appeared satisfactory, BMD remained stable since 2022 without any improvement despite treatment. Ophthalmic examination revealed no progression of retinopathy. Considering the limited impact of nonsurgical HPT treatment on skeletal health, parathyroidectomy was recommended.
Conclusions
This case highlights a nine-year remission period following successful simultaneous pancreas-kidney transplantation in a T1D patient. However, it also underscores the progressive nature of complications post-transplantation, necessitating careful monitoring and timely intervention to prevent further complications.

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EP65

Prevalence and risk factors for steatosis and liver fibrosis measured by magnetic resonance elastography in adults with cystic fibrosis-related diabetes

Ana Piñar Gutiérrez, Silvia García Rey, María del Carmen Roque Cuéllar, Andrés Jiménez Sánchez, Ángeles Pizarro, Esther Quintana Gallego, Francisco Javier Castell, Manuel Romero-Gomez, Alfonso Soto & Pedro Pablo Garcia-Luna
Virgen del Rocío University Hospital, Sevilla, Spain

Introduction
Cystic fibrosis-related diabetes (CFRD) has a prevalence of 40-50% in adults. Given what we know about metabolic liver disease, studies are needed to assess whether CFRD is also related to steatosis (LS) and liver fibrosis (LF).
Objectives
To determine the prevalence of LS and LF by magnetic resonance elastography (Mre) in a cohort of adults with CFRD. Secondary: to determine the diagnostic yield of transitional elastography (Fibroscan®) and the factors associated with both entities.
Methods
Cross-sectional study of adults with CFRD in a multidisciplinary unit. Clinical evaluation, morphofunctional assessment, MRe, transitional elastography and noninvasive markers were performed. Quantitative variables are expressed as n(%); qualitative variables as P50(P25-P75). Diagnostic accuracy tests were performed. Logistic regression was performed to study risk factors.
Results
$n=28$. Women$n=15(53.6\%)$. Age$=34(28.7\text{-}40.5)$years. Time of evolution$=28(19.5\text{-}34)$years. Malnutrition(GLIM)$=15(53.6\%)$. Exocrine pancreatic insufficiency$=26(92.9\%)$. BMI$=23.2(19.7\text{-}24.5)$kg/m^2. Insulin treatment$=20(71.4\%)$. The prevalence of LS was 25% and of LF 32.1%. In Fibroscan® it was 28.6% (71.4% sensitivity and 85.7% specificity) and 17.9% (55.5% sensitivity and 100% specificity) respectively. The AUROC of the Fibroscan® was 0.915(0.81-1) in HD and 0.936(0.838-1) in FH. We did not find any factors associated with LS. Those associated with LF are shown in the Table. Multivariate analysis could not be performed due to the low sample size.
Conclusions
This is the first study of LS and LF in adults with CFRD performed with MRe. The prevalence was 25% and 31.1% respectively. FibroScan® demonstrated excellent diagnostic accuracy. Alterations in blood count and transaminases, as well as fat-soluble vitamin deficiencies seem to be associated with increased risk of LF.

	OR(CI 95%)	p
Hemoglobin	5.6(1.01-338.59)	0.05
Total bilirubin	11.46(1.032-127.3)	0.047
Platelets	0.981(0.964-0.998)	0.031
Lymphocytes	0.038(0.002-0.615)	0.021
AST	1.128(1.02-1.247)	0.019
Vitamin A	0.866(0.752-0.997)	0.046
Vitamin E	0.997(0.993-1)	0.047

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EP67

Enavogliflozin, an sglt2 inhibitor, improves nonalcoholic steatohepatitis induced by high-fat high-cholesterol diet

Heesung Kim[1], Haein Hwang[1], Thi Minh Phuc Pham[2], Seon Mee Kang[3] & Eun-Hee Cho[3]
[1]Kangwon National University Hospital, Internal medicine, chuncheon, Korea, Rep. of South; [2]Kangwon National University, chuncheon, Korea, Rep. of South; [3]Kangwon National University Hospital, Endocrinology, chuncheon, Korea, Rep. of South

Objective
Non-alcoholic fatty liver disease (NAFLD) is a progressive disease caused by a build-up of fat in the liver and onsets with simple steatosis, potentially advancing to non-alcoholic steatohepatitis (NASH) in the presence of inflammation and fibrosis, severely leading to cirrhosis or hepatocellular carcinoma. There is increasing cumulative evidence indicating that sodium-glucose cotransport 2 (SGLT2) inhibitor agents efficaciously alleviate NASH in a novel mouse model, but there is no study mentioning the effect of Enavogliflozin on liver disease. Consequently, in this present study, we investigated the impact of this sodium-glucose cotransport 2 inhibitor on high-fat high-cholesterol diet (HFHCD)-induced NASH mice.

Methods
Male C57BL/6 mice were fed a chow diet, HFHCD, or HFHCD with Enavogliflozin for 12 weeks. Enavogliflozin was administered at a dose of 1.28 mg/kg/day in these experiments. *In vitro*, human hepatic stellate cells (LX-2 cells) were treated with transforming growth factor beta 1 (TGF-β1) in the presence or absence of Enavogliflozin.
Results
HFHCD induced excessive hepatic lipid accumulation, immune cell infiltration, and severe fibrosis. Enavogliflozin administration not only ameliorated hepatic steatosis and fibrotic condition but also suppressed the production of inflammatory cytokines (IL-6, IL-1β). In the *in vitro* study, in addition to decreasing SGLT2 expression induced by TGF-β1, enavogliflozin inhibited hepatic stellate cell activation by reducing proliferation, wound healing migration, and suppressing the expression of αSMA.
Conclusion
Our results suggest that enavogliflozin shows efficacy in a mouse model of NASH and liver fibrosis by attenuating hepatic steatosis, suppressing inflammation, and inhibiting hepatic stellate cell activation *in vitro*.
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EP68

Assessment of dietary patterns in patients with type 2 diabetes mellitus and different expressed insulin resistance
Diana Simoniene
Lithuanian University of Health Sciences, Endocrinology, Kaunas, Lithuania

What factors contribute to the development and progression of insulin resistance in diabetes is not fully understood.
The aim was to evaluate the intake of carbohydrates, vegetables and meat intake according to sex, age, BMI, duration of diabetes, diabetes complications and HOMA - IR scores in the groups with different IR.
Methods
This was a case-control study. Total of 122 subjects were enrolled. Subjects matched by age and sex were divided into two groups. Subjects with high insulin doses (> 1–2 IU/kg/day) and poor diabetes control (HbA1c > 9%) were referred to the case group (60 participants). Subjects with low insulin requirement (< 1 IU/kg/day) and HbA1c < 8 % were referred to control group. Usual dietary intake was assessed by using semiquantitative FFQ (unique, created by study author). Participants were asked to report their frequency of consumption of a given serving of each food item during the previous month on a daily basis.
Results
A significantly higher proportion of control group subjects consumed slow-release carbohydrates (≥ 2 times per week) and had a lower HOMA-IR < 10 (70.6%), compared with the case group subjects, who consumed more fast-acting carbs and had a high HOMA-IR ≥ 10 (29.4%) ($P=0.041$). Younger than 60 years case group participants consumed vegetables less frequently than control subjects (61.9% in the case group vs 100% in the control group, $P = 0.043$). Case group women (82.1%, $P=0.033$), subjects over 60 years (85.3%, $P=0.020$) and subjects with diabetes duration >10 years (84.8%, $P=0.017$) consumed red meat more often than 1 time per week. Irrespective of BMI, subjects in the control group were statistically significantly more likely to report no or infrequent intake of the red meat (16.1% vs. 3.6% in the case group, $P=0.006$). A higher proportion of subjects who rarely ate red meat (less than 1 time a week) had no diabetes complications (33.3%) compared to 8.6% of subjects who rarely ate red meat and had diabetes complications ($P=0.051$).
Conclusions
Subjects who frequently consumed slow carbohydrates were more likely to have lower HOMA-IR. Vegetables were less frequently consumed by case group subjects, younger than 60 years. Red meat was consumed more frequently by female, subjects over 60 years, obese and long diabetes duration subjects. The rate of chronic diabetes complications was lower in subjects who consumed red meat less than 1 time a week.
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EP69

Painful diabetic peripheral neuropathy among Tunisian geriatric patients suffering from diabetes mellitus
Dhoha Ben Salah, Mariem Abdelmouleh, Siddiqa Soomauroo, Mona Elleuch, Khouloud Boujelben, Faten Hadjkacem, Nadia Charfi, Fatma Mnif, Mouna Mnif, Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Distal and symmetrical peripheral polyneuropathy is the most frequent type of diabetic neuropathy. Its painful form (PDN) is the most common cause of non-traumatic neuropathic pain and can place a heavy burden on elderly patients' lives. Despite the major impact that it can have on the quality of life, PDN is generally underdiagnosed because of a large interindividual variability of symptoms and in the absence of well-established diagnostic criteria.
Aim
To determine the prevalence of PDN and to identify the different risk factors of its occurrence within Tunisian geriatric patients.
Methods
This was a cross-sectional study conducted in the endocrinology-diabetology department of Hedi Chaker hospital Sfax Tunisia, in which we collected elderly patients with diabetes. The DN4 Questionnaire was used to diagnose PDN.
Results
A total of 52 elderly patients were recruited. The mean age of patients was 70.6 years with a slight female predominance (55.8% Vs 44.2%). All the patients had type 2 diabetes. The mean duration of diabetes' evolution was 13.54 years. The average of HbA1c level was 10.35%. Among diabetes' complications, PDN was the most frequent in our study (53.8%). The mean DN4 score was 3.83. Significant predictors of PDN included long history of diabetes ($P=0.04$), high levels of glycated hemoglobin (HbA1c) ($P=0.04$) and insulin therapy within type 2 diabetic patients ($P=0.029$), in addition to some comorbidities such as sweating disorders and history of leg ulcer. Some features of foot examination were also found to be risk factors of PDN namely trophic disorders ($P=0.05$), dry skin ($P=0.004$), hyperkeratosis ($P<0.001$), abolition of Achilles reflexes ($P<0.001$) and positive monofilament test ($P<0.005$).
Conclusion
The present study demonstrated that the prevalence of PDN is high among our geriatric population. This emphasizes the need to screen periodically diabetic elderly patients using a simple instrument such as the DN4 questionnaire and to educate at risk patients about predictors of PDN regularly.
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EP71

Analysis of the work of the office of diabetic foot care "minsk city clinical endocrinilogy center" for 2019-2023
Hanna Bliznets, Volha Shyshko, Inesa Pukita & Alena Yurenia
Minsk City Clinical Endocrinology Center, Minsk, Belarus

Objectives
Analysis of the work of the diabetic foot office (DFO), the number of amputations and the causes that led to this complication of diabetic foot syndrome (DFS) underlies the development of preventive measures that help to reduce the level of disability and lethality, which is an urgent and socially significant medical problem.
Objective
To study the indicators characterizing the provision of medical care to patients with diabetes and lower limb lesions in Minsk from 2019 to 2023 and the relationship of these indicators with the developed regulatory documentation determining the optimal routing of this group of patients.
Materials and Methods
Annual reports were analyzed according to the database of the "Diabetic Foot" department of the health care institution "Minsk City Clinical Endocrinology Center" (MCCEC). Indicators for 2019-2023 of adult patients with diabetes were evaluated.
Results
After implementation of a regulatory document defining the sequence of patient referral and routing the number of patients per year admitted to the MCCEC increased from 6883 in 2019 to 7633 in 2023. The percentage of patients initially admitted with DFS in 2019 was 19% and increased to 35.7% in 2023. There is a decrease in high amputations: at the hip level from 17.9% in 2019 to 15.2% in 2023, at the tibial level from 10.5% in 2019 to 8.9% in 2023. There is a gradual increase in the percentage of finger-level amputations from 61% in 2019 to 67% in 2023.
Conclusions
The analysis of statistics of specialized care for patients with DFS for 5 years has shown that the development of thematic documents and optimization of patient routing significantly increase the capacity of specialized care, which leads to early

detection of patients with DFS, and as a result - a decrease in the frequency of high amputations, which may reflect the improvement of the quality of patient management by endocrinologists and surgeons at the outpatient stage, and increase the effectiveness of prevention of lower limb lesions.

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EP72

Mitochondrial diabetes in relation to 40 patients from 30 tunisian families: phenotypic and genotypic heterogeneity

Hamdi Frikha, Yesmine Elloumi, Souhir Maalej, Khouloud Boujelben, Dhoha Ben Salah, Faten Haj Kacem Akid, fatma mnif, nadia charfi, mouna mnif, mouna elleuch, Mohamed Abid & Nabila Rekik Majdoub
Hedi Chaker University Hospital, Department of Endocrinology, Tunisia

Introduction
Mitochondrial diabetes (MD) is characterized by a wide spectrum of phenotypic and genotypic manifestations. Through a cohort study of 40 patients with MD, we attempted to establish a correlation between this diversity of phenotypic expression and the biomolecular substrate of the mitochondrial genome within the Tunisian population.
Results
Epidemiologically and anthropometrically, our series aligns with literature data, with an onset age of 31.6 years (5-52), a female predominance (82.5%), and a normal BMI in 60% of cases. Diabetes had a MIDD2 phenotype in % of cases, with a significantly higher frequency of diabetic retinopathy (42.5%) compared to 8-13% in the literature. Regarding extra-pancreatic manifestations, the reticulated macular dystrophy, highly characteristic of MD, was absent in all our patients, as well as retinitis pigmentosa (15% vs 57-86%). Perceptive deafness, classically almost constant, was present in only half of the cases. Dilated cardiomyopathy was found in only one case vs 18-34% in the literature. The biomolecular study of the mitochondrial genome revealed the absence of the most frequently described mutation associated with MD: m.3243A>G (tRNA Leu). This led us to investigate the m.14709T>C (tRNA Glu) mutation, found in 6 patients from 3 different families; however, the study of heteroplasmy levels within 2 families did not reveal a correlation with the phenotypic spectrum. Moreover, whole mitochondrial genome sequencing revealed other polymorphisms not described in the literature, playing a key role in the functioning of the mitochondrial respiratory chain.
Conclusion
Our cohort is characterized by phenotypic and genotypic heterogeneity within a sample of the Tunisian population. It appears that the m.3243A>G mutation is not specific to our Tunisian population, and the m.14709T>C mutation was more frequent. A larger-scale study is necessary to establish the impact of heteroplasmy levels on the phenotypic spectrum.

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EP73

Impact of socio-economic status on glycemic control in type 2 diabetic patients: a study of 216 cases

Nabil Skouta, Nassim Essabah Haraj, Siham El aziz & Asma Chadli
UHC Ibn Rochd, Casablanca, Morocco, Department of Endocrinology, Diabetology and Metabolic Diseases, Casablanca

Introduction
Type 2 diabetes constitutes a major public health problem. In 2017, the International Diabetes Federation estimated that 425 million people worldwide suffer from diabetes, and by 2045, this number is projected to rise to 629 million.
Objectives
The aim of our study is to assess the impact of patient's socio-economic status (SES) on their glycemic control.
Patients Et Methods
This is a descriptive cross-sectional study involving 216 type 2 diabetic patients, followed in the Diabetology department at Ibn Rochd University Hospital in Casablanca from March 2023 to November 2023. The classification used for socio-economic status is provided by the High commission for planning of Morocco: Low SES (income < 350$/month), Moderate SES (income between 350-2300$/month), High SES (income > 2300$/month). Data were collected using an exploitation form and analyzed using IBM SPSS Statistics 27.0.
Results
Our study included 216 patients with a mean age of 59 years and a M/F ratio of 2.48. The average duration of diabetes was 13 years. Regarding cardiovascular risk factors, 67% were hypertensive, 39% were obese, 41% had dyslipidemia, and 13% had toxic habits. Ischemic heart disease and peripheral arterial disease were found in 15% and 16% of cases, respectively, while retinopathy and diabetic nephropathy were present in 54% and 20% of cases, respectively. In our series, 20% of patients had a moderate SES with an average HbA1c of 7.02%, while 80% had a low SES with an average HbA1c of 11.25%. The mean difference in HbA1c levels between low and moderate SES individuals was 4.22% (95% CI 3.83;4.61) ($P < 0.0001$).
Conclusion
Our study indicates that socio-economic status influences the stability of individuals with type 2 diabetes. Individuals with a higher socio-economic status face fewer challenges in adhering to treatments such as GLP-1 agonists, SGLT2 inhibitors, or the latest-generation insulins, which are costly but more effective.

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EP74

Predictors of carbohydrate metabolism disorders within 1 year after COVID-19

Zilya Kalmykova, Marina Shestakova, Irina Kononenko & Natalia Mokrysheva
Endocrinology Research Centre, Moskva, Russian Federation

Background
The potential impact of SARS-CoV-2 on glucose metabolism has been discussed since the first days of the COVID-19 pandemic, and now has been confirmed by research results and clinical practice data about new-onset carbohydrate metabolism disorders after COVID-19. Determining the predictors of their development will help to determine the best treatment tactics.
Aim
To determine predictors of carbohydrate metabolism disorders within 1 year after COVID-19.
Materials and methods
We included consecutive patients hospitalized with viral pneumonia caused by COVID-19. All underwent a clinical and laboratory examination, including assessment of carbohydrate metabolism indicators (blood glucose on admission, fasting plasma glucose, HbA1c, proinsulin, insulin, C-peptide, HOMA-IR). The prospective part of the study included patients without previous history of diabetes mellitus, who had HbA1c > 6.0% during the acute period of the COVID-19. In this group, patients underwent an oral glucose tolerance test (OGTT) 6-8 weeks and 1 year after discharge. In patients, which developed prediabetes and diabetes after COVID-19, we performed a comparative analysis of clinical and laboratory parameters.
Results
We included 155 hospitalized patients with acute phase of COVID-19: median age 59 years [47;72], male/female ratio (%) - 49,4/50,6, BMI – 28,9 kg/m2 [25,4;32,9]. Among these patients, 55 had elevated HbA1c values without previous DM history: HbA1c 6,1-6,4% - 36 patients, HbA1c ≥ 6,5% - 27 patients. During the follow-up 1 year after COVID-19, 33 patients were lost to follow-up, 12 patients developed carbohydrate metabolism disorders, and 10 were euglycemic. We found differences in baseline proinsulin levels between groups with and without carbohydrate metabolism disorders on follow-up: 0,58 mIU/l [0,26; 0,94] and 1,16 mIU/l [0,98; 2,47], respectively ($P < 0,001$). AUC for baseline proinsulin levels estimated 0,906 (95% CI, 0.784-1.000, $P < 0.001$), with cut-off 1,10 mIU/l to distinguish patients with/without carbohydrate metabolism disorders at follow-up. The model had acceptable NPV, 93,8% (83,5%- 99,6%), however, PPV was low, 54,4% (14,1%- 77,2%).
Conclusion
Baseline proinsulin levels with a cut-off at 1,10 mIU/l could be potential predictor of long-term carbohydrate metabolism disorders in patients without previous DM history after COVID-19. However, further studies with extended groups and longer follow-up are needed to confirm this finding.

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EP75

Fournier's gangrene in diabetic women: 2 case reports

Ilham Midhat, Mennani Fatimaeezzahra, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Centre Hospitalo-Universitaire Mohammed Vi Marrakech, Endocrinology, Marrakech, Morocco

Introduction
Fournier's gangrene is a rare and serious poly-microbial necrotizing fasciitis of the perineum and external genitalia, characterized by a fulminant evolution and a high morbidity and mortality. Annual incidence is between 1.6 and 3.3 cases/100,000 patients, with type 2 diabetics accounting for 30% to over 50% of cases, and 66% in women.
Observations
Case 1: 48-year-old female, diabetic for 8 years on Metformin, admitted for diabetic ketosis on Fournier's gangrene, revealed by a swelling associated with pain in the perianal and gluteal region, rapidly complicated by perianal necrosis extending to the left thigh, evolving for 7 days in a context of fever quantified at 39°c. Biological work-up revealed a frank infectious syndrome with Enterococcus Feacalis on pus sampling.
Case 2: Patient aged 43, admitted for diabetic ketoacidosis inaugurated by Fournier's gangrene, revealed by an ulcerated lesion in the left perianal area 4 months previously. The lesion was manipulated, and rapidly spread to the left buttock area, evolving in a context of fever at 39.4°c. Biological tests revealed a frank infectious syndrome with Streptococcus Agalactiae in the pus sample. Both patients received triple broad-spectrum probabilistic antibiotic therapy, then adapted to the antibiogram, and underwent immediate broad-spectrum surgical debridement with insulin initiation followed by intensification. The average hospital stay was 20 days. One patient had a favorable outcome after a stay in intensive care, with good progress in directed healing. After stabilization, patients received therapeutic education on the need for hygiene and early consultation in the event of any injury to the perineal region.
Discussion and conclusion
Necrotizing skin and soft-tissue infections are characterized by rapid, deep-seated spread along the fascia and destruction of the skin, hypodermis and muscles. Clinical presentations vary according to the location and extent of lesions, the bacteria involved and predisposing factors linked to the infected subjects. They may be monomicrobial (especially streptococci/staphylococci) or polymicrobial. Fournier's gangrene most often occurs in an immunocompromised environment: diabetes (40-60% of cases), alcoholism, malnutrition and poor sanitary conditions are frequent predisposing factors, as are immune deficiencies: chemotherapy, AIDS, advanced age.... Women are affected much more rarely, and the starting point of the disease is often gynecological. Treatment must be initiated urgently, based on broad-spectrum antibiotic therapy, hemodynamic stabilization measures and, above all, rapid surgical cure by debridement and radical excision of necrotic tissue, in order to reduce the still high mortality rate, as well as aesthetic and functional sequelae.

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EP76

Complications and metabolic control in adults with diabetes aged 16-25 years old

Francisca Leitão[1], Sae Zambre[2], Lucy Du[2], Maria Carlos Cordeiro[1] & Ana Quitalo
[1]Hospital Garcia de Orta; [2]Translational Research Institute

Introduction
Diabetes mellitus (DM) is a chronic disease with increasing incidence worldwide, mostly in younger ages. Diabetic kidney disease (DKD) is a main complication, with a prevalence of 20-40%, associated with high cardiovascular mortality. Despite the association of type 2 diabetes (T2D) in young adults with rapid progression to DKD, in type 1 diabetes (T1D) this is not well established. Other complications have also a high impact on life quality.
Objective
Evaluate the difference in the metabolic control and incidence of complications associated with T1D and T2D in young adults.
Methods
Retrospective cohort study including all cases of patients with DM aged 16 to 25 who attended MYAHC (Mater Young Adult Health Centre, Brisbane), between 2016-2020. Cases with less than 2 GFR measurements were excluded. Values of glycated haemoglobin (HgA1c) were collected.
Results
Were analysed 576 patients, 548 with T1D and 28 with T2D. In total, 59% were female, the mean age at first visit was 19.3 and the median time since diagnosis was 16 years. CKD of diabetic aetiology was found in 14.4% of T1D group, 2 of them with ESKD (0.3%), compared with 71.4% in T2D group, none with end-stage kidney disease (ESKD). Cases of CKD of another aetiology were found only in T2D group (10.7%). GFR was lower than 90 ml/min/1.73 m^2 in 19.9% of T1D group, compared to 7.1% in T2D group. GFR below 60ml/min/1.73 m^2 was only found in 0.7% of T1D group. Overall, the decrease in GFR per year was an average of 2.11 ml/min/1.73 m^2 in T1D group compared to 0.98 ml/min/1.73 m^2 in T2D group. For other chronic complications: peripheral neuropathy was found only in T1D group (3.1%); 12.2% of T1D presented with retinopathy compared to 7.1% in T2D group; autonomic neuropathy was present in 64.3% of T2D group, compared with 2.2% in T1D group. Better metabolic control was noted in T2D, with a HgA1c of 7.2 compared to 7.8 in T1D group.
Conclusion
Regardless higher incidence of DKD in the T2D group, there was higher incidence of ESRD along with greater decline in eGFR/year in T1D group. Also, overall incidence of other complications was higher in T1D. Although these can possibly be explained by the small number of young people diagnosed with T2D, these results suggests that the progression rate towards DKD is higher and more abrupt in young adults with T1D. Better metabolic control in T2D reinforces the importance of intensive treatment in T1D.

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EP79

Common disease rare complication: diabetic myonecrosis

Selin Çetin[1], Alperen Onur İşler[2], Büşra Torun Alp[1], Adalet Elçin Yıldız[3], Tolga Yıldırım[4] & Uğur Ünlütürk[2]
[1]Hacettepe University School of Medicine, Department of Internal Medicine, Ankara, Turkey; [2]Hacettepe University School of Medicine, Division of Endocrinology and Metabolism, Department of Internal Medicine, Ankara, Turkey; [3]Hacettepe University School of Medicine, Department of Radiology, Ankara, Turkey; [4]Hacettepe University School of Medicine, Division of Nephrology, Department of Internal Medicine, Ankara, Turkey

Background
Diabetic myonecrosis is a rare complication associated particularly with prolonged dysregulation of blood glucose in diabetes. While the exact pathophysiology remains not fully understood, it is suggested that atherosclerosis, diabetic microangiopathy, vasculitis, ischemia-reperfusion injury and hypercoagulability might contribute to this condition. Diabetic nephropathy is the most blamed risk factor. Here, we present a case of diabetic myonecrosis followed up after renal transplantation due to diabetic nephropathy.
Case Presentation
A 40-year-old female patient with known type 1 diabetes, situs inversus and hypertension, who had a kidney transplant from a living donor due to diabetic nephropathy, was admitted to the internal medicine clinic due to progressive decrease in glomerular filtration rate (9 ml/dk). She had uncontrolled type 1 diabetes for 30 years with retinopathy, neuropathy, hypertension and nephropathy leading to ESRD. She had a diabetic foot arthroplasty in her history. HbA1c value was 11.7%. One week before the patient's admission, she developed swelling, pain, and restricted mobility in the upper left thigh. The findings were significant in terms of infectious-inflammatory processes. WBC was $14.54 \times 10^3/\mu L$ (4.49-12.68×10^3), sedimentation rate was 15 mm/hour (0-25), CRP was 17.9 mg/l ($<$ 0.5) creatine kinase total was 58 U/l ($<$145) in laboratory examination. A lower extremity Doppler ultrasound was performed and didn't reveal any evidence of deep vein thrombosis (DVT). The skin ultrasound result showed edematous changes and thickening in the subcutaneous tissue of the symptomatic area with no significant drainable abscess or collection detected. In a contrast-free MRI imaging performed for differential diagnosis, myositis and fascial edema were observed in the vastus medialis and intermedius muscles on the left, along with a focal area suggesting necrosis within the vastus medialis. MRI findings indicated diabetic myonecrosis. During this period, blood glucose control was achieved with insulin glargine and insulin aspart. In the treatment of diabetic myonecrosis, bed rest and elevation of the extremity were applied. NSAIDs could not be given because her kidney functions were impaired. Oxycodone 10 mg/day was given for pain palliation. The patient's complaints and symptoms regressed in 15 days.
Conclusions
Despite diabetes being a common disease, diabetic myonecrosis is an uncommon and challenging complication to diagnose. In the diabetic patients especially who have diabetic nephropathy, in situations of sudden onset pain and swelling in the lower extremities, diabetic myonecrosis, should be considered in the differential diagnosis and MRI should be performed.

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EP92

Analysis of glycated hemoglobin trajectories in chd patients with dm 2

Raisa Trigulova[1] & Shahnoza Mukhtarova[2,2]
[1]Republican Specialized Scientific and Practical Medical Center for Cardiology, Tashkent, Uzbekistan; [2]Tashkent Pediatric Medical Institute, Tashkent, The Republic of Uzbekistan, Tashkent

Introduction
The stability of glycated hemoglobin (HbA1c) as a key to the prevention of micro-and macrovascular complications continues to be discussed.
Purpose
to analyze the interrelations between HbAc trajectories and clinical and biochemical parameters in patients with CHD and DM 2.
Material and methods
130 patients with CAD and DM-2 aged 63.9±8.8 years. Therapy: DPP-4 inhibitors, GLP agonists. Groups: HbA1c <7.0 (n-27; A); 7.0<HbA1c<8.0 (n-25; B); HbA1c > 8.0 (n-78; C). 2 years of observation.
Results
In patients with unchanged HbA1c, there is an increase in vitamin D: with HbA1c<8, n-47 Δ 6.54 ng/ml, $P=0.003$; HbA1c>8.1, n-50 Δ 8.24 ng/ml, $P=0.004$. CRP and BNP in dynamics: HbA1c<8, n-47 Δ 4.18 ng/ml, $P=0.002$ and Δ 363.0 pg/ml, $P=0.01$, respectively. HbA1c > 8.1 CRP and BNP n-50 Δ 2.75 ng/ml, $P=0.02$ and Δ 432.2 pg/ml, $P=0.02$. A high content of UA is recorded in group C and Ć (with HbA1c > 8.1) ($P=0.02$). With HbA1c<8, there is a decrease in vitamin D 16.65[10.00-22.50] and a high BNP 2052.78 [1247.50-2977.50] pg/ml. A direct correlation was established between PPG and the metabolic index ($r=0.367$; $P=0.009$); vitamin D and BNP ($r=0.336$; $P=0.017$) and vitamin D with eGFR ($r=0.429$; $P=0.002$) in group C (HbA1c remained >8.1).
Conclusion
A two-year follow-up of HbA1c showed that alternating target values were recorded. Correlations of vitamin D in the blood (both deficiency and insufficiency) with high BNP in patients with HbA1>8.1 were revealed, which confirms the role of vitamin D in the progression of heart failure and renal dysfunction.

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EP97

Resilience in patients with fabry disease and its association with disease course, psychosocial factors and quality of life: a multicentre cross-sectional study

Albina Nowak[1,2] & Yaroslav Winter[3]
[1]university Hospital Zurich, Endocrinology, Zurich, Switzerland; [2]University Hospital of Zürich, Zürich, Switzerland; [3]University Hospital Mainz, Neurology

Fabry disease (FD) is an X-linked lysosomal storage disorder originating from mutations in the GLA-gene causing deficiency in alpha-Galactosidase A (GLA) which leads to the accumulation of glycosphingolipids, particularly globotriaosylceramide (Gb3) and globotriaosylsphingosine (Lyso-Gb3). The classic phenotype is characterized by neuropathic pains and pain crises, anhidrosis, abdominal cramping. With advancing age, the disease leads to life-threatening complications such as renal dysfunction, left ventricular hypertrophy, hypertrophic cardiomyopathy or cryptogenic stroke. These debilitating symptoms are associated with depression and impaired quality of life. Resilience is known as an individual's ability of coping with stressors and is characterized as high self-esteem, optimism and self-efficacy. Resilience enhancement programmes were shown to have a benefit on resilience, depression, anxiety and quality of life. 122 genetically confirmed FD patients from the university hospitals of Zurich Switzerland and Mainz Germany completed self-report questionnaires Resilience Scale 11 (RS-11), Beck Depression Inventory (BDI), Pain Disability Index (PDI), Pittsburgh Sleep Quality Index (PSQI), Trierer Inventory for Chronic (TICS-SSCS). Women indicated higher resilience scores than men (59 ± 14.4 vs 54.4 ± 19.2) and patients without enzyme replacement therapy (ERT) higher than on ERT (64.5 ± 15.9 vs 55.8 ± 16.5). Among females, resilience was higher if the FD diagnose was made at younger age ($r=-0.40$, $P=0.02$), while resilience declined with increasing age ($r=-0.26$, $P=0.04$). More symptomatic patients showed lower resilience scores ($r=-0.24$, $P=0.01$). The RS-11 showed a significant adverse correlation with BDI ($r=-0.59$; $P=0.001$), PDI ($r=-0.31$, $P=0.006$), PSQI ($r=-0.53$, $P=0.001$) and TICS-SSCS ($r=-0.42$, $P=0.001$). Our analyses show that impaired resilience is associated with depression, pains, poor sleep and chronic stress. All these factors are modifiable and treatable. Importantly, resilience enhancement programs should be offered to Fabry patients.

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EP99

Association between eating behavior and post-operative diabetes mellitus remission

Paula Sprovera, Carolina Monteiro Antunes, Maria Leonor Guia Lopes, Margarida Oliveira, Catarina Gama, Bruna Pimentel, Catarina Saraiva & João Manuel Sequeira Duarte
Egas Moniz Hospital, Endocrinology, diabetes and metabolism, Lisbon, Portugal

Introduction
Type 2 Diabetes Mellitus (DM2) remission after bariatric surgery can be achieved in 72% of cases. This mechanism is not fully dilucidated; however, it could be caused by the action of glucose direct deposit in the jejunum.
Objective
To assess the preoperative eating behavior impact in postoperative DM2 remission.
Materials and methods
A retrospective chart review among obese and type 2 diabetic patients that underwent bariatric surgery in a tertiary hospital center. Preoperative BMI and eating behavior were evaluated, as well as postoperative diabetes status and BMI.
Results
A total of 198 patients underwent bariatric surgery, of which 128 presented an altered glucose metabolism, corresponding to 64 cases of DM2 and 64 pre-diabetic patients. Most diabetic patients were women (78%), with initial mean weight of 114.7 kg, while male patients presented 154.5 kg. The mean BMI was 42.1 kg/m2 and 49 kg/m^2, respectively. In the eating behavior evaluation, 28% of the diabetic patients were classified as 'volume-eater', 15.6% as 'sweet-eater' and 6.25% as 'snack-eater'. Half of the sample presented a mixed-pattern eating behavior, being the most frequent combination the 'Volume-sweet-eater' mixture. Most diabetic patients (71.8%) underwent a gastric bypass (GBP) and 28.2% underwent a vertical sleeve gastrectomy (VSG). In the GBP group, 46% of patients achieved diabetic remission at 5 years of assessment and there were no cases of remission in the VSG group. The eating behavior that presented most cases of remission was the 'volume-sweet-eater' pattern with 100% of cases of normoglycemia after bariatric surgery ($P=0.004$). The other patterns did not present statistically significant remission.
Conclusion
It seems that therés an association between the 'volume-sweet-eater' behavior and post-operative DM2 remission.

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EP100

Exogenous insulin antibodies syndrome: challenges in management

Sahar Abidi, Manel Jemel, Emna Naccache, Marwa Chiboub & ines Kammoun
Departement of Endocrinology, National Institute of Nutrition, Tunis, Tunisia

Introduction
Exogenous insulin antibodies syndrome (EIAS) is a clinical syndrome associated with insulin antibodies induced by exogenous insulin in diabetic patients. It represents a rare cause of hyperinsulinemic hypoglycemia and glycemic instability. The management of EIAS remains a challenge.
Case presentation
We present the case of a 12-year-old female with type 1 diabetes for 6 years treated with insulin analogues (Glrargen and Aspart). She experienced significant glycemic instability, leading to frequent hospitalizations for diabetic ketosis and ketoacidosis with no apparent cause, resulting in an average HbA1c of 14%. Her mother reported discontinuation of rapid insulin due to recurrent hypoglycemia. The patient weighed 32 kg, had a height of 145 cm (-2DS), and investigations revealed an isolated growth hormone deficiency. The anti-exogenous insulin antibody titer was elevated at 24 UI/ml (VN <0.4). Treatment with a high dose of corticosteroids (30g of prednisolone) resulted in a favorable response, marked by a significant improvement in glucose stability and no unexplained hypoglycemia. Corticosteroids were maintained for 4 months and then gradually tapered. However, after discontinuation, a recurrence of glycemic instability was observed.
Discussion
EIAS typically manifests months or years after initiating insulin treatment and can affect both type I and II diabetes patients. It is a rare cause of glycemic instability, characterized by daytime hyperglycemia due to insulin uptake by anti-insulin antibodies and nocturnal hypoglycemia due to insulin release. The initial treatment of EIAS involves glucocorticoids. In our case, we initiated treatment with 2 UI/kg of prednisolone for 4 months, with a gradual dose reduction. The

literature suggests alternative treatments, including oral or IV immunosuppression such as mycophenolate mofetil, cyclophosphamide, and azathioprine, although outcomes vary. Plasmapheresis can serve as effective therapy in patients who are refractory to other therapeutic modalities based on the results of literature review and case reports.
Conclusions
EIAS should be considered in T1D patients with unexplained glycemic instability and hypoglycemia. The laboratory plays an integral diagnostic role. The management of EIAS is poorly codified. Longer-term follow-up is necessary, as recurrence is classic in this type of pathology

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EP101

Side effects of mesenchymal stem cell transplantation in type 1 diabetics department of endocrinology, diabetology, metabolic

Mennani Fatima Ezzahra, Sana Rafi, Ghizlane EL Mghari & Nawal EL Ansari
Centre Hospitalo-Universitaire Mohammed VI Marrakech, Endocrinolgy, Marrakech

Introduction
According to numerous studies, mesenchymal stem cell therapy is one of the best therapeutic approaches for the treatment of type 1 diabetes. The aim of our study is to provide an update on the contribution of mesenchymal stem cells to glycaemic control and the screening of short-and long-term side effects.
Results
We included 5 patients who met our inclusion criteria. The mean age was 21.2 years, with a sex ratio of 0.6. The average duration of diabetes in our patients was 2 years and 3 months. Minor incidents in the immediate postoperative period were nausea and vomiting in 30% of patients, pain at the sampling site in 10%, and no patient presented a major incident in the immediate postoperative period. In terms of glycaemia: GAJ and GPP fell from 1.63 and 2.01 pre-transplant to 1.28 and 1.52 respectively after 18 months post-transplant, the mean daily dose of basal insulin fell from 0.46 IU/Kg/d pre-transplant to 0. 37 IU/Kg/d after 18 months' follow-up, for rapid insulin requirements fell from 17.5 IU/d pre-transplant to 11.5 IU/d, and marked weight gain was observed in 40% of patients after 18 months' post-transplant follow-up.
Discussion
Dave and trivedi published in 2013 their results of post-MSC transplant follow-up in 2 T1DM patients, insulin requirements reduced from 64 and 56 IU/day to 18 and 22 IU/day after 23 months of follow-up, HbA1c levels reduced from 9.1%, to 6.3% in the 1st patient and 12.4%, to 6.8% in the 2nd patient, without any side effects. Another review published in China in March 2022 by Xin Xing Wan showed that stem cell transplantation had beneficial effects in newly diagnosed type 1 diabetics, with no obvious adverse effects.
Conclusions
Mesenchymal stem cells represent an avenue for the future that will open up new therapeutic prospects in T1DM because of their immunomodulatory properties, ease of isolation, abundance and safety of use.

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EP104

Quality of life of patients with diabetes type 1 and type 2 in the conditions of military conflict

Oksana Khyzhnyak, Miroslava Mykytyk & Urii Karachentsev
V. Danilevsky' Institute of Endocrine Pathology Problems, Clinical Endocrinology, Kharkiv, Ukraine

The military conflict in Ukraine triggered the internal migration of millions of Ukrainians. Internally displaced persons (IDPs) and residents of territorial communities (RTCs) located in zones of war with Diabetes mellitus (DM) are at high risk of developing post-traumatic stress disorder (PTSD), anxiety and depression.
The aim of the study was to assess the health-related quality of life (HRQoL) of patients with DM type 1 (DM T1) and type 2 (DM T2) in the context of military conflict.
Materials and methods
26 patients with DMT1 ((34.7 $\pm$ 8.79) yrs, disease duration (DD) (11.0 $\pm$ 10.5) yrs) and 65 patients with DMT2 ((56.5 $\pm$ 10.79) yrs, DD (6.9 $\pm$ 5.1) yrs) were examined. 43.9% ($n=40$) were IDPs and 56.1% ($n=51$) RTCs located in the war zone. The Ukrainian-language version of the "SF-36®Health Survey" questionnaire was used to assess the health care system. Subjective feelings of patients were analyzed using the HADS Hospital Anxiety and Depression Assessment Scale. Statistical processing of the results was performed using Package for Social Sciences v.16.0 (SPSS Inc, Chicago, Il, USA).
Results and discussion
It was found that the physical activity of patients with DM was significantly limited by their health status. Patients with DM T1 rated their general health status higher on the 'general health status' scale than patients with DMT2. In patients with DMT2, the average score on the 'mental health' scale was significantly lower than in patients with DMT1, which indicated the possible development of PTRs. It was determined that the physical activity of MTG-patients is significantly limited by their health status compared to the IDPs group. Assessment of the severity of depressive symptoms on the HADS-D subscale showed that in 46.2% ($n=42$) of the examined the total score was within the normal range, in 24.2% ($n=22$) it corresponded to subclinical depression and in 29.7% ($n=27$) – clinically significant depression. The total score on the HADS-D subscale in MTG-patients is significantly higher than in the IDPs group ((7.81 $\pm$ 0.34) and (4.86 $\pm$ 0.29), respectively; $P < 0.04$).
Conclusion
In conditions of war conflict, patients with DMT2 compared to patients with DMT1 experienced a more significant deterioration in PCH and mental component of health (MCH). MTH-patients with DM due to the deterioration of PCH and MCH, have more significant restrictions in daily activities, social contacts, and a decrease in the level of communication than IDPs. 53.9% of patients with DM in the conditions of a military conflict develop clinical depression of varying severity, 50.6% - clinical anxiety.

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EP105

Comorbidity of autoimmune diseases in pediatric patients with type 1 diabetes mellitus: a retrospective analysis

Irina Bojoga[1,2], Sorin Ioacara[1,2] & Simona Fica[1,2]
[1]'Elias' University Emergency Hospital, Endocrinology and Diabetes, Bucharest, Romania; [2]'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania

Background and Aims
The concurrent presentation of Type 1 diabetes mellitus (T1DM) with other autoimmune disorders, notably autoimmune thyroiditis and celiac disease, has been substantiated in numerous studies. Established guidelines advocate for routine screenings for these disorders at the onset of T1DM diagnosis, followed by periodic evaluations — biennially for thyroid pathologies and every 2-5 years for celiac disease. This research endeavours to elucidate the prevalence of these autoimmune comorbidities in pediatric patients with T1DM receiving care at our Endocrinology and Diabetes Department.
Methods
We engaged in a meticulous retrospective analysis encompassing pediatric patients diagnosed with T1DM and monitored systematically for associated autoimmune pathologies within our facility. Thyroid anomalies were scrutinized through assessments of TSH, anti-thyroid peroxidase antibodies, and antithyroglobulin antibodies, supplemented by examinations for thyroid stimulating hormone receptor antibodies in instances of suppressed TSH to preclude Basedow-Graves disease. Meanwhile, the prevalence of celiac disease was determined through the measurement of anti-transglutaminase IgA antibodies alongside the total IgA level.
Results
The cohort incorporated 565 patients characterized by a median age of 7.3 $\pm$ 4 years at the time of T1DM diagnosis, with a slight male predominance (50.8%). A substantial fraction, 25.6%, manifested at least one additional autoimmune disorder, itemized as follows: autoimmune thyroid disease (20%), differentiated further into Hashimoto thyroiditis (19.2%) and Basedow-Graves Disease (0.8%); celiac disease (2.65%); and other autoimmune maladies, including psoriasis and megaloblastic anemia (0.7%). Moreover, a smaller segment encountered dual diagnoses: Hashimoto thyroiditis and celiac disease (2.1%), and a singular case exhibited coexistence of thyroiditis and psoriasis. Of those diagnosed with Hashimoto Disease, a noteworthy 27.6% necessitated substitution therapy with levothyroxine.
Conclusions
The data delineates a significant incidence of autoimmune comorbidities in pediatric patients with T1DM treated at our department, with one in four patients afflicted. The findings underscore the imperative of regular screenings to facilitate timely diagnosis and intervention, a practice integral in fostering the well-being and normative development of pediatric patients.

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EP108

Chrono-type of obese patients

Mouna Elleuch, Wissal Ghamgui, Nadia Charfi, Feten Hadj Kacem, Nabila Rekik & Mohammed Abid
Hedi Chaker Hospital, Endocrinology and Diabetology department, Sfax, Tunisia

Introduction
The chrono-type, intrinsic to each individual, is the tendency of an individual to prefer activities carried out in the morning or evening. The aim of our study was to determine the chronotype of our obese patients.
Materials and methods
This is a descriptive cross-sectional study involving obese adults consulting the service of Endocrinology of Sfax, Hedi Chaker University Hospital, during the period extending from December 2022 until March 2023. Our patients were subject to the typology questionnaire circadian of Horne and Ostberg.
Results
We recruited 40 obese patients. The average age was 43.47 years × 16.56. The sex ratio was 0.21. Fifteen percent of patients were smokers. The average duration of obesity was 20 years × 13.25. The average weight was 95.17 kg. BMI average was 35.96 × 5.04 kg/m^2. The average score of Horne's circadian typology and Ostberg was 55.93 × 11.28. The chrono-type of our patients was distributed as follows: 5% were very morning, 47% were moderate morning, 32% were neutral, 15% were moderate evening and no patient was entirely in the evening.
Conclusions
Only 15% of patients had an evening chronotype. According to several authors, people with an 'evening' chrono-type are more at risk of developing overweight or obesity mechanisms to explain this association are not yet fully elucidated, which must push us to carry out more research on this subject.

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EP112

Diabetic pregnancy: adherence and benefits of regular physical activity on blood sugar control in diabetic pregnant women

Rakia Bachir Moctar, Salma Bensba, Nassim Essabah Haraj, EL Aziz Siham & Asma Chadli
CHU Ibn Rochd, Casablanca, Morocco, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Casablanca, Morocco

Introduction
Regular physical activity, the right diet and medication can help diabetics achieve optimal glycemic and mental balance.
The objective of the study is to assess the prevalence of regular physical activity (APR: ≥30 min/day, 3 times/week) and its effect on glycemic control.
Patients and methods
Our work is a retrospective study, including 449 patients with diabetic pregnancies followed at the Endocrinology-Diabetology department between January 2016 and January 2022. To do this work, we used SPSS software.
Results
The study included 449 patients with a mean age of 32 years. The prevalence of patients engaged in regular physical activity was 42.14% (n = 189). Two groups of patients, G1: patients with regular physical activity and G2: "sedentary" patients. The mean BMI of the G1 was 25.4 kg/m^2 compared to 29.8 kg/m^2 for the G2. G2 had an average fasting blood glucose of 1.8 g/l vs G1: 0.86g/l. Glycemic control was significantly better in G1: mean HbA1C = 6.8% vs 7.2% G2. This, with less severe hypoglycemia in the G1 but not significant.
Discussion and Conclusion
Our study showed the importance of APR on glycemic control. As a result, it is an inexpensive and effective prevention of cardiovascular disease. Hence the need for therapeutic education to encourage RPA.

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EP119

Phospholipid composition of hippocampal membranes in rats with the induced sporadic neurodegenerative condition

Talat Saatov, Gulnora Artykbaeva, Tokhir Ishankhodjaev & Mukhammadjon Mustafakulov[1,1]
Institute of Biophysics and Biochemistry, Mirzo Ulugbek National University of Uzbekistan, lab of metabolomics, Tashkent, Uzbekistan

Alzheimer's disease is closely associated with type 2 diabetes mellitus (DM); being considered as type 3 DM due to common molecular peculiarities of type 2 DM and insulin resistance associated with the memory deficit and decline in the cognitive functions in elderly persons. We generated a model of sporadic neurodegenerative condition (NDC) or type 3 DM. The work was initiated to study profile of phospholipids in the hippocampal membranes of rats with the induced sporadic NDC.
Materials and methods
Within long period of time, the animals have been kept on the high calorie diet subsequently administered with neurotoxin. The phospholipids were fractionated by thin-layer chromatography. All experiments with animals were conducted in compliance with the regulations of the Committee on bioethics at the Institute of Biophysics and Biochemistry.
Results and discussion
Monitoring of the type 3DM was conducted by regular testing of behavior functions of animals, as well as their blood biochemical examination. The sporadic model of NDC with symptoms of Alzheimer's disease or type 3 DM induced, the lysoforms of phospholipids (14.1 ± 0.6 vs 10.3 ± 0.5 μg of phosphorus/g of tissue in the controls), phosphatidic acid (18.2 ± 1.2 vs 14.9 ± 0.8 μg of phosphorus/g of tissue) and cholesterol (22.6 ± 0.3 vs 19.0 ± 0.3 μg of phosphorus/g of tissue, P < 0.05) were found increased next to insignificant reduction in macro-components, to name phosphatidylcholine (542.0 ± 21.6 vs 559.8 ± 25.6 μg of phosphorus/g of tissue), sphingomyelin (108.1 ± 3.221 vs125.2 ± 3.8 μg of phosphorus/g of tissue), phosphatidylethanolamine (488.3 ± 19.1 vs 491.4 ± 21.4 μg of phosphorus/g of tissue), in micro-components, such as phosphatidylserine (147.4 ± 6.1 vs 187.5 ± 9.5 μg of phosphorus/g of tissue), phosphatidylinositol (83.5 ± 3.5 vs 88.7 ± 4.8 μg of phosphorus/g of tissue), as well as in total phospholipids (1464.7 ± 32.3 vs 1537.4 ± 31.3 μg of phosphorus/g of tissue). As the components of intermediate part of bio-membranes, phospholipids make impact on the condition and functionality of a cell, as a whole. Phospholipids maintain functioning of the essential cell mechanisms, to name ion exchange, inner reparation, bio-oxidation, influencing fixation of enzymes in mitochondria and oxidative phosphorylation. Increase in lysoforms of phospholipids and phosphatidic acid under induction of the NDC model indicates activation of phospholipases, possibly producing effects on the microenvironment of acetyl choline receptors of the brain cells and neuroplasticity of the nerve cells.

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EP120

Association of AGEs and alcohol consumption with the incidence of diabetic neuropathy

Deimante Paskeviciene, Rasa Verkauskiene & Lina Radzeviciene
Lithuanian University of Health Sciences, Institute of Endocrinology, Kaunas, Lithuania

Background
Diabetic neuropathy (DN) is a major complication of diabetes, affecting one in three people with diabetes. The presence of peripheral neuropathy increases their risks of developing foot ulceration and subsequent necrosis that results in lower limb amputation. Good diabetes control helps to lower the risk of diabetic complications, which can be accelerated by advanced glycation end-products (AGEs) or alcohol consumption. AGEs are heterogeneous group of molecules, that normally accumulate slowly and in healthy people with natural ageing. Higher AGEs levels were associated with metabolic syndrome, cardiovascular disease, and diabetes-related complications such as DN. Alcohol consumption by persons with diabetes can worsen glucose control and diabetes-related medical complications, such as disturbances in fat metabolism or nerve damage. This study aimed to analyze the relationship between AGEs levels, patients' alcohol consumption and the presence of DN.
Materials and methods
AGEs concentration in the skin was non-invasively measured using ultra-violet light to excite autofluorescence with AGE Reader in 151 patients (age 18-85): no DN (78), with DN (73). Data on patients' clinical characteristics were collected from medical records and used to investigate associations between the presence of DN and the patients' AGEs concentration and alcohol consumption.
Results
The median diabetes duration was 14 years, age – 55 years. The study cohort consisted of 83 (55.0%) women and 68 (45.0%) men. The presence of DN significantly depended on alcohol consumption ($r_{cramer's}$ = 0.232, P < 0.01). Patients who consume alcohol are more likely to have complications of DN than patients who do not consume alcohol (P < 0.01). There were no significant associations between AGEs concentration and alcohol consumption (P = 0.232) and the presence of DN complication (P = 0.575). However, there was a positive correlation between AGEs concentration and age (r = 0.474, P < 0.001), BMI (r =

0.161, $P<0.05$), duration of diabetes ($r=0.293$, $P<0.001$). The odds of developing DN is 2.57 (CI 1.33 – 4.96) times greater for people, who consume alcohol ($P<0.01$).
Conclusions
Patients consuming alcohol were more likely to have a DN complication. Alcohol consumption did not have any influence on the levels of AGEs.
Funding
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EP121

Comparison of admissions for diabetic ketoacidosis in patients with autoimmune diabetes and type 2 diabetes in the san cecilio clinic university hospital

Javier García Sánchez, Elena Martínez Silla, Raúl Rodríguez Juárez, Laura Cánovas Noguera, Enrique Redondo & Pablo José López-Ibarra Lozano
San Cecilio Clinical University Hospital, Endocrinology and Nutrition, Granada

Introduction and objectives
Diabetic ketoacidosis (DKA) is a severe acute complication of Diabetes Mellitus (DM) and may require hospital admission. Our aim was to compare the characteristics of DKA occurring in patients with autoimmune DM (AMD) and type 2 DM (DM2) in our setting.
Methods
Retrospective observational study. Patients with AMD and DM2 admitted for DKA at the Hospital Universitario San Cecilio de Granada between January 2019 and December 2023 were compared. Variables related to the disease and to the episode of CAD were analyzed. Analyses were carried out with SPSS 25.0.
Results
85 patients with AMD and 16 with DM2 were included (48.5% women, with no significant differences between the two groups). The mean age was significantly higher in DM2 (35.21 vs. 56.13 years, $P<0.05$) and the time of evolution was similar in both groups (15.37 $\pm$ 11.53 and 14.77 $\pm$ 9.97 respectively). BMI was significantly higher in the DM2 category (31.47 vs 21.4 kg/m^2, $P<0.05$). Admission for CAD was the manner of debut in 25.9% of patients with AMD and in 31.25% of DM2. Of the patients with AMD, 64.5% had previously presented an episode of DKA. The most important precipitating factor in AMD was omission of treatment while in DM2 it was concomitant infections. No significant differences were found in terms of the need for ICU stay or the number of days in the ICU and on the hospital ward between the two groups. In those patients with DM debut, patients with DM2 have higher basal and rapid insulin needs (31 vs 15.6 IU, $P<0.05$; and 34.67 vs 21.6 IU, $P<0.05$; respectively). Metabolic control in terms of HbA1c was worse, with a tendency to significance, in the AMD group (11.01 vs 10.02%, $P=0.064$). No significant differences were observed in analytical parameters (blood glucose, pH, HCO3 and lactic acid) at admission.
Conclusions
In our work, it was observed that admissions for DKA in our center were more frequent in patients with AMD, despite the fact that these present better metabolic control and lower insulin requirements at debut. On the other hand, there is a tendency for most episodes of DKA in DM2 to be associated with infections, while the main risk factor in patients with AMD is the omission of treatment.
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EP122

Type 1 diabetes mellitus and metabolic syndrome

Dhoha Ben Salah, Siddiqa Soomauroo, Mouna Elleuch, Khouloud Boujelben, Faten Hadjkacem, Nadia Charfi, Fatma Mnif, Mouna Mnif, Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Metabolic syndrome (MS) is responsible for the increased cardiovascular risk in type 2 diabetics. There is a scarcity of research on the metabolic syndrome among individuals diagnosed with type 1 diabetes (T1DM). The aim of this study is to describe clinical, biochemical and therapeutic characteristics of T1DM with MS.
Materials and Methods
Retrospective study including 36 patients, with T1DM and MS, hospitalized in the department of Endocrinology in Hedi-Chaker Universital Hospital in Sfax/Tunisia, from 1997 to 2020. MS was defined according to the NCEP-ATP III criteria.
Results
The average age of our patients was 53 years (extremes: 26-80). A male predominance was noted with a sex ratio of H/F to 1,4. The average duration of diabetes was 15 years. Metabolic syndrome occurred after an average duration of diabetes of 13.7 years. Hypertension was noted in 21 patients (58.3%). The mean BMI was 26 kg/m^2, 19.7% of patients were obese. The average waist circumference was 95.5 cm $\pm$ 10.7. An android distribution of fat was present in 14 women. The mean total cholesterol level was 4.59 mmol/l $\pm$ 1.18 and mean triglycerides level was 1.67 mmol/l $\pm$ 0.81. Hypertriglyceridemia was present in 17 cases. The average HDL cholesterol level was 0,96 mmol/l $\pm$0.29. Low HDL-cholesterol level was present in 20 cases. The MS comprised of 3 criteria in 22 cases, 4 criteria in 11cases and 5 criteria in 3 cases. In the majority of cases, it was the combination of dyslipidemia, hypertension and diabetes (80%). Therapeutically, the average dose of insulin used was 0.8 IU/kg/day. The association of metformin was required in 18 cases (50%). Microvascular complications were present in all patients consisting of retinopathy (55.6%) and nephropathy (41.7%) and neuropathy (63.9%). Macrovascular complications, such as coronary insufficiency, were present in 20% of cases. The Cardiovascular risk was very high in all patients.
Conclusions
The prevalence of metabolic syndrome during type 1 diabetes is increasing. It indicates an increased risk for micro-and macrovascular complications.
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EP123

Insulin resistance and body composition in a pediatric population of acute lymphoblastic leukemia survivors

Iustina Grosu[1], Luminita Nicoleta Cima[1,2], Sabina Maria Dumitrache[1], Raluca Stan[1], Ana Zubaci[1], Marina Iliescu[1], Diana Puscasu[1], Cristina Jercan[3], Andreea Serbanica[3], Anca Colita[2,3] & Simona Fica[1,2]
[1]Elias Emergency University Hospital, Endocrinology and Diabetes, Nutrition and Metabolic Diseases, Bucharest; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [3]Fundeni Clinical Institute, Pediatrics, Bucharest, Romania

Background
Childhood acute lymphoblastic leukemia (ALL) is no longer a death sentence. With survival rates approaching 90%, focus needs to shift towards improving long-term quality of life. Compared to the general population, adult survivors have four-fold excess risk of mortality secondary to cardiovascular diseases. Thus, modifiable risk factors, such as altered glucose metabolism, are of great importance and should be actively sought after. Studies show high prevalences of insulin resistance(IR) from an early age in this population, but its pathophysiology is poorly understood. Proposed mechanisms include body compostion alterations, with increased fat mass, fat redistribution and decreased lean mass.
Study aim
We aimed to investigate the early development of glucose homeostasis disturbances in ALL survivors while still children and to determine the relationship of IR with body composition.
Methods
We registered 20 ALL survivors, aged under 18, in remission for at least one year, evaluated in the Pediatric Endocrinology Department between 2016 and 2022 (mean age 9.85 +/-3.68 years, range 4-17; average time from diagnosis 4.7 years). Anthropometric measurements (BMI, waist circumference, waist-to-hip ratio) and glycemic indices (fasting glucose and insulin, HbA1c, OGTT) were collected and compared with results from 12 healthy children matched for age and sex. IR was evaluated using HOMA-IR and QUICKI. DXA was performed to assess body composition in 12 survivors.
Results
Glycemic profile (fasting glucose, HbA1c, OGTT) was normal in both groups. However, ALL survivors were 50% more likely to have IR compared to healthy subjects (RR=1.5, 95%CI 1-2.23, $P=0.047$), despite no significant difference in BMI (mean z-score 0.26 $\pm$ 1.38 vs 0.05 $\pm$ 1.24, $P=0.7$). Higher mean HOMA-IR (2.76 $\pm$ 1.88 vs 0.97 $\pm$ 0.73, $P=0.0095$) and lower mean QUIKI (0.34 $\pm$ 0.04 vs 0.425 $\pm$ 0.08, $P=0.02$) were observed in ALL survivors. In the study population, HOMA-IR correlated with BMI ($r=0.57$, 95%CI 0.06-0.84, $P=0.03$), android-gynoid fat ratio ($r=0.65$, 95%CI 0.09-0.90, $P=0.02$) and appendicular lean mass index(ALMI) ($r=0.75$, 95%CI 0.24-0.93, $P=0.01$).
Conclusions
As children in remission after ALL are 50% more likely to have IR compared to healthy subjects, an early and regular screening for metabolic disturbances should

be implemented in order to diminish cardiovascular risk among the growing population of survivors. Surprinsingly, in our study group, IR had a positive relationship not only with fat distribution, but aslo with ALMI, a surrogate for skeletal muscle mass. This is contrary to the general belief that high lean mass is beneficial for glucose regulation. Further studies are needed to clarify the effect of muscle mass on glucose homeostasis in ALL survivors.

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EP124

Perioperative management of diabetes

Belhadi Leila, Nassim Essabah Haraj, El Aziz Siham & Chadli Asma
University Hospital Center Ibn Rochd, Department of Endocrinology and Metabolic Diseases, Casablanca, Morocco

Introduction
Perioperative hyperglycemia is associated with several adverse effects, including infection and cardiovascular events. Glycemic control is likely to be beneficial in reducing postoperative mortality.
Objectives
Our study aims to assess glycemic balance in the perioperative period and the impact of glycemic imbalance on postoperative complications.
Patients and Methods
A retrospective descriptive study was conducted on 185 patients hospitalized in the surgical departments of CHU Ibn Rochd Casablanca, from January 2022 to January 2023. The analysis was performed using the SPSS software.
Results
The average age was 60.2 years, with a female predominance (sex ratio: 1.26). The average duration of diabetes was 9.6 years. Type 2 diabetes accounted for 94.7% of cases, and type 1 diabetes for 4.9% of cases. An endocrinologist's opinion was sought preoperatively in 76.8% of cases and postoperatively in 23.2% of cases. The glycemic imbalance was judged based on HbA1C in 35.7% of cases and on a glycemic cycle with an average blood glucose level of 2.6 g/l in 55.7% of patients. The average HbA1C was 9.5%. Regarding treatment, 37.8% of patients were on oral antidiabetic drugs (ADO), 52.6% were on insulin therapy, and 2% were on a diet. All patients were put on insulin therapy (basal-bolus in 84.2% of cases and rapid bolus in 14.7% of cases). Surgical management was urgent in 89.4% of patients. Glycemic control was achieved in an average of 5.2 days. Among our patients, 6.3% experienced postoperative infectious complications, and one patient died from a pulmonary embolism.
Conclusion
Preoperative identification of patients with poorly controlled diabetes and intensification of treatment improve glycemic control, reduce the risk of complications, and shorten hospital stays.

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EP125

Impact of travel on diabetes: a cross sectional study

Zayneb Sassi, Houcem Elomma Mrabet, Asma Ben Mabrouk, boubaker Fadia, Haifa Sfar, Ghofrane Belaabed, Amine Bayoudh, Najoua Lassoued, zantour baha, alaya wafa & Sfar Mohamed Habib
University Hospital Tahar Sfar, the Endocrinology Department, Mahdia, Tunisia

Introduction
The prevalence of diabetes has risen in recent years, leading to a growing number of travellers with diabetes. While travel can be therapeutic, it poses specific challenges for diabetic patients, requiring meticulous precautions.
Objective
To assess the occurrence of complications during travel and diabetes control after travel.
Methods
Cross-sectional study using a questionnaire, including out-patients with type 1 (T1DM) or type 2 diabetes (T2DM) aged $\geq$ 18 years and who had past travel experiences while diagnosed with diabetes at the Endocrinology Department at Tahar Sfar University Hospital Mahdia between October and December 2023.
Results
Twenty-one patients were included. The mean age was 57 years ranging from 35 to 73 years. Eighteen patients (85%) had T2DM. Among them, eight patients (44%) were on insulin therapy. The onset of diabetes occurred at 10 $\pm$ 6 years. The duration of travel had an average of 30 days and a median of 15 days. Ten patients (47 %) traveled alone, while 11 patients (52%) traveled with their families ($n=11$). Fifteen patients went on a pilgrimage to Saudi Arabia. Only six patients (28%) sought pre-travel advice and had a pre-travel consultation. None of the patients brought a medical prescription for their diabetes treatment during travel. Eleven patients (52%) were non-adherent to treatment. This was attributed to the lack of time and organization in 4 cases (36%), episodes of hypoglycemia resulting from changes in exercise patterns in 3 cases (27%), a shortage of rapid insulin analogs in one case, and a lack of therapeutic education, along with deviation from dietary measures in the remaining cases. Acute metabolic complications occurred in 4 cases (19%) during the trip, with two cases of hyperglycemia and two cases of ketoacidosis. A three-day hospitalization for ketoacidosis was reported in a patient with T1DM who had a shortage of rapid insulin analogs for 2 days. A significant decline in diabetes control after traveling was observed in 61% of the patients ($n=13$), as determined by comparing HbA1C levels before and after the trip, with an average increase of 1.08 % (t= -2, $P=0.028$).
Conclusion
Our series was characterized by a high frequency of altered diabetes control during and after traveling. This can be attributed to the absence of pre-travel advice, insufficient education regarding potential emergencies, and a lack of thorough review of diabetes. Diabetic patients must be guided in understanding that they can travel with diabetes, not from diabetes.

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EP127

ENT mucormycosis in diabetic patients: report of 5 cases

Rachida Bouattay, nawres bouaziz, Hela Guizeni, Mahdi Ferjaoui, Amel El Korbi, Naourez Kolsi, Khaled Harrathi & Jamel Koubaa
مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Objectives
Mucormycosis is an opportunist infection usually affecting immunocompromised patients. It is rare and often fatal. The pathogen is filamentous fungus of the mucorales order. Transmission is air-borne, with predominantly sinonasal tropism (40% of cases). Other locations are possible but much rarer. Diagnosis is founded on anatomopathologic and mycologic examination. Prognosis is severe, depending essentially on early diagnosis and treatment. The present study and review of the literature updates clinical, paraclinical, evolutive and therapeutic aspects of ENT mucormycosis.
Material and methods
A retrospective study included 5 patients with ENT mucormycosis diagnosed over a 14-year period, from January 2006 to December 2019.
Results
The study included 2 male and 3 female patients, with a mean age of 45.6 years (range: 27-61 years). All patients were diabetic. Mean duration of diabetes was 10.6 years, with extremes ranging from 3 to 24 years. Complications related to diabetes were observed in 3 cases. A patient had advanced kidney failure and another had systemic lupus erythematosus. A glycaemic imbalance was noted in 100% of patients with a mean HbA1C of 8.78. All five patients had sinonasal mucormycosis. Imaging was performed for all patients. Computed tomography was performed in all cases and imagnetic resonance imaging in one case. Mucorales filaments were founded on anatomopathologic and mycologic examination. Liposomal amphotericin B was progressively initiated for many weeks, with surgical curettage in all cases. The equilibration of diabetes was obtained. Subsequent evolution was unfavorable in four cases and the patients died a few days after surgery, from severe sepsis and multi-organ failure.
Conclusions
Otorhinolaryngologic mucormycosis is a rare fungal infection, which needs to be borne in mind. Rhinocerebral lesions are the most common clinical manifestations. Diagnosis is often difficult, but should be as early as possible. Treatment, initiated urgently, associates antifungal treatment, surgical resection and control of risk factors. The prognosis remains in all cases severe.

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EP128

Self-assessment by type 2 diabetics of their knowledge about their disease

Mouna Elleuch[1], Insaf Nasri[1], Wissal Ghamgui[1], Younes Derbel[1], Mouna Mnif[1], Fatma Mnif[1], Dhouha Ben Salah[1], Charfi Nadia[1], Mohammed Abid[1], Feten Hadj Kacem[1] & Nabila Rekike[1]
[1]Hedi Chaker Hospital, Endocrinology and Diabetes Department, Sfax, Tunisia

Background
To be able to manage their disease and live with it, type 2 diabetic patients need to understand and be aware of their disease. Educational diagnosis should therefore assess patients' perception of their diabetes.
Aims
This study aims to carry out a self-assessment of diabetic patients' knowledge of their disease
Methods
Our study is a descriptive and analytical cross-sectional study which took place during the period from November 2022 to January 2023 among T2DM patients hospitalized in the endocrinology department in Sfax as well as patients followed at the basic health centre
Results
Our study find out that almost half of the patients did not know the origin of their disease. In terms of knowledge of the various complications, half of our patients said that they were aware of some of them. With regard to treatment (57.4%), they only recognized their current treatment and no longer knew about the other therapeutic alternatives for T2DM. The majority of patients admitted that diabetes aggravates underlying co morbidities. Only 31.1% of patients were aware of the use of insulin therapy. Patient autonomy was significantly associated with better knowledge of ADO intake (P-value = 0.021), hyperglycemia sign (P-value = 0.011) and glucometer use (P-value = 0.023); the more autonomous the patient, the better his or her knowledge of these areas. Knowledge of complications was strongly associated with diabetes control (HbA1c) (P-value = 0.003). The correlation was negative (-0.238). Furthermore, the higher the level of knowledge, the lower the HbA1c. There was an association between theoretical knowledge of the complications of the disease and the number of T2DM patients in the complication stage. A higher level of knowledge of the complications of T2DM was observed in patients who already had one of the complications of T2DM. Patients on ADO alone also appeared to have better knowledge of the disease than those on insulin. However, this did not reach statistical significance (P-value = 0.254).
Conclusion
Patients admitted that their knowledge of their illness was inadequate. Autonomy and the socio-economic conditions of the population meant that the quality of patient education depended on how well patients were educated.

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EP129

Non-arteritic anterior ischemic optic neuropathy (NAION) in diabetic patients: A case report

Ilham Midhat, mennani fatimaeezzahra, Sana Rafi, Ghizlane EL Mghari & Nawal EL Ansari
Centre Hospitalo-Universitaire Mohammed VI Marrakech, Marrakech, Morocco

Introduction
Non-arteritic anterior ischemic optic neuropathy (NOIAN) is acute ischemia of the optic nerve head. It is one of the most common causes of blindness in diabetic patients, especially in the elderly. Visual impairment in NAION may be due to deterioration in visual acuity (VA) and/or visual field (VF) loss.
Observation
51-year-old female patient, diabetic for 14 years on insulin, not well controlled, and hypertensive for 15 years on treatment, who presented for one and a half months with a brutal and painless decrease in visual acuity of the right eye (RE), at the etiological investigation performed: fundus showed a drop in visual acuity in the (RE), with visual acuity in the left eye: 8/10th; normal papilla, flat retina, a few patchy haemorrhages at the posterior pole and punctiform, macula embedded in the chorioretinal anastomoses (ACR). Fluorescein angiography is in progress. Orbito-cerebral MRI: signal abnormalities in supratentorial white matter. Visual evoked potentials showed right axonal optic neuropathy. Lumbar puncture was normal. Biological workup revealed a slightly disturbed lipid profile and HBA1c 11.8%. Immunological tests revealed anti-SSA and anti-SSB autoantibodies, anti-native DNA antibodies, anti-phospholipid antibodies (IgG/IgM) and paraneoplastic antibodies. Serologies were negative. Patient received a bolus of 500 mg/day of Solumedrol for 3 days with slight improvement of decrease in visual acuity, responsible for major hyperglycemias suppressed by insulin therapy, with progressive attainment of optimal glycemic control, in order to avoid worsening of RE decrease in visual acuity and prevent contralateral damage.
Discussion et conclusion
Ischemic optic neuropathies include all vascular pathologies of the optic nerve. The classic distinction is between anterior ischemic optic neuropathy, in which there is papilledema, and posterior ischemic optic neuropathy, in which the optic disc appears normal. Non-arteritic acute anterior ischemic optic neuropathy is the most common form of ischemic optic nerve damage. Its exact physiopathology remains poorly understood. It is seen in patients with a papilla at risk (small and unexcavated). There is no effective preventive or curative treatment. In all cases of ischemic optic neuropathy, it is essential to eliminate an arteritic cause, both clinically and through further investigations. Treatment with methylprednisolone should then be started as a matter of urgency to limit visual decline and prevent damage to the adelphic eye. Optimal glycemic control remains an indispensable weapon in the prevention of NOIAN. When the condition has already set in, it can be stabilized or even corrected.

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EP130

Diabetes mellitus in beckwith-wiedemann syndrome: an unusual co-occurence

Yesmine Elloumi, Abbes Wissal, Frikha Hamdi, Maalej Souhir, Ben Salah Dhoha, Boujelben Khouloud, Hadj Kacem Faten, Mnif Fatma, Nadia Charfi, Mnif Mouna, Elleuch Mouna, Mohamed Abid & Nabila Rekik Majdoub
Hospital of Hedi Chaker

Background
Beckwith–Wiedemann syndrome (BWS) is an imprinting disorder characterized by overgrowth, tumor predisposition, and congenital malformation(s). Diabetes mellitus is not characteristic of BWS. If anything, BWS is associated with hypoglycaemia which is believed to be related to hyperinsulinaemia due to an unknown mechanism. The presentation of concurrent BWS and permanent diabetes mellitus (DM) is uncommun.
Case Report
We report the case of a two year old girl with a past medical history of BWS. She was a term baby. She had earlobe crease, macroglossia and omphalocoele requiring immediate surgical repair. Genetic testing detected a decreased methylation intensity of the KvDMR1 (differentially methylated region) in the chromosome region 11p15.5, consistent with a diagnosis of BWS. Paternal uniparental isodisomy of 11p15 was unlikely but couldn't be excluded and her DNA methylation was normal at H19. At the age of two, she presented to her primary care physician with weight loss, polyuria, and polydipsia. She was diagnosed with new-onset diabetes and was started on a basal-bolus insulin regimen. At ten years old, she consulted with a poorly controlled DM. Lab results showed negative testing for the autoantibodies against Glutamic Acid Decarboxylase (GADA), insulinoma antigen-2 (IA-2A) and islet cells (ICA). Insulin blood level and c peptid level were respectively < 7 pmol/l and $< 0{,}03$ µg/l for a concomitant blood sugar at 5,13 g/l. We can postulate as a mechanism for such paradoxal association, a loss of imprinting control region (IC2) methylation that regulates the expression of CDKN1C which has been previously reported to be associated with permanent diabetes, as reported in 2023. A loss of methylation in imprinted PLAG1 locus on chromosomes 6q24 responsible for transient neonatal diabetes mellitus (TNDM) is the second hypothesis but it was described to be associated with transient DM as reported in 2015.
Conclusion
Our case illustrates the second case in the literature associating paradoxal permanent DM and BWS. Further biomolecular investigations are required to identify the possible interactions between BWS and glucose homeostasic abnormality.

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EP153

Successful medical treatment of congenital hyperinsulinism with pasireotide: case-report

Kammoun Fatma, Ibtissem Ben Nacef, Sabrine Mekni, Sawsen Essayeh, Rihab Laamouri, Mchirgui Nadia, Karima Khiari & Imen Rojbi
Charles Nicolle Hospital, Endocrinology, Tunisia

Introduction
Congenital hyperinsulinism (CHI) is the most common cause of persistent hypoglycmia in neonatles and children. CHI causes persistent hypoglycemia due to inappropriate over-secretion of insulin. Promt diagnosis and immediate management is important to avoid long-term neurological damage. Medical therapy includes the use of the somatostatin analog octreotide as a second line-treatement in diazoxide-unresponsive cases. Here we report a case of a patient with CHI successfully treated with pasireotide, a somatostatin analog with high affinity for somatostatin receptor 5.

Case description
The patient presented at the age of 8 years with recurrent episodes of nonfasting hypoglycemia with neuroglycopenic symptoms. A diagnosis of autonomous insulin secretion was biochemically confirmed by identifying an elevated insulin level of 22,9 μ UI/ml > 3 μ UI/ml and C-peptide was elevated (3,43 ng/ml > 0,6 ng/ml) measured during hypoglycemia (glucose 2.03 mmol/l). Glucose infusion rate to maintain euglycemia was 7 (mg/kg/min). Abdominal ultrasound, computed tomography and magnetic resonance imaging (MRI) did not identify any pancreatic abnormalities. Endoscopic ultrasound and octreotide receptor scintigraphy revealed no pathological findings. The patient was initially treated with frequent feeding with carbohydrate-enriched formula and diazoxide 10 mg/kg/j. At the age of 12 years treatment with sc injections of octreotide was added because of recurrent hypoglycemia. At the age of 12 years 6 months and after parental consent, we started therapy with the long-acting somatostatin analog pasireotide at the dose of 40 mg every 28 days. Potential side effects of pasireotide (elevated liver enzymes, hypothyroidism, and adrenal insufficiency) were monitored and did not occur. With this therapy, the patient was normoglycemic with a good growth rate, normal weight gain, and excellent neurodevelopment.
Discussion
Pasireotide is a second-generation somatostatin analogue with a strong affinity for four of the five SSTRs especially SSTR5, followed by SSTR2, SSTR3, and SSTR1 receptors. Pasireotide was first introduced for treating Cushing disease and acromegaly and is known to cause hyperglycemia as a side effect due to inhibition of insulin secretion. It has been proposed as a new treatment for CHI. Pasireotide has a much higher affinity for SSTR5 than the first-generation somatostatin analogues) and might be more effective in controlling hyperinsulinism.

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EP164

Oligoelements deficiency in adult patients consulting for underweight

Dorra Ben Salem[1], Emna Bornaz[1], Selma Mohsen[2], Haifa Abbassi[1], Sana Khamassi[1], Fatma Boukhayatia[1], Asma Ben Brahim[1], Rym Yahyeoui[1], Kamilia Ounaissa[1] & Chiraz Amrouche[1]
[1]National Institute of Nutrition, Outpatient Department and Functional Exploration, Tunis; [2]Tahar Sfar Hospital, Endocrinology, Mahdia, Tunisia

Introduction
Oligoelements are essential for body metabolism and normal physiological processes. Deficiency of these micronutrients is associated with multiple situations such as malnutrition. Despite numerous reports linking micronutrient deficiencies to serious health complications, attention to this issue is poor among clinicians.
Objective
We investigated the nature of oligoelements deficiencies that arose in underweight patients in order to determine the frequency of deficiency in each element in this situation and to identify associated factors.
Materials and methods
An assessment of the serum calcium (Ca), phosphorus (P) and magnesium (Mg) levels was done on adult patients with underweight consulting our specialized nutrition unit in the outpatient department of the National institute of Nutrition of Tunis. Socio-demographic and anthropometric parameters were collected. To diagnose undernutrition, we referred to the high health authority (HAS) 2021 definition.
Results
Thirty-five adult patient was included with a female predominance (80%). The mean age was 36.64 ±13.45 years [22; 69]. The average weight, BMI, weight loss and calf circumference were 47.45±12.34 kg, 17.14±3.3 kg/m^2, 15.88±9.63% and 30.82±4.11 cm respectively. The prevalence of undernutrition was 62.84%. Only a third of patients (33.32%) had a known disease explaining their malnutrition on admission to the unit. The average Mg, Ca and P were 0.8±0.07 mmol/l, 2.35±0.11 mmol/l and 1.13±0.16 mmol/l respectively. Hypomagnesemia was met in 20% of cases, hypocalcemia in 5.7% of cases and hypophosphoremia in 2.9% of them. No significant correlation was found between (Mg), gender, anthropometric and other biological parameters. (Ca) was neither correlated to weight nor to weight loss. (P) was significantly correlated with calf circumference ($P=0.05$).
Conclusion
Oligoelement deficiencies seem to be frequently found in undernutrition situations. Proper monitoring and tests are recommended whenever the diagnosis is established, followed by specific and individual nutritional supplementation treatments.

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EP165

Severe hypertriglyceridemia in type 2 diabetes with systemic lupus accompanied by acute pancreatitis

Hemmat el Haddad, Rokaya Abdel Aziz, Heba Moustafa, Heba Murad, Nehal Hamdy, Ahmed Fayed, Ihab Sameeh, Randa Salam, Samar Amin, Mona Youssry & Fatma Fayed
Cairo University, Internal medicine, endocrinology, Cairo, Egypt

Introduction
Severe HTG usually occurs in a patient with genetic predisposition encoding various apolipoproteins (APOE, APOA5, APOC2, APOB), lipoprotein lipase (LPL), exacerbated by secondary factors as diabetes, obesity, high alcohol intake
Case report
35 yr old diabetic male presented with repeated vomiting with severe epigastric pain He had similar attack 1 year ago diagnosed as acute pancreatitis. 3 years ago he was diagnosed SLE with antiphospholipid on prednisone 5 mg, mycophenolate mofetil 1.5 mg, hydroxychloroquine 400 mg, warfarin 4 mg Upon admission, he was alert, Pulse: 140 beat/minute Blood pressure: 80/40 Respiratory rate: 32/minute. Temperature: 38ºC, tenderness over the epigastrium. Laboratory investigations; RBS 500 mg/dl, A1C: 14.7 %, ABG (PH: 7.38 HCO3: 26 Mm/l SaO2 98.0%) HB;12.4 g/dl, TLC: 24/ul PLT:77,000/uL/CRP: 265 mg/dl/Chol: 425 mg/dl, LDL: 257 mg/dl, HDL: 25 mg/dl, TG: 1547 mg/dl Amylase: 1323U/l, Lipase: 2278U/l/Na: 141mEq/l, K: 3.8 mEq/l, Urea: 100 mg/dl Creatinine: 2.1 mg/dl., ALT: 73 IU/l, AST: 73IU/l, Bil T: 4.5 mg/dl, Albumin: 4 g/dl Abdominopelvic sonar showed: Pancreatic edema with pancreatic cyst (9×7 cms). CT abdomen: Enlarged pancreatic head, perihepatic& peri pancreatic free fluid collection for pigtail insertion. Culture and sensitivity of collected fluid: E.coli, candida. The patient started, antifungal, fluids and insulin, NPO Icosapent Ethyl 2 gm and fenofibrate 320 mg, cholesterol dropped to 102 mg/dl, triglycerides to 293 mg/dl discharged on fibrates with life style modification
Conclusions
Patients with severe hypertricylcerideamia require fast and effective lowering of TG levels in order to reverse the lipotoxic effect

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EP166

Blood phospholipid profile in patients with type 1 diabetes mellitus combined with ischemic heart disease

Gulnora Artykbaeva & Talat Saatov
Institute of Biophysics and Biochemistry, Mirzo Ulugbek National University of Uzbekistan, lab of metabolomics, Tashkent, Uzbekistan

For quite a long period of time, diabetes mellitus (DM) has been considered as the carbohydrate metabolism disorder; to maintain blood glucose normal was believed to be the only mission of insulin. By now, findings from many studies have proved that DM is accompanied by the complex disorder of metabolism not only for carbohydrates, but also for lipids and proteins. Atherosclerotic injury of large vessels and ketoacidosis are known to be the main DM complications. The work was initiated to study disorders of phospholipid metabolism in patients with type 1 DM and its combination with ischemic heart disease (IHD).
Materials and methods
We examined 34 patients with type 1 DM. The group of DM+IHD included 25 patients. The control one consisted of 11 healthy persons. The blood phospholipids were fractionated by thin-layer chromatography.
Results and discussion
Significant increase in the concentrations of total phospholipids was found in fractions of these phospholipids in groups of patients with DM only and in those with DM and IHD combination. Phosphatidylinositol was found unchanged in the DM group (12.23 ± 3.59 vs 11.85 ± 3.38%), but it was significantly decreased in the DM+IHD group (3.74 ± 0.83 vs 11.85 ± 3.39, $P<0.05$). There was no difference between concentrations of phosphatidylcholine in patients with DM only (23.89 ± 4.41 vs 23.82 ± 5.12%), but significant reduction as compared to the normal concentrations was observed in the DM+IHD group (10.03 ± 2/07 vs 23.82 ± 5.12%, $P<0.05$). Phosphatidylethanolamine was found decreased both in the DM group (9.55 ± 3.44 vs 17.14 ± 3.14% in the controls), and in the DM+IHD group (11.62 ±4.5 vs 17.14 ± 3.14%, $P<0.05$). No significant differences could be seen in the concentrations of phosphatidic acid between the groups. Sphingomyelin was within normal limits in both groups of patients. Only traces of lysophosphatidylcholine could be observed in the controls. This was found in the DM group, but in the DM+IHD group significant increase of the parameter was seen (13.9 ±2.97%, $P<0.05$). Thus, the most significant alterations could be seen in the patients with the IHD-accompanied DM. In this group, increases in lysophospholipids next to the reduction in phosphatidylcholine, phosphatidylinositol and phosphatidylethanolamine, turned out the most sensitive ones. The sum

of phospholipids was most pronounced in DM, reducing in DM+IHD, but being significantly higher than the one in the controls. We have shown alterations in the phospholipid profile in patients with IHD-accompanied DM.

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EP167

Bempedoic acid role in treating familial hyperlipedemia

Aida Kanaan & Daniel Kannappan
Wrightington, Wigan & Leigh NHS Foundation Trust, Appley Bridge, United Kingdom

Bempedoic acid, an innovative medication targeting cholesterol synthesis through ATP citrate lyase inhibition, gained FDA and EMA approval in February 2020 for familial hypercholesterolemia and cardiovascular disease. UK NICE TA694, on April 28, 2021, extended its recommendation to include Bempedoic acid with ezetimibe for primary hypercholesterolaemia and mixed dyslipidaemia in adults, alongside dietary measures. This retrospective clinical audit assessed Bempedoic acid's effectiveness and safety, particularly in patients intolerant to statins, familial hyperlipidaemia, and atherosclerotic cardiovascular disease. Examining 16 patients from the Leigh Lipid Clinic (January 2021 to June 2023), results showed a significant reduction in LDL-C levels, with a peak percentage reduction of 18.98% at 6 months. Total cholesterol reached its lowest mean at 6 months, with a maximum reduction of 13.51%. However, a notable percentage of patients developed prediabetes or diabetes, warranting further exploration. Contrary to expectations, triglyceride levels increased by 30.4%, challenging previous literature suggesting Bempedoic acid's benefits in diabetes patients. In the audit of Bempedoic acid treatment for hypercholesterolemia in 16 patients, all participants experienced at least one treatment-emergent adverse event (TEAE), but none led to treatment discontinuation. New onset hypertension occurred in 12.5% of patients, while musculoskeletal symptoms and other specific adverse events, were reported in smaller percentages. Biochemical changes, such as elevated creatine kinase and alanine aminotransferase levels, as well as shifts in HbA1c with some patients transitioning to diabetes or prediabetes, were observed. Notably, 45.5% of patients had a significant drop in hemoglobin levels. Descriptive statistics of urea levels over time revealed a notable increase at the 1-year mark, reaching a mean of 7.75 mmol/l, with a maximum observed percentage increase of 30.64%. Triglyceride levels peaked at the 6-month interval with a mean of 2.6 mmol/l and a maximum observed percent increase of 30.4%. HDL-C levels showed the lowest mean at the 6-month interval (1.1725 mmol/l) with a maximum observed percent reduction of -28.08%. These findings highlight the prevalence of adverse events and biochemical changes associated with Bempedoic acid treatment, emphasizing the need for careful monitoring and further investigation. Acknowledging study limitations, such as a small sample size and missing data, this research provides valuable insights into Bempedoic acid's safety and side effects in a challenging patient population, advocating for a larger sample size in future evaluations.

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EP168

Treatment with adalimumab and combined hormonal contraception as a cause of hypertriglyceridemia induced acute pancreatitis: a case report

Matej Rakusa[1,2] & Darko Siuka[2,3,4]
[1], Department of Endocrinology, Diabetes and Metabolic Disease, University Medical Centre Ljubljana, Ljubljana, Slovenia; [2]Department of Internal Medicine, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia; [3], Department of Gastroenterology, University Medical Centre Ljubljana, Ljubljana, Slovenia; [4]Japljeva ulica 2, Department of Gastroenterology, University Medical Centre Ljubljana, Ljubljana, Slovenia

Introduction
Hidradenitis suppurativa (HS) is a chronic and debilitating inflammatory skin disease, that is characterised by painful lesions in apocrine gland-bearing areas. Patients also present with significantly increased rates of cardiovascular risk factors, such as dyslipidaemia, diabetes, metabolic syndrome. Adalimumab a fully human IgG1 monoclonal antibody that specifically binds to TNF-α is an established treatment for HS. Combined hormonal contraception is commonly used in general female population. Both medications are known to moderately increase cholesterol and triglycerides (TG).
Case report
We report a case of 34-year-old woman who was admitted to emergency department because of acute abdominal pain. Patient was treated with adalimumab 40 mg QW for previously diagnosed HS and used etonogestrel/ethinylestradiol vaginal ring (VR) for contraception. On admission she complained about sudden onset of nausea and dull abdominal pain, propagating to the back. She denied alcohol abuse. Blood pressure was 140/85 mmHg, height 158 cm, weight 93 kg, body mass index 37.3 kg/m^2. Abdominal examination revealed generalised tenderness on palpation. Bowel sounds were silent, but present. On admission blood was lipemic and could not be analysed. On abdominal ultrasound liver steatosis was present, cholecystolithiasis and cholecystitis were excluded. Computed tomography of abdomen revealed inflammation of the pancreas and retroperitoneal fat of 10 cm in diameter. We treated her with parenteral hydration, analgesics and plasmapheresis. Results of blood test after initial treatment were: white cell count 15.5×10^9/l (normal range $4\text{-}10\times10^9$/l), C-reactive protein (CRP) 135 mg/l (<5 mg/l), amylase 2.22 μkat/l (0.52-1.78 μkat/l), lipase 4.68 μkat/l (<1.07 μkat/l), cholesterol 19.5 mmol/l (<5 mmol/l), TG 49.1 mmol/l (<1.7 mmol/l). Liver function tests were normal. We discontinued treatment with adalimumab and removed VR. During hospitalisation TG level gradually decreased to 8.0 mmol/l, and CRP transiently increased to 368 mg/l and then normalised. No antibiotic treatment was necessary. On follow-up visit additional trend of normalisation of TG was noted.
Discussion and conclusion
To our knowledge this is the first case of hypertriglyceridemia induced pancreatitis, caused by combination of treatment with adalimumab for HS and with VR, without any other predisposing conditions. When combining treatment with known side effects on lipid metabolism, we should consider possible multiplicative effect, especially in patients prone to metabolic complications. Prior to initiating and during treatment regular laboratory test should be performed.

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EP170

Myocardial infarction in patients with type 2 diabetes and coronary heart disease

Elena Brutskaya-Stempkovskaya, Lizaveta Tsitova & Karina Liahkova
Belarusian State Medical University, Belarus

Objective
Coronary heart disease (CHD) is one of the leading causes of death worldwide. According to WHO experts, one out of 4 deaths in the world is due to CHD (17.8 million people annually). Type 2 diabetes is an independent risk factor for CHD. Thrombotic complications of atherosclerosis are the main cause of death in 80% of patients with type 2 diabetes.
Materials and Methods
We studied the prevalence of myocardial infarction in patients with CHD and type 2 diabetes. A cross-sectional controlled study of 50 hospitalized cardialogical patients with chronic CHD was conducted. The main group - patients with chronic CHD and type 2 diabetes, average age was 68.5±9.63 years (women - 44.12%, men - 55.88%). The comparison group was patients with CHD without type 2 diabetes, averageage was 69.5±13.14 years (women – 43.75%, men – 56.25%).
Examination
ECG, HЬA1c, blood chemistry, glucose, heart ultrasound, coronary angiography.
Results
Patients of both groups were comparable in gender, age (U=243,5, P=0,56), laboratory data: cholesterol (4.62 (3.8-5.3) vs 4.78 (3.67-5.67) mmol/l, P=0.7), TG (1.55 (1.21-1.94) vs 1.60 (1.34-2.76) mmol/l, P=0.74), HDL (1.1 (0.9-1.3) vs 1.13 (0.87-1.38) mmol/l, P=0.88), LDL (2.4 (1.9-3.0) vs 3.0 (2.0- 3.7) mmol/l, P=0.12), VLDL (0.58 (0.37-0.72) vs 0.64 (0.54-1.03) mmol/l, P=0, 26), AST (23 (18-40) vs 24 (18-42) U/l, P=0.77), ALT (22 (15.9-41) vs 28 (23-40) U/l, P=0.14), creatinine (102.0 (77.5-144.6) vs 90.3 (75.3-132.9) μmol/l, P=0.47), total protein (71 (66-74) vs 71.35 (66-74) g/l, P=0.89) in blood serum. The blood glucose level in patients of the main group was significantly higher compared to the comparison group (6.8 (5.5-8.5) vs 5.5 (5.2-6.0) mmol/l, P=0.01). HbA1c = 7.7 ± 1.73% in patients of the main group, the experience of type 2 diabetes according to the anamnesis was 8.2 ± 3.14 years. According to the anamnesis data, acute myocardial infarction was diagnosed in 79.41% (n=27) of patients in the main group and in 56.25% (n=9) of patients in the comparison group. The prevalence of a history of myocardial infarction was 23.16% higher in patients of the main group ($\chi2$ = 2.9, P=0.089).
Conclusion
the results of the study indicate an increasing incidence of acute myocardial infarction by 23.16% in patients with coronary heart disease in combination with type 2 diabetes compared to patients with coronary heart disease without type 2 diabetes.

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EP172

Predictors of antenatal insulin requirement in gestational diabetes mellitus

Sawsen Nouira, Taieb Ach, Asma Ben Abdelkrim, Amel Maaroufi, Yosra Hasni & Molka Chaieb
University Hospital Farhat Hached, Endocrinology, Sousse

Introduction
Gestational diabetes mellitus (GDM) arises from elevated glycemia during pregnancy, posing risks to both mother and fetus. Managing GDM involves close monitoring and dietary control, with antenatal insulin therapy (AIT). The aim of this study was to evaluate the efficiency of diverse maternal characteristics and biological indicators identified during GDM diagnosis in anticipating the inadequacy of dietary measures and the requirement for AIT to achieve glucose targets.
Materials
We conducted a retrospective longitudinal study that included women diagnosed with GDM and who were monitored at the Endocrinology Department of Farhad Hached Hospital in Sousse between January 2017 and March 2020.
Results
We analyzed 380 records of patients diagnosed with GDM. The average age in our patient group was 34 $\pm$ 5 years, ranging from 20 to 46 years. Among them, 73% (280 individuals) needed AIT, while 100 patients achieved glycemic goals solely through Medical Nutrition Therapy (MNT). Notably, those requiring insulin had prior history of obesity (24%), gestational diabetes (12%), and macrosomia (18%) ($P=10^{-3}$). Patients meeting glycemic targets via MNT had higher total carbohydrate intake upon GDM diagnosis ($P=0.02$). Those necessitating AIT were diagnosed at an average gestational age (GA) of 24 ± 6 weeks, significantly earlier than the 25 ± 6 weeks observed in patients following MNT ($P<10^{-3}$). Fasting glucose levels did not exhibit a notable difference between the two groups. Patients requiring insulin showed a median HbA1c level of 5.5%, surpassing levels observed in the group under MNT. Elevated HbA1C emerged as the only independent predictor for the necessity of AIT.
Conclusion
Recognizing the diverse spectrum of glucose intolerance severity among women with GDM necessitates a stratified classification for management strategies. This approach allows for the optimal allocation of human and financial resources. Notably, a higher HbA1C at diagnosis signals the potential need for intensified monitoring by specialized healthcare providers.

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EP174

Frequency and risk factors of medication non-adherence in elderly diabetics

Dhoha Ben Salah[1], Abir Larayedh[2], Mouna Elleuch[1], Khouloud Boujelben[1], Faten Hadj Kacem[1], Fatma Mnif[1], Mouna Mnif[1], Nadia Charfi[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Endocrinology Department, Hedi Chaker University Hospital, Sfax, Tunisia; [2]Department of Family Medicine, Faculty of Medicine, Sfax, Tunisia

Background
Low medication adherence is a frequent problem in elderly individuals with chronic diseases such as diabetes. The objective is to assess the level of medication adherence and identify predictive factors for poor adherence among elderly diabetic patients.
Methods
We conducted a descriptive, cross-sectional study among diabetic patients aged 65 years and older, who were attending the Endocrinology Department at Hedi Chaker University Hospital in Sfax from January to March 2022. Medication adherence was assessed using a validated Arabic version of the 8-item Morisky Medication Adherence Scale (MMAS-8). Univariate analysis followed by multivariate logistic regression was used to identify predictors of low medication adherence.
Results
This study included a sample of 137 elderly patients, with a mean age of 71.49 years ($\pm$6.2) and a sex-ratio of 0.9. The prevalence of low medication adherence was 56.2%, and it was independently and significantly correlated with five distinct factors: the absence of self-monitoring of blood glucose [OR = 2.987; 95% CI (1.295-6.889), $P=0.01$], irregular medical visits [OR = 5.383; 95% CI (1.353-21.419), $P=0.017$], non-adherence to prescribed treatments [OR = 4.644; 95% CI (1.457-14.804), $P=0.009$], high HbA1C levels (>7%) [OR = 3.008; 95% CI (1.194-7.580), $P=0.02$] and diabetic retinopathy[OR = 2.987; 95% CI (1.327-6.725), $P=0.008$].
Conclusions
Medication adherence was insufficient in our study. Therapeutic education programs are needed for patient management.

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EP176

Feature of technology in therapeutic education of diabetes patient: 61 cases

Mouna Elleuch, Insaf Nasri, Wissal Ghamgui, Younes Derbel, Charfi Nadia, Feten Hadj Kacem, Mouna Mnif, Fatma Mnif, Mohammed Abid, Dhouha Ben Salah & Nabila Rekike
Hedi Chaker Hospital, Endocrinology and diabetology department, Sfax, Tunisia

Background
Interest health applications and networks for self-management of diabetes are growing. Furthermore, the potential influence of social media on health information spread is remarkable.
Aim
This study aims to determine the role of the new telecommunication technology in the dissemination of therapeutic education in our population.
Methods
Our study is an descriptive and analytical cross-sectional study which took place during the period from November 2022 to January 2023 among 61 T2DM patients hospitalized in the endocrinology department in Sfax as well as patients followed at the basic health centre.
Results
The involvement of new telecommunication technologies in the choice of therapeutic education's interface occupied the second priority in the different educational objectives, but in different proportions. Moreover, 24 patients (39.3%) preferred telephone applications for disseminating instructions on dietary hygiene measures. The role of the media was also in demand, especially for general information (26.2%), diet (24.6%) and how to use current treatment (21.3%). Internet platforms dedicated to diabetic patients were among the choices of 10 patients (16.4%) in the area of preventing complications of the disease. Social networks were also integrated into the development for health care resources, especially to prevent complications (23%). The correlation between patients' objective assessment of their knowledge and their possession of telecommunication resources (smart phones, computers…) was significant (0.316, $P=0.006$). The statistical study showed a positive correlation between the use of new technologies and patients' level of knowledge. This relationship was significant for glucometer use ($P=0.002$).
Conclusion
In our study, we recognized that whatever the integration of new telecommunication technologies that patients needed, the medical and paramedical staff were always involved in the dissemination of therapeutic education.

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EP179

Impact of obesity and android fat distribution on the progression of hepatic fibrosis in metabolic steatopathy

Ahmed Mohamed Nefzi, Bouchabou Bochra, El Mouldi Yosr, Nakhli Abdelwahab, Hemdani Nesrine, Benzarti Zeineb, Ben Nejma Houda & Ennaifer Rym
Hôpital Mongi Slim, Hepato-gastroenterology, Marsa, Tunisia

Introduction
Metabolic steatopathy is a public health problem, and its therapeutic management remains a challenge primarily relying on lifestyle and dietary measures. The degree of liver fibrosis represents the major prognostic factor for this condition. The objective of this study was to investigate the impact of obesity and android fat distribution on the progression of hepatic fibrosis in metabolic steatopathy.
Patients and Methods
We conducted a prospective, descriptive study including patients diagnosed with metabolic steatopathy between March 2021 and December 2022. Age and various medical histories were collected. Anthropometric measurements were taken, and a biological assessment, including metabolic and hepatic panels, was performed. liver fibrosis assessment using transient elastography was conducted, with advanced fibrosis defined as liver elasticity $\geq$ 9.7 kPa.
Results
We included 139 patients with an average age of 54.2 ± 10.7 years and a gender ratio of 0.53. Histories of type 2 diabetes, hypertension, and dyslipidemia were

noted in 43.5%, 46.4%, and 31.2% of patients, respectively. Obesity was found in 52.6%, and android fat distribution was observed in 87.3% of patients. Advanced hepatic fibrosis was noted in 15.6% of patients. In analytical study, patients with advanced fibrosis had significantly higher body mass index (BMI) and waist circumference (WC) with *P*-values of 0.03 and 0.024, respectively. The study of BMI and WC performance in predicting advanced fibrosis showed the superiority of WC with areas under the ROC curve of 0.63 (95% CI 0.5–0.779) and 0.7 (95% CI 0.6–0.833), respectively. The BMI cutoff was 30.6 kg/m^2 with a sensitivity of 65% and specificity of 50%. The WC cutoff was 103.5 cm with a sensitivity of 82.4% and specificity of 40%.
Conclusion
Android-type obesity has a more pronounced correlation with advanced fibrosis than overall obesity. Therefore, it is imperative to systematically include the assessment of this parameter in the management of this pathology.

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EP184

Postnatal growth and weight gain in term and near-term infants with severe neonatal hypoglycemia: a comparison between offspring of diabetic and non-diabetic mothers

Nada Alaaraj, Ashraf Soliman, Fawzia Alyafei, Noor Hamed, Shayma Mohamed & Hamdy Ali
Department of Pediatrics Hamad Medical Centre, Doha, Qatar

Introduction
Hypoglycemia occurs more frequently in infants of diabetic mothers as well as in preterm and small for gestational age babies (SGA). Severe neonatal hypoglycemia can adversely affect the neurodevelopment and metabolism of the infant on the long run. Postnatal growth of these infants has not been studied in depth.
Objective
This study aimed to evaluate postnatal growth patterns in infants with neonatal hypoglycemia, comparing infants of diabetic mothers (IDM) with infants of non-diabetic mothers (INDM) from birth to 3 years of age.
Methods
We retrospectively analyzed the growth data of 79 IDM and 51 INDM infants who were treated for severe neonatal hypoglycemia at a single center. Anthropometric measurements, including weight-for-age Z score (WAZ), length-for-age Z score (LAZ), and weight-for-length Z score (WLZ), were collected at birth and at several intervals up to 36 months.
Results
IDM were born at a higher gestational age and with better growth indices than INDM. During the first year, IDM had a progressive increase in WAZ, which stabilized thereafter, while INDM demonstrated a significant catch-up in WAZ and LAZ, particularly in the first 18 months. After 2 months, IDM maintained higher WLZ scores than INDM. By 36 months, IDM had significantly higher WAZ and WLZ, suggesting a tendency towards increased weight relative to length.
Discussion
IDM exhibited a distinct growth pattern, characterized by larger size at birth and slower postnatal catch-up growth compared to INDM. Despite severe neonatal hypoglycemia, IDM and INDM infants showed the ability to reach normal growth velocity by 18 months, although IDM had a higher risk of increased adiposity. These findings align with previous research, highlighting the impact of maternal diabetes on the growth trajectory of infants and the potential for long-term metabolic implications.
Conclusion
The growth patterns of infants with neonatal hypoglycemia are influenced by maternal diabetes status. While IDMs are at risk for increased adiposity, both groups show resilience in growth, underscoring the need for ongoing monitoring to support their growth needs.

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EP187

A case of rhino-orbital mucormycosis precipitated by a state of diabetic keto-acidosis

Najoua Lassoued[1], Bougossa Rebeh[2], Bayoudh Amine[1], Larbi Fatma[2] & Sfar Habib[1]
[1]Taher Sfar University Hospital, Endocrinology Department, Mahdia, Tunisia; [2]Taher Sfar University Hospital, Department of Infectious Diseases, Mahdia, Tunisia

Background
Mucormycosis, also known as black fungus, is a rare, aggressive, locally invasive, and life-threatening fungal infection that can occur in healthy individuals but that is more frequently seen in immuno-compromised patients especially in diabetics in the context of diabetic keto-acidosis. Early diagnosis is a key for good prognosis.
Case Presentation
We report the case of a 66-year-old Tunisian male, with a history of uncontrolled type 2 diabetes treated with metformin, who presented with fever, acute hemifacial and palpebral oedema and right unilateral epistaxis. The patient reported a 10-day history of dental pain initially diagnosed as a dental abscess and treated with amoxicillin. The initial presentation revealed a state of Keto-acidosis, adequate insulin therapy, as well as fluid and electrolyte replacement were initiated. An emergency CT scan revealed orbital cellulitis stage 2 of Chandler associated with cervical-facial extension without signs of collection, along with right maxillary and ethmoidal sinusitis, the patient was admitted and the diagnosis of dental-origin cellulitis with orbital extension was initially retained, the patient was placed under a triple antibiotic treatment, in 24 hours rapid lesion extension was noted with central necrotisation of skin lesions along with necrosis of the lateral wall of the right nasal cavity and ulceration of the right vestibular grove in nasal fibroscopy. Tissue samples were taken and an urgent pathological examination confirmed the diagnosis of Rhino-orbital mucormycosis precipitated by the state of keto-acidosis the patient was placed under anti-fungal treatment and surgical removal and care for necrotic lesions were done in the ENT department. Glycemia targets were met with intensive intravenous insulin treatment followed by a basal-bolus insulin regimen. Clinical improvement was noted in a few weeks and the patient benefited from a facial skin graft;
Conclusions
This case shows a rare case of rhinorobital mucormycosis precipitated by diabetic ketoacidosis and uncontrolled type 2 diabetes. This case highlights the need for an early diagnosis of mucormycosis as well as the need for optimal control of diabetes and rapid treatment of acute metabolic complications.

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EP188

Mauriac syndrome in poorly controlled type 1 diabetes: case report

Rokia Abd Al Aziz, Ghada Rabie, Dina Farouk & Randa Salam
Cairo University, Internal medicine, endocrinology, Cairo, Egypt

Introduction
Mauriac syndrome (MS) is considered a glycogenic hepatopathy characterized by growth failure, delayed puberty, hepatomegaly with abnormal liver enzymes, hypercholesterolemia. These features were attributed mainly to insulin deficiency and sub-optimal diabetic management
Case report
18 years old male, presented with short stature and delayed puberty. The patient was diagnosed to have type 1 DM at the age of 6. He was on a premixed insulin regimen but non compliant to treatment. His disease course was complicated by diabetic retinopathy, and neuropathy frequent admissions for recurrent diabetic ketoacidosis (DKA) There was a history of right hypochondrial dragging pain with no jaundice
Physical examination
Height was 145 cm, $<$3rd percentile, proportionate. BMI was 19.9 kg/m^2, mid-parental height was 168 cm. Blood pressure: 110/70 mm Hg, Pulse: 80/mint, normal RR and temperature. Absent secondary sexual characters and infantile male genitalia tanner stage 1 The abdominal examination showed soft hepatomegaly. liver span of 22 cm Cardiac and chest examination were normal
Investigations
HbA1c was 9.9%, A/C ratio: 500 mg/g His hepatic panel revealed high ALP: 490 U/l (N: 40-150 U/l), high liver transaminases. ALT: 235 U/l(10-50 U/l), AST: 259 U/l (N: 0-38 U/l) cholesterol: 319 mg/dl, LDL: 233 mg/dl, Serum triglycerides: 191 mg/dl Thyroid function test was normal LH: 0.22 mIU/ml (1.7-8.6 mIU/ml) FSH: 1.9 mIU/ml(N: 1.5-12.1) Total testosterone: $<$0.025 ng/ml (2.5 -8.4) indicative of hypogonadotropic hypogonadism ANA: 29 IU/ml, Anti -DNA, Anti–LKM, ASMA, anti-TTG IgA: negative Normal Ceruloplasmin: 24 hr urinary copper, HbsAg and HCV Ab: negative Abdominal ultrasound: Enlarged liver with uniform soft fatty echo pattern, span of right lobe 22 cm, bone age: 13 years The patient was prescribed a basal-bolus insulin regimen With improvement of his blood glucose, liver enzymes. And liver size decreased significantly. follow-up labs after 6 weeks: ALT: 54 U/l, AST: 40 U/l, ALP: 292 U/l, GGT: 44 U/l LH: 2.8 mIU/ml, FSH: 4.3 mIU/ml, Total testosterone: 0.2 ng/ml During his follow-up, he got his puberty, and his final height was 149 cm.
Conclusion
In spite of advancement in diabetic management, MS a rare complication in poorly controlled T1DM still exists. A high index of suspicion is needed in T1DM

with delayed growth and puberty since good metabolic control could reverse this rare condition.

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EP192

Infrared thermography may be considered a new tool for the early detection of diabetic neuropathy

Mahmoud Younis
Egypt Ministry of Health, كفر الشيخ, Egypt

Introduction
Diabetes mellitus is a multifaceted condition that involves both metabolic and inflammatory processes. Diabetic neuropathy is a progressive disorder that affects the nerves throughout the body. Thermography is a non-invasive, painless, and radiation-free test that uses infrared light to detect changes in the surface temperature of the body. Thermography can be used to monitor the progression of diabetic neuropathy. Thermography can be utilized to assess the effectiveness of treatment for diabetic neuropathy. Thermography can be used to monitor the progression of diabetic neuropathy. Thermography can be utilized to assess the effectiveness of treatment for diabetic neuropathy.
Materials and Methods
Grouping: 60 Participants with type 2 diabetes and mild diabetic peripheral neuropathy (DPN) and 60 healthy controls were divided into 2 groups: The first group: patients with type 2 diabetes mellitus with mild neuropathy and mild scoring on biothesiometer measurements from 16 to 20.30 female patients and 30 male patients. The second group are controlled healthy peoples not having diabetes mellitus.30 female patients and 30 male patients. This study used medical infrared imaging to visualize the temperature distribution of the feet of participants with diabetes mellitus (DM) and healthy controls. An infrared thermal imaging camera (BENETECH GT3251) was used to measure the temperature of the dorsal surface. The room temperature was kept at 25 degrees Celsius. Before the measurement, participants were required to remove their shoes and socks. Each participant was in a supine position, with the knee joint fully extended. This posture was maintained for 5 minutes so that the epidermal temperature could adapt to the standard room temperature.
Results
The results show that infrared thermography shows increased dorsum of the foot temperature compared to controls with pvalue <0.0001. The results show a direct correlation between the temperature of the dorsum of the foot and the vibration perception threshold of diabetic neuropathic patients with P-value <0.0001.
Conclusion
Infrared imaging can detect changes in skin temperature, which can indicate nerve damage. This technology has been used to identify early signs of diabetic neuropathy before symptoms become severe. By detecting neuropathy early, clinicians can intervene with treatments that may slow the progression of the disease.

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EP197

Fatal rhinosinus disease in diabetic patients: about 8 cases

El Omri Malika[1], Jemli S[1], Lazid Sarra[1], Bellakhdher Mouna[1], Meherzi Abir[1], Houas Jihene[1], Ghammem Monia[1], Ach Taieb[2], Kermani Wassim[1] & Abdelkefi Mohamed[1]
[1]ENT department Farhat Hached hospital, Sousse, Tunisia; [2]Endocrinology department Farhat Hached hospital, Sousse, Tunisia

Introduction
Mucormycosis is a rare opportunistic aggressive fungal infection usually occurs patients with immune deficiency especially in diabetic. Extension is rapid, with a high rate of mortality. The pathogen is a filamentous fungus of the zygomycete class of the Mucorales order. The aim of this study to reveal clinical, paraclinical manifestations of this entity and its prognosis.
Material and methods
A retrospective study about 8 cases of mucormycosis diagnosed and treated in our ENT department between January 2000 and December 2023
Results
The mean age was 49 years with male predominance, the average duration of diabetes follow up was over 12 years. We noticed an orbital involvement in one case. Rhinocerebral mucormycosis was diagnosed in one patient. The infection was limited to the rhinosinus space in 6 cases. The causative agent was, exclusively, *Rhizopusarrhizus*. In all cases, surgical evaluation was immediately performed for debridement of the necrotic tissues, and multiple biopsies were performed for diagnostic purposes. The medical treatment was based in intravenous liposomal amphotericin B. The main complication was septicemia, seen in one case, after one week of evolution. We noted a complete recovery in 5 cases. Outcomes had been marked by the death of one patient who had a cerebral involvement.
Conclusion
ENT mucormycosis is a rare and severe fungal infection, to be borne in mind in diabetic patients. Late diagnosis and treatment inevitably incurs severe or even fatal complications. Only adequate early treatment, associating amphotericin B, necrotic tissue resection and control of risk factors can improve prognosis.

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EP200

Immune checkpoint inhibitor (ICPi)-induced de novo type 1 diabetes mellitus: a case report

Maria Borg[1], Zachary Busuttil[1], Simon Mifsud[1], Arlène Gatt[1], Kelly Mifsud Taliana[2] & Sandro Vella[1]
[1]Mater Dei Hospital, L-Imsida, Malta; [2]Sir Anthony Mamo Oncology Centre, L-Imsida, Malta

Background
Immune checkpoint inhibitors (ICPis) have become a cornerstone of cancer management. Whilst endocrine-related adverse effects are one of the most common immune-related adverse events, ICPi-induced *de novo* diabetes occurs at low frequencies[1]. We describe a case of ICPi-induced *de novo* type 1 diabetes presenting with severe diabetic ketoacidosis (DKA) in a female with metastatic melanoma.
Case report
A 50-year-old lady was being treated with ICPis for metastatic melanoma. She initially received four cycles of combined ipilimumab (a cytotoxic T-lymphocyte-associated protein 4 [CTLA-4] checkpoint inhibitor), and nivolumab (a programmed cell death-1 [PD-1] checkpoint inhibitor) therapy followed by maintenance nivolumab. After the tenth cycle of nivolumab, she presented to the emergency department with fatigue, abdominal pain, vomiting, and polyuria. Laboratory investigations confirmed severe DKA as evidenced by plasma glucose of 67 mmol/l, blood ketones >7 mmol/l, and metabolic acidosis (pH:6.91, serum bicarbonate:8mmol/l). Treatment with intravenous fluids, a fixed rate of intravenous insulin infusion at 0.1 units/kg/hour, and electrolyte replacement was commenced immediately. Low-molecular-weight heparin was also prescribed for thromboprophylaxis. Further investigations including liver function tests, amylase, and inflammatory markers were normal. A septic screen excluded an infectious source. Antibodies to glutamic acid decarboxylase, tyrosine phosphatase-related islet antigen 2, islet cell, and insulin were negative. Following resolution of her DKA and review by the diabetologists, diabetes specialist nurses, and caring oncologist the patient was discharged on daily insulin glargine and thrice daily insulin aspart. She remained well upon review at her follow-up appointment where in the interim she was recommenced on nivolumab.
Conclusions
The use of PD-1 inhibitors is associated with an increased risk of type 1 diabetes when compared to CTLA-4 inhibitors, but when PD-1 inhibitors are combined with CTLA-4 inhibitors, this leads to an increased risk of diabetes at an earlier stage[1,2]. This case highlights how DKA is the most common presentation of ICPi-induced type 1 diabetes as a result of swift β-cell destruction and resultant insulin deficiency[2]. ICPi-induced type 1 diabetes is irreversible. Hence, such patients require life-long insulin treatment regardless of whether ICPi therapy is withheld[2]. Patients receiving ICPis, especially PD-1 inhibitors, should be informed about the symptoms and signs of diabetes, and to monitor their glucose levels.
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EP201

Evaluation of the prevalence phenotypic criteria of GLIM on hospitalized patients in a third-level hospital: a cross-sectional study

Laura Mola Reyes, Rosa María García Moreno, Mary Llaro, Gonzalo Miñon Sanchez, Bricia López Plaza & Samara Palma Milla
La Paz University Hospital, Madrid, Spain

Rationale
The Global Leadership Initiative on Malnutrition (GLIM) criteria was recently proposed as the world's first diagnostic criteria for malnutrition in adults in hospital settings. The GLIM approach is based on the assessment of three phenotypic and two etiologic criteria, with diagnosis confirmed by any combination of one phenotypic and one etiologic criterion fulfilled. The purpose of this study was to evaluate the prevalence phenotypic criteria of GLIM in hospitalized patients.
Methods
A cross-sectional study was performed on adult patients admitted to Hospital Universitario La Paz who were assessed by the Nutrition Unit staff through interconsultation between August 2019 and November 2020 ($n=1036$) GLIM criteria were applied. The phenotypic criteria (unintentional weight loss [UWL] defined as weight loss $>5\%$ within the last 6 months or $>10\%$ beyond 6 months; low BMI defined as <20 kg/m^2 or <22 kg/m^2 in participants younger and older than 70 years, respectively; and reduced muscle mass [RMM] from mid-upper arm circumference) were analyzed according to the age group, sex, and underlying pathology. The Chi-square test was used in statistical analysis.
Results
The prevalence of GLIM phenotypic criteria in the population was: 56.7% UWL, 30.1% low BMI, and 23.4% RMM. Regarding age, we found significant differences in RMM, with a greater prevalence of RMM in those <70 years ($P<0.001$). In relation to sex, there was a higher prevalence of UWL and RMM in men ($P<0.001$ and $P<0.001$, respectively), while low BMI criterion was more common in women ($P=0.043$). The underlying pathology had a significant effect on the phenotypic criteria of low BMI and RMM ($P=0.001$ and $P=0.002$, respectively), with the higher prevalence of low BMI in patients admitted for gastrointestinal diseases and RMM in those admitted for infections.
Conclusion
Our results suggest that the age and gender of the hospitalized patients and their underlying pathology may have an impact on the prevalence of phenotypic GLIM criteria in this population.

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EP203

Osteomielitis enfisematosa en pacientes diabéticos

Maria Jose Vallejo Herrera & Veronica Vallejo Herrera
Hospital Regional Málaga, Malaga

Introduction/Objectives
Emphysematous osteomyelitis is a rare disease, characterized by the presence of intraosseous gas associated with an infectious process. It occurs in patients with chronic pathologies such as diabetes mellitus, and has high mortality. The most common location is the vertebral, sacral, femur, pelvis, tibia and fibula, while it is extremely rare in the foot.
Material/Method
With the help of the Radiology service of our hospital, we collected cases of emphysematous osteomyelitis diagnosed by imaging (CT or MRI) in diabetic patients at the Regional Hospital of Malaga during the year 2023: one in the pubis and two in the foot. 2 men and 1 woman with an average age of 60-70 years and diabetes with poor metabolic control, case 1 died during admission. Case 1 70-year-old man, ex-smoker, type 2 diabetes and dyslipidemia. He was admitted for grade IV peripheral arterial disease with dry necrotic plaque on both forefeet of MMII and dry necrosis in the toes of the left foot, leukocytosis and elevated CRP. In Angio - CT of the Lower Limbs, he presented radiological signs of osteomyelitis in both feet, affecting the left calcaneus (emphysematous osteomyelitis) and phalanges bilaterally. Subcutaneous emphysema and collections adjacent to both calcaneus. EXITUS Case 2: A 62-year-old man, poorly controlled type 2 diabetes, poor adherence to treatment, diabetic polyneuropathy, previous amputations and peripheral arterial disease with ulcers in both lower limbs. He went to the emergency room due to metabolic decompensation and poor progress of a left plantar ulcer. Computed tomography and magnetic resonance imaging showed emphysematous osteomyelitis in the midfoot and forefoot, with extensive abscessed inflammatory involvement of adjacent soft tissues. Intravenous antibiotic treatment was initiated with subsequent infratuberosal amputation. HOSPITAL DISCHARGE Case 3. 63-year-old woman, DM on insulin. Cutaneous lupus. He was admitted for left pyelonephritis with areas of abscessation, with probable superinfection of the cortical cyst in the upper pole complicated with emphysematous osteomyelitis affecting the pubis. Complicated evolution with pelvic collections and emphysematous osteomyelitis of the pubis. Percutaneous drainage was performed, isolating E. coli, the same germ isolated in urine and blood cultures. HOSPITAL DISCHARGE
Conclusion
Imaging tests play an essential role in making early diagnosis and treatment, and reducing the mortality rate. CT can evaluate bone gas and MRI can evaluate soft tissues. Treatment is based on surgical debridement, amputation and intravenous antibiotic therapy.

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EP204

A comprehensive assessment of some pathogenetic aspects of sarcopenic obesity

Svitlana Opalenyk[1], Olga Oleksyk[2] & Oksana Khyzhnyak[3,3]
[1]Uzhhorod National University, Medical faculty 2, Department of Internal Medicine, Uzhhorod, Ukraine; [2]A. Novak' Transcarpathian Clinical Regional Hospital, Endocrinology, Uzhhorod, Ukraine; [3]V. Danilevsky' Institute of Endocrine Pathology Problems, Clinical Endocrinology, Kharkiv, Ukraine

Introduction
Early diagnosis of obesity, as well as prevention of its occurrence in high-risk patients, plays an important role in the prevention of severe cardiovascular and cerebrovascular diseases. The study of leptin and ghrelin are one of important pathogenetic aspect of obesity. At the same time, such factors as hypodynamia, low physical activity and insulin resistance contribute to the formation of sarcopenic obesity, which is characterized by the loss of muscle tissue and muscle strength with replacement by adipose tissue.
The aim of the study was to carry out a comprehensive assessment of some pathogenetic aspects of diagnosis of sarcopenic obesity.
Materials and methods
68 obese and overweight patients were examined: 32 men and 36 women. The average age of the patients was 45 ± 11.73 years. Depending on the body mass index, all patients were divided into 2 groups: group I -31 overweight patients, group II - 37 patients with obesity I and II degrees. The control group - 20 healthy people. All patients underwent a bioimpedance examination with a study of the component composition of the body. Determination of the serum levels of ghrelin and leptin was carried out by the ELISA method. Statistical data processing was performed using the STATISTICA 10.0 computer program (StatSoftInc, USA).
Results
According to the results of the bioimpedance examination, all patients had a deficiency of muscle. The level of leptin in overweight patients was higher compared to the control group (3.1 ± 0.28 ng/ml), but was within the reference values (6.57 ± 0.39 ng/ml). At the same time, a significant statistically significant increase in the level of leptin was observed in obese patients compared to both studied groups (up to 41.72 ± 5.22 ng/ml). Ghrelin levels were increased in both groups and were highest in group 1 (up to 247.5 ± 10.09 ng/ml) and moderately increased in patients in group 2 (up to 120.93 ± 5.57 ng/ml), $P=0.005$ compared to controls. A positive correlation between serum leptin and the content of fat mass was also established ($r=0.89203$; $p=0.01303$). At the same time, a negative correlation between the level of ghrelin and fat mass ($r=-0.70641$; $P=0.030251$) was found in all studied patients.
Conclusion
Determining the level of ghrelin in blood serum is a more sensitive and informative pathogenetic marker for detecting the sarcopenic form of obesity at an early stage of the disease.

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EP207

Estimated glucose disposal rate as a predictor of chronic complications in type 1 diabetes – a cross-sectional study

Nuno Jesus, Patrícia Tavares, Henrique Alexandrino, José Silva, Margarida Gonçalves, Ana Sousa, Gustavo Rocha, Marta Ferreira, Sara Correia, Sara Monteiro & Maria Oliveira
ULS Gaia e Espinho, Endocrinology Department, Vila Nova de Gaia, Portugal

Introduction
Insulin resistance, often implicated in the pathophysiology of Type 2 Diabetes Mellitus, can also occur in patients with Type 1 Diabetes Mellitus (T1DM), giving rise to a distinct phenotype that some authors describe as Double Diabetes - a population with a higher risk of developing chronic complications. The estimated glucose disposal rate (eGDR) is a validated marker of insulin resistance

in Type 1 Diabetes (T1DM), based on data obtained from the hyperinsulinemic-euglycemic clamp method. The eGDR formula uses common predictor variables in clinical practice: body mass index (BMI), glycated hemoglobin (HbA1c), and the presence of arterial hypertension (HTN). Insulin resistance is often reported as eGDR <8 mg/kg/min, and its relationship with macro-and microvascular complications is unclear. This study aims to investigate the relationship between eGDR and macro-and microvascular complications in T1DM patients from our Endocrinology – Diabetes outpatient clinic.

Methods

Patients with T1DM followed in the Endocrinology – Diabetes outpatient clinic were included, excluding those with hemoglobinopathies, pregnant individuals, and those with less than 5 years of disease duration. The eGDR was calculated using the formula: 19.02 - [0.22 $\times$ BMI (kg/m^2)] - [(3.26 x HTN (0 = absent; 1 = present)] - [0.61 $\times$ HbA1c(%)]. Prevalences of complications and comorbidities were compared between insulin-resistant and insulin-sensitive groups, and odds ratios were calculated for three eGDR categories (<6; 6-7.99; ≥ 8 mg/kg/min), defined according to an observational study that related eGDR to mortality differences, whenever possible.

Results

A total of 182 individuals with T1DM were included, with 51% being male. The average age was 38.5 years, and the average disease duration was 18.5 years. Approximately 30.9% of the sample was overweight, and 12.6% had obesity. The eGDR was less than 8 mg/kg/min in about 44% of individuals, and this group was associated with the presence of at least one chronic complication of T1DM (OR 5.344 [95% CI 2.824–10.112], *P*-value <0.001). The eGDR inversely varied with the prevalence of microvascular complications, with statistical significance for diabetic kidney disease, diabetic retinopathy, and peripheral neuropathy. Due to the low prevalence of macrovascular complications in the sample, it was not possible to calculate statistically significant odds ratios.

Conclusions

The eGDR is a validated tool for estimating insulin resistance. It is associated with the prevalence of chronic complications of T1DM, making it a potentially helpful tool for personalized therapy in T1DM patients.

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EP209

Impact of blood glucose control on clinical outcomes in type 2 diabetes patients hospitalized with COVID-19 infection

Elena Chertok shacham[1,2], Nimra Maman[2] & Avraham Ishay[3]
[1]Israel Institute of Technology, Haifa, Israel, Medicine; [2]Emek Medical Center, Afula, Israel; [3]Technion - Israel Institute of Technology, Medicine, Haifa, Israel

COVID-19 infection is associated with worse outcomes in patients with hyperglycemia. Our study evaluates the relationship between diabetes control

(Abstract EP209)

Table 4. Logistic regression of variables predicted 30 days mortality.

Predictor variables	*Adjusted OR*	*95% CI*	*P-value*
Gender	1	0.4-2.2	0.99
Age	1.35	0.8-2.2	0.2
BMI <30	0.97	0.47- 2	0.9
HbA1C before admission	0.8	0.6-1.1	0.15
Length of Hospital stay	0.97	0.9-1.1	0.1
COVID-19 severity	12.4	6.53-25.7	<0.001
Insulin treatment	1.8	0.69-4.9	0.22
Dexamethasone treatment	0.79	0.28-2.18	0.64
Metformin treatment	1	0.34-3	0.94
SGLT-2	0.48	0.12-1.7	0.27
CRP level	1.05	1.0-1.08	0.047
Average glucose in hospital	1	0.99-1	0.74
Acute renal failure	3.85	1.52-10	0.005
Cardiovascular disease	0.57	0.28-1.9	0.13
Congestive heart failure	2.4	1.04-5.8	0.04
Chronic pulmonary disease	0.8	0.37-1.8	0.64

Predictor variables	*Adjusted OR*	*95% CI*	*P-value*
Age	*0.99*	*0.77-1.27*	*0.937*
BMI	*1.19*	*0.81-1.76*	*0.372*
HbA1C before	*1.8*	*1.5-2.1*	*<0.001*
Length of Hospital stay	*0.99*	*0.97-1*	*0.28*
COVID-19 severity	*0.99*	*0.73-1.35*	*0.97*
Insulin treatment in hosp	*0.2*	*0.12-0.31*	*<0.001*
Dexamethasone treatment	*0.81*	*0.49-1.3*	*0.395*
Metformin treatment before	*0.78*	*0.49-1.23*	*0.276*
Metformin treatment in hosp	*0.71*	*0.39-1.3*	*0.27*
SGLT-2 before hosp	*2.1*	*1.26-3.59*	*0.005*
SGLT2 in hospital	*1.8*	*0.96-3.69*	*0.067*
CRP level	*1*	*0.99-1*	*0.48*
Cardiovascular disease	*1.26*	*0.84-1.87*	*0.26*
Acute renal failure	*2*	*1.18-3.43*	*0.011*

before and during hospitalization, the severity of SARS-CoV-2 infection, and mortality in patients with type 2 diabetes
Methods
The 857 patients were divided into four groups according to blood glucose control. The first group included 365 patients with an average blood glucose ≤ 140 mg/dl, the second group included 201 patients with an average blood glucose of -140-180 mg/dl, the third group included 198 patients with an average blood glucose of 180-250 mg/dl, and 93 patients in the fourth group had an average blood glucose >250 mg/dl. In all subjects, we assessed preadmission diabetes treatment and prior diagnoses of major comorbidities (atherosclerotic cardiovascular disease, congestive heart failure, chronic renal disease, chronic pulmonary diseases, and dementia). Glucose control during hospitalization, diabetes medications before and during hospitalization, renal function, and glucocorticoid treatment were retrieved from electronic health data. COVID-19 death at 30 days was assessed in the four groups.
Results
Among patients with poor preadmission glucose control (Hba1c>9%), one-third had average blood glucose >250 mg/dl during hospitalization and only 8% had adequate blood glucose control. The overall 30-day mortality rate was 19% (192 patients out of 857) and was highest among patients with uncontrolled blood glucose during hospitalization compared to well-controlled blood glucose (32% vs. 14%). Significant predictors of mortality were the severity of COVID-19, acute renal failure, and a diagnosis of congestive heart failure before hospitalization
Conclusion
In patients with type 2 diabetes hospitalized with COVID-19, poor long-term glycemic control is associated with the level of hyperglycemia during hospitalization, and the COVID-19 severity.

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EP219

Non-alcoholic fatty liver disease. change from F3 to F1 fibrosis after 12 months of combined pioglitazone and dulaglutide treatment

Luisa Lener[1], Marco Chianelli[2], Filomena Graziano[2], Irene Misischi[2], Lucilla Petrucci[2], Roberta Rinaldi[2], Enrico Papini[2] & Rinaldo Guglielmi[2]
[1]Catholic University of Sacred Heart, University Hospital 'A. Gemelli', IRCCS, Internal Medicine, Endocrinology and Diabetology, Rome, Italy; [2]Regina Apostolorum Hospital, Unit of Endocrinology and Metabolism, Albano, Italy

Background
Liver fibrosis is the result of the chronic hepatocyte damage due to different causes. Among them, Non-alcoholic Fatty Liver Disease (NAFLD) is estimated to account for nearly 30% of cases, representing a leading cause of chronic liver disease. NAFLD can evolve into non-alcoholic steatohepatitis, with or without fibrosis, whose diagnosis requires a liver biopsy, a costly and invasive procedure. Non-invasive tests have recently been proposed to screen patients at risk of fibrosis. For instance, fibrosis-4 index (FIB-4) is an effective screening tool for the selection of patients at risk of fibrosis who have indication to liver biopsy. Although there is no established treatment for NAFLD, studies suggested a favorable influence of specific anti-diabetes drugs, such as glucagon-like peptide-1 receptor agonist (GLP-1 RA) and peroxisome proliferator-activated receptor γ (PPARγ) agonists. It is still debated, however, whether these drugs are effective once liver fibrosis has occurred.
Clinical case
A 64-year-old woman referring to our outpatient clinic for dyslipidemia and type 2 diabetes was treated with Vildagliptin 50 mg/bid. and Simvastatin 20 mg/die. She complained of mild right upper quadrant abdominal pain thus, in consideration of her clinical history, FIB-4 was calculated (2.39, n.v. <1.45); Metavir score at liver elastography was F3 (severe fibrosis); liver biopsy confirmed mild fibrosis. Diabetes treatment was shifted to dulaglutide 1.5 mg/week and pioglitazone 30 mg/die. After 12 months, Metavir score at elastography was F1 (fibrosis absent or mild). FIB-4 decreased to 1.63, thus liver biopsy was not performed. 6 months later, weight gain and fluid retention occurred. Empagliflozin 25 mg/die was added to treatment, reducing the symptoms.
Discussion
Recent studies proved the efficacy of dulaglutide in reducing liver fat content and preventing the progression of fibrosis. Pioglitazone promotes the uptake of free fatty acids and lipogenesis, reducing the saturation of subcutaneous adipose tissue, a key factor in the deposition of visceral fat. The reduction of visceral fat and the anti-inflammatory effects of these drugs may explain why they could induce a partial regression of the fibrosis, particularly in early stages. Preclinic studies have demonstrated that, activating the PPARγ pathway, pioglitazone directly inhibits IGF-1-induced collagen deposition in hepatic stellate cells. This might enable hepatic progenitor cells to differentiate into functional hepatocytes and replace the damaged liver tissue. Nevertheless, pioglitazone is rarely used due to its unfavorable effects on weight gain. In our patient, the addition of a Sodium/Glucose Cotransporter 2 inhibitor partially counterbalanced these side effects.

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EP220

Bilateral charcot foot: case report

Imane el ghebir & Ait Abderrahmane Samir
Army Central Hospital, Diabetology, Algiers, Algeria

Introduction
Charcot foot is a rare and particular form of diabetic foot that presents a diagnostic and therapeutic challenge. It can lead to gross structural deformities of the foot and ankle, and subsequent skin ulceration and lower limb amputation from soft tissue or bony infection.
Case report
We report the case of Mr B.D, aged 55, type 2 diabetic for 29 years, poorly controlled despite intensified insulin treatment, at the stage of micro and macroangiopathic complications. He is hypertensive on triple therapy and has a history of multiple episodes of infection in both feet, resulting in amputation of the distal phalanx of the left big toe. He was admitted to our department for treatment of a left plantar neuropathic ulcer. Clinical examination revealed a plantar ulceration on the left foot opposite the 1st metatarsal head measuring 3 cm, painless, surrounded by significant hyperkeratosis and not infected, claw-like deformity of the 2nd toe. Both feet flat, oedematous, dry skin and hyperkeratosis of the heels, monofilament tactile sensitivity and achilles reflex abolished, neuropathic pain graded 5/10 according to DN4, permanent pain in both ankles. Normal IPS at 1.18 on the right and 1.12 on the left. This the lesion can be classified P1E2D2I1S2 according to the PEDIS classification on feet classified guard 3 according to podological risk. Investigation revealed fasting blood glucose of 1.24, HbA1c of 11% and a negative inflammatory panel. The standard X-ray of the left foot was without abnormality, while the MRI revealed extensive remodelling of the Chopart's joint space, suggestive of Charcot foot. Standard radiography of the right foot revealed major osteoarticular destruction of the ankle, suggestive of Charcot foot, confirmed by CT and MRI. Treatment consisted of progressive control of diabetes, strict off-loading of both feet by Aircast with preventive anticoagulation. Local care and oily dressings twice a week.
Discussion
Diabetic osteoarthropathy is a serious complication of diabetes whose early diagnosis is complex and often delayed. It manifests itself in the acute phase by localized inflammation of the foot or ankle, and in the absence of discharge. It leads to severe bone damage. Cases of bilateral Charcot's Foot are not frequent, from 5.9-39.3% of cases according to studies. Accurate diagnosis can lead to appropriate treatment and subsequent reduction in the risk of skin ulceration and lower limb amputation among an already high risk population.

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EP221

The effect of physical activity on sleep quality in middle-aged diabetic patients

Sana Khamassi, Emna Bornaz, Haifa Abdesselem, Marouani Nouha, Kamilia Ounaissa & Chiraz Amrouche
National Institute of Nutrition, Outpatient Department and Functional Explorations, Tunis, Tunisia

Introduction
Sleep and physical activity (PA) are crucial lifestyle components for primary prevention. Governments worldwide have aimed to promote regular PA among diabetic patients to prevent complications and reduce mortality rates. Furthermore, literature data suggests that physical activity contributes to an enhancement in sleep quality[1]. This study aims to assess the level of PA and the sleep quality (SQ) in adults with type 2 diabetes and analyze the correlation between these two parameters.
Materials
One hundred adults with type 2 diabetes were enrolled in this study. Physical activity level was assessed using the Ricci and Gagnon questionnaire. Patients

were asked to complete Pittsburgh sleep quality index (PSQI) to assess SQ[2]. The total PSQI score was obtained by adding seven scores corresponding to seven components of SQ and a total score >5 indicates significant sleep disturbance and categorizes the subjects as poor sleepers.

Results

Mean age was 54.45±7.13 years with female predominance (72%). High blood pressure was reported in 40% of the study population and more than two thirds of patients (70%) had dyslipidemia. Mean diabetes duration was 12.67±7.35 years, 79% used insulin while 21% of patients used oral glucose-lowering drugs (OGLDs) only. Mean BMI was 29.49 ±4.97 kg/m^2. Half of our sample was obese (49%). Mean Ricci and Gagnon total score was 18.20±8.11 with extremes ranging from 9 to 38. More than half of our sample (57%) were inactive, 40% were active, and only 3% of patients were very active. The mean PSQI score was 7.89±3.69 and 69 % of our patients had poor sleep quality. The Ricci and Gagnon score was negatively correlated with the PSQI total score ($P=0.024$; $r=$ - 0.236). Regarding its relationship with sleep components our study revealed that the physical activity level was negatively correlated with self-reported sleep quality ($P=0.013$; $r=$-0.257), habitual sleep efficiency ($P=0.032$, $r=$-0.224) and daytime dysfunction ($P=0.003$; $r=$ - 0.303).

Conclusion

Our study suggests that physical activity could be an area of focus for interventions to improve sleep quality, which is often compromised in diabetic population.

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EP224

Association of glycoregulation, microvascular complications and comorbidities in patients with diabetes mellitus in the republic of srpska/bosnia and herzegovina - cross-sectional study

Snjezana Popovic Pejicic[1,2], Anja Jankovic Pejicic[3], Nina Pejicic[1,2] & Ljiljana stanivuk[4]

[1]University of Banja Luka, Faculty of Medicine, Banja Luka, Bosnia and Herzegovina, Banja Luka, Bosnia and Herzegovina; [2]University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina, Banja Luka, Bosnia and Herzegovina; [3]Medical University of Vienna, Vienna, Austria; [4]Institute of Public Health of Republika Srpska, Banja Luka, Bosnia and Herzegovina

Introduction and objective

Unsatisfactory glycoregulation is the main cause of the development of diabetic microvascular complications. The gold standard for monitoring glycoregulation is glycated hemoglobin (HbA1c). The aim of the research is to determine the association between glycoregulation, microvascular complications and comorbidities in patients with diabetes in Republika Srpska (RS).

Methods

The study was conducted as a cross-sectional study, with the participation of 1088 patients with diabetes in RS. Anthropometric measurements, blood pressure measurement, serum albumin and creatinine, the ratio of albumin and creatinine in urine (ACR), total cholesterol (C), LDL-C, HDL-C, tryglicerides and HbA1c were performed in all patients. For screening of diabetic retinopathy, a nonmydriatic fundus camera with a field of 45 degrees was used, and for the diagnosis of neuroischemic and polyneuropathic changes in the foot was used neurological hammer, sound fork 128Hz and monofilament test with 10 g with mandatory neurological examination.

Results

The study included 1037 patients with diabetes, T1D4.6 % and T2D95.4 %, 576 women (55.5 %) and 461 (44.5%) of men, with an average age of 64.0 ±10.58. Unsatisfactory glycoregulation (HbA1c ≥ 6.5%) had 61.1% of patients ($\chi^2=$ 4.874, df=1, $P=0.027$). The duration of diabetes affected the deterioration of glycoregulation, statistically significantly more common in T2D ($\chi^2=62{,}070$, df=2, $P=0.000$). Patients with diabetes over 10 years (84.60% T1Di 76.10% T2D) had more frequent unsatisfactory glycoregulation (HBa1c≥ 6.5%) Based on the value of BMI, 50.1% of these patients were obese (≥30 kg/m^2), and based on waist circumference, abdominal obesity had 75.6% with a higher frequency in T2D compared to T1D (50.1:15.7%). Elevated blood pressure values (≥ 130/80 mmHg) were recorded in 88.61% i.e., 918 of these patients. Patients with unsatisfactory glycoregulation had significantly higher ACR values compared to satisfactory (79.50 mg/g: 39.00 mg/g) ($P<0.001$). Microalbuminuria was the most common microvascular complication (48.10%), polyneuropathy (42.5%) and retinopathy (25.0%). Polyneuropathy (T2D 43.0%; T1D31.4%) and microalbuminuria (T2D 49.10%; T1D 26.0%) were more common in patients with T2D ($\chi^2=10.217$, df =1, $P=0.001$), while retinopathy (T2D 24.6%; T1D31.4%) was more common in T1D.

Conclusion

Patients with diabetes in RS have a high percentage of unsatisfactory glycoregulation associated with microvascular complications and comorbidities, primarily obesity and hypertension. The results are similar to many studies in developing countries and indicate the need to implement additional measures to improve glycoregulation and reduce microvascular complications and comorbidities.

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EP227

Amyotrophic lateral sclerosis (als): analysis from a nutritional perspective

Irene Zayas Aguilar, María González Pachecho, María del Mar Roca Rodríguez, María Alarcón Manoja & Francisco Javier Vilchez

Hospital Universitario Puerta del Mar, Endocrinology and Nutrition Department, Cádiz, Spain

Introduction

ALS is a neurodegenerative disease with a high prevalence of malnutrition. Nutritional diagnosis is important because of its prognostic implication.

Objective

To determine the clinical and morphofunctional characteristics in a series of patients with ALS.

Materials and methods

Cross-sectional descriptive study of patients seen at the multidisciplinary ALS clinic of the Hospital Puerta del Mar (Cádiz).

Results

17 patients, 58.8% women, mean age 68 years and weight 64.9 kg. The mean time of symptoms evolution was 39 months (64.7% spinal symptoms). Distribution according to disease stage: I 5.9%, II 35.3%, III 41.2% and IV 17.6%. The mean ALSFRS-R scale score 32 (moderate progression). 64.7% had dysphagia, with mean duration 6 months and 35.3% had nutritional risk or were classified as malnourished (The Subjective Global Assessment (SGA) B or C). Mean nutritional ultrasound parameters: (1) Anterior rectus quadriceps: area 3.17 cm^2, Y axis 1.07 cm, (2) Abdominal adipose tissue: total 1.73 cm and preperitoneal 0.55 cm, (3) Masseter: 1.12 cm. BIA: Phase angle 3.7º, Hydration 73.8%, Fat free mass 42.8%, Fat mass 23.1 kg, BCM 17.3 and ASMM 14.3 kg. Patients with SGA B or C had a higher weight percentage (11.1 vs 1.65%; P 0.032) and lower fat mass (16.7 vs 24.2 kg; P 0.039). There was a negative correlation between ALFRS-R score and preperitoneal fat ($r=$ - 0.837, $P<0.001$), and positive correlations between weight and fat mass ($r=$ 0.752, $P<0.001$), between lean mass and ASMM ($r=$ 0.966, $P<0.001$) and between lean mass and BCM ($r=0.776$, $P<0.001$).

Conclusions

In our cohort, malnutrition is highly prevalent. Overall, there is a marked decrease in phase angle, with a significant reduction in fat mass in malnourished patients. The prognostic value of these findings in the follow-up of the disease needs to be assessed.

Ultrasound parameters	**Median**
Area anterior rectus quadriceps	**3.17 cm^2**
Y axis anterior rectus quadriceps	**1.07 cm**
Abdominal adipose tissue: total	**1.73 cm**
Abdominal adipose tissue: total	**0.55 cm**
Masseter	**1.12 cm**
BIA Parameters	**Median**
Phase angle	**3.7º**
Hydration	**73.8%**
Fat free mass	**42.8%**
Fat mass	**23.1 kg**
BCM	**17.3**
ASMM	**14.3 kg**

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EP228

Variables of diabetes distress and glycated hemoglobin in patients with type 2 diabetes mellitus

Volodymyr Pankiv
Ukrainian Scientific and Practical Center of Endocrine Surgery, Transplantation of Endocrine Organs and Tissues of MoH of Ukraine, Prevention and Treatment of Diabetes Mellitus and its Complications, Kyiv, Ukraine

Background
Among potential barriers for people with diabetes mellitus (DM) to reach glycemic goals is diabetes distress. Accumulating evidence suggests diabetes distress may be linked to individuals' emotion regulation capacities.
The aim of this study was to explicate the relationships between variables of glycated hemoglobin (HbA1c), diabetes distress, emotion regulation, and self-care variables through the analysis of cross-sectional data from individuals with type 2 DM.
Materials and methods
We used structural equation modeling to assess the cross-sectional relationships between variables of HbA1c, diabetes distress, emotion regulation, and self-care variables through the analysis of cross-sectional data from 95 individuals with Type 2 DM. After giving informed consent agreeing that their data would be used for research purposes without identifying them, study participants were evaluated by clinical psychologists with a structured clinical assessment and a series of other assessments relevant to DM.
Results
Study examined two potential explanatory models with one of the models showing a more comprehensive view of the data revealing a total effect of poor emotional regulation on HbA1c levels. Diabetes distress in adults is linked with heightened negative emotionality (Emotion Regulation-Experience) and reduced skill at emotional regulation (Emotion Regulation-Skill) in adults, both of which are related to elevated HbA1c levels and that these relationships are stronger than that with diabetes self-care.
Conclusions
This study suggests that, in people with DM, elevated HbA1c levels and diabetes distress are linked with poor emotion regulation. These data suggest that targeting difficulties in emotion regulation may hold promise for maximizing improvement in diabetes distress and HbA1c in individuals with DM.

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EP229

Bridging the gap between short stature and metabolic alterations in children born small for gestational age: an exploratory study

Giulia Rodari[1,2], valeria citterio[2], Valentina Collini[2], Alessandro Risio[2], Eriselda Profka[1,2], Federico Giacchetti[1], Giovanna Mantovani[1,2] & Claudia Giavoli[1,2]
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, [2]University of Milan, Department of Clinical Sciences and Community Health

Introduction
Children born small for gestational age (SGA) represent a heterogeneous population, displaying different phenotypes for both growth and metabolic status. Low birth length and/or weight increases the risks for not only growth impairment but also for metabolic derangements, the latter with an even amplified risk in children with rapid postnatal weight gain. Variability in metabolic parameters, catch-up growth as well as different GH treatment responses are still poorly understood.
Aims
We investigated a possible association between anthropometric/metabolic parameters in SGA children.
Methods
This cross-sectional observational study evaluated a series of 58 children aged between 4 and 15.7 years, with birth weight and/or length $<$ -2.0 SDS according to INeS Growth Charts. All patients with underlying chronic conditions, GH deficiency, other endocrinopathies and known genetic syndromes were excluded. Anthropometric (height-HT, Mid-parental height-MPH, weight, weight gain at 24 months, Body Mass Index-BMI, Tanner stage, body composition by Body Structure Analyzer BC-420MA TANITA) and metabolic (fasting glycemia and insulin, glycosylated hemoglobin-HbA1c) parameters were collected. Insulin resistance (HOMA-IR) and sensitivity (QUICKI) were calculated.
Results
Fifty-eight SGA patients (F 33/58, 57%), with a mean age of 9.5 $\pm$ 2.9 years were consecutively enrolled. In 22.4% of patients HT was below -2.0 SDS. Mean HT was 129.8 $\pm$ 17.7 cm, -0.88 $\pm$ 1.29 SDS according to WHO Growth Charts with a MPH distance (MPH SDS-HT SDS) of 0.70 $\pm$ 1.36 SDS. As far as glycemic profile was concerned, glycemia was in the normal range in all study patients apart from one with impaired fasting glucose (107 mg/dL), mean glycemia was 82.7 $\pm$ 7.9 mg/dl, mean HbA1c 35 $\pm$ 3 mmol/mol, with a median HOMA I of 1.45 (IQR 0.74-2.7) and QUICKI of 0.36 (IQR 0.32-0.39). At multiple regression, HbA1c was positively associated with HT SDS ($P = 0.005$), even after correction for MPH ($P = 0.01$). Moreover, weight gain at 24 months was positively associated with HT SDS ($P = 0.021$). No association was found between weight gain and metabolic parameters.
Conclusions
Our results suggest a possible relationship between postnatal height catch-up growth and metabolic impairment, as underlined by the association found between HT and HbA1c, even after correction for mid-parental height. This is only an explorative analysis; we would like to confirm our results on a larger scale in order to eventually bridge the gap between height gain and metabolic impairment in SGA children.

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EP235

A rare cause of glucosuria and aminoaciduria in a patient with well-controlled diabetes mellitus

Saohoine Inthasot[1], Julien Vanderhulst[1], Sien Van Daele[2], Evelien Van Hoof[2], Cyrielle Kint[3], Laura Iconaru[4] & Jeroen de Filette[4]
[1]CHU Brugmann, Department of Internal Medicine, Université Libre de Bruxelles, Brussels, Belgium; [2]University Hospitals Leuven, Center for Human Genetics, Catholic University Leuven, Leuven, Belgium; [3]KU Leuven, Centre of Microbial and Plant Genetics, Leuven, Belgium; [4]CHU Brugmann, Department of Endocrinology, Université Libre de Bruxelles, Brussels, Belgium

Background
Familial renal glucosuria (FRG) is a rare renal tubular disorder characterized by increased urinary glucose excretion despite normoglycemia. The sodium-glucose cotransporter 2 (SGLT2) is expressed in the proximal renal tubule and is crucial for glucose reabsorption. *SLC5A2* is a member of the solute carrier family V transporter genes and encodes for this cotransporter. Mutations in *SLC5A2* are the primary cause of FRG.
Case presentation
We report the case of a 44-year-old male who was referred for unexplained glucosuria despite well-controlled diabetes mellitus (with fasting glycemia 138 mg/dl and HbA1c 6,5%) treated with metformin and gliclazide. He was diagnosed with diabetes mellitus at the age of 38. He complained of an unintentional 5-kg weight loss in one year (despite normal appetite) and nycturia. A 24-hour urinary collection revealed overt glucosuria (24,2 g/1,73 m^2/24 h) as well as generalized aminoaciduria (hydroxyproline, serine, glycine, alanine, valine, cystine, isoleucine and lysine) and increased uric acid excretion. Renal function was preserved and proteinuria was absent. Whole exome sequencing with analysis of the nephropathy gene panel was performed (with specific attention to the *SLC5A2* and *HFN1A* genes (MODY 3)) and revealed a novel heterozygous c.469-1G $>$ A variant in the *SLC5A2* gene. This mutation was classified as class 4 (likely pathogenic) according to the American College of Medical Genetics guidelines. In-silico analysis predicted a possible splice defect. No other pathogenic variants were detected. Familial genetic testing was recommended to the patient and his children.
Discussion
The *SLC5A2* gene encodes the kidney-specific low-affinity/high-capacity sodium-glucose cotransporter, SGLT2. Mutations in *SLC5A2* are associated with FRG, which is considered to be a benign disorder of proximal tubular glucose transport. FRG can be inherited in an autosomal recessive or autosomal dominant pattern. Individuals with bi-allelic pathogenic variants are considered to have a more severe phenotype than patients who only have a heterozygous variant. Generalized or selective aminoaciduria is a feature of FRG, although it has been suggested that aminoaciduria in this setting is a consequence of the impairment of glucose reabsorption rather than directly related to the *SLC5A2* mutation.
Conclusion
We describe a patient with renal glucosuria despite well-controlled diabetes mellitus, associated with a novel heterozygous c.469-1G $>$ A mutation in the *SLC5A2* gene. The pathogenesis of aminoaciduria and hyperuricosuria with aberrant renal glucose transport remains to be established.

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EP236

Association of advanced glycation end products with diabetic retinopathy in type 1 and type 2 diabetes

Diana Simoniene[1], Lina Radzevičienė[1,2], Deimantė Paškevičienė[2] & Rasa Verkauskienė[1,2]
[1]Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Endocrinology, Kaunas, Lithuania; [2]Institute of Endocrinology, Lithuanian University of Health Sciences Kaunas Clinics, Endocrinology, Kaunas, Lithuania

Some studies suggest that Advanced Glycation End products (AGEs) formation represent important and interconnected pathogenic mechanisms in diabetic retinopathy (DR).
The aim of this study was to investigate the association of AGEs products with DR in a cohort at Hospital of LHUS.
Methods
It was a cross-sectional study of a cohort of adults with type 1 or 2 type diabetes (T1D/T2D).
Results
78 patients with T1D and 81 with T2D were recruited. The overall incidence of any DR was 50.9 %. The prevalence of DR was significantly higher among patients with T1D compared to T2D group (70.5 vs 32.1 %, $P<0.001$). Patients with T1D had higher risk for DR in comparison to T2D (OR 5,059 [2,578-9,927], $P<0.001$). Univariate logistic regression revealed that higher risk for DR in T1D was related with diabetes duration > 11 years OR 60,563 [13,75-266,752], $P<0,001$, mean AGE Reader level > 1,8 OR 6,947[2,242-21,526], $P=0,003$, male gender OR 2,938[1,007-8,569] ($P=0,044$) and dyslipidaemia OR 3,231[1,103-9,464] ($P=0,029$). Higher risk for DR in T2D was related with diabetes duration > 13 years OR 4,604 [1,701-12,462], $P=0,002$, OR 6,947 [2,242-21,526], $P<0,001$ and albuminuria > 6.3 mg/24 hrs OR 10,431[2,681-40,586], $P=0,001$. In binary logistic regression analysis, the highest risk for DR was associated with dyslipidaemia OR 6 (0.99-36.26) $P=0.051$ and diabetes duration > 11 years OR 76 (13.63-423.73), $P<0.001$ in T1D. In T2D DR was associated with HbA1c > 7.5 % OR 7.42 (2.23-24.58), $P=0.001$ and diabetes duration > 13 years OR 4.35 (1.42-13.34), $P=0.01$.
Conclusions
Diabetic retinopathy prevalence in Lithuanian cohort was 50.9 %. Patients with T1D had a five times higher risk for DR in comparison to T2D. In univariate models, DR in T1D was significantly associated with mean AGE score, diabetes duration, male gender and dyslipidaemia, in T2D - with HbA1c level, increased albuminuria level and diabetes duration. In binary logistic regression analysis, diabetes duration remained the most significant predictor for DR in both types of diabetes. T1D patients with diabetes duration > 11 years and T2D patients with diabetes duration > 13 years, will have the highest rate risk of DR.

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EP243

Hypoglycemia and beyond

Felicia Visconti, Marcella Libera Balbo, Daniela Rosso, Francesca Garino, Daniela Sansone & Salvatore Endrio Oleandri
ASL Città di Torino, S.C. Endocrinologia e Malattie Metaboliche, Torino, Italy

Introduction
Hirata Syndrome (SH) is a rare cause of autoimmune hypoglycemia, characterized by elevated circulating insulin levels without concomitant increase in C-peptide, anti-insulin antibodies positivity and pancreas alterations absence in patients never exposed to exogenous insulin. It is also known as insulin autoimmune syndrome (IAS) and is a relatively rare cause of spontaneous hypoglycemia. The syndrome was first described in 1970 by Yukimasa Hirata in Japan, the country where the highest number of cases was subsequently recorded.
Case report
77-year-old woman came to the emergency room for an episode of profuse sweating and aphasia. -for two months she had frequent lipothymic episodes for which she had undergone cardiological tests, the results of which were normal. Blood sugar levels were found to be 27 mg/dl on blood chemistry tests, whereby 10% glucose solution was administered, reaching glycemic values at the lower limits of normality, making it impossible to reduce or suspend therapy. Abdominal CT and echoendoscopy were negative for pancreatic lesions and hypoadrenalism was excluded (ACTH: 20 pg/ml, cortisolemia: 10.7 mg/dl). Fasting test was started: after 3 hours, the patient complained of sweating and tremor, with concomitant findings on blood tests: glycemia 29 mg/dl, insulinemia: 747 microU/ml, c-peptide: 4.9 mg/l, anti-insulin Ab: 11 U/ml (nv.: < 2.4). Autoimmune hypoglycemia was diagnosed, and patient started steroid therapy with prednisone 25 mg/day. The patient started flash glucose monitoring, showing an adequate response to steroid therapy, with progressive reduction of hypoglycemic episodes and normalization of glycemic levels. The patient was discharged, and at the endocrinological visit after one month steroid tapering was possible, according to the glycemic values.
Conclusion
Autoimmune forms of hypoglycemia are rare among Caucasians but should be taken into consideration in the setting of unsuppressed insulin levels, to avoid misdiagnosis of insulinoma. Treatment involves primarily the use of corticosteroid therapy or, in more severe cases, greater immunosuppressive drugs such as azathioprine. In extreme cases plasmapheresis can be necessary.

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EP248

Diabetes mellitus after ocrelizumab treatment for primary progressive multiple sclerosis

Marco Grasso, Nino Cristiano Chilelli, Vera Frison & Alessio Filippi
Hospital of Cittadella, Diabetology Unit, Cittadella, Italy

Introduction
immune reconstitution therapies, which include cell-depleting monoclonal antibodies targeting CD20+ (ocrelizumab) or CD52+ (alemtuzumab) leukocytes, are approved for the treatment of multiple sclerosis. Autoimmune thyroid disease is the most common adverse effect of alemtuzumab, but some cases of autoimmune diabetes have been reported. To date, diabetes mellitus has not been reported after CD20-targeting monoclonal antibodies therapy.
Case presentation
A 41-year-old Caucasian man with primary progressive multiple sclerosis was started on ocrelizumab in July 2021, after the finding of active disease on MRI and progression of neurological symptoms. The patient had a family history of autoimmune thyroiditis. He was non-smoker, not overweight (BMI 24.5 kg/m^2), and treated with lamivudine for chronic hepatitis B and baclofen. There were two previous findings of impaired fasting glucose. In January 2022, before the second ocrelizumab administration, the urine test showed glycosuria (> 1000 mg/dl) and proteinuria, without ketonuria. In the last few weeks, the patient had reported polyuria and polydipsia, but no blurred vision or weight loss. HbA1c and blood glucose level confirmed the diagnosis of diabetes mellitus (87 mmol/mol and 442 mg/dl, respectively). The patient underwent further tests to clarify the etiology of hyperglycemia. GADA, IA-2A and ICA were found negative; C-peptide indicated a well-preserved beta-cell function (2.7 ng/ml). Renal and liver function were normal. Other autoantibodies related to endocrine diseases, such as TPO-Ab and ACA, were found negative. We started a strict glucose monitoring and basal-bolus insulin treatment (total daily dose 58 IU, 0.75 IU/Kg). Down-titration of insulin dosage had been progressive and relatively rapid: 43 IU after two weeks, 36 IU after the first month, 24 IU after six weeks. We added metformin 1000 mg and, after four months, insulin treatment has been permanently discontinued. The patient continued ocrelizumab treatment, but severe hyperglycemia has no longer occurred. In August 2023, the blood test showed a HbA1c level of 39 mmol/mol, indicative of an optimal glycemic control with only metformin.
Conclusions
this is the first case of diabetes mellitus reported after ocrelizumab administration. The timing of onset and course are similar to alemtuzumab-induced autoimmune diseases, usually defined as an 'immune reconstitution syndrome'; nevertheless, cell depletion induced by ocrelizumab shows some differences in duration and cell population affected. This case suggests the need for screening and follow-up of glycemic status in patients treated with this monoclonal antibody. Further investigation is required to elucidate the correlation between hyperglycemia and ocrelizumab.

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EP259

A ketogenic diet as feasible treatment for post bariatric weight regain

Fiammetta Cipriani[1], Maria chiara Massari[1], Maria Letizia Spizzichini[1], Davide Masi[1], Ilaria Ernesti[2], Alfredo Genco[2], Silvia Migliaccio[1], Stefania Mariani[1], Lucio Gnessi[1], Carla Lubrano[1] & Mikiko Watanabe[1]
[1]Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza University of Rome, 00161 Rome, Italy; [2]Surgical Endoscopy Unit, Department of Surgical Sciences, Sapienza University of Rome, Rome, Italy

Introduction
Metabolic surgery is the most effective long-term treatment for obesity. However, studies reveal that up to 40% of post-bariatric subjects experience long-term weight regain (WR), particularly those who discontinue surgical and nutritional follow-ups. In contrast, the ketogenic diet emerges as a pivotal therapy for obesity, showing convincing evidence in weight loss and improvement of weight-related complications.
Purpose
This study aims to evaluate the safety and efficacy of a very-low calorie ketogenic diet (VLCKD) in the treatment of post-bariatric WR.
Materials and Methods
This prospective, single-center pilot study involved patients with previous metabolic surgery (RYGB or Sleeve gastrectomy) who had clinically significant WR after successful initial weight loss. Inclusion criteria included age between 18 and 65 years, a BMI ≥ 30 kg/m^2, while exclusion criteria included pregnancy/lactation, type 1 diabetes mellitus, renal and hepatic disease, alcoholism, and major psychiatric disorders. The primary outcome was weight loss, while secondary outcomes focused on safety, improvements in metabolic profile, and body composition. All participants followed an 8-week nutritional intervention with VLCKD, limiting their carbohydrate intake to less than 50 g/day and with adequate protein intake at 1.2-1.5 g/kg of ideal body weight. Dietary counseling was provided every 4 weeks by an experienced dietitian, and compliance was assessed by dietary recalls and beta hydroxybutyrate measurements. Patients underwent biochemical and body composition assessment by DXA scan at baseline and after dietary intervention.
Results
Fifteen patients were enrolled (10 females, 5 males) with a mean age of 49 ± 11 years and a mean BMI of 40.27 ± 6.59 kg/m^2. After 8 weeks, patients showed an average weight loss of 7.2%, a significant reduction in waist circumference ($P < 0.001$), hip circumference ($P = 0.007$) and improvement in body composition indices: reduction in fat mass ($P < 0.001$) and lean mass to fat mass ratio ($P = 0.03$). Favorable changes in glyco-metabolic balance were reported with a significant reduction in LDL cholesterol levels ($P = 0.03$). Safety parameters (renal function, uric acid, electrolytes) remained stable; the only adverse event reported was mild constipation.
Conclusions
This study emphasizes the efficacy of the VLCKD in the management of post-bariatric WR, demonstrating satisfactory weight loss and improved body composition without safety concerns. However, long-term weight loss maintenance remains uncertain without significant changes in lifestyle or pharmacotherapy. Further studies should explore the efficacy of dieting, including different weight loss scenarios and emphasizing maintenance strategies.

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EP263

Reactive hypoglycaemia: A challenge in clinical practice

Usman Shah, Anna Hawkins, Raj Tanday, Azin Mohammadpoor, Nancy Enriquez & Khash Nikookam
Barking, Havering and Redbridge Hospitals University NHS Trust, United Kingdom

This is a case of a 38-year-old lady with a past medical history of Ehlers Danlos Syndrome, functional neurological syndrome and unremarkable cardiac investigations for palpitations. She was referred by her general practitioner (GP) with episodic shaking, excessive sweating, recurrent hypo-and hyperglycaemia recorded by her own capillary blood glucose (CBG) meter, ranging from 1.9mmol/l to 19mmol/l. The episodes would mostly occur 1 to 3 times per week, usually in the afternoon and last for approximately 15 minutes. She denied loss of consciousness and the episodes would leave her feeling either weak or fine. All her medications (Duloxetine, bisoprolol and oral contraceptive pill) were stopped prior to her endocrine appointment. She was admitted following recurrent hypoglycaemia and with presenting symptoms suggestive of urinary tract infection. She had various investigations including a normal IGF-1, coeliac screen, a short synacthen test (SST) with 0, 30 and 60mins serum cortisol response of 452, 658 and 820 respectively, normal 24 hr urine metanephrine and a 72 hour fast which did not reveal any spontaneous hypoglycaemia. Subsequent prolonged oral glucose tolerance test (OGTT) was indicative of Type2 Diabetes Mellitus with a CBG at 0 mins of 6.3 and at 120 mins of 12.1mmol/l. She experienced symptoms of headache, tiredness and sweating at 240 mins with a CBG of 3.5mmol/l. The patient has continued to experience hypoglycaemic episodes in daily life. She has therefore been advised to have smaller meal portions but more frequent intake which she reports have reduced her hypoglycaemia episodes.
Conclusion
Reactive hypoglycaemia could be a cause of recurrent hypoglycaemia in individuals with or without diabetes mellitus. Reactive hypoglycaemia can be a debilitating condition with a significant impact on one's general wellbeing and daily activities. Diagnosing and understanding of reactive hypoglycaemia would potentially change one's life for the better.

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EP264

Depression in elderly diabetics: prevalence and impact on glycemic control

Maryam Cheikhrouhou, Kamilia Ounaissa, Chaima Sdiri, Haifa Abdesslem, Sana Khamessi, Emna Bornaz & Chiraz Amrouche
national nutrition institute, Department of Nutritional Diseases D, Tunisia

Introduction
Depression is a frequent pathology in elderly subjects, due to lifestyle changes, age and the high frequency of comorbidities. Our study aimed to assess the prevalence of depression in a group of elderly diabetics and to investigate its impact on diabetes control.
Methods
This was a cross-sectional study, conducted in a group of 200 type 2 diabetic patients, aged 70 years or more. We screened for depression using the 15-point geriatric depression scale (GDS15). The diagnosis of depression was made if the score was < 5. Depression was considered mild to moderate if the score was between 5 and 9 and severe if the score was ≥ 10.
Results
The meanage was of 74.7 ± 4.2 years, ranging from 70 to 90 years. A female predominance wasn oted with a sex ratio M/F = 0.62. The mean duration of diabetes was 16.5 ± 9.26 years. The mean GDS15 score was 4.35 ± 2.8. Depression was diagnosed in 45.5% of patients. It was severe in 7.5% of cases and it was more frequent in the 75-80 yearsage group. It was more frequent in women then in men (60.2% vs 22.1%, $P < 0.001$). Patients with a GDS15 score below 5 had a better glycemic control than those with GDS15 scores more then 5 (51.4% vs 34.1%, $P = 0.014$). Likewise, we found a statistically significant relationship between depression on one hand and the occurrence of hypoglycemia ($P < 0.001$), the presence of diabetic retinopathy ($P = 0.04$) and diabetic neuropathy ($P = 0.004$) on the other hand.
Conclusion
Systematic screening and appropriate management of depression are essential in elderly diabetic patients in order to improve patients' quality of life.

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EP273

The association between heat exposure and hospitalization for diabetic ketoacidosis, hyperosmolar hyperglycemic state, and hypoglycemia. a scoping review

Emmanuel Sandoval Garcia[1] & Stephani Rubi Hellwege[2]
[1]Royal Infirmary of Edinburgh, United Kingdom; [2]University Hospital of Zürich, Zürich, Switzerland

Introduction
Global mean surface air temperatures have risen by about 1 °C in the past century and are projected to increase by another 1–6 °C by 2100 depending on greenhouse gas emissions. As a result of the increase in mean temperatures, heatwaves have become more severe, frequent, and prevalent. Heat exposure in ambient temperature is associated with all-cause diabetes mortality and all-cause hospitalisation in people with diabetes. However, there is a paucity about the current evidence of the association between heat exposure and hospitalisation for hyperglycaemic emergencies, such as diabetic ketoacidosis (DKA), hyperosmolar hyperglycaemic state (HHS), and hypoglycaemia. This scoping review aims to map existing literature and provide a summary of diabetic ketoacidosis (DKA), hyperosmolar hyperglycemic state (HHS), and hypoglycaemia and heatwaves in people with diabetes. This includes risk factors, interventions and identification of research gaps in the literature.
Methods
Electronic databases (MEDLINE, EMBASE, and, Global Health) were systematically and independently searched following the Joanna Briggs Institute (JBI)

guidelines. Two independent researchers assessed the literature and conducted the review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines for Scoping Reviews (PRISMA-ScR). Covidence was used for for title/abstract screening, full-text screening, data extraction, and quality assessment.
Results
Of the 4406 articles screened, 75 articles met inclusion criteria and 12 were included for this scoping review. The majority of studies were cross-sectional concentrated in the Americas, Asia and Australia. The findings indicated that heat exposure was associated with an increased risk of hospitalisations for DKA, HHS but not hypoglycaemia. There was a lack of information regarding other environmental conditions such as humidity, air pollution and extreme weather events which may interact with these outcomes.
Conclusions
People with diabetes face heightened susceptibility to health threats linked to climate change, such as increased heat exposure. This research has the potential to inform proactive measures against the elevated risk of hyperglycaemic emergencies. These findings offer an opportunity for developing public health initiatives aimed at managing heatwaves in the contemporary context of global warming. Implementing policies that acknowledge the interplay between climate change and diabetes outcomes could improve the overall health of the diabetic population. Clearly, further studies are necessary for investigating potential solutions to tackle this crisis

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EP275

Endocrine disorders in adult patients with inherited metabolic diseases: their diagnosis and long-term management

Adrian Heald[1], John Bassett[1], John Warner-Levy[1], Nuria Puente-Ruiz[2], Peter Clayton[3] & Karolina Stepien[2]
[1]Salford Royal Hospital, Salford, Department of Endocrinology and Diabetes, Salford, United Kingdom; [2]Northern Care Alliance NHS Foundation Trust, Adult Inherited Metabolic Disorders, Salford, United Kingdom; [3]Royal Manchester Children's Hospital, Manchester University NHS Foundation Trust, Manchester, UK, Manchester, United Kingdom

Background
Inherited metabolic disorders (IMDs) are a group of heterogenous genetic disorders resulting in substrate accumulation, energy deficiency or complex molecular defects due to the failure of specific molecules to act as enzymes, cofactors, transporters, or receptors in specific metabolic pathways. The pathophysiological changes seen in IMDs sometimes impact on the endocrine system. We here describe our experience at one UK centre where patients are seen jointly by an endocrinologist and an IMD specialist.
Methods
The study has two parts: 1) a review of the types of IMDs and the endocrine problem, to understand the molecular mechanisms in the metabolic pathways that might have led to the hormonal dysfunction; 2) service development for joint working between the endocrinology and metabolic specialities.
Results
61.0% of the attendees are women and 67.5% of patients have a solitary endocrine disorder with (sub)infertility problems being the most frequent reason for attendance. 28.2% had 2 endocrine conditions and 4.435% had at least 3 endocrine complications. The most prevalent IMDs related to endocrine complications included Classical Galactosemia (15.2%), X-linked Adrenoleukodystrophy (10.9%), Mucopolysaccharidosis type I Hurler (8.7%) who underwent Haemopoietic Cell Transplantation in childhood, and mitochondrial disorders. The mechanisms of endocrinopathy were directly related to the metabolic pathway of an IMD in most patients. Learning disability was a feature of several IMDs; in our cohort, 26.0% had mild/moderate type of learning disability.
Conclusion
Endocrine disorders are long-term complications of IMDs. Thus awareness among endocrinologists of the potential for an IMD to be the underlying cause of an endocrine presentation is important. Signs and symptoms of common hormonal problems may be wrongly attributed to the underlying IMD, if not diagnosed promptly. Hormonal dysfunction may be the first manifestation of previously unknown IMDs in adults in both men and women and further investigations may lead to a diagnosis of an attenuated form of an IMD in adulthood. Advice on hormonal replacement therapy choice should consider its effects on metabolism and efficacy.

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EP277

Plasma SHBG levels as an early predictor of response to bariatric surgery

Pablo Gabriel-Medina[1], Roser Ferrer[1,1,2,2], Francisco Rodriguez-Frias[1], Marta Comas[3], Ramon Vilallonga[4], Andreea Ciudin[3] & David Selva[5]
[1]Vall d'Hebron University Hospital, Clinical Biochemistry Department, Barcelona, Spain; [2], Clinical Biochemistry Department, Barcelona; [3], Vall d'Hebron University Hospital, Endocrinology and Nutrition Department, Barcelona, Spain; [4]Center of Excellence for the EAC-BC and Vall d'Hebron University Hospital, Endocrine, Metabolic and Bariatric Unit, Barcelona, Spain; [5]Vall d'Hebron Research Institute, Diabetes and Metabolism, Barcelona, Spain

Background
Obesity is a growing global health problem and currently bariatric surgery (BS) is the best solution in terms of sustained total weight loss (TWL). However, a significant number of patients present weight regain (WR) in time. There is a lack of biomarkers predicting the response to BS and WR during the follow-up. Plasma SHBG levels, which are low in obesity, increase one month after BS but there is no data of plasma SHBG levels at long term. We performed the present study aimed at exploring the SHBG role in predicting TWL and WR after BS.
Methods
Prospective study including 62 patients with obesity undergoing BS. Anthropometric and biochemical variables, including SHBG were analyzed at baseline, 1, 6, 12, and 24 months; TWL $\geq$25% was considered as good BS response.
Results
Weight loss nadir was achieved at 12 months post-BS where maximum SHBG increase was reached. $\geq$25% TWL patients presented significantly higher SHBG increases at 1st and 6th month follow-up respect to baseline (100% and 150% respectively, $P=0.025$), than $<$25% TWL patients (40% and 50% respectively, $P=0.03$). Also, these presented 6.6% WR after 24 months. The 1st month SHBG increase predicted BS response at 24 months (OR=2.71; 95%CI=[1.11-6.60]; $P=0.028$) and TWL in the 12th month ($r=0.330$, $P=0.012$) and the WR in the 24th month after BS ($r=-0.301$, $P=0.028$).
Conclusion
Our results showed for the first time that increase in plasma SHBG levels within the first month after BS is a good predictor of TWL and WR response after two years.

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EP278

The effects of different weight-loss interventions on Bile acid and FGF-19 metabolism and correlation with metabolic improvement

Preeshila Behary[1,2], Kleopatra Alexiadou[1], Tracey Mare[3], Julian Walters[4], David Taylor[3], Royce Vincent[3] & Tricia Tan[1,2]
[1]Imperial College London, Section of Endocrinology and Investigative Medicine, London, United Kingdom; [2]Imperial College Healthcare NHS Trust, Department of Endocrinology, London, United Kingdom; [3]King's College Hospital NHS Foundation Trust, Department of Clinical Biochemistry (Synnovis), London, United Kingdom; [4]Imperial College Healthcare NHS Trust, Department of Gastroenterology, London, United Kingdom

Background
Bariatric surgery, dietary restriction and gut hormones treatment for obesity, lead to distinctive changes in weight-loss maintenance and glycaemia. We previously showed that Roux-en-Y Gastric Bypass (RYGB) and Very-Low-Calorie-Diet (VLCD) were superior in weight-loss, compared to a tripeptide hormone infusion of G lucagon-like Peptide-1, O xyntomodulin and P eptide-YY over a month (**GOP**, infused at doses to replicate their peak post-prandial concentrations as seen at 1 month after RYGB). However, better glycaemic improvement with superior glucose variability attenuation were observed with GOP (1). Bile acids (BA) are important mediators of energy and glucose metabolism. The aims of this study are to investigate the acute and long-term changes in BA metabolism post-RYGB, relative to other weight-loss interventions and to correlate with metabolic improvement.
Methods
Obese participants with type 2 diabetes/pre-diabetes underwent RYGB or a VLCD or were randomised to GOP infusion. Fasted and post-prandial BA and FGF-19 were measured following a mixed meal test, at baseline and 1-month after all 3 interventions, and additionally at 2-3 years post-surgery. Fifteen plasma BA fractions were measured using a liquid chromatography-tandem mass spectrometry. A mixed-effects analysis with Bonferroni correction was applied for within-group comparison.

(Abstract EP278)

	Weight loss (%)		Fructosamine (μmol/l)			Fasting BA (μM/l)		
	1-month	2-3 years	Baseline	1-month	2-3 years	Baseline	1-month	2-3 years
RYGB ($n=20$)	8.8±0.6*	26.7±2.5*	248.3±8.0	216.4±4.8*	241.1±5.1	3.9±0.4	3.2±0.5	4.4±0.8
GOP ($n=14$)	3.7±0.4*		304.1±17.2	261.7±12.7*		3.1±0.3	2.2±0.1*	
VLCD ($n=20$)	7.6±0.4*		254.9±8.5	225.1±7.3*		2.8±0.3	3.0±0.6	

Mean ±SE, *$P<0.05$ compared to baseline

Results
Study subjects were well matched for baseline characteristics. Changes in weight, fructosamine and fasting BAs are described below:
At 1-month, fasting and post-prandial BA remained statistically unchanged after RYGB and VLCD, but there was a significant reduction in total and other BA parameters with GOP. Post-prandial FGF-19 concentrations decreased with GOP, but no significant change was noted from baseline after RYGB and VLCD at 1-month. However, at 2-3 years post-RYGB, there were significant increases in post-prandial total BAs and the 12 hydroxylated:12 non-hydroxylated BA ratio, as well as an increase in post-prandial FGF-19 concentrations were observed.
Conclusion
Different weight-loss interventions have distinctive effects on the BA/FGF-19 axis. Despite its lowering effect on several BA fractions and FGF-19 concentrations, significant weight loss and improvement in glycaemia were still observed following a tripeptide gut hormone infusion. Total post-prandial BAs and FGF-19 were only increased at 2-3 years post-RYGB, suggesting a potential role in the long-term rather than short-term efficacy of RYGB.
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EP279

Prediction of post-COVID syndrome development in type 2 diabetes: retrospective analysis based on national survey in Ukraine
Anton Matviichuk[1], Vitalii Gurianov[1], Viktoriia Yerokhovych[1], Oleksandr Livkutnyk[2], Tetyana Falalyeyeva[3,4], Iuliia Komisarenko[1], Oksana Sulaieva[4] & Nazarii Kobyliak[4,5]
[1]Bogomolets National Medical University, Kyiv, Ukraine; [2]Kyiv City Clinical Endocrinology Center, Kyiv, Ukraine; [3]Taras Shevchenko National University of Kyiv, Kyiv, Ukraine; [4]Medical Laboratory CSD, Scientific, Kyiv, Ukraine; [5]Bogomolets National Medical University, Endocrinology, Ukraine

Background
Post-COVID-19 condition (long COVID-19, post-acute COVID-19, long-term effects of COVID-19) is an emerging health problem in people recovering from COVID-19 infection within the past 4-6 months. Patients with type 2 diabetes (T2D) are in the risk group for a more severe course of COVID-19 and the development of its complications.
Aim
to define the prevalence and prediction of post-COVID-syndrome development in patients with T2D according to retrospective analysis based on national survey in Ukraine.
Method
The retrospective analysis include data from 403 patients who suffered from COVID-19 infection in different regions on Ukraine. Among these patients, 168 (41.7%) developed post-COVID syndrome and 235 (58.3%) reported it absence. Patients were asked to fill out specially developed questionnaires for the purpose of retrospective assessment of the main parameters. The questionnaires included the following information: anthropometric indicators, year of diagnosis ofT2D, existing T2D complications history of COVID-19, COVID-19 severity and treatment, post-COVID phenotype and symptoms, duration of post-COVID syndrome, hypoglycemic therapy, levels of HbA1C, lipids and basic biochemical indicators. The stepwise multivariate logistic regression and PNN (Probabilistic Neural Network) models were used to select independent risk factors. The ROC curve analysis was used to assess the accuracy of models.
Results
As a result of the selection, 8 independent factor associated with the risk of post-COVID development in T2D patients were selected: treatment of COVID-19 with steroids (OR 1.73, 95% CI 1.06 – 2.84; $P=0.029$), remdesmevir (all patient presented), mechanical ventilation (OR 36.9, 95% CI 4.2 – 322; $P=0.001$), myocardial infarction (OR 2.68, 95% CI 1.3 – 5.5; $P=0.007$) and stroke (OR 4.18, 95% CI 1.79 – 9.75; $P=0.001$) in anamnesis, T2D duration (OR 0.94, 95% CI 0.9 – 0.97; $P=0.001$), commbination of anti-diabetic drugs with insulin (OR 2.98, 95% CI 1.35 – 6.58; $P=0.007$) and used of insulin analogues (OR 2.94, 95% CI 1.34 – 6.48; $P=0.007$). It should be noted that the indicators. In ROC analysis 8-factorial model constructed with PNN AUROC 0.831; 95% CI 0.791–0.866) significantly better predict post-COVID syndrome development as compared multiple regression model (AUROC 0.759; 95% CI 0.714–0.800; $P=0.004$)
Conclusion
Treatment of COVID-19 with steroids, remdesmevir, mechanical ventilation, myocardial infarction and stroke in anamnesis, T2D duration, commbination of anti-diabetic drugs with insulin and use of insulin analogues are the main predictors of post-COVID development. The prediction of post-COVID with PNN are clearly accurate as compared to step-wise logistic regression model.
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EP281

Fluasterone buccal tablets: a promising therapy for the metabolic effects of hypercortisolemia and cushing syndrome
Dionysios Vrachnis[1], Zoi Efstathiadou[2], Dimitrios Goulis[3], Eva Kassi[4], Christina Lymniati[5], Georgia Ntali[6], Melpomeni Peppa[7], Konstantinos Stavrinos[8], Andromahi Vryonidou[9], Paraskevi Xekouki[10] & Constantine Stratakis[11,12,13]
[1]National and Kapodistrian University of Athens, Medical School, Greece; [2]Department of Endocrinology, "Hippokration" General Hospital of Thessaloniki, Thessaloniki 54642, Greece; [3]Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece; [4]Endocrinology Unit, 1st Department of Propaedeutic and Internal Medicine, School of Medicine, National and Kapodistrian University of Athens, Laikon University Hospital of Athens, 11527 Athens, Greece; [5]Department of Endocrinology, Metabolism and Diabetes Mellitus, Nikea-Piraeus General Hospital "Agios Panteleimon", Athens, Greece; [6]Department of Endocrinology and Diabetes Center, Endo ERN Center, Evaggelismos Hospital, Athens, Greece; [7]2nd Department of Internal Medicine, Research Institute and Diabetes Center, National and Kapodistrian University of Athens, Attikon University Hospital 1 Rimini Street, 12462, Chaidari, Greece; [8]Pharmassist, Nea Ionia, Greece; [9]Department of Endocrinology and Diabetes Center, Hellenic Red Cross Hospital, Athens, Greece; [10]Department of Endocrinology and Diabetes, University General Hospital of Heraklion, School of Medicine, University of Crete, Heraklion, Greece; [11]Human Genetics & Precision Medicine, IMBB, FORTH, Heraklion, Greece; [12]NICHD, NIH, Bethesda, MD, USA; [13]Medical Genetics, H. Dunant Hospital, Athens, Greece

Fluasterone (16-α-fluoro-5-androsten-17-one) is a structural analogue of dehydroepiandrosterone (DHEA) that retains DHEA clinical properties without its androgenic effects. In animal models, fluasterone exhibits DHEA-like effects, including anti-inflammatory, anti-proliferative, and anti-diabetic properties but is consistently more potent than DHEA. An orphan-drug designation for fluasterone has been granted by the FDA for treatment of Cushing's syndrome (CS), including hyperglycemia, nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatosis (NAS). Oral DHEA was shown to produce remission of hyperglycemia in mice. Oral fluasterone was shown to be superior to control in reduction of plasma glucose levels and while DHEA is highly androgenic, producing 25-fold increase in plasma testosterone levels and a dose-related increase in seminal vesicle weights, these findings were not present in mice treated with fluasterone. The mechanism of the anti-glucocorticoid effect of fluasterone has not been established. Fluasterone prevents thymic involution induced by treatment with pharmacological doses of dexamethasone in mice, which indicates marked anti-glucocorticoid action independent of any changes in endogenous glucocorticoid levels. In mice, fluasterone, when injected subcutaneously at 5 mg/kg, decreased plasma corticosterone levels, and this was correlated with lowering of fasting plasma glucose. As the dose of fluasterone was increased, corticosterone and fasting plasma glucose levels both rebounded due to increased corticotropin. In mice that develop NAFLD, 8-wk treatment with fluasterone lowered inflammation and NAS fibrosis. In humans, a total of 105 adults have received one or more oral or buccal doses of fluasterone during seven phase-1 and phase-2 trials. Because oral fluasterone underwent extensive first-pass metabolism, oral dosing was discontinued. Nevertheless, oral studies showed efficacy in patients having either rheumatoid arthritis or hypertriglyceridemia. Buccal fluasterone was then investigated in a phase 1/2 study of 24 adults with metabolic syndrome who received an 8-wk, once-daily buccal tablet of fluasterone or placebo. The triglyceride levels in the 80 mg fluasterone group

declined from baseline by 34% at week 2, 4, 6, and 8 and by 35% at week 8. In the placebo group, at the corresponding time points the triglyceride levels increased by 6% and 7%, respectively. The decline in triglyceride level from baseline in the 80 mg buccal fluasterone group was significantly greater than that in the placebo group with no adverse events reported. Thus, we propose a double-blind, placebo-controlled, crossover pilot study of the efficacy and safety of buccal Fluasterone in the control of hyperglycemia in adults with CS.

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EP285

Enigma of hypogonadism in men with type 2 diabetes: central or peripheral origins?

Anis Grassa[1], Manel Jemel[1], Salma Salhi[1], Marwa Chiboub[1], Brahim Khalfa[2], Rahma Mahjoub[2], Emna Talbi[2], Hager Kandara[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technologies, Zouheir Kallel, Endocrinology, Tunisia; [2]National Institute of Nutrition and Food Technologies, Zouheir Kallel, Biochemistry, Tunis, Tunisia

Introduction
Male hypogonadism (HG), characterized by a decrease in testosterone levels, becomes more prevalent with age, significantly impacting the quality of life. A noteworthy association with type 2 diabetes (T2D) has increasingly captured medical interest. The critical question persists: is the HG observed in T2D patients of central or peripheral origin? This study delves into this inquiry to enhance our understanding and inform better management.
Methods
We recruited 68 adult male patients with type with T2D and HG from outpatient clinics at the National Institute of Nutrition and Food Technology. Testosteronemia, Sex Hormone-Binding Globulin and albumin, for calculating Free Testosterone (FT) and Bioavailable Testosterone (BT) using the Vermeulen formula[1]. The diagnostic criterion for HG included specific thresholds: Total Testosterone (TT) below 231 ng/dl, FT below 6.5 ng/dl or BT below 150 ng/dl. Hypogonadism was Hypergonadotropic (HGHyper) if LH $>$ 8.6 mIU/ml, and hypogonadotrophic (HGHypo) if LH values $\leq$ 8.6 mIU/ml. For HGHypo cases, magnetic resonance imaging (MRI) was performed in case of clinical and/or biological signs, indicating pituitary hypersecretion or insufficiency, or if TT was below 150 ng/dl.
Results
The median age of the studied population was 59 years with an interquartile range of [56–64]. The highest prevalence of HG was observed in patients aged 60 to 65, reaching 49%. The prevalence of HG did not show statistical significance ($P=0.270$) in the age groups. The central origin of HG was identified in 75% of cases ($n=51$). There was no significant correlation between patients' age and the nature of HG (58.4 $\pm$ 5.6 vs 59.9 $\pm$ 6.4; $P=0.366$). Four patients required an MRI-HH justified by TT $<$150 ng/dl. The etiological investigation didn't reveal anomalies in all cases.
Conclusion
The study demonstrates a predominance of the central origin of hypogonadism in patients with type 2 diabetes, irrespective of their age. Emphasis is placed on the importance of thorough hormonal exploration for this population. Further investigations are necessary to elucidate underlying mechanisms and guide the development of more personalized therapeutic strategies.
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EP289

Evaluation of nurses 'knowledge on diabetic foot wounds management

Dhoha Ben Salah, Kouloud Boujelben, Mohamed Khairi Arous, Mouna Elleuch, Faten Haj Kacem Akid, Fatma Mnif, Nadia Charfi, Mouna Mnif, Mohamed Abid & Nabila Rekik Majdoub
Hedi Chaker Hospital, Endocrinology, Sfax, Tunisia

Introduction
Diabetic foot wounds (DFW) are one of the most challenging complications of diabetes. DFW is one of the leading causes of foot ulceration and amputation in patients with diabetes mellitus. Then, a multidisciplinary approach is of a great importance in the prevention and management of DFW. Healthcare personnel, particularly nurses, have an important role in this process. The objective of our study was to evaluate nurses 'knowledge on diabetic foot wounds management.
Patients and methods
We conducted a cross sectional study between September and November 2021. Knowledge were assessed by referring to a questionnaire based on International Working Group on the Diabetic Foot (IWGDF) recommendations, designed to evaluate the knowledge levels of 50 nurses, working in various departments of diabetology, regarding DFW management.
Results
The average age was 30,9 years (25-58 years). There were 45 females and only 5 males. Twenty four percent of nurses reported that patients with diabetes mellitus should be referred to podiatric physicians when they developed hyperkeratosis. Sixty six percent of our population reported that hyperkeratosis may be removed by a 20 minute bathfoot. Thirty eight percent of nurses knew principal characteristics of neurological wounds. Thirty four percent of asked population were able to identify ischemic wounds. Thirty percent of nurses recognized that a wound is considered chronic when the healing process exceeds 4 to 6 weeks. Thirty four percent of respondents were familiar with chronic wound cleaning with saline physiological serum. Fourty four of nurses knew that the removal of fibrinous tissue requires mechanical debridement. Only 8% of patients knew the infected wounds classification according to Texas University systems.
Conclusion
Levels of foot care knowledge and approach are various among studies. Our study highlights the importance of foot care in patients with diabetes mellitus and the need of regular training courses for nurses.

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EP290

Association between emerging lipid indicators and diabetic degenerative complications

Youssef Gharbi, Bchir Najla, Bel Hadj Sliman Chayma, Annam Benchhida, Dorra Dorraelguiche, Zouaoui Chadia & Haroun Ouertani
Military Hospital of Tunis, Endocrinology, Tunis, Tunisia

Introduction
Screening and preventing the onset of degenerative complications of type 2 diabetes is the cornerstone of patients follow up. Recently, new emerging indicators have been suggested to be more sensitive for the early detection of the onset of micro and macroangiopathies. These indicators emerge from the involvement of metabolic syndrome, dyslipidemia and glycemic imbalance in endothelial dysfunction. Among these indicators, we cite the atherogenic index (TC-(HDL-C))/HDL-C), the atherogenic plasma index (LDL-C/HDL-C) and the HbA1C/HDLc ratio. The objective of our study was to evaluate the association between these indicators correlated with atherosclerosis and degenerative complications of diabetes.
Methods
It was a cross-sectional study that included 100 type 2 diabetic patients followed at the Tunis Military Hospital for a period of 3 months. An assay of the various biological parameters dating back for less than six months as well as an evaluation of micro and macroangiopathies were carried out.
Results
In our population, patients had an average HbA1C of 10.51% $\pm$ 2.44% and 88% of patients had dyslipidemia. Regarding the impact of diabetes, the distribution of degenerative complications was 50% for diabetic retinopathy, 61% for diabetic neuropathy, 43% for diabetic nephropathy, 7% for stroke, 32% for coronary heart disease and 9% for peripheral arterial disease. Diabetic nephropathy was significantly associated with the atherogenic plasma index ($P=0.041$) and the HbA1C/HDLc ratio ($P=0.003$). As for microalbumiuria, it was associated with the atherogenic index ($P=0.024$) and atherogenic plasma index ($P=0.007$). However, no association between these different indicators and the other degenerative complications of diabetes has been found.
Conclusions
Positive associations suggest that the atherogenic index, the atherogenic plasma index and the HbA1C/HDLc ratio may be good indicators of the occurrence of diabetic nephropathy in the Tunisian population. However, larger multicenter studies are needed to determine their exact place as an indicator of the occurrence of degenerative complications of diabetes.

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EP291

Defining male hypogonadism in type 2 diabetes: a fresh approach and diagnostic insights

Anis Grassa[1], Manel Jemel[1], salma salhi[1], Brahim Khalfa[1], Meriem Adel[1], Asma Krir[2], Ahlem Benhmid[2], Hager Kandara[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technologies, Zouheir Kallel, Tunis, Tunisia; [2]Pasteur Institute of Tunis, Tunis, Tunisia

Introduction
The association between male hypogonadism (HG) and type 2 diabetes (T2D) has become a growing focus in medical research. However, a major challenge stems from the lack of consensus in defining HG, leading to variations in diagnostic thresholds among different medical societies. This study addresses this challenge by proposing a new perspective on the classification and thresholds of HG.
Methods
The research focused on a group of 250 adult male individuals with T2D. A comprehensive assessment of gonadal hormones was conducted to calculate Free Testosterone (FT) and Bioavailable Testosterone (BT) using the Vermeulen formula, available at https://www.issam.ch/freetesto.htm[1], and adhering to the suggested cut-off values[2]. Diagnostic criteria for male HG included specific thresholds, such as Total Testosterone (TT) below 231 ng/dl or TT$\geq$ 231 ng/dl with FT below 6.5 ng/dl, and/or BT below 150 ng/dl. Additionally, participants responded to an Arabic-validated ADAM questionnaire [3]
Results
The median age of our population was 58 years, with an interquartile range (IQR) of [52.7–62]. The prevalence of HG was 27.2% ($n=68$). In our study, a significant correlation was observed between responses to the ADAM questionnaire and the diagnosis of HG ($P<10^{-3}$). The most notable differences in clinical signs between the HG and non-HG groups were the decrease in muscle strength and endurance, present in 86.6% vs 46.1% ($P<10^{-3}$), followed by erectile dysfunction, present in 82.1% vs 52.2% ($P<10^{-3}$), and a decrease in libido, present in 65.7% vs 37.8% ($P<10^{-3}$). Biologically, the differences between the HG and non-HG groups for mean levels of TT, FT, and BT were 301 vs 491.5 ng/dl ($P<10^{-3}$), 5.6 vs 9.8 ng/dl ($P<10^{-3}$), and 124.6 vs 213.9 ng/dl ($P<10^{-3}$), respectively. A TT level $>$ 350 ng/dl was noted in 173 (69.2%), among whom 17 were diagnosed as having HG (6.8%).
Conclusion
In conclusion, this study offers a new perspective on addressing the definition of male hypogonadism within a T2D population and emphasizes the importance of standardizing diagnostic criteria for HG to enhance sensitivity and clinical management within this population.
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EP292

arGLP-1: our experience in a tertiary hospital in southern spain

Víctor Siles-Guerrero[1], Patricia Vílchez-Fernández[2], Piedad Santiago-Fernández[1] & Martín López-de-la Torre Casares[1]
[1]Hospital Universitario Virgen de las Nieves, Servicio de Endocrinología y Nutrición, Granada, Spain; [2]Hospital Universitario Virgen de las Nieves, Servicio de Cirugía General, Granada, Spain

Objectives
The development of drugs to aid weight loss as an adjunct to dietary and lifestyle recommendations prior to surgical treatment of obesity may help in the management of these patients. To compare the percentage of weight loss among patients who received dietary recommendations (Group 1) and lifestyle recommendations vs those who added arGLP1 semaglutide 1 mg sc (Group 2) or liraglutide 3 mg sc (Group 3) to these recommendations, analysing other variables such as the presence of diabetes mellitus.
Methods
Patients undergoing bariatric surgery from 01/01/2022 to 01/09/2023 were reviewed using normality, t-Student, ANOVA and non-parametric tests with the Jamovi v2.3.28 software.
Results
Included were 67 females and 31 males with a mean age 49.2 $\pm$ 8.97 SD years with a baseline weight 128 $\pm$ 20.1 kg, who followed treatment for 29.2 $\pm$ months: (1) diet: 48 patients 28.33 $\pm$ 22.9 SD months, (2) diet with semaglutide 1 mg sc: 21 patients 22.14 $\pm$ 18.23 SD months and (3) diet with liraglutide 3 mg sc: 19 patients 11.42 $\pm$ 14.15 SD months. At the end of follow-up they lost: - 5.98% $\pm$7.82 SD kg. In the percentage of weight loss there were no differences between sexes, whether or not they used aGLP1, but the loss was greater in those treated pharmacologically ($P<0.001$), being -10.2 $\pm$ 7.89 SD with diet and drugs and -3.09 $\pm$ 6.37 SD Kg with diet alone. 83% achieved losses greater than 5% and 48% greater than 10% with pharmacological treatment. There was no difference when comparing Liraglutide sc vs Semaglutide sc in weight loss. In the 26 DM2 patients treated with arGLP-1, weight loss was lower (-8.8% $\pm$ 6.42 kg) than in non-DM2 patients (-10.6% $\pm$ 7.29 kg) ($P<0.05$).
Conclusions
Adding arGLP-1 to dietary and lifestyle changes treatment improves the percentage of weight loss achieved before bariatric surgery, reaching the usual recommended 10% weight loss, being more effective in non-DM, without differences between sexes or arGLP-1 used.

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EP306

Diabetes and psychiatric disorders: optimizing dual care

Manal Bennani, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital - Clinical Neuroscience and Mental Health Laboratory Faculty of Medicine and Pharmacy - Hassan II University-, Department of Endocrinology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
A mental disorder is characterized by a significant clinical impairment in an individual's cognitive state, emotional regulation, or behavior. It typically accompanies a sense of distress or functional impairments in crucial areas of life. The coexistence of diabetes and mental illness is not uncommon. However, due to the necessity of a collaborative approach between healthcare providers and patients to optimize treatment and considering the chronic nature of both conditions, it is essential to explore specific aspects.
Objective
Our study aims to assess factors influencing the management of diabetic patients with psychiatric disorders to enhance their adherence to treatment and follow-up.
Materials and Methods
This is a retrospective descriptive study conducted at the Endocrinology and Diabetology Department of CHU IBN ROCHD in Casablanca. It focuses on diabetic patients with psychiatric disorders requiring specialized hospital care in either the psychiatry or endocrinology department from January 2021 to December 2023; data were collected using Excel.
Results
In our study, 112 patients were included, comprising 68 men and 44 women. The overall average age of diabetic patients with psychiatric disorders was 40 years (ranging from 15 to 61 years). Two distinct peaks were observed: one during adolescence, where depression predominated, and another around 54 years, with a clear prevalence of psychoses. The prevalence of type 1 diabetes was higher in adolescence, with the basal-bolus regimen being essential, necessitating educational, medicinal, and psychotherapeutic support to prevent multiple hospitalizations due to complications such as ketoacidosis or hypoglycemia. Underlying depressions were often identified during stays in the endocrinology department in 22% of cases. For patients with type 2 diabetes or those with a debated diabetes type, representing 50% and 28% of the sample, respectively, and facing challenges in the applicability of educational strategies during psychoses or situations of hetero-aggression, oral antidiabetics were preferred if HbA1c values and diabetes duration allowed. Otherwise, premixed or basal-plus regimens were considered.
Conclusion
Managing diabetic patients with mental disorders remains a challenge for both healthcare professionals and caregivers. Thus, collaboration between endocrinologists, psychiatrists, and psychotherapists is crucial to mitigate the complications associated with these conditions.

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EP307

Management of bell palsy in diabetic patients

Meherzi Samia[1], Omri Rihab[2] & Iansari Salma[2]
[1]Universitu of Sousse, Faculty of Medecine of Sousse, ENT Department, Tunisia; [2]University of Sousse, Faculty of Medecine of Sousse, ENT Department, Tunisia

Objective
Our study aims to review the therapeutic management guideline of diabetic patients who presented with Bell's palsy.

Materials and Methods
A retrospective study which consisted of 35 diabetic patients with idiopathic peripheral facial paralysis (PFP) over a period of 3 years (from January 2020 to December 2022). All patients underwent a complete ENT examination, a neurological examination, and a minimal assessment including a complete blood count, blood glucose measurement, and an audiometry (tonal audiometry + impedance audiometry).
Results
Our series identified 10 female and 25 male, with an average age of 47 years (26–65 years). Others than diabetes, risk factors for PFP were found within 29 patients, involving hypertension, hematological disorders, and pregnancy. Twenty-four cases were classified as type 2 diabetes, 22 of them were treated with Oral antidiabetic medications. All patients presented with an unilateral facial asymmetry, with an average delay of consultation of 3 days. In the initial physical examination, 20 patients presented with mild-to-moderate facial palsies (grades I-III), while moderate-to-severe palsies (grades IV–VI) were observed in fifteen of the patients. Twelve patients underwent a cerebral computed tomography, completed in one case of a magnetic resonance imaging, showing normal results. Stapedial reflex was absent in 19 cases. Eleven patients were treated on an outpatient basis while twenty-four patients required hospitalization, including 4 children. Corticosteroid therapy based on prednisolone or methylprednisolone was initiated in all patients with an average duration of 7 days. Antiviral treatment, always in combination with corticosteroid therapy, was prescribed for 21 patients with an average consultation delay of 3 days. All patients received vasodilators and vitamin therapy. Facial rehabilitation was initiated in all cases with an average delay of 7 days (3–10 days). After 1 year of follow-up, 19 patients recovered normal facial tone
Conclusion
Bell's palsy is the most common form of facial paralysis therefore it remains a diagnosis of exclusion. The therapeutic management in diabetics relies on an early combination of corticosteroids and antivirals. The prognosis is often favorable, with the potential for aesthetic and functional sequelae.

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EP308

Hypogonadism and and chronic complications in type 2 diabetic males

Anis Grassa[1], Manel Jemel[1], Salma Salhi[1], Brahim Khalfa[1], Rahma Mahjoub[1], Emna Talbi[1], Asma Krir[2], Radhouane Gharbi[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technologies, Zouheir Kallel; [2]Pasteur Institute of Tunis

Introduction
Type 2 Diabetes (T2D) is a widespread metabolic disorder associated with chronic complications. Few studies have explored the relation between **chronic** complications in type 2 diabetic males presenting an hypogonadism (HG). Understanding how T2D, its complications, and HG are connected is crucial for overall health. This study aims to explore these links in simpler terms.
Methods
This is a descriptive cross-sectional study that included 250 adult men with T2D. Participants underwent a clinical examination and metabolic and hormonal assessments. The diagnosis of HG was established based on the Vermeulen criteria, involving the measurement of total testosterone and the calculation of free testosterone.
Results
The prevalence of impaired glucose was 27.2% ($n=68$). The average duration of diabetes was 12.5 ± 7.4 years [Range: 1-31]. Patients with a diabetes duration exceeding 10 years accounted for more than half of the cases (62.2%). In total, 52% of the patients exhibited chronic complications of diabetes. Microangiopathic complications were present in one hundred and nine patients, accounting for 44.1% of the total. In 37.6% of cases, retinopathy was observed, while nephropathy affected 25.6% ($n=64$) and neuropathy impacted 18% of the total. One-fourth of the patients had macroangiopathic complications, accounting for 25.8%. Among these complications, 50 patients (20%) exhibited coronary involvement. A history of stroke or transient ischemic attack (TIA) was found in 2.4% of the patients. Lower limb arteritis was observed in 9.7% of the cases. Sixty-eight patients were diagnosed with HG, representing 27.2%. When comparing the HG and non-HG groups, there was no correlation between the prevalence of impaired glucose and microangiopathic complications ($P=0.071$). Regarding retinopathy (42.4% vs 39.9%; $P=0.402$), nephropathy (27.3% vs 25.7%; $P=0.452$), and neuropathy (18.2% vs 19.2%; $P=0.516$), no significant differences were observed. Similarly, for macroangiopathy, coronary insufficiency and lower limb arteriopathy were nearly identical in the two groups, HG and non-HG, respectively: 19.7% vs 20.8%; $P=0.511$ and 9.1% vs 10.2%; $P=0.514$. Regarding stroke/TIA, they were more frequent in patients with hypogonadism, 4.5% vs 1.7%, but this correlation was not statistically significant ($P=0.199$).
Conclusion
The study reveals no significant correlation between HG and key parameters, including diabetes duration, micro and macroangiopathic complications. The lack of association prompts further investigation into the complex relationships between HG and diabetic complications.
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EP312

The role of a behavioral approach in the treatment of obesity

Anna Brodovskaia
Normed Medical Center, Yerevan, Armenia

Approximately 2.6 billion people worldwide (38% of the planet's population) are already overweight or obese. In 12 years, according to analysts' forecasts, every second person on the planet will have an excess of fat. Unfortunately, adhering to diets only contributes to weight gain. Under calorie restriction, physiological adaptation mechanisms are activated in the body, which increase hunger and reduce basal metabolism. In such conditions, weight loss is possible only in the case of sustainable food restriction, which inevitably leads to breakdowns and relapses. The only method that will help reduce weight in the long term is changing eating habits and working on food behavior.
Aim
To evaluate the effect of behavioral interventions in the treatment of overweight/obesity in adults.
Methods
The study was conducted in obese/overweight adults in an outpatient setting and with remote monitoring. The behavior modification included goal-setting, motivational counseling, self-monitoring and self-motivation, reward system, problem-solving, and social support. The observation period consisted of weekly sessions for the first three months and then monthly supporting meetings. Evaluation of the results of observation was carried out after 9 months.
Results
A total of 17 patients at the age from 23 to 45 years old were examined. The average body mass index was 31.3 ± 3.14 kg/m^2. Average weight loss was 8.2%; average rate of weight loss - 2.7 kg/month. Patients had good adherence to recommendations and continued to maintain/lose weight after the active intervention period.
Conclusion
Long-term weight loss is possible when abandoning restrictions and under conditions of adequate activity. There is a need for a more holistic approach that includes behavioral treatments to promote adherence to treatment and maintain lifestyle modifications.

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EP314

Ocular infections: distinctive aspects in diabetic patients

Manal Bennani, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital - Clinical Neuroscience and Mental Health Laboratory Faculty of Medicine and Pharmacy - Hassan II University-, Department of Endocrinology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
Ocular infections are a serious threat to the visual prognosis of diabetic patients. Often exacerbated by glycemic imbalance and pre-existing eye conditions, their progression remains unpredictable due to the limited therapeutic options available. Factors contributing to this unpredictability include the restricted diffusion of antibiotics within the eye, the toxicity associated with prolonged use of certain fortified eye drops, and the emergence of antibiotic-resistant strains.
Objective
The aim of our study is to assess predisposing factors for specific types of ocular infections and their prevalence among diabetic patients, with the ultimate goal of enhancing preventive measures.

Materials and Methods
This study is an observational statistical analysis conducted at the Endocrinology and Diabetology Department of CHU IBN ROCHD in Casablanca, using the SPSS software. It focuses on diabetic patients who presented with severe ocular infections requiring specialized ophthalmological care from January 2021 to December 2023.
Results
In our study, 92 patients were included, comprising 38 men and 54 women, all of whom had ocular infections. The average age was 61 years (ranging from 27 to 81 years), with 93% having type 2 diabetes and an average diabetes duration of 12 years. The identified pathologies included endophthalmitis (42%), corneal abscesses (31%), and retro-orbital cellulitis (15%). Initial treatment involved local and intravenous antibiotics, and 12 patients eventually underwent evisceration. A1c levels were below 7% in 27% of cases, between 7% and 8% in another 27%, and above 8% in the remaining patients. The majority of diabetic patients were initially on insulin therapy (93%).
Conclusion
The severity of ocular infections in diabetic individuals is heightened by age, diabetes duration, and underlying glycemic imbalance. The risk of progressing to loss of ocular function underscores the need for strict glycemic control and close monitoring to mitigate these avoidable complications.

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EP336

Secondary failure of oral therapy in patients with type 2 diabetes mellitus - possibilities of overcoming

Aleksandra Markovic[1,2], Mirjana Bojic[1], Tamara Dojcinovic[1,2], Ivona Risovic[1,2], Milena Brkic[2], Valentina Soldat Stankovic[1,2] & Djuro Macut[3,4]
[1]University Clinical Centre of the Republic of Srpska, Internal Medicine, Banja Luka, Bosnia and Herzegovina; [2]University of Banja Luka, Faculty of Medicine, Banja Luka, Bosnia and Herzegovina; [3]University Clinical Centre of Serbia, Belgrade, Serbia; [4]University of Belgrade, Faculty of Medicine, Belgrade, Serbia

Introduction
Secondary failure (SF) of oral therapy in patients with type 2 diabetes is a common clinical phenomenon, which often puts the practitioner in a dilemma as to which therapeutic regimen to choose for continuing therapy. The dilemma primarily applies to patients in whom there is no clear clinical and biochemical evidence of significant insulin deficiency. This is precisely why there has been an increased interest in the use of short-term intermittent insulin therapy. The aim of the study was to examine the acute and residual effects of short-term mono insulin therapy on glycoregulation and insulin secretory function.
Methods
The prospective study took place in two phases and included 69 patients with type 2 DM and SF oral therapy. The first phase represents the introduction of insulin therapy (monoinsulin or combined) for three months, and the second phase represents the assessment of the residual effects of insulin therapy on glycoregulation and insulin secretory function (postinsulin period). During the second phase of the study, which lasted for 3 months, the patients again used the oral therapy they used until the diagnosis of SF. Glycoregulation and insulin secretory function were evaluated at the beginning and at the end of both phases.
Results
After three months of insulin therapy, there was a significant improvement in all observed parameters: morning glycemia (6.1 vs 9.5; $P<0.001$), postprandial glycemia (6.9 vs 11.6; $P<0.001$), glycemia from all-day profile (7.3 vs 10.3; $P<0.001$), while in the post-insulin period there was a certain deterioration of these parameters. Also, after three months of insulin therapy, the values of basal C-peptide increased (1.23 vs 1.67; $P<0.001$), while the level of basal insulinemia was reduced (9.17 vs 11.46; $P<0.001$). In the post-insulin period, there were no significant changes in C-peptide and insulin values compared to the period immediately after insulin therapy.
Conclusion
Short-term monoinsulin therapy represents a rational alternative to permanent insulin therapy in properly selected patients who do not have clear clinical and biochemical parameters of significant insulin deficiency. It can cause a state of re-sensitivity to oral therapy and delay permanent insulin treatment.

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EP337

Subgroup analysis of phase 3 study of fixed-dose combination of dapagliflozin, glimepiride and metformin IR in type 2 diabetes mellitus patients aged <45 years and 45 to 65 years

Prakash Kurmi[1], Manish Singh[2], Vishal Gupta[3], Chikkalingaiah Siddegowda[4], Jitendra Shukla[5], Sandip Gofne[6], Nilesh Lomte[7], Kaustubh Shendkar[8], Dinesh Gangwani[9], Surendra Kumar[10], Sandeep Gupta[11], Aravind G Nagarajaiah[12], Amit Bhaskar[13], Prabhat Sharma[14], Arjun Baidya[15], Animesh Maiti[16], Ambana Gowda[17], Jayesh Ambaliya[18], Balachandra Giriappa K[19], Sunil Mahavar[20], Hemant Gupta[21], Mandodari Rajurkar[22], Supriya Sonowal[22], Piyush Patel[23], Dipak Patil[22], Lalit Lakhwani[23], Pravin Ghadge[22], Suyog Mehta[24] & Sadhna Joglekar[25]
[1]Shivam Hospital, Ahmedabad, India; [2]Maya Hospital & Maternity Centre, Department of General Medicine, Kanpur, India; [3]GSVM Medical College, Department of Medicine, Kanpur, India; [4]Medstar Speciality Hospital, Bangalore, India; [5]Moti lal Nehru Medical College, Department of Medicine, Prayagraj, India; [6]District Civil Hospital, Aurangabad, India; [7]Hormone Care, Aurangabad, India; [8]Global Hospital and Research Institute, Department of Diabetology, Pune, India; [9]Priyadarshini Nursing Home, Mumbai, India; [10]S. P. Medical College & A.G of Hospitals, Bikaner, India; [11]M.V. Hospitals and Research Center, Department of Medicine, Lucknow, India; [12]Victoria Hospital, Department of General Medicine, Bangalore, India; [13]Janta Hospital, Varanasi, India; [14]Maharaja Agrasen superspeciality Hospital, Department of General Medicine, Jaipur, India; [15]Nilratan Sircar Medical College and Hospital, Kolkata, India; [16]Medical College and Hospital, Kolkata, India; [17]Citizen hospital, Bangalore, India; [18]Pagarav Hospital & ICU, Department of Medicine, Gandhinagar, India; [19]BGS Global Institute of Medical Sciences, Department of General Medicine, Bangalore, India; [20]SMS hospital, Department of Medicine, Jaipur, India; [21]Grant Govt. Medical College and Sir J. J. Group of Hospital, Department of Internal Medicine, Mumbai, India; [22]Sun Pharma Laboratories Limited, India Clinical Research, Mumbai, India; [23]Ex Sun Pharma Laboratories Limited, India Clinical Research, Mumbai, India; [24]Sun Pharma Laboratories Limited, Head Medical Affairs, Clinical Research, India & EM, Mumbai, India; [25]Ex Sun Pharmaceutical Industries Limited, Medical Affairs and India Clinical Research, Mumbai, India

Background and Objective
Fixed-dose combination (FDC) of dapagliflozin + metformin + sulfonylurea with complementary mechanisms can provide effective glycaemic control, preserve beta-cell function, improved compliance without risk of weight gain, and reno-protective action in type 2 diabetes mellitus (T2DM) patients. This subgroup analysis assessed efficacy and safety of triple-drug FDC vs (vs) two-drug combination in T2DM Indian patients aged <45 years and 45-65 years.
Method
This is a subgroup analysis of phase 3, open-label, four-arm, active-controlled study (CTRI/2022/06/043249) in T2DM patients (glycated haemoglobin [HbA1c] 8%-11%) taking metformin 1000 mg 2000 mg/day and glimepiride 2 mg/day at screening. Patients received FDC of dapagliflozin + glimepiride + metformin IR tablet twice-daily (BID) (5 mg + 1 mg + 500 mg [test-1]/5 mg + 1 mg + 1000 mg [test-2]) OR co administration of glimepiride tablet + metformin IR BID (1 mg + 1 tablet of 500 mg [comparator-1]/1 mg + 2 tablets of 500 mg [comparator-2]) for 16 weeks. Post Week 16, up titrated dose of glimepiride (2 mg) in respective treatments was provided to patients with HbA1c ≥7% in each arm. This subgroup analysis evaluated glycaemic and safety parameters from Baseline till Week 28 in two age subgroups; subgroup 1 (S1:age <45 years) and subgroup 2 (S2:age 45-65 years).
Results
At baseline, 223 patients aged <45 years (S1) and 310 patients aged 45-65 years (S2). Adjusted mean change (SE) in HbA1c in S1 was statistically significant in test-1 vs comparator-1 [2.48% (0.14%) vs 1.64% (0.14%), $P<0.0001$) and in test-2 vs comparator-2 [-2.31% (0.13%) vs -1.65% (0.13%), $P=0.0004$) at Week 16. Adjusted mean change (SE) in HbA1c in S2 was statistically significant in test-1 vs comparator-1 (2.1% (0.12%) vs -1.63% (0.12%), $P=0.0043$)] and in test-2 vs comparator-2 [-2.18% (0.12%) vs -1.75% (0.12%), $P=0.0116$] at Week 16. In S1, proportion of patients achieving HbA1c <7% were significantly higher in test-1 vs comparator-1 (74.5% vs 46.9%, $P=0.0047$) and test-2 vs comparator-2 (85.5% vs 58.1%, $P=0.0011$) at Week 16. In S2, proportion of patients achieving HbA1c <7% were significantly higher in test-1 vs comparator-1 (70.1% vs 46.8%, $P=0.0032$) and test-2 vs comparator-2 (73.7% vs 47.1%, $P=0.0011$) at Week 16. Significant reduction in HbA1c, fasting and post prandial blood glucose was observed from Baseline to Weeks 12 and 16 in each arm in both subgroups. No patient reported hypoglycaemia or required rescue medication. Both treatments were well tolerated.
Conclusion
Triple FDCs of dapagliflozin + glimepiride + metformin IR tablets showed statistically significant reduction in HbA1c from Baseline to Week 16 as

compared to dual combinations in T2DM patients of both age groups (<45 years and 45-65 years) and is a treatment option for all age groups.

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EP378

Patient with type 1 diabetes mellitus with poor glycemic control with adrenocorticotropic hormone (ACTH)-secreting pituitary macroadenoma

Paloma González Lázaro[1], Maria Zhao Montero Benítez[1], Pedro Jimenez Torrecilla[1], Juan A. Mascuñana Calle[1], Cristina Contreras Pascual[2] & Ines. R Gomez García[1]
[1]Hospital General La Mancha Centro, Alcázar de San Juan, Spain; [2]Hospital Santa Barbara, Soria, Spain

Introduction
Diabetes mellitus is the most common chronic disease in children, with type 1 diabetes accounting for 80% of diabetic patients under the age of 19 years. Though hyperglycemia in pediatric patients with diabetes mellitus commonly occurs due to poor adherence to insulin therapy, other etiologies should be considered when hyperglycemia is refractory and additional systemic signs and symptoms are present. We discuss a case of a female patient presenting with signs and symptoms of elevated cortisol levels several years after being diagnosed with T1DM.
Case Presentation
We present the case of a 19-year-old woman diagnosed with type 1 diabetes mellitus and celiac disease at 3 years and 9 months. Come to our consultation after follow-up in Pediatric Endocrinology for follow-up of type 1 DM. Screening for Cushing's syndrome is requested due to reports of increased insulin needs, weight gain, rounder face and menstrual alterations since 2020. On examination, attention is drawn to facial plethora, a full moon face, vinous red striae on the abdomen and accumulation of retrocervical and supraclavicular fat. A functionality study was performed (Suppression with 1 mg of Dexamethasone, urinary free cortisol, salivary cortisol, cortisol rhythm, strong suppression with Dexamethasone and CRH test) suggestive of ACTH-dependent syndrome. A subsequent brain MRI showed pituitary gland with an increase in size of 9.9×8.6 mm in the sagittal plane suggestive of pituitary adenoma. Normal appearing pituitary stalk and optic chiasm. Medical treatment with ketoconazole was initiated with improvement in glycemic control and normalization of urinary free cortisol until complete transsphenoidal resection of the adenoma was performed. Following resection her long-acting insulin requirement decreased by 50%. At his three-month postoperative follow-up, the patient's striae and facial edema had improved significantly and her weight decreased by 9 kg.
Conclusions
We described the case of a 19-year-old Spanish female, with poorly controlled T1DM and Cushingoid features, who was found to have a functioning pituitary macroadenoma. An ACTH-secreting pituitary adenoma is an extremely rare phenomenon in such young patients, but it should be considered in patients presenting with refractory hyperglycemia and other signs and symptoms of Cushing disease.

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EP398

Gender affirming hormonal care induces a gender-concordant gut metagenome transition in transgender individuals

Matthias Auer[1], Timur Liwinski[2], Johanna Schröder[3], Ina Pieknik[4], Christian Casar[5], Günter Stalla[6], Undine Lang[2], Alina von Klitzing[4], Corinna Bang[7], Peer Briken[4], Christoph Schramm[8] & Johannes Fuss[8]
[1]Klinikum der Universität München, Medizinische Klinik and Poliklinik IV, Munich, Germany; [2]University of Basel, Clinic for Adult Psychiatry, Basel, Switzerland; [3]Medical School Hamburg, Institute for Clinical Psychology and Psychotherapy, Hamburg, Germany; [4]University Medical Center Hamburg-Eppendorf, Institute for Sex Research, Sexual Medicine and Forensic Psychiatry, Hamburg, Germany; [5]University Medical Centre Hamburg-Eppendorf (UKE), I. Department of Medicine, Hamburg, Germany; [6]Medicover Neuroendocrinology, Munich, Germany; [7]Christian-Albrechts-University Kiel, Institute of Clinical Molecular Biology, Kiel, Germany; [8]University Medical Centre Hamburg-Eppendorf, Hamburg Centre for Translational Immunology (HCTI), Hamburg, Germany

Aim
There is no data on gender-specific microbial alterations during the gender-affirming transition of trans people, along with inconsistent investigations regarding the specific impact of sex steroids on gut microbiota taxonomy and function.
Method
Our study included 36 transgender participants (17 trans women and 19 trans men). We collected stool samples before and three months post-GAHT initiation, employing shotgun metagenomic sequencing to evaluate the microbiota's response.
Results
Taxonomically, alpha and beta diversity did not differ between trans men and trans women before transition. Moreover, transition was not associated with changes in overall alpha or beta diversity. Nevertheless, four species, namely *Parabacteroides goldsteinii* (FDR = 0.0264), *Coprococcus sp. ART55/1* (FDR = 3×10^{-4}), *Coprococcus eutactus* (FDR = 0.0289), and *Escherichia coli* (FDR = 0.0019), exhibited significant abundance changes in response to hormonal treatment aligning with the participants' affirmed gender. Our analysis revealed a statistically significant effect of gender and transition on the overall functional metagenome ($R^2 = 4.1\%$, $P = 0.0115$). Single pathway analysis demonstrated alignment of the transition-related changes with the affirmed gender, particularly in fatty acid-related metabolism, which was more pronounced in the high testosterone state.
Conclusion
The study highlights distinct microbial profiles in men and women's gut microbiomes. GAHT tends to masculinize the microbiome in trans men and feminize it in trans women. These changes could influence various health outcomes, emphasizing the importance of considering the gut microbiome in transgender health care.

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EP422

Variation in metabolic control in children with DM1 after a summer camp

Javier García Sánchez[1], María Cristina Palma Conesa[2], María Teresa Zarco Martín[4], Raquel María López Ortiz[1], Enrique Redondo[1] & Pablo José López-Ibarra Lozano[1]
[1]San Cecilio Clinical University Hospital, Endocrinology and Nutrition, Granada; [2]San Cecilio Clinical University Hospital, Pediatrics, Granada

Introduction and objectives of the study
Every year the Diabetes Association of Granada (AGRADI), organizes a summer camp for children with Diabetes Mellitus type 1 with the aim of combining leisure activities and facilitating learning and developing autonomy in their pathology. The presence of health professionals is essential to ensure the monitoring and safety of children and a good diabetological education. The aim of this study is to evaluate the clinical characteristics and compare different parameters of the diabetic control of the participants before and during the activity.
Material and methods
Retrospective descriptive observational study that analyzes the participants in two camps for children with DM1 in the years 2022 and 2023. Clinical, glucometric and pharmacological variables were measured. The analysis was performed with SPSS 25.0.
Results
Sixty-five subjects aged 7 to 16 years were included, being 33 males and 32 females. The time of evolution of DM was 5 ± 2.8 years with a mean HbA1c of $7.07 \pm 0.6\%$. Of these, 31 were continuous insulin pump infusion (CIIP) users and 34 used multiple doses of insulin (MDI). With respect to insulin dose, a significant reduction in total insulin dose was found overall and in both groups. The reduction occurred in slow insulin doses in users with MDI (21.6 Units (U) vs 14.9 U) and bolus in the case of CIIP (30.7 U vs 25.8 U), both significant. A significant increase in the sensitivity factor was also observed in global terms and in the ISCI group. Regarding glucometry, there was an improvement in mean glucose with an increase in time in range with no significant difference in time below range, during the camp, compared to previous weeks. In addition, there was no significant difference in the use of glucose sensors and the number of glucose sensor readings compared to the pre-camp discharge.
Conclusions
In conclusion, an improvement in metabolic control was observed during the summer camp. Time in range improved without a significant increase in the number of hypoglycemia. The insulin dose was reduced without requiring a greater number of controls during the camp. Diabetic education, therefore, is key to correct metabolic control.

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EP423

Semaglutide therapy in people with type 2 diabetes and obesity: efficacy on glycated hemoglobin and weight loss

Michela Del Prete[1], Olga Eugenia Disoteo[1], Renato Cozzi[2], Gianleone Di Sacco[1], Federico Vignati[1], Lidia Gavazzi[1] & Fabrizio Muratori[1]
[1]Sant'Anna Hospital – ASST Lariana, Division of Endocrinology, Diabetology and Clinical Nutrition, Como, Italy; [2]Niguarda Hospital, Division of Endocrinology, Milan, Italy

Introduction
The long acting GLP-1 analogue, Semaglutide (S), is indicated for the treatment of adults with type 2 diabetes mellitus (T2DM). Since November 2021, S has also been approved by the European Medicines Agency (EMA) at a dose of 2.4 mg for the treatment of obesity. Here, we report the efficacy of S, either alone or in combination with other antidiabetic drugs, in patients with T2DM and obesity on glycated hemoglobin (HBA1C) and weight loss.
Patients and Methods
We retrospectively evaluated 129 patients (75 F and 54 M; mean age 61.2 ± 9.8 years) with T2DM and obesity treated with S for glycemic control and for weight loss. At the first visit, mean weight was 101.8 ± 24.6 kg and mean body mass index (BMI) was 36.7 ± 8.7 kg/m^2. At baseline mean HBA1C was 7.7 ± 1.5%. S was administered as monotherapy or in combination with metformin. S was administered once-weekly subcutaneously at starting dose of 0.25 mg and with monthly increases up to 1.0 mg. The aim of this study was to evaluate the efficacy of S on HBA1C and according to the weight loss reduction more than (>) 5% or > 10% in this setting of patients.
Results
After 6-month follow up, 115/129 patients had a mean weight of 95.2 ± 24.3 kg and mean BMI of 34.3 ± 9.4 kg/m^2, with a mean percentage weight reduction of -9.5 ± 6.5% and mean BMI reduction of -3.7 ± 3.1 kg/m^2. After 6-month of therapy HBA1C was 6.4 ± 0.9%, with a mean reduction of -1.8 ± 1.5%. In 55.4% of patients that lost > 5% of weight, mean HBA1C reduction was -1.6 ± 1.2%, while in 44.6% patients that lost > 10% of weight from baseline, there was a mean HBA1C reduction of -2.1 ± 1.7%. After 12-month follow up, 47/129 patients had a mean weight of 88.9 ± 17.9 kg and mean BMI of 31.9 ± 5.6 kg/m^2 with a mean percentage weight loss of -9.2 ± 7.6% and mean BMI reduction of -3.3 ± 2.8 kg/m^2. After 12-month follow up mean HBA1C was 6.4 ± 0.9%, with a mean reduction of -1.6 ± 1.6%. In 42.6% of patients with a weight loss > 5%, there was a mean HBA1C reduction of -1.4 ± 1.6%. In 57.4% of patients with a weight loss > 10%, mean HBA1C reduction was -1.7 ± 1.5% from baseline. S was well tolerated and no patient experienced serious adverse events.
Conclusions
Our results confirm the efficacy and safety in glycometabolic control of S therapy in patients with T2DM and obesity. In our study S provide significant weight loss and reduction in HBA1C, probably further reduced also due to the significant weight loss.

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EP425

Assessment of the Exsel Test to detect excessive salt consumption in type 2 diabetic patients

Rym Ben Othmen[1], Emna Talbi[2], Nesrine Dhieb[1], Ramla Mizouri[1], Brahim Khalfa 2[2], Skandar Msolly1[1], Rahma Mahjoub2[2], Olfa Berriche1[1] & Henda Jamoussi1[1]
[1]1National Institute of Nutrition and Technology, Department A, Tunis, Tunisia; [2]Zouhair Kallel Institute of Nutrition and food technology, Clinical Biology Laboratory, tunis, Tunisia

Introduction
Despite the fact that excessive salt consumption is a risk factor in the development of a number of diseases. There is no doubt that dietary intake of sodium chloride remains well above recommended levels. The aim of our study was to evaluate the effectiveness of the Exsel Test in detecting excessive salt consumption in type 2 diabetic patients.
Methods
This was a cross-sectional study of 106 type 2 diabetic patients hospitalised in department A of the National Institute of Nutrition and Food Technology in Tunis. Each patient benefited from a physical examination, a biological check-up and an Exsel Test.
Results
The mean age was 55.46 ± 7.51 years. The majority of patients were women (57). The mean BMI was 29.68 ± 5.92 kg/m.2 We noted a significant difference ($P = 0.001$) in BMI between patients with a positive Exsel Test and those with a negative test. In our study, the Exsel test was associated with the frequency of consumption of salted cheese ($P = 0.001$), tinned food ($P = 0.005$), dried fruit ($P = 0.01$), variants ($P = 0.005$) and sauces ($P = 0.03$). The mean 24 h natriuresis was reported as 106.45 ± 63.82 mmol/24 h and the mean salt intake predicted by natriuresis as 6.22 ± 3.73 g/. The kappa test for comparing the relationship between the exsel test and predicted salt intake was 0.9 and the chi-square was 0.7. The sensitivity of the self-questionnaire was 25%, specificity 74%, PPV 4% and NPV 96%. The area under the curve was equal to 0.577, which is a very low value for a threshold of positivity for the Exsel Test self-questionnaire.
Conclusions
We suggest improving the Exsel test to adapt it to people's culinary habits.

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EP426

SGLT-2 inhibitors-induced erythrocytosis: a case series

David Verissimo, Beatriz R Pereira, Joana Vinhais, Catarina Ivo, Ana Cláudia Martins, Joao Silva, Dolores Passos, Luis Lopes, J Jácome Castro & Mafalda Marcelino
Armed Forces Hospital, Department of Endocrinology, Lisboa, Portugal

Introduction
Sodium-glucose co-transporter 2 inhibitors (SGLT2i) have emerged as a promising class of medications, demonstrating a significant reduction in the risk of cardiovascular events. An associated consequence of SGLT2i is an increase in hematocrit levels, with cardiovascular outcome trials revealing frequent hematocrit mean elevations varying from + 2.3% to 3.5%. This rise in hematocrit introduces a potential dilemma when evaluating the risk-benefit profile of SGLT2i in patients with high cardiovascular risk. While effectively reducing the relative risk of major cardiovascular events, the associated secondary polycythemia raises concerns about an elevated risk of thrombotic events. Notably, existing guidelines and recommendations do not address this specific concern, emphasizing the need for further exploration and guidance in managing hematological alterations associated with SGLT2i therapy.
Case series
To address this issue, we present a case series involving five male patients, with a median age of 53 years [41-61], diagnosed with type 2 diabetes for 6 years [1-12], all prescribed a daily dose of the SGLT2 inhibitor dapagliflozin. Only one patient was a former smoker. Baseline blood tests revealed normal hemogram values, including hemoglobin at 16.2 g/l [15.5-16.9], hematocrit at 47.2% [44.7-49.8], and erythrocytes at 5.33×10^{12}/l [5.28-5.33]. Following a mean treatment duration of 3 ± 1 months, a substantial increase was observed in both hemoglobin (17.8 g/dl [17.3-18.3], $P = 0.043$) and hematocrit (51.2% [49.5-53.4], $P = 0.043$), reaching peak values of 18.4 g/dl and 54.2%, respectively. However, there was no significant change in erythrocyte count ($P = 0.109$). All patients underwent normal blood smear assessments, and their erythropoietin levels, electrolytes, kidney, and liver functions remained within the normal range. The absence of the JAK2 v617f mutation in all five patients ruled out Polycythemia Vera and other myeloproliferative disorders. In two cases, dapagliflozin was suspended, resulting in decreased hemoglobin levels (15.9 and 16.4 g/l) and reduced hematocrit (44% and 46.5%) after three and four months, without the need for phlebotomy. Conversely, for the remaining three patients, the cardiovascular benefits of dapagliflozin were deemed superior, and consequently, treatment continued in conjunction with periodic phlebotomies. In conclusion, these case reports demonstrate that SGLT2i-induced erythrocytosis accompanies the cardiovascular benefits of these drugs. Clinicians should maintain close monitoring of patients' hemogram and carefully weigh the risk-benefit profile in an individualized approach, considering potential interventions such as drug suspension or therapeutic phlebotomy.

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EP427

The effect of SGLT-2 inhibitor switching from TZD with triple combination treatment in type 2 diabetes

Yonghyun Kim & Donghyun Shin
Jesaeng Hospital, Endocrinology and Metabolism, Seongnam-si, Korea, Republic of South Korea

Before launching of SGL-2 inhibitor, triple combination of TZD with metformin and DPP-4 inhibitor was best option for delaying progression of diabetes by improving insulin resistance and secretory dysfunction. But due to side effects of TZD such as weight gain and edema, SGL-2 inhibitor can be

another option instead of TZD. So we tried to know the effect of SGLT2 inhibitor switching from TZD with triple combination therapy in type 2 diabetes. In 80 patients treated with triple combination of metformin, DPP4 inhibitor and 15 mg of pioglitazone –the usual dose in this country, pioglitazone was switched to 10 mg of dapaglifozin or empagloflozin. The 6 months after HbA1c was compared with mean HbA1c of 3 months and just before switching. Weight change was compared and other clinical characteristics were assessed. The mean age was 59.6±11.4, duration of diabetes was 9.3±4.3 year and BMI was 28.3±3.6. The HOMA-IR was 3.59±3.5 and fasting c-peptide was 2.42±1.16. The mean of HbA1c 3 month and just before switching was 6.90±0.58%. HbA1 was increased in 44%, decreased in 39% and mean elevation and reduction was 0.49 and 0.64, each in 52 patients with dapaglifozin group. HbA1 was increased in 46%, decreased in 46% and mean elevation and reduction was 0.33 and 0.48, each in 28 patients with empagloflozin group. HOMA-IR was improved by 3.79 in 62% and aggravated by 1.90 in 38%. Body weight was reduced in 100% by 4.92±2.38 kg. So, triple combination of SGLT-2 inhibitor with metformin and DPP-4 inhibitor was similar effec in glucose control, but efficient in weight control compared to TZD as expected.

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EP428

Clinical and laboratory factors associated with response to therapy with sodium-glucose cotransporter 2 inhibitors in patients with type 2 diabetes mellitus

Sophia Pitsiava[1], Vasilis Tsimihodimos[2], Kalliopi Kotsa[3] & Theocharis Koufakis[4]
[1]Thessaloniki, School of Medicine, Aristotle University of Thessaloniki, Greece; [2]Ioannina, Department of Internal Medicine, Faculty of Medicine, University of Ioannina, Greece; [3]Thessaloniki, Division of Endocrinology and Metabolism and Diabetes Centre, First Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA University Hospital, Greece; [4]Thessaloniki, Second Propedeutic Department of Internal Medicine, Hippokration General Hospital, Aristotle University of Thessaloniki, Greece

Background
Response to therapy with glucose-lowering agents, in terms of glycemic control and weight loss, presents significant interindividual variability. This study investigated the association between clinical and laboratory parameters and response to therapy with sodium-glucose cotransporter 2 inhibitors (SGLT2i) in patients with type 2 diabetes mellitus (T2DM).
Methods
We retrospectively analyzed the medical records of people with T2DM in whom SGLT2i was started, without the concomitant initiation of any other pharmaceutical agent. Clinical and laboratory parameters were recorded before, at 3 and 6 months after starting treatment. We defined a good response in terms of glycemic control, as meeting one of the following criteria, at 3 or 6 months: i. Glycated hemoglobin (HbA1c) $<7\%$ ii. Reduction in HbA1c $\geq 1\%$ compared to baseline iii. Maintaining HbA1c $<7\%$ that a patient had before starting SGLT2i. A good response in terms of weight loss was defined as losing $\geq 3\%$ of the baseline weight at 3 or 6 months.
Results
We included 50 individuals (64% men) with a mean age of 65.8 ± 8.5 years. 86% and 64% of the participants were classified into good response categories for glycemic control and weight loss, respectively. Good responders in terms of glycemia had lower high-density lipoprotein cholesterol levels at baseline compared to bad responders (43.3 vs 57.4 mg/dl, $P=0.044$). Both the good and bad responders in terms of weight loss experienced a significant reduction in HbA1c levels between baseline and 3 months (-0.6%, $P=0.002$ and -0.8%, $P=0.003$, respectively). Only good responders in terms of glycemic control and weight loss experienced a significant improvement in the estimated glomerular filtration rate values at 3 months compared to baseline ($+2.9$ ml/min/1.73 m^2, $P=0.015$ and $+3.68$ ml/min/1.73 m^2, $P=0.006$, respectively). In logistic regression analysis, a higher baseline weight was associated with a better response to therapy in terms of weight loss ($P=0.04$).
Conclusions
Specific clinical and laboratory parameters are associated with response to SGLT2i treatment. Responses in terms of glycemic control and weight loss appear to be two distinct outcomes, despite the common underlying mechanism. These findings can contribute to a more personalized approach to T2DM care.

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EP429

The influence of individual learning at the Diabetes School on the achievement of glycemic control goals in patients with type 1 diabetes

Volha Shyshko[1,2] & Uladzislau Marozik[1]
[1]Minsk City Clinical Endocrinology Center, Minsk, Belarus; [2], Belarusian State Medical University, Department of Endocrinology, Minsk, Belarus

Introduction
Despite the emergence of all new means of control and treatment of type 1 diabetes (T1DM), the achievement of target indicators of glycemia remains a serious problem, which leads to the development of chronic complications. Therapeutic training of the basics of life with diabetes allows patients with T1DM to improve glycemic control.
Target
Evaluate the influence of individual learning at the Diabetes School on HbA1c.
Methods
For the study were selected 103 patients in the Minsk City Clinical Endocrinological Center. The selection criterion was the nonattendance of the target HbA1c. The average HbA1c was 9.26% (± 1.51%). Men amounted to 33.98% ($n=35$), women 66.02% ($n=68$). Average age 36.9±11 years. Diabetes experience 17.2±9.7 years. All patients in the past were trained under the standard program of the Diabetes School.
Results
Each patient underwent individual counseling with a teacher of the Diabetes school. The first control of HbA1c showed a decrease in its average level to 8.87±1.47% ($P=0.025$). The difference with the starting indicator HbA1c is 0.39%. Only 94 patients participated in the second control of the HbA1c. The average level of HbA1c was 9.02±1.48 % ($P=0.037$), which is 0.25 % less than HbA1c before consultation, but already higher than after 1 control of HbA1c. Only 46 people have reached a persistent decrease in HbA1c after 1 and 2 control. The average level of HbA1c was 8.62±1.43 % ($P=0.016$).
Conclusions
Individual consultations at the Diabetes School improve glycemic control One consultation is not enough to achieve the goals of HbA1C in the long term It is necessary to develop individual learning standards for its implementation in everyday practice.

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EP434

Effect of Diabetes education through social media in young patients with type 1 diabetes

Bharat Saboo[1], Aniket Inamdar[2], Vipul Chavda[3] & Dhruvi Hasnani[3]
[1]Prayas Diabetes Center, Indore, India; [2]Samarpan clinic, Omerga, India; [3]Rudraksha Institute of Medical Sciences, Ahmedabad, India

New modalities of patient education have come up, young people are more attracted towards social media WhatsApp is very common messaging and networking tool. This study compared the effects of WhatsApp-based patient education and routine care on the disease knowledge and glycemic control of adolescents and young adults with T1D in a low-resource setting. A two-month three diabetes clinics in India. The intervention group received six WhatsApp sessions of patient education, while the control group followed their usual care. Diabetes knowledge, acute events, and glycemic control were assessed before and after the intervention. The study enrolled 42 patients, 22 in the intervention group and 20 in the control group. The median age was 19 (16-21) years for both groups. The intervention group showed a significant increase in diabetes knowledge from 12/20 to 17/20 ($P< 0.01$) after two months, while the control group showed a no change from 12/20 to 12/20 ($P=0.33$). The intervention group also had a lower mean proportion of acute complications, from 24% to 18% ($P=0.52$), while the control group had a higher proportion, from 8% to 36% ($P=0.01$). There was no difference in glycosylated hemoglobin level between the groups. The study concluded that patient education via WhatsApp improved diabetes knowledge and reduced acute events, but did not affect glycemic control, after two months.

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EP438

Obesity-related comorbidities as potential factors influencing features of premature ageing in severely obese patients

Alicja Dudek[1,2], Barbara Zapała[3], Karol Ciszek[1], Ilona Kawa[1], Wojciech Zgliczyński[2] & Piotr Major[1]

[1]Jagiellonian University Medical College, 2nd Department of General Surgery, Krakow, Poland; [2]Department of Endocrinology CMKP, Warsaw, Poland; [3]Jagiellonian University, Department of Pharmaceutical Microbiology, Krakow, Poland

Background
Obesity poses a considerable threat to health, increasing the likelihood of accompanying conditions such as type 2 diabetes, hypertension, dyslipidemia, and cancer. Ageing results in the accumulation of damaging factors leading to the development of chronic diseases. Inflammation levels, telomere length, level of neurocognitive function, metabolic age serve as acknowledged indicators of biological aging. The prevalence of premature ageing in obesity has been evidenced. The precise factors driving this premature aging in obese individuals remain uncertain.
Objectives
The aim of the study was to assess the impact of comorbidity on premature ageing in obesity.
Methods
In this prospective cohort study the interleukin-6 (IL-6), C-reactive protein (CRP), telomere length (TL), speed of attention in Colour Trailed Test and metabolic age were evaluated in patients with severe obesity (SG, BMI $\geq$ 40 kg/m^2 or $\geq$35 kg/m^2 with obesity comorbidities, $n=100$) and the healthy volunteers (CG, BMI 18.5 - 24.9 kg/m^2, $n=30$). SG was divided into two subgroups: subjects with comorbidities ($n=78$) and subjects without comorbidities ($n=21$). The regression model tested the effect of dyslipidaemia, hypertension, diabetes and pre-diabetes on markers of ageing.
Results
Our results demonstrated that both SG subgroups presented higher levels of IL-6 (4.75 vs 3,96 vs 1.13 pg/ml), CRP (22.45 vs 17.8 vs 0.43 pg/ml); shorter TL (4002 vs 3809 vs 5353 bp) than never-obese subjects ($P<0.05$). However, there were no differences between patients with obesity and comorbidities and without comorbidities. The effect of BMI on increased inflammation has been demonstrated. The effect of the presence of hypertension on cognitive decline was observed.
Conclusions
Our study showed that obesity regardless of comorbidity causes premature ageing. An interesting point is the association of hypertenstion with cognitive function decline.

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EP439

Improvement of non-alcoholic steatohepatitis as measured by elastography in obese diabetic and non-diabetic patients undergoing bariatric surgery, after one-year follow-up

Víctor José Simón Frapolli[1,2,3], Ana Sánchez García[1,3], Esther Garvi Peláez[1,3], Raquel Sancho Marín[3], Isabel Arranz Salas[3,4], Gema Gómez Casado[1,3], Rocío Soler Humanes[3,5], José Pinazo Bandera[3,6], Francisco Tinahones Madueño[1,3] & Lourdes Garrido Sánchez[1,3]
[1]Hospital Universitario Virgen de la Victoria, Endocrinology and Nutrition; [2]; [3]BIONAND, Málaga, Spain; [4]Hospital Universitario Virgen de la Victoria, Pathological Anatomy, Málaga, Spain; [5]Hospital Universitario Virgen de la Victoria, General Surgery, Málaga, Spain; [6]Hospital Universitario Virgen de la Victoria, Digestive System, Málaga, Spain

Introduction
Bariatric surgery (BS) is an effective strategy for the remission of non-alcoholic steatohepatitis (NASH) in morbidly obese (MO) patients, producing an improvement in comorbidities and better glycaemic control in patients with DM2. Liver biopsy remains the definitive test to classify a patient with NASH/NASH, however, the use of non-invasive techniques such as fibroscan would avoid the limitations and risks that biopsy can cause in this type of patient. Therefore, in this study we determined the improvement of NASH by fibroscan in patients with OM undergoing BC and classified according to diabetes (DM2).
Material and Methods
We included 38 patients with OM classified according to the presence of DM2, who underwent BC and were followed up 1 year after BC. Fibroscan was performed before surgery and one year after BC. Anthropometric and biochemical variables and liver fibrosis scores were measured.
Results
Of the 38 patients included, 22 (non-DM2), and 16 (DM2), only 7 patients remained DM2 at 1 year after BC, which meant a remission of 56.3%. BMI before and 1 year after BC were similar in the two cohorts studied. Fibroscan was also similar in both groups before surgery, reflecting a significant improvement, especially in non-diabetics, but also in diabetics after surgery.
Conclusions
According to this study, liver improvement is equal in both groups of patients after one year. It shows that elastography is a valid technique to assess NASH remission in OM patients undergoing bariatric surgery. Therefore, it is important to use fibroscan to evaluate those patients with NAFLD with liver fibrosis and to prioritise their surgical intervention over those without obesity-associated comorbidities.
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EP487

Correlation between depression and type 2 diabetes mellitus in durres community

Ira Xhemollari[1], Edlira Elezi Bucpapaj[2] & Agron Ylli[3]
[1]Municipial Hospital, Endocrinology, Kavaje, Albania; [2]Municipial Hospital, Endocrinology, Lac, Albania; [3]Mother Teresa University Hospital Center, Endocrine and Metabolic Diseases Unit, Tirane, Albania

Background
Worldwide, depression is the second-leading cause of disability and diabetic patients have more chances to develop depression compared to non-diabetic people. The aim of our study is to estimate the prevalence of depression among type 2 diabetes patients and to investigate the sociodemographic and clinical factors associated with the presence of depression among these patients in Regional Hospital of Durres, Albania.
Methods
Through a cross-sectional study were prospectively analyzed 111 consecutive patients with diabetes mellitus admitted to the regional hospital of Durres between January and February 2022. For each patient was assessed the sociodemographic and clinical characteristics and screening of depression was performed through questionnaire according to the patient health questionnaire Beck's depression Inventory (BDI). SPSS 16.0 was used for data analysis.
Results
The prevalence of depression was 73.9 % among the diabetic patients and the female patients had a higher percentage of depression compare to men. Multivariate logistic regression analysis showed that gender female (OR=3.4), unemployment (OR=9), poor economic level (OR 4.7), the duration of diabetes mellitus over 3 years (OR=4) and marital status (OR=6) are the independent factors that influence the onset of depression.
Conclusion
Many factors as being female, unemployment, poor economic level, marital status, duration of diabetes above three years, are the independent factors that influencing the onset of depression. It is a need to develop an integrated care program to manage depression in diabetic patients. Early recognition of predictive factors associated with anxiety and depression in diabetic people is necessary to promote adherence with the treatment and compliance to diabetes control.
Key word: depression, diabetic, risk

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EP491

Applicability of intermittent intersticial glucose monitoring in patients admitted to the intensive care unit of the hospital universitario san cecilio in granada

Raúl Rodríguez Juárez[1], María Del Carmen Andreo-Lopez[1], Elena Martínez Silla[1], Javier García Sánchez[1], Laura Cánovas Noguera[1], Juan Luis Delgado Montoya[1], Maria Teresa Cruces Moreno[2] & Pablo José López-Ibarra Lozano[1]
[1]Granada, UCG Endocrinología y Nutrición, Granada, Spain; [2]Granada, UCG Cuidados Intensivos, Granada, Spain

Objective
Optimal glycemic management in critically ill patients with diabetes or stress hyperglycemia has prognostic value. For adjustment, the most used measurement in the Intensive Care Unit (ICU) is the capillary glucose. In this study, we compare interstitial glucose (IG) and capillary glucose (CG) concentrations to assess the applicability of sensor placement in patients requiring vasoactive agents.

Materials and Methods
Prospective longitudinal observational study with 6 diabetic patients or stress hyperglycemia admitted to the ICU. Demographic (sex, age), clinical (DM, high blood pressure, obesity), hemodynamic (need for vasoactives) and metabolic (A1c-type glycosylated hemoglobin (HbA1c) determined by laboratory analysis, presence of angiopathic complications, CG and IGM measurements (in mg/dl)) variables were collected. The statistical analysis was performed with the IBM SPSS v.25 programme (Statistical significance $P<0.05$).
Results
67% were males with a mean age of 65.5 ± 21.5 years. 100% have high blood pressure and 50% obese. 67% were type 2 diabetic with a mean HbA1c 6.5 ± 1.6% and 75% had angiopathic complications. The mean CG was 205 ± 66.9 and the mean IG was 152.2 ± 53.4. 67% required vasoactive agents. There was a positive correlation between capillary and interstitial measurements both in patients with and without vasoactive agents ($r=0.8$ and $r=0.7$, respectively, $P=0.0$).
Conclusions
There's a positive and strong correlation between capillary and interstitial measurements, with or without vasoactive agents. This suggests that, regardless of the patient's hemodynamic situation, IG could be useful as a glycemic measurement instrument in critically ill patients, thus improving their comfort.

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EP492

Inflammatory cardiovascular marker IP-10/CXCL-10 in patients with diabetes mellitus type 2

Sylvia Pashkunova[1], Valentina Gavazova[1], Stefan Tsonev[2], Detelina Vitanova[3], Joana Vangelova[4], Nikolay Kostadinov[5], Maya Zheliazkova[6], Dimitar Vassilev[7] & Teodora Daneva[8]
[1]Military Medical Academy, Endocrinology, Sofia, Bulgaria; [2]Agrobioinstitute, Sofia, Bulgaria; [3]3University of Library Studies and Information Technologies, Sofia, Bulgaria; [4]Medical University, Varna, Bulgaria; [5]Medical University, Burgas, Bulgaria; [6]Sofia University 'St. Kl. Ohridski', Faculty of Mathemathics and Informathics, Faculty of Mathemathics and Informathics, Sofia, Bulgaria; [7]Sofia University 'St. Kl. Ohridski', Faculty of Mathemathics and Informathics, Sofia, Bulgaria; [8]Bulgarian Academy of Sciences, Institute of Biology and Immunology of Reproduction "Acad. Kiril Bratanov, Sofia, Bulgaria

Interferon gamma-induced protein 10, a proinflammatory chemokine, has a significant effect in inflammatory diseases. Interferon-inducible protein of 10 kD (IP-10/CXCL10), is a member of the C-X-C chemokine superfamily. It is a potent chemoattractant for activated T lymphocytes and is reported to be involved in various disease states, including atheroma plaque formation, inhibition of tumor angiogenesis and maintenance of podocyte function. However, the involvement of IP-10 in DMT2, especially in its vascular and renal complications, is not thoroughly studied. A study domain with promising potential of the IP-10 influence is its relation with patients with DMT2 with macrovascular complications in the context of disbalanced lipid profile LDL, HDL, Total cholesterol, triglycerides, BMI >30 kg/m^2, poor Glycaemic control.
Materials. Methods
To elucidate the etiopathological role of IP-10 in DMT2, we measured the concentrations of IP-10/in plasma samples from 130 patients with various degrees of macrovascular complications, and with high level of BMI and poor Glycaemic control and dyslipidemia. We focus our research on measuring of the IP-10/CXCL10 as an inflammatory marker in DM2T and its relation to the above-mentioned complications. IP-10/CXCL10 is related to patients with dyslipidaemia. Patients with higher BMI are potentially associated with increased levels of IP-10/CXCL10. To examine the dependencies between the studied blood test parameters and IP-10/CXCL10 we set up a study including following data: IP-10/CXCL10 plasma levels of 56 men and 74 women with DMT2 were measured by ELISA and compared with dose in 115 healthy control subjects. Some significant differences (t-test) between averages were obtained for all blood test parameters measured for patients with DMT2 related to IP-10CXCL10.
Results
The IP-10/CXCL10 levels were higher in diabetics than in healthy controls (251 pg/ml vs 209 pg/ml $p = 0.043$). IP-10/CXCL10 were significantly increased in hyperlipidemic men and women as compared to those with normal lipidemic profile, respectively within the group of DMT2 patients. The distribution of the number of the controlled patients in both DMT2 subgroups is not well-balanced, where very often is observed different directions of the levels of such parameters like HbA1c and BMI as compared to lipid panel. All the lab tests are significantly differentiated as related to the introduced groups of DMT2 patients and healthy controls as well as within the groups of DMT2 patients having different referent levels of the blood tests and IP-10. IP-10/CXCL10 is related to patients with high levels of LDL, HDL, Total cholesterol and triglycerides.

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EP493

The role of COVID-19 in the development of diabetic nephropathy

Dilafruz Khudaybergenova[1], Dilorom Najmutdinova[1] & Khilola Mirakhmedova[2]
[1]Tashkent medical academy, Endocrinology, Tashkent; [2]Tashkent medical academy, The propaedeutics of internal disease, Tashkent

Introduction
COVID-19 is the disease caused by a new coronavirus, now called severe acute respiratory syndrome coronavirus. Long COVID is a wide range of new, returning, or ongoing health problems that people experience after being infected with the virus that causes COVID-19. Diabetic nephropathy(DN) is a frequent comorbidity in patients with COVID-19.
Aim
The aim of the present work was to study the relationship between chronic kidney disease (CKD) and SARS-CoV-2 infection and early detection of CKD.
Methods
A cohort of patients were studied with confirmed COVID-19 infection examined at the Department of infectious disease, Zangiata Infectious Diseases Hospital, Tashkent region. Bloodwithdrawalwas carried outwhen the recruited adolescents tested negative for the SARS-CoV-2 ('post-infected COVID-19'), 90 to 95 days after the last molecular test.
Results
120 adult patients were examined: 80 patients with type 2 diabetes complicated by CKD (main group) who had suffered COVID-19, and 30 patients with type 2 diabetes complicated by CKD who had not suffered COVID-19 (control group). Patients in the main (COVID-19 in combination with T2DM) and control groups (T2DM) did not differ, as expected, in gender (7 men (33.3%) in each group; $P=1.00$), age (64.3 ± 8.50 and 62.3 ± 5.96 years; $P=0.333$), HbA1c level (9.8 ± 2.09 and 9.6 ± 1.82%; $P=0.670$), as well as body mass index (30.7 ± 5.15 and 29.2 ± 5.83 kg/m^2; $P=0.131$). Both groups had the same number of patients with diabetes experience of more than 5 years (16 people each, or 76.2%; $P=1.00$). The study and control groups did not differ in the frequency of detection of such diabetes complications as nephropathy (10 (47.6%) and 11 (52.4%); $P=0.762$), retinopathy (7 (33.3%) and 11 (52.4%); $P=0.213$) and polyneuropathy (16 (76.2%) and 11 (52.4%); $P=0.110$). Analysis of tissue growth factor (TGF-β1) indicators in patients with covid 19 and diabetic nephropathy showed that TGF-β1 in this group was 1.9 times higher than normal (54.7 ± 6.1 ng/ml), compared with the control group it was 0.65 times higher ($P< 0.05$). Scientific studies have determined the levels of sensitivity and specificity of TGF-β1 as diagnostic markers in the early detection of CKD.
Conclusions
The results of our study are in accordance with those of the literature regarding in early diagnosis and prevention is the use in clinical practice of highly diagnostic laboratory research methods to identify CKD of various etiologies among the population.

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EP494

Dazzeling evolution with unusual metastases of a medullary thyroid carcinoma: about a case

amira bouchenna, Benabdelatif Katia & Bensaleh meriem
central hospital of army, endocrinology, algiers, Algeria

Introduction
At the time of diagnosis of medullary thyroid carcinoma (MTC) 10 to 15% of patients have distant metastases, 25% of them develop them over a longer or shorter period of time. The usual metastases concern cervical lymphadenopathy, bone, lung and liver. There are also unusual secondary localisations. We report a case.
Observation
A 56-year-old patient who consulted a year after apparition of cervical lymphadenopathy, whose fine needle aspiration returned in favor of a MTC with serum thyrocalcitonin (TCT) level at 2000 pg/l. The extension assessment was negative, the patient was operated on and the anatomopathological study confirmed the diagnosis of MTC classified as PT3N1bM0. The genetic study of the RET mutation could not be carried out. 6 weeks after surgery the TCT level returns to 1500 pg/l. At 3 months after surgery, the patient presented with inguinal lymphadenopathy, the fine needle aspiration of which revealed a carcinomatous process with a TCT level in the liquid washing was 2342 pg/l. the serum TCT level returned to 3789 pg/l, and the extension assessment found a right adrenal metastasis of 14mm (the diagnosis of pheochromocytoma was ruled out), multiple right femoral and vertebral bone metastases with spinal cord compression of L1,

the latter's surgery is rejected, so he benefits from decompression radiotherapy. The patient is put on vandetanib

Discussion

The rapid evolution in our patient with the appearance of multiple metastases, two of which are unusual in 2 months, raises fears of a codon 918 mutation of the RET proto-oncogene. Few studies specify the proportion of rare localizations of MTC; one study of 19 patients reported 10% adrenal and digestive metastases, while another of 35 patients found no cases. In our reading we found only two described cases of metastatic inguinal lymphadenopathy.

Conclusion

Metastases from unusual locations do not seem so rare, they must be sought in the event of a doubling of TST values and be treated in patients whose survival is sometimes very prolonged.

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EP495

Relationship of the mediterranean diet with vitamin d status in patients with obesity

Javier García Sánchez[1], Maria Hayon Ponce[2], María Teresa Zarco Martín[1], Socorro Leyva Martínez[1], Maria Luisa Fernández Soto[1] & Verónica Ávila Rubio[1]

[1]San Cecilio Clinical University Hospital, Endocrinology and Nutrition, Spain; [2]Virgen de las Nieves University Hospital, Endocrinology and Nutrition, Spain

Introduction

Obesity is a known risk factor for hypovitaminosis D and although several studies point out that higher adherence to the Mediterranean Diet (Diet-Med) is associated with higher dietary vitamin D intake, there are very limited data on the influence of Diet-Med on serum 25-Hydroxy Vitamin D (25OHD) levels. Our aim was to evaluate the relationship between adherence to Diet-Med and vitamin D status in obese patients.

Material and Methods

Retrospective observational study of a sample of 125 candidates for bariatric surgery evaluated during 2018-2022 at the UNCyD of the Hospital San Cecilio of Granada. Sociodemographic, anthropometric data and serum 25OHD levels were analyzed. Adherence to Diet-Med was assessed using the PREDIMED-score (<7 points = low adherence).

Results

Prevalence of good adherence to Diet-Med: 54.4%. 68.8% women. Mean age 45.3 ± 12.4 years. Mean weight 126 ± 24 kg and mean BMI 45 ± 6.8 kg/m^2. The group with good adherence to Diet-Med presented higher age (47.6 ± 10.6 vs 42.6 ± 12.8, $P = 0.03$) and higher number of patients with vitamin D sufficiency (25OHD ≥ 20 ng/ml: 46.3% vs 28.1%, $P = 0.037$). Furthermore, a statistically significant positive relationship was observed between good adherence to Diet-Med and vitamin D sufficiency ($r = 0.187$, $P = 0.038$) with an odds ratio of 2.207 (95% CI: 1.0141-4.677, $P = 0.039$).

Conclusion

The association between adherence to Diet-Med and vitamin D status in obese subjects is demonstrated.

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EP498

Clinical characteristics of people with type 1 diabetes at the axarquia hospital

Luis Ignacio Navas Vela, Viyey Kishore Doulatram Gamgaram, Javier Gómez Pino, María José Vallejo Herrera & Monica Tomé García

Hospital Regional Universitario, Endocrinology and Nutrition

Introduction

For the past three years, patients with type 1 diabetes have been treated with basal-bolus therapy at the Axarquia Hospital by doctors from the Clinical Management Unit of Endocrinology and Nutrition at the Malaga Regional University Hospital. Treating patients in their own health area avoids travel and could have an impact on better follow-up, metabolic control, and the incidence of complications. The aim of this study is to describe the socio-demographic and clinical characteristics of the patients seen in this clinic.

Material and Methods

Cross-sectional descriptive observational study of patients with type 1 diabetes mellitus followed up at the Diabetes Clinic of the Axarquia Hospital. Data were obtained from their electronic medical records. The analysis was carried out using the JAMOVI programme.

Results

Data were collected from 335 people with type 1 DM. The mean age was 42.9 ± 14.8 years (16-82). Forty percent were women. The mean BMI was 26.6 ± 5.27 (15.1-51.1). 22.9% were smokers and 25.7% were ex-smokers. 25.8% had hypertension and 45.5% were on lipid-lowering therapy. 9.8% had diabetic nephropathy, 32.4% had diabetic retinopathy and 12.9% had diabetic neuropathy. The mean glycated haemoglobin was 7.70 ± 1.15. Regarding the glucose activity profile recorded by the intermittent glucose monitoring systems, sensor usage was $89.6 \pm 10.3\%$, mean glucose 174 ± 38.9 mg/dl, glucose variability $37.6 \pm 7.65\%$, mean interstitial glucose (MIG) $7.49 \pm 0.94\%$, time in range (70-180 mg/dl) $56.6 \pm 18.5\%$, time above range (181-250 mg/dl) $23.9 \pm 8.78\%$, time in very high range (>250 mg/dl) $15.8 \pm 15.4\%$, time below range (55-69 mg/dl) $3.24 \pm 3.21\%$ and time far below range (<54 mg/dl) $0.6 \pm 1.52\%$. Regarding basal insulin use, 48.2% used degludec, 49.3% used glargine U100 and the remaining 2.5% used a first-generation basal insulin analogue. For rapid insulin, 70.7% used Fiasp and the remaining 29.3% used rapid insulin analogues.

Conclusions

The Diabetes Unit of the Axarquia Hospital treats patients with complex characteristics and a high percentage of microvascular complications. It would be interesting to follow the long-term evolution of these patients and to analyse the impact of the care provided in the regional hospital on the achievement of glycaemic targets.

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EP499

Impact of the world diabetes day in greece

Dimitra Ragia, Sofia Dionysopoulou, Eleni Kouroglou, Konstantinos Belis, Stella Proikaki & Ioannis Ilias

Hippokration General Hospital, Department of Endocrinology, Athens, Greece

Introduction/Aim

In this study, we aimed to evaluate the long-term impact of the diabetes awareness day in Greece (in 2016-2023), which is organized every year in November, by examining the relevant local internet searches.

Materials/Methods

We collected monthly data with Google Trends, exclusively from Greece, on relevant [online] search volumes (RSVs), with keywords "diabetes" (study group; in medical/scientific and lay terms, in Greek and in English) and "breast cancer" (control group - in Greek). The data were collected and analyzed in three periods: 2016-2019 (period A), 2020-2021 (COVID-19 period, period B), 2022-2023 (period C; Google Trends implemented a major change in the algorithms to calculate RSVs on January 1, 2022). RSVs for diabetes and breast cancer were compared by month (Kruskal-Wallis test). In addition, RSVs for diabetes were compared with those for breast cancer and were also assessed for longitudinal trends using the Sign test and Spearman's correlation analysis, respectively (statistical significance was set at $P < 0.05$).

Results

In period A, searches for diabetes-related terms outnumbered those for breast cancer, but with no differentiation in months with corresponding days of awareness for the diseases. Searches for "[blood] sugar" and "breast cancer" increased with time. In period B, searches for diabetes terms outnumbered those for breast cancer (except for "[blood] sugar"). Months with disease awareness days had more searches compared to other months. Searches for "diabetes" showed a downward trend. In period C, searches for diabetes terms outnumbered those for breast cancer. The months with diabetes awareness days showed more searches compared to other months and showed an increasing phase. Overall, of the diabetes terms, searches for "[blood] sugar" stood out for their predominance over the other terms combined with their increasing trend.

Discussion/Conclusions

Diabetes was more popular in online searches than breast cancer and interest in it online, with the exception of the Covid-19 period, had an increasing trend in Greece. Based on these results, the effectiveness of the diabetes day is judged positively, in spite of critics of such actions. The trend of the lay search term "[blood] sugar" could be attributed to the doubling of the percentage of people over 65 years of age in the country accessing the Internet in the last decade. In addition, it is important to note that the study's reliance on internet searches and the potential influence of other factors on search trends may introduce limitations.

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EP502

The main risk factors in type 2 diabetes for cognitive dysfunction, depression, and psychosocial problems

Maarja Randväli[1], Toomas Toomsoo[2] & Jekterina Šteinmiller[1]
[1]Tallinn Health Care College, Nursing, Tallinn, Estonia; [2]Tallinn University, Natural Science and Health, Tallinn, Estonia

The aim of this study is to analyze the risk factors that lead to cognitive impairment, depression, and psychosocial problems in type 2 diabetes and discern what aspects they have in common. Type 2 diabetes is associated with a higher risk of cognitive impairment, including dementia, which in turn increases the risk of hospitalization, falls, and premature mortality. In this study, we conducted a systematic review to achieve this goal, including searches on electronic databases such as PubMed, Medline, Web of Science, EBSCO Discovery, EBSCO host, Scopus, and ScienceDirect, from 2016 onwards. Additionally, we carried out manual searches in leading journals in the field. After evaluating and analyzing the articles, 60 remained, focusing on the following four main themes: disorders due to biological, psychological, social, and pharmacological causes that lead to neuropsychological complications. Based on the results, consistently analogous risk factors contributing to the onset of cognitive impairments, depression, and psychosocial predicaments encompass comorbid ailments, dysglycemia, gender, heightened levels of apprehension and anxiety, educational attainment, socio-economic standing, and pharmaceutical interventions. Furthermore, in the realm of type 2 diabetes, factors such as disease duration, adiposity, specifically overweight and obesity, and advancing age were also identified as significant contributors to cognitive impairments and depression. Concomitantly, the absence of a robust support system and social network emerged as a shared risk factor, predisposing individuals to psychosocial challenges and depressive states. These findings emphasize that the risk factors for cognitive impairments, depression, and psychosocial issues for type 2 diabetes are similar, highlighting the importance of psychosocial support, education, and patient-centered treatment to optimize outcomes and quality of life.

Keywords: type 2 diabetes; depression;cognitive dysfunction; psyhosocial challenges

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EP503

Determination of diabetes care profile and diabetes management in individuals with type 2 diabetes: turkey survey

Saadet Can Cicek[1], Muhammed Emin Demirkol[2], Emine Kir Biçer[3] & Derya Kocadag[4]
[1]Bolu Abant izzet Baysal University, Department of Nursing, Bolu, Turkey; [2]Abant izzet Baysal Üniversitesi, Department of Internal Medicine, Turkey; [3]Mustafa Kemal Üniversitesi Tayfur Sökmen Kampüsü, Turkey; [4]Bolu Provincial Health Directorate, Turkey

Objective
This study aimed to determine the diabetes care profile and diabetes management in individuals with type 2 diabetes.
Methods
The population of the cross-sectional study consisted of individuals with Type 2 diabetes who received treatment in the internal medicine services of Public Hospitals in a province, and 377 individuals who met the inclusion criteria constituted the sample. Data was obtained using the Information Form, the Summary of Diabetes Self Care Activities Questionnaire (SDSCA) and the Diabetes Care Profile Scale.
Results
The mean age of the participants was 60.7 ± 9.7 years, 65.3% were female, the duration of diabetes was 10.71 ± 7.0 years, the HbA1c level was 7.2 ± 1.4, the most common type of diabetes treatment was nutrition and oral antidiabetic medication, and 7.2% developed diabetes-related complications. Among the subscales of the diabetes care profile scale, control problems (4.87 ± 1.14), which is one of the factors that impede diabetes control, and long-term results (4.41 ± 1.07), which is one of the factors that improve diabetes control, received the highest scores. Control problems was higher in women who were illiterate, living with their parents, using nutrition + oral antidiabetic medication + insulin and did not receive training on diabetes ($P < 0.05$). The long-term care benefits sub-scale was higher in smokers, those who take nutrition + oral antidiabetic medication + insulin therapy, and those with a family history of diabetes. An inverse correlation was found between diabetes self-care activities and the factors that impede diabetes management difficult except for medical barriers while a positive correlation was found between diabetes self-care activities and the factors promoting diabetes management except for long-term care benefits and blood glucose monitoring ($P < 0.05$).
Conclusion
It was seen that factors impeding and promoting diabetes management differed in terms of sociodemographic and diabetes-related characteristics of individuals with diabetes, and a significant relationship was determined between diabetes care profile and diabetes self-care activities.

Keywords: Diabetes Care Profile; Type 2 Diabetes; Diabetes Self-Care Activities; Diabetes Management.

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EP504

Evaluation of knowledge and practices of individuals with diabetes towards diabetes technologies

Emine Kir Biçer[1] & ilker Tutur[2]
[1]Mustafa Kemal Üniversitesi Tayfur Sökmen Kampüsü, Demartment of Internel Medical Nursing, Turkey; [2]Kırıkhan Devlet Hastanesi, Turkey

Objective
This study was conducted to evaluate the knowledge and practices of individuals with diabetes towards diabetes technologies
Method
A total of 514 people consisted of the sample of the descriptive and cross-sectional study. Data were collected through a questionnaire developed by the researchers, and the Unified Theory of Technology Acceptance and Use Scale-2 was applied using an online Google survey distributed through social media.
Results
The study's participants, with a mean age of 29.9 ± 12.2 years, displayed a diverse demographic profile, with 68.3% being female, 38.9% holding a bachelor's degree or higher, and 59.3% being single. The mean duration of diabetes among participants was 10.4 ± 6.6 years, primarily managed with insulin (82.7%). Among insulin users, 67.7% favored insulin pens, 19.3% opted for insulin pumps, and 13.0% used insulin injectors. Participants checked blood glucose levels an average of 7.9 ± 8.0 times per day and injected insulin 3.6 ± 0.7 times daily. Regarding technology usage, 94.9% of participants reported using mobile phones, 91.4% owned smartphones, and 77.8% used computers. Notably, 72.6% were aware of Continuous Glucose Monitoring Systems (CGM), 78.4% knew about insulin pump therapy, 77.8% were familiar with insulin pens, and 34.0% recognized mobile applications related to diabetes. In terms of technology adoption, 39.9% used CGM, 51.8% utilized glucometers, 20.2% employed insulin pumps, 1.8% accessed telehealth services, and 16.3% utilized mobile technology. Participants expressed interest in receiving information about CGM (21.4%), insulin pumps (41.8%), hypoglycemia warning wristbands (45.1%), and insulin ports (37.7%). Overall, 80% of individuals reported that diabetes-related devices significantly influenced their lives, with 82.3% finding them effective. Internet usage in relation to diabetes included participation in social networks (58.9%), seeking information (58.4%), and gaining social support (20.4%). Participants most frequently searched for information on nutrition (67.1%) and insulin treatment (53.5%). The frequency of use of mobile services by individuals with diabetes was found to be every day at the highest rate (66.3%). The mean score of the Unified Theory of Acceptance and Use of Technology Scale-2 was 132.2 ± 47.8 (min = 27-max = 188).
Conclusion
The study revealed predominant use of insulin pens and a high reliance on mobile technology among individuals with diabetes. While interest in advanced technologies exists, the adoption of telehealth services remains low. The study suggests a moderate level of technology acceptance and use among the participants.

Keywords: Diabetes, technology, telehealth, mobile applications

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EP505

Correlation between kalemia and biochemical parameters in patients with diabetic ketoacidosis

Ines Mezghani[1], Omaima Hammami[1], Rim Marrakchi[1], Faten Hajkacem[2], Mariem Boudaya[1], Kamel Jammoussi[1], Nabila Rekik[2], Mohamed Abid[2] & Mouna Turki[1]
[1]Hedi-Chaker University Hospital, Biochemistry Departement, sfax, Tunisia; [2]Hedi-Chaker University Hospital, Endocrinology Departement, sfax, Tunisia

Introduction
Ketoacidosis is a frequent and life-threatening complication of diabetes. Our aim was to study the Correlation between kalemia and biochemical parameters in patients with diabetic ketoacidosis.

Methods
This is a retrospective descriptive study concerning all patients hospitalized in the Endocrinology Department for Diabetic Ketoacidosis (DKA) between August 2021 to December 2022. Acidosis markers were measured using an ABL 80 FLEX blood gas analyser, and the biochemical parameters using the DXI 700 AU (Beckman Coulter) analyser. IBM SPSS was used for statistical analyses.
Results
Out of 30 patients, 19 (63,3%) patients had type 1 diabetes and 11(36.7%) had type 2 diabetes. The mean age of patients was 26.7 ± 10.4 years (type 1 diabetes 22 ± 6.5 years; type 2 diabetes 34.9 ± 11 years). The sex-ratio (H/F) was 0.66. There was significant difference in the initial laboratory evaluation between type 1 and type 2 diabetes patients only for the pH and serum bicarbonate ($P=0.010$ and $P=0.024$, respectively). Among patients, 26.66% had hypokalaemia (potassium concentration (k^+C) <3.3 mmol/l), 16.66% had k^+C between 3.3 and 3.5 mmol/l. In 26.66% of cases the k^+C was between 3.5 and 4 mmol/l and 16.66% of patients had k^+C between 4 and 4.5 mmol/l. In 10% of patients the k^+C was between 4.5 and 5 mmol/l. Only one patient was presented with hyperkalemia. The mean age of the group who presented hypokalemia was 27.12 years ± 8.62 and 50% of them were Type 1 diabetes. None of the patients had neuromuscular or electrical signs of dyskalemia. Potassium levels were correlated with serum glucose($r=0.523$), glycated hemoglobin ($r=0.468$), pH ($r=0.597$), serum bicarbonate($r=-0.380$), PCO2($r=0.309$), PO2($r=0.257$) and creatinine($r=0.293$).
Conclusion
Hypokalemia was observed in 26.66% of patients with DKA. Further research is needed to better determine the risks and benefits of administering insulin before obtaining serum potassium values.

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EP506

Post-absorptive and post-prandial glucose and fat metabolism in post-menopausal women with breast cancer after chemotherapy compared to healthy controls

Kristian Buch-Larsen[1], Simone Marstrand[1], Djordje Marina[1], Linn Gilberg[2], Michael Andersson[1], Gerrit Hall[1] & Peter Schwarz[1]
[1]Rigshospitalet, København, Denmark; [2]Copenhagen University, København, Denmark

Background
Breast cancer survivors are a growing population due to improved treatment. It is known that postmenopausal women treated for breast cancer may experience weight gain and increased insulin resistance, but detailed knowledge on how chemotherapy impact metabolic and endocrine mechanisms remain unknown.
Objective
We performed a thorough, preliminary study to elucidate the differing mechanisms of post-prandial absorption and metabolism in postmenopausal early breast cancer (EBC) patients treated with adjuvant chemotherapy compared to healthy controls. We hypothesize that chemotherapy has a negative impact on metabolism in EBC patients.
Methods
We examined four postmenopausal women shortly after treatment with chemotherapy for EBC and four age-matched healthy women who served as controls using isotopic tracers during a mixed meal-test. Blood was sampled during the 240 min meal-test to examine post-prandial absorption and endogenous synthesis of lipid and carbohydrate metabolites.
Results
We found that insulin concentrations were numerically higher before the meal-test in the EBC patients compared to controls (76.3 pmol/l vs 37.0 pmol/l; $P=0.06$). Glucose kinetics was increased post-prandial (most pronounced at 30 minutes, 9.46 mmol/l vs 7.33 mmol/l; $P=0.51$), with no difference between the groups regarding liver glucose output. Fatty acid kinetics showed a numeric increase in oleic acid rate of appearance in BC patients, but only during the first hour after the mixed meal. There was no significant difference in VLDL-TAG synthesis between the two groups.
Conclusions
This preliminary study is unique in using advanced tracer methods to investigate *in vivo* metabolism of EBC patients after chemotherapy although no statistical differences in glucose and fatty acid kinetics was seen compared to controls. However, during the first two post-prandial hours, oral glucose and oleic acid appearance in the systematic circulation was elevated in the EBC patients. This could be due to changes in gastrointestinal uptake and further studies with altered set-up could provide valuable insights.

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EP509

Differences in sleep quality of patients with type 2 diabetes experiencing low perceived psychological stress and high perceived psychological stress

Lina Radzeviciene & Lina Lasaite
Lithuanian University of Health Sciences, Institute of Endocrinology, Kaunas, Lithuania

Aim
to assess sleep quality in patients with type 2 diabetes (T2D) experiencing low perceived psychological stress and high perceived psychological stress.
Methods
Perceived stress level and sleep quality were assessed in 154 patients with T2D (58 men, 96 women, age 58.7 ± 11.8 years), using Perceived Stress Scale (a higher score denotes a higher level of perceived stress) and Pittsburgh Sleep Quality Index (a higher score denotes worse sleep quality).
Results
Patients with T2D with high stress level had worse subjective sleep quality ($P=0.027$), higher use of sleeping medication ($P=0.023$), daytime dysfunction ($P<0.001$) than those with low stress level. No significant differences were found in sleep latency, sleep duration, habitual sleep efficiency and sleep disturbances as well as in T2D duration, body mass index and glycated haemoglobin (HbA1c) level between patients experiencing low and high perceived stress. Perceived stress level in patients with T2D correlated with subjective sleep quality ($r=0.260$, $P=0.002$), sleep duration ($r=0.228$, $P=0.005$), use of sleep medication ($r=0.245$, $P=0.004$), daytime dysfunction ($r=0.326$, $P<0.001$).
In conclusion, patients with type 2 diabetes experiencing high perceived psychological stress level have worse subjective sleep quality, higher use of sleeping medication, daytime dysfunction than patients experiencing low perceived stress level. Perceived stress level in patients with type 2 diabetes is related to subjective sleep quality, sleep duration, use of sleep medication, daytime dysfunction.

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EP510

Type 2 diabetes and cancer: phenotyping of patients followed in a tertiary diabetic centre

Edoardo Luigi Maria Mollero[1], Carola Ciamparini[1], Davide Vimercati[1], Leonardo Bighetti[1], Giulia Marsan[1], Lorenza Scotti[2], Paolo Marzullo[1], Marina Caputo[1,3], Gianluca Aimaretti[1] & Flavia Prodam[1,3]
[1]SCDU Endocrinologia, University of Eastern Piedmont, Department of Translational Medicine, Novara, Italy; [2]University of Eastern Piedmont, Department of Translational Medicine, Novara, Italy; [3]University of Eastern Piedmont, Department of Health Sciences, Novara, Italy

Background
Data on the relationship between type 2 diabetes (T2D) and cancer consistently suggests the involvement of metabolic mechanisms such as inflammation, obesity, and glucose alteration. These mechanisms, including the activation of factors like IGF-1 or m-TOR, may influence the development of cancer.
Aim
Our study had two main objectives. Firstly, we aimed to investigate the relationship between specific identifiable factors associated with T2D and the timing of cancer onset. Secondly, we sought to examine the relationship among cancer recurrence, second primary cancers, and the presence of either of them, while considering the same variables.
Methods
We selected 1089 patients affected by both T2D and cancer, carried out from the Smart Digital Clinic electronic medical record system using relevant key words related to the field of cancer. The variables of interest were measured at baseline and during the last visit of follow-up. For statistical purposes, only the variables at baseline were compared to the time of cancer onset. Subsequently, all variables were stratified by sex. Various types of cancers were classified based on the organ system they affected.
Results
Almost all the variables considered had not a statistically significant relationship with the time of cancer onset. Smoking resulted the only factor that can influence it ($P=0.0024$). Furthermore, when considering cancer recurrence, second primary cancer, or either of them, none of the variables showed a relationship with them. The same variables were stratified by sex at baseline and at the last visit of follow-up. Females were found to be more overweight ($P=0.0314$) and in need of higher doses of insulin ($P=0.0181$) compared to males. This is because they had worse glucose control, with higher levels of HbA1c ($P=0.0004$) and fasting blood glucose ($P=0.0348$) compared to males both at baseline and at the last visit. On the

contrary, males had a higher rate of smoking and alcohol consumption compared to females (both $P<0.0001$). Lastly, among the variables considered and the three events (cancer recurrence, second primary cancer and either of them), the only variable found to be sex-related was the LDL-cholesterol compared to cancer recurrence, which was slightly higher in female than males ($P=0.0356$).
Conclusion
We observed that, apart from smoking, all the variables considered identifiable factors with T2D had not an influence on the time of cancer onset, as well as on cancer recurrence, second primary cancer or either of them.

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EP511

Necrotizing otitis externa in diabetic patients: clinical features and out come

Meherzi Samia[1], Lansari Salma[2] & Omri Rihab[3]
[1]University of Sousse, Faculty of Medecine of Sousse, ENT Departement, Tunisia; [2]University of Sousse, Faculty of Medecine of Sousse, Ent Department, Tunisia; [3]University of Sousse, Faculty of Medecine of Sousse, Ent Department, Tunisia

Objective
Describe clinical features and therapeutic modalities of diabetic patients hospitalized for necrotizing otitis externa in our department.
Materials and methods
Retrospective study about 19 diabetic patients treated for necrotizing otitis externa in our department over a period of 7 years (2016 - 2022). All patients had a bacteriological and mycological otorrhea sampling, computed tomography and laboratory test.
Results
The average age of our patients was 60 years old (22-91 years old) with female predominance. Severe otalgia resistant to standard treatments was observed in all cases. Two patients suffered from facial palsy. All patients received pre-hospital antibiotic therapy for an average duration of 7 days (5 – 21 days). The average time for germ isolation was 4 months (3 days – 3 months). The bacteriological study of the initial samples was positive in 12 cases. The most common germ was Pseudomonas Aeruginosa (9 cases). 4 patients had an aspergillary infection (fungal transformation in 3 cases). Aspergillus serology was positive in two patients who still had negative samples. Treatment was based on parenteral antibiotic therapy combining a Fluoroquinolone (Ofloxacin) with a Third Generation Cephalosporin (Ceftazidim) or a Carbapenem in the majority of cases, with an average duration of 45 days. The fungal forms received antifungal treatment (Itraconazole) for an average duration of 3 months (66 days– 5 months). The evolution was favorable in all cases. No recurrence was noted with an average follow-up of 15 months.
Conclusion
Necrotizing otitis externa represents a diagnostic and therapeutic challenge for any ENT practitioner. Fungal forms are clearly on the rise. The multiplicity of bacteriological and mycological samples improves the rate of positive results and establishes the appropriate treatment.

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EP512

Coronary arteries atherosclerosis in patients with type 2 diabetes and coronary heart disease

Elena Brutskaya-Stempkovskaya[1], Alexandr Aleshkevich[1], Oleg Kozak[2], Iryna Subota[2], Karina Liahkova[1], Lizaveta Tsitova[1] & Yuliya Dydyshka[1]
[1]Belarusian State Medical University, Minsk, Belarus; [2]Minsk Scientific and Practical Center for Surgery, Transplantology and Hematology, Minsk, Belarus

Type 2 diabetes (T2D) is an independent risk factor for coronary heart disease (CHD). CHD in patients with T2D develops at an earlier age and is characterized by severe damage to the distal coronary arteries.
Materials and Methods
A cross-sectional controlled study of 50 hospitalized cardiac patients with chronic CHD was conducted to assess the effect of T2D on the condition of the coronary arteries using coronary angiography. The main group: patients with CHD and T2D, age-68.5$\pm$9.63 years (women-44.12%, men-55.88%). The comparison group: patients with CHD without T2D, age–69.5$\pm$13.14 years (women–43.75%, men–56.25%).
Results
Patients of both groups were comparable in gender, age ($P>0.05$), laboratory data: cholesterol, TG, HDL, VLDL, AST, ALT, creatinine, total protein ($P>0.05$) in blood serum. The blood glucose level in patients of the main group was significantly higher compared to the comparison group (6.8 (5.5-8.5) vs 5.5 (5.2-6.0) mmol/l, $P=0.01$). HbA1c=7.7$\pm$1.73% in patients of the main group, the experience of T2D according to the anamnesis was 8.2$\pm$3.14 years. The HbA1c level in patients of the main group was 7.7$\pm$1.73, which indicates insufficient control of T2D. According the coronary angiography results, hemodynamically significant stenosis involving coronary arteries peripheral parts were identified in 43.7% of patients in the comparison group: in the left coronary artery, right coronary artery, anterior interventricular branch, circumflex branch, diagonal branch, obtuse edge branch. In 79.4% of patients in the main group the number of hemodynamically significant stenosis involving peripheral parts was identified in the left coronary artery, circumflex branch, diagonal branch, and obtuse margin branch, and right coronary artery, anterior and posterior interventricular branches. The results indicate a significant increasing of hemodynamically significant stenosis involving the peripheral parts of the coronary arteries in patients with CHD and T2D ($\chi2 = 6.4$, $P=0.012$). The higher prevalence and depth of the pathological process was recorded in patients with CHD and T2D.
Conclusions
The results of the study show an increasing prevalence of the coronary atherosclerosis confirmed by coronary angiography in patients with coronary heart disease and type 2 diabetes compared with patients with coronary heart disease without type 2 diabetes by 35.7%. More severe coronary atherosclerosis was identified in patients with coronary heart disease and type 2 diabetes, included hemodynamically significant stenosis involving predominantly peripheral parts of the coronary arteries, caused by the development of atherosclerotic plaques and arterial tortuosity, which is likely due to diabetic angiopathy against the background of chronic hyperglycemia.

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EP514

Incidence of new onset type 1 diabetes in children during the covid-19 global pandemic

Nataliia Kurmacheva[1], Michail Svinarev[2], Olga Gumeniuk[1] & Yuriy Chernenkov[1]
[1]Saratov State Medical University, Hospital Paediatrics, Saratov, Russian Federation; [2]Saratov State Medical University, Paediatrics, Saratov, Russian Federation

The COVID-19 pandemic has an impact on the incidence of type 1 diabetes. It is important to synthesize estimates of changes in incidence rates.
Aim
To compare the incidence rates of type 1 diabetes mellitus (T1DM) in children of Saratov region during and before the COVID-19 pandemic.
Patients and methods
This is a retrospective multicenter study involving new onset T1DM paediatric patients (0-17 y.o.) in Saratov region, during periods 1994-2023 years.
Results
Incidence of T1DM in children of Saratov from 1994 to 2019 it increased by 3 times (8 cases in 1994 and 24 cases in 2019 per 100,000 paediatric person). The type 1 diabetes incidence rate increased during the COVID-19 pandemic vs before the pandemic among children and adolescents (32 cases in 2020 and 28 cases in 2021 per 100,000 paediatric person). The incidence of new onset DM1 among children in the Saratov region remains high (26 cases in 2022 and 29 cases in 2023 per 100,000 paediatric person).
Conclusions
New onset T1DM increased during the pandemic. Further studies are required to evaluate the mechanism leading to this rise to guide intervention measures. It is important to further study the prevalence and features of the course of T1DM in children who have been ill COVID-19, compared with those who have not had coronavirus infection and vaccinated children.

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EP516

Micronutrients intake and cellular protection in type 2 diabetics

Hana Ben jemâa, Berriche Olfa, Rym Ben Othman, Ramla Mizouri, Ben Amor Nadia, Amel Gamoudi, Emna Talbi & Jamoussi Henda
National Institute of Nutrition, A

Introduction
Micronutrients play a crucial role in cellular protection against external aggressions, particularly combating oxidative stress and aging. The aim of our study was to

determine the association between micronutrient intake and cellular protection in diabetic patients.
Methods
A descriptive study was performed on 115 type 2 diabetics. Each patient underwent a dietary survey to assess micronutrient intake. We used the Functional Food Questionnaire (FFQ) related to cellular protection and validated by the European Institute of Dietetics and Micronutrition (IEDM) to classify the patient's dietary habits into favorable, less favorable, and unfavorable categories based on the obtained score.
Results
The median age of patients was 57.93 ± 7.48 years. The majority of included patients were female (67.8%) with a sex ratio (female/male) of 2.1. For vitamins, a deficiency in vitamin D intake was the most observed among our patients (51.4%). Regarding minerals, a magnesium intake deficiency was the most frequent and encountered in 52.2% of patients. Favorable, less favorable, and unfavorable dietary habits were observed in 22.6%; 38.3%; and 39.1% of the patients, respectively, using the FFQ. In our study, we found positive and significant associations between the FFQ score relative to cellular protection and intake of vitamin A ($P=0.033$), vitamin C ($P<0.001$), and manganese ($P=0.031$). In multivariate analysis favorable habits were associated with vitamin C intake ($P=0.002$).
Conclusion
A well-balanced diet rich in antioxidants, especially in vitamin C, vitamin A, and manganese, enables the body to combat oxidative stress. A deficiency in micronutrient intake may clinically manifest through various functional signs such as skin disorders and infectious issues, potentially altering the quality of life of patients.

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EP518

Charcot foot in diabetes: review of 35 cases

Hani Meriem[1], Imane el ghebir[1,2], Rehaimia Amina[1] & Ait Abderrahmane Samir[1]
[1]Algiers Province, Algeria; [2]

Background and aims
Charcot neuroarthropathy (CN) is a devastating and destructive disease of the bone structure and joints. Despite the fact that its description was published almost 130 years ago, its pathophysiology, risk factors, diagnosis, and treatment remain areas that need to be described. This study aims to describe patient characteristics and comorbidities as well as the clinical and morphological characteristics of these neuroarthropathies.
Material and methods
This is a retrospective and prospective study of 35 patients with neuro-arthropathy among patients hospitalized in our department between 2002 and 2022. Data for sex, age, diabetes type, duration, complications and treatement as well as the anatomical classification, stage of CN, diabetic foot ulcer, Hba1c were collected.
Results
35 patients aged 56 years on average, were included. Patients are mostly type 2 diabetics (79%), aged 56 on average, male (66%) and overweight (average BMI 27.57 kg/m^2). Diabetes is of long evolution (17 years on average) with poor glycemic control (average Hba1c at 9.39%), insulin-requiring (83%) and presents multiple micro and macrovascular complications (diabetic neuropathy 100%, diabetic retinopathy 83%). The majority of neuroarthropathies are chronic (79%), with acute cases (21%) being rarely diagnosed in time. An ulcer is revealing in nearly half of the cases (51%). Midfoot involvement is classically the most frequent: Type 2 (31%), Type 3 (17%). We observed a large number of simultaneous attacks on several areas. The radiological stages were as follows: Stage 0 (3%), Stage 1 (14%), Stage 2 (14%), Stage 3 (69%). MRI is performed in 41% of cases: grade 1 (4%), grade 3 (10%), grade 4 (17%), grade 5 (10%).
Conclusion
Charcot's foot constitutes a diagnostic and therapeutic challenge. Indeed, an early diagnosis makes it possible to avoid the installation of sometimes severe and disabling deformations.

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EP519

Can micronutrients intake really impact brain health ?

Berriche Olfa, Hana Ben jemâa, Rym Ben Othman, Amel Gamoudi, Emna Talbi & Jamoussi Henda
National institute of nutrition, A

Introduction
Micronutrients are involved in numerous physiological processes at the cellular level. They play an essential role in the synthesis of neurotransmitters, crucial for the brain's optimal functioning. The aim of our study was to determine the association between micronutrient intake and brain function in type 2 diabetic patients using a validated questionnaire.
Methods
A descriptive analysis was conducted on 115 type 2 diabetics. Each patient underwent a dietary assessment to evaluate their micronutrient's intake. The Dopamine Norepinephrine Serotonin questionnaire (DNS) is used to assess the impact of diet on brain function. The DNS is validated by the European Institute of Dietetics and Micronutrition (IEDM) and it classify individuals into 4 groups: low score, moderate score, high score, and very high score based on the functional disorders presented by the patients.
Results
The median age of patients was 57,93 ± 7,48 years. The majority of included patients were obese (53.4%). For the DNS score related to dopamine, moderate, high, and very high scores were noted in 30.4%, 19%, and 18.8% of patients, respectively. Regarding norepinephrine, a high score was most observed among patients (36.5%). Low, moderate, and very high scores were noted in 25.2%, 35.7% and 2.6% of patients, respectively. As for serotonin, patients predominantly had a low score (44.3%). Moderate, high, and very high scores were noted in 36.5%, 15.7% and 3.5% of patients, respectively. Negative and significant associations were found between dopamine score and intake of vitamin B9 ($P=0.002$), magnesium ($P=0.003$), and copper ($P=0.007$). Negative and significant associations were found between Noradrenaline score and intake of vitamin C ($P=0.046$), vitamin B6 ($P<0.001$), magnesium ($P=0.024$), and zinc ($P=0.009$). Negative and significant associations were found between Serotonin score and intake of vitamin B12 ($P=0.001$), magnesium ($P=0.027$), and zinc ($P=0.047$).
Conclusion
As cofactors in neurotransmitter synthesis, Micronutrients influence not only the brain but the entire body functioning. In fact, nourishing the cellular city with a balanced diet help patients particularly type 2 diabetics having optimal brain functioning and long-term prosperity.

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EP521

Benefits of Moringa oleifera on metabolic parameters in type 2 diabetics

Khouloud Boujelbene, Maryam Cheikhrouhou, Fatma Mnif, Dhouha Ben Salah, Mouna Elleuch, Mouna Mnif, Nadia Charfi, Faten Hadj Kacem, Mohamed Abid & Nabila Rekik
Hedi Chaker Sfax, Endocrinology Department, Tunisia

Introduction
Moringa is a common tropical tree in Africa that has become a subject of interest for scientists due to its interesting composition and nutritional qualities. The objective of this study was to evaluate the effects of Moringa oleifera powder on metabolic parameters in diabetic patients in the short term.
Method
We conducted a randomized controlled study with ten type 2 diabetic patients treated with oral antidiabetic medications. Each patient received 5 g of Moringa powder per day for 15 days, followed by 8 g per day for the next 15 days. Glycemic and lipid profiles were assessed before the protocol, on day 15, and on day 30.
Results
There was a female predominance (80%) in the study. Hypertension was found in 80% of patients, and obesity was present in 20% of patients. Before the protocol, the average fasting blood glucose was 8.61 ± 3.51 mmol/l, and the average HbA1C was 7.93 ± 3.67%. After 30 days of Moringa powder consumption, a decrease of 18.73% in fasting blood glucose was observed. Regarding HbA1C, no significant change was noted after 30 days. Analysis of the lipid profile showed a decrease of 13.05% in total cholesterol and a decrease of 19.62% in triglyceride levels after 30 days of Moringa powder consumption.
Conclusion
While further research is needed to confirm these observations, these results suggest that Moringa oleifera could be considered as a potential dietary supplement to improve metabolic parameters in individuals with type 2 diabetes.

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EP523

Diabetics Retinopathy Knowledge and Awareness Assessment among Tunisian patients with Type 2 Diabetes

Mouna Elleuch, Hamdi Frikha, Dhoha Ben Salah, Khouloud Boujelben, Faten Haj Kacem Akid, Fatma Mnif, Nadia Charfi, Mouna Mnif, Mohamed Abid & Nabila Rekik Majdoub
Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Diabetic retinopathy (DR) is the most common cause of acquired blindness. Patient information about its course and prognosis is key to insure therapeutic adherence and reduce the risk of blindness. The aim of this study is to assess Tunisian patients' level of knowledge about DR and to correlate it with DR severity.
Methods
We conducted a cross-sectional descriptive and analytical study of diabetic patients with DR followed at outpatient unit of the endocrinology department of Hedi Chaker University of Sfax, Tunisia. Patients' knowledge about DR was assessed using a open-end survey in Arabic language.
Results
We enrolled 41 T2DM patients in the study. Mean age was 49 years. Patients were predominantly male. Funduscopic examination showed that 76% of patients had pre-proliferative DR while 24% had proliferative DR. We found that 51% of patients were unaware of the risk of DR. The majority of patients (69%) were unable to specify the types of ocular damage related to diabetes. Preventive measures were poorly understood and executed: In fact 84% of patients could not enumerate any effective method to delay the onset of DR and 78% have never undergone a specialized ophthalmological assessment of retina throughout the course of the disease. We found that a lesser survey global score was associated with more severe DR phenotype (OR = 3.2; $P = 0.04$).
Conclusion
DR is emerging as an important cause of visual impairment. Proactive participation of patient is key to insure better management outcomes. Our results showed poor global level of knowledge among Tunisian patients, in contrast with results by Almalki *et al*. (2018). Adequate therapeutic education about DR has been linked to better outcomes in a study by Assem *et al*. (2020). These results should prompt practitioners to develop therapeutic education programs regarding DR.

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EP524

Knowledge of diabetes mellitus during Ramadan fasting among Tunisian patients with diabetes mellitus

Khouloud Boujelben, Dhoha Ben Salah, Feriel Touzi, Elleuch Mouna, Mouna Mnif, Fatma Mnif, Faten Hadj Kacem, Charfi Nadia, Abid Mohamed & Rekik Nabila
Hedi Chaker Hospital, endocrinology department, Sfax, Tunisia

Introduction
For individuals adhering to the Islamic faith, the observance of Ramadan fasting introduces a multitude of challenges, particularly regarding patients' non-adherence to mitigating increased risks of glycemic imbalance and associated complications. This study aimed to assess the depth of knowledge among Tunisian Muslim patients diagnosed with diabetes mellitus (DM) regarding their self-management practices while fasting during the holy month of Ramadan.
Patients and Methods
A cross-sectional and descriptive study was conducted, involving 70 patients diagnosed with diabetes mellitus, at the Endocrinology Department of Hedi Chaker Hospital in Sfax, Tunisia. The study was conducted from March 15 to the end of April 2021, targeting adult individuals with diabetes mellitus who observed fasting for at least 15 days per month. Data were collected through a questionnaire in French, comprising 76 questions, translated into Arabic, and aligned with the Tunisian consensus on the management of diabetes during Ramadan.
Results
Seventy patients were enrolled, with an average age of 55 years and a female predominance, resulting in a sex ratio (M/F) of 0.3. Eighty-six percent of patients were diagnosed with type 2 diabetes, and 41% were prescribed oral antidiabetics, predominantly metformin, used as a monotherapy in 62% of cases. The mean HbA1c was recorded at 10%. Diabetic risk stratification revealed that 22.8% of patients were classified as high risk. More than half (56%) of patients demonstrated awareness that hypoglycemia poses a significant risk, especially for younger individuals. Nineteen (27%) patients could accurately identify high-risk treatment scenarios. Sixty-four percent of respondents were aware that the pre-dawn meal (suhoor) should be consumed as late as possible. Relating to clinical practices, fifty-five (79%) patients underwent a pre-Ramadan consultation. The medical practitioner advised against fasting in 36 patients. Moreover, thirty patients (43%) were equipped with a glycemic monitoring device. Hypoglycemic events were reported in 25 (36%) patients. However, forty-seven (67%) individuals did not alter their prescribed medication regimen. A notable 33% of patients skipped the pre-dawn meal. Additionally, 53 patients (76%) refrained from engaging in regular physical activity.
Conclusions
This study underscores the importance of providing clear and practical guidance on dietary choices, glycemic control, physical exercise, and potential therapeutic adjustments for individuals with diabetes observing fasting during Ramadan.

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EP527

Diabetic retinopathy: Is neuropathy part of its etiopathogenesis?

Youssef Gharbi, Bchir Najla, Salma Salhi, Annam Benchhida, Dorra Dorraelguiche, Zouaoui Chadia & Haroun Ouertani
Military Hospital of Tunis, Endocrinology, Tunis, Tunisia

Introduction
Diabetic retinopathy (DR) is the leading cause of blindness before the age of 50. The etiopathogenesis of DR is still controversial. Even if the microvascular damage is undeniable, the place and importance of the nerve damage must be defined. Our objective was to evaluate the association between DR and diabetic neuropathy (DN) in type 2 diabetics.
Methods
It was a cross-sectional, comparative study that included 100 type 2 diabetic patients divided equally into two groups according to the presence or absence of DR, matched according to age, gender and duration of diabetes. We detected neuropathic damage using the DN4 score. We also evaluated the deep tendon reflexes and looked for signs of autonomic neuropathy such as gastroparesis, intractable constipation, and erectile dysfunction.
Results
The average age of our population was 62.01 ± 9.37 years and the sex ratio (Men/Women) was 1.08. DR had a mean duration of progression of 3.84 ± 2.63 years. 39% of the total population had diabetic neuropathy distributed as follows: 71% peripheral neuropathy, 11% autonomic neuropathy, 18% peripheral and autonomic neuropathy. DN was 4.57 times more present in the group with DR than in the group without DR (64% vs 14%) and DR was significantly associated with DN ($P < 0.001$). Multivariate analysis confirmed this association ($P < 0.001$, OR = 9.6).
Conclusion
Our study showed a strong association between DN and DR. These results support the involvement of ophthalmic nerve damage to a greater extent than our prerequisites, giving rise to a promising field of investigation (with extensive ophthalmic and neurological imaging).

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EP529

Association of type 1 diabetes and autoimmune diseases

Fatima Zahra Zerrouki[1], Fatimzahra Bentebbaa[1], Magouri Oumaima[1], Siham Rouf[2] & Hanane Latrech[2]
[1]Department of Endocrinology-Diabetology and Nutrition CHU Mohammed-VI Oujda, Oujda, Morocco; [2]Department of Endocrinology-Diabetology and Nutrition CHU Mohammed-VI Oujda, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy Oujda, Mohammed Premier University Oujda, Morocco, Oujda, Morocco

Introduction
Type 1 diabetes (T1DM) is an autoimmune disease that accounts for over 90% of diabetes in children and adolescents. It may be associated to other autoimmune diseases, especially thyoiditis, celiac and Addison's diseases. These associations may represent a challenge for management of this disease for the child and his family. The aim of this study is to describe the different aspects of this association.
Patients and Methods
This is a retrospective descriptive study including 428 type 1 diabetic patients hospitalized at the Endocrinology Diabetology and Nutrition Department of the university hospital Mohammed VI of Oujda, between 2016 and 2023. All our

patients had a complete clinical examination and a biological workup including the autoimmune workup.
Results
The mean age of our patients was 20±10.7 years, ranging from 2 to 78 years, women was predominant (sex ratio 0.8), the mean duration of diabetes was 12±8 years, and the mean glycated hemoglobin was 10.3%. Of all patients, 59 had autoimmune disease (14% of cases), with a higher incidence in women (70% of cases). 8 of these patients had familial autoimmune disease (13% of cases) Autoimmune thyoiditis was present in 63% of cases. 21 patients had hypothyroidism (36% of cases) including 12 patients with positive anti-TPO antibodies, and 16 cases of hyperthyroidism (27% of cases), including 11 with Graves' disease. Celiac disease was revealed by positive anti-transglutaminase antibodies in 16 patients (27% of cases). Addison's disease was present in 2 patients (3.3% of cases) same percentage for ovarian insufficiency and psoriasis.
Conclusion
Our results confirm the frequent association of type 1 diabetes with autoimmune diseases, mainly dysthyroidism, as well as celiac disease, this result confirm the importance of screening according to recommendations to ensure optimal and comprehensive management.
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EP532

Anxiodepressive disorders in Type 1 Diabetics
Deus Niyongabo, Nassim Essabah Haraj, Siham El aziz & Asma Chadli
Ibn Rochd University Hospital of Casablanca, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca

Introduction
Individuals with type 1 diabetes have an increased risk of depression, which can worsen their health condition and elevate the risk of complications. This study aims to estimate the prevalence of anxiety and depression in these patients and evaluate their impact on disease management.
Patients and Methods
A retrospective study over six years (2018-2023), including 168 hospitalized type 1 diabetic patients, assessed for their mental state using the Hamilton and Beck scores. Statistical analysis was performed using Epi-Info 7.2 software.
Results
The mean age of the patients was 26 years, with a sex ratio of 1.3 males to 1 female. The prevalence of toxic habits was 39.2%. The average diabetes duration was 8.5 years, and glycemic imbalance was observed in 88.6% of patients. Degenerative complications (retinopathy, nephropathy, neuropathy) were present in a quarter to a third of patients. Acute complications (ketosis, acidosis, frequent hypoglycemia) were very common, affecting 89.8%, 32.1%, and 82.1% of patients, respectively. Depression and anxiety were present in 20.2% and 61.3% of patients, respectively, with co-occurrence observed in 18.4%. Diabetes and anxiodepressive disorder follow-up were irregular in 78.3% of cases. Treatment mainly included supportive psychotherapy, as well as anxiolytics and antipsychotics as needed.
Conclusion
Detecting anxiodepressive disorders in the management of type 1 diabetic patients is of paramount importance. Appropriate psychological intervention could promote better glycemic control and more effective disease management.
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EP533

Metabolic syndrome in type 1 diabetes: About 638 cases
Imane Hasbi[1], Nassim Essabah Haraj[2], Siham El Aziz[3] & Asma Chadli[2]
[4]Ibn Rochd University Hospital, Endocrinology and Metabolic Diseases, casablanca, Morocco; [2]Ibn Rochd University Hospital, Endocrinology and Metabolic Diseases, Casablanca, Morocco; [3]Endocrinology and Metabolic Diseases, Endocrinology and Metabolic Diseases, Casablanca, Morocco

Introduction
The increasing association between metabolic syndrome and type 1 diabetes, along with its impact on micro and macrovascular complications, is becoming more evident. The aim of our study was to assess the prevalence of different components of metabolic syndrome in type 1 diabetic patients and identify any possible correlation with various complications related to type 1 diabetes
Materials and Methods
This is a descriptive retrospective study involving 638 patients with type 1 diabetes, hospitalized at the endocrinology department of Ibn Rochd University Hospital in Casablanca. All patients underwent a clinical examination, including anthropometric measurements for calculating body mass index (BMI) and waist circumference (WC). A metabolic assessment was also conducted. Metabolic syndrome was defined according to the criteria of the International Diabetes Federation (IDF). The statistical analysis was performed using the SPSS software, version 25.
Results
The mean age was 25.7 years with a gender ratio (M/F) of 1.1, the mean duration of diabetes was 9.5±2 years. Metabolic syndrome (MS) was identified in 15.8% of patients. Analysis of patients with MS revealed an average age of 31.3 years, ranging from 15 to 60 years, an average BMI of 27.4/m2, and an average WC of 91 cm. Most participants exhibited evident glycemic imbalance, reflected by an average HbA1c level of 12.2%. Arterial hypertension was observed in 61.4% of cases. The mean levels of total cholesterol, HDL cholesterol, and triglycerides were 1.78 g/l, 0.44 g/l (with hypo-HDLemia in 68.5% of cases), and 1.48 g/l (with hypertriglyceridemia in 33.7% of cases), respectively. Participants with MS were older (31.3 vs 24.9 years, $P=0.01$) and predominantly female (75.2% vs 41.3%, $P=0.001$), had longer diabetes duration (15.3 vs 8.6 years, $P=0.001$), and a higher prevalence of microangiopathy (66.3% vs 23.9%, $P=0.001$), although no significant difference was observed for macroangiopathy. Therapeutically, patients with MS had a higher average insulin dose ($P=0.001$), and the use of an insulin sensitizer was necessary in 18.8% of cases
Discussion and Conclusion
The prevalence of metabolic syndrome in type 1 diabetes is increasing. Its presence indicates an increased risk of micro and macrovascular complications. This subgroup of type 1 diabetes requires optimal glycemic control and a reduction in other risk factors.
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EP534

Necrotizing fasciitis of the upper extremity complicated by ulnar vein thrombophlebitis revealing diabetes: A case report
Ilham Midhat, Hanane Boualam, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Centre Hospitalo-Universitaire Mohammed VI Marrakech, Marrakech, Morocco

Introduction
Necrotizingfasciitis is a severe infection of deep subcutaneous tissue and hypodermal fascia with secondary skin necrosis.
Observation
Patient M.A., aged 67, with no particular pathological history, presented with an 11-day history of a boil on the left forearm, treated with traditional herbs. The evolution was marked by the development of an inflammatory placard on the forearm with extensive necrotic lesions. Ultrasound revealed extensive infiltration of the soft tissue, organized into micro and macro logettes. Biological findings included a predominantly neutrophilic hyperleukocytosis, CRP 406 mg/l, and bacteriological sampling of the pus isolated multi-sensitive Pseudomonas aeruginosa. With the onset of edema and insomniac pain, the investigation was completed by a venous echodoppler of the left upper limb, which revealed thrombophlebitis of the ulnar vein. The patient underwent necrosectomy. Treatment consisted of curative anticoagulation, intensified insulin therapy and strict glycemic control. Triple intravenous probabilistic antibiotic therapy was instituted, then adapted to the antibiogram. The evolution was favorable, with a good clinico-biological improvement and good directed healing.
Discussion and conclusion
Necrotizing fasciitis of the upper limbs remains a relatively rare infection. It can occur at any age, although advanced age is considered a risk factor. Necrotizing fasciitis is a major medical and surgical emergency, and the rapidity of its evolution makes it essential to establish the diagnosis as soon as possible, in order to reduce the risk of mortality and disabling functional sequelae. Clinically, differentiating a necrotizing infection from a common soft-tissue infection is difficult when cutaneous necrosis does not dominate the clinical presentation. The germs responsible are varied (frequently streptococci, multi-microbial flora in over half of cases). It requires early, intensive management based on three pillars (early surgical excision, broad-spectrum antibiotic therapy and resuscitation) in parallel with strict glycemic control. The prognosis is clouded by the severity of lesions and delays in treatment. Prevention must be encouraged through effective patient education, with targets to be set consistently.
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EP536

Epidemiology of type 2 diabetes and prediabetes in the adult population of the Republic of Moldova

Lorina Vudu[1], Aristia Seremet[1], Vlada Furdui[2], Stela Bacinschi-Gheorghita[1], Diana Munteanu[1], Carolina Piterschi[1] & Stela Vudu[1]
[1]Nicolae Testemitanu State University of Medicine and Pharmacy, Endocrinology, Chisinau, Moldova; [2]Nicolae Testemitanu State University of Medicine and Pharmacy

Background and Aim
Diabetes mellitus (DM) represents a substantial burden on health care systems, being the 8th leading cause of death and disability in the world in 2019, associated with long-term microvascular (neuropathy, retinopathy, and nephropathy) and macrovascular (ischemic heart disease, stroke, peripheral vascular disease) complications. DM comorbidities lead to a substantial decrease in quality of life, as well as important socio-economic consequences. In 2022, the health system in the Republic of Moldova (RM) had records of 131,550 people with DM. Data on the prevalence and incidence of DM and prediabetes are limited due to the lack of studies in this direction. The aim of the study was to assess the prevalence of diabetes, prediabetes and obesity in the adult population of RM.
Methods
This is the first cross-sectional, epidemiological study that analyzes the prevalence of DM, prediabetes, and dyslipidemia in the population of RM. The diagnosis of DM was established based on the diagnostic criteria of the American Diabetes Association: HbA1c $\geq$ 6.5%, fasting glucose (FG) $\geq$ 7 mmol/l, blood glucose 2h after the oral glucose tolerance test (OGTT) $\geq$ 11.1 mmol/l or the presence of diabetes history - reported by the patient. The diagnostic criteria for prediabetes were: HbA1c value between 5.7 and 6.4 %, FG – 5.6 – 6.9 mmol/l, blood glucose 2 hours after OGTT 7.8 – 11 mmol/l. Statistical analysis used Spearman's correlation test, chi-square, and Wilcoxon tests.
Results
A total of 1039 persons were enrolled (66.4% women and 33.6% men, with an average age of 49 $\pm$ 13 years). 10,8 % of the investigated persons were with diabetes mellitus, 1.9 % of whom had unknown DM. 51 % of persons with DM were men; 71 % of whom – with a BMI $\geq$ 25 kg/m^2; 93 % - with abdominal obesity. 69 % of women with DM were with BMI $\geq$ 25 kg/m^2 and 94 % - with abdominal obesity. Prediabetes was diagnosed in 29.6% of the investigated persons, with a prevalence of 48 % in men vs 52 % in women. Advanced age, obesity, and dyslipidemia were the diabetes influencing factors.
Conclusion
The study showed an increased prevalence of carbohydrate metabolism disorders, including prediabetes, as well as a high prevalence of abdominal obesity. Persons with unknown diabetes mellitus have been identified.

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EP537

Assessment of oxidative stress levels in gestational diabetes mellitus (GDM) patients: a cross-sectional study

Justyna Hryniewicka[1], Angelika Buczyńska[2], Katarzyna Siewko[1], Popławska-Kita Anna[1], Agnieszka Adamska[1], Adam Krętowski[1] & Małgorzata Szelachowska[1]
[1]Medical University of Bialystok, Department of Endocrinology, Diabetology and Internal Medicine, Bialystok, Poland; [2]Medical University of Bialystok, Clinical Research Centre, Bialystok, Poland

Background
Gestational Diabetes Mellitus (GDM) is a common pregnancy-related metabolic disorder associated with increased maternal and fetal complications. Oxidative stress has been implicated in the pathogenesis of various pregnancy-related disorders, including GDM. This cross-sectional study aims to evaluate and compare oxidative stress levels among GDM patients, shedding light on potential implications for maternal and fetal health.
Methods
A total of 47 pregnant women, comprising 27 GDM patients and 20 normoglycemic pregnant controls, were enrolled in this study. Oxidative stress levels were assessed using reliable biomarkers and assays, including photometric test system for the determination of the total antioxidative status/capacity (TAS/TAC) and for the determination of the total oxidative status/capacity (TOS/TOC). Demographic and clinical data, including age, gestational age, and relevant medical history, were collected and analyzed. GDM and the control group were matched to ensure no differences in age, weight, and BMI.
Results
The study revealed a statistically significant difference in oxidative stress levels between GDM patients and normoglycemic pregnant controls. GDM patients exhibited higher levels of oxidative stress markers during whole pregnancy and also 3 month postparum in comparison to control group. Significantly higher levels of oxidative stress markers was observed in first trimester of pregnancy, before GDM diagnosis, comprehensively suggesting an increased burden of oxidative damage. According to ANOVA results we hypothesize that TOS/TAS may be a potential future marker of GDM. Further subgroup analyses explored potential correlations between oxidative stress levels and key clinical parameters within the GDM group.
Conclusion
This cross-sectional study provides valuable insights into the heightened oxidative stress observed in GDM patients compared to normoglycemic pregnant individuals. Understanding the role of oxidative stress in GDM pathophysiology may contribute to the development of targeted therapeutic interventions aimed at mitigating maternal and fetal complications associated with GDM. Future longitudinal studies are warranted to explore the temporal dynamics of oxidative stress throughout the course of GDM and its impact on pregnancy outcomes.

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EP542

Effect of chemotherapy on glucose metabolism in breast cancer patients

Simone Diedrichsen Marstrand[1], Djordje Marina[1], Valdemar Mendez[1], Michael Andersson[2], Kristian Buch-Larsen[1] & Peter Schwarz[1]
[1]Rigshospitalet, Department of Endocrinology, København, Denmark; [2]Rigshospitalet, Department of Oncology, København, Denmark

Background
Observational studies indicate that breast cancer survivors more often are diagnosed with type 2 diabetes mellitus (T2DM) up to several years after treatment completion. As the population of breast cancer survivors increase due to improved diagnostic and treatment methods the importance of understanding possible long-term side effects of the treatment such as T2DM becomes more central. It is reported that women receiving adjuvant chemotherapy experience weight gain and altered body composition with loss of muscle mass and increasing fat mass. Furthermore, studies have shown elevated fasting insulin levels in breast cancer patients before and after treatment. Obesity can lead to insulin resistance and thereby a risk of developing T2DM. It is relevant to consider if changes in glucose and insulin metabolism are seen in relation to breast cancer treatment to further explore the risk of T2DM.
Aim
to examine if adjuvant chemotherapy negatively affects glucose metabolism, outlined by changes in glucose and HbA1c.
Method
Women with early breast cancer stages I-III eligible for chemotherapy were prospectively recruited by Department of Oncology at Rigshospitalet, Denmark. Exclusion criteria were prior malignancy or endocrine disease. Blood samples were drawn immediately before initiation of chemotherapy and after completed chemotherapy. Furthermore, in a subgroup of women an oral glucose tolerance test (OGTT) was performed after completed chemotherapy. Patients drank a concentrated glucose solution and blood samples were drawn at times 0 min, 30 min, 45 min, 60 min, 90 min, and 120 min.
Results
103 women with early breast cancer were include in the study. 79 patients completed examinations before and after chemotherapy. All women underwent breast surgery and chemotherapy regimens including at least one of the following drugs docetaxel, paclitaxel, epirubicin, and cyclophosphamide. High-dose prednisolone was given as antiemetics. Statistical analysis showed no significant difference in HbA1c before and after chemotherapy with mean values 37.1 mmol/mol and 36.7 mmol/mol respectively and $P = 0.28$. The OGTT was performed in 11 of the breast cancer patients after completed chemotherapy. Furthermore, 7 healthy controls completed an OGTT. Glucose levels at 120 min did not significantly differ between patients and controls with $P = 0.44$ and mean glucose for patients 6.9 mmol/l and controls 6.2 mmol/l.
Conclusion
HbA1c is not significantly altered by chemotherapy in early breast cancer patients. In addition, we find no significant difference in response to a glucose load between a subgroup of patients and controls.

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EP561

Effects of vitamin D on the heart failure with preserved ejection fraction in women with prediabetes

Lileia Petrovska[1], Iryna Kostitska[1] & Anna Hryb[2]
[1]Ivano-Frankivsk National Medical University, Endocrinology, Ivano-Frankivsk, Ukraine; [2]Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine

Introduction
Heart Failure with Preserved Ejection Fraction (HFpEF) morbidity and mortality are increasing at an alarming rate in patients with prediabetes, insulin resistance and obesity. Vitamin D deficiency is associated with the risk of impaired glucose and lipid metabolism. All this substantiates the need to monitor the concentration vitamin D in women with this comorbid pathology.
Aim of the study
is to investigate the severity of vitamin D deficiency in females with prediabetes and HFpEF.
Materials and methods
Participants were comprehensively phenotyped including physical examination, laboratory results and echocardiography (left ventricular ejection fraction (LVEF) $>50\%$). Main group included 30 women with prediabetes and HFpEF (initially mean aged 49.54 $\pm$1.63 years, body mass index (BMI) - 35.24$\pm$2.21 kg/m^2, glycated hemoglobin (HbA_1C) - 6.05$\pm$0.13% and duration of prediabetes - 3.22$\pm$2.19 years, N-terminal pro-brain natriuretic peptide (NT-proBNP) - 161.51$\pm$7.27 pg/ml, left ventricle (LV) mass index 112$\pm$24, LVEF – 59.43$\pm$7.39%) were divided into groups: I group (Gr I, $n=15$) females with insufficiency of 25-hydroxycholecalciferol (25(OH)D - 20-30 ng/ml) and II group (Gr II, $n=15$) subjects with hypovitaminosis D (25(OH)D below 20 ng/ml. The patients were treated metformin XR (daily dose - 500-1500 mg) combination cholecalciferol (vitamin D3) (daily dose Gr I – 5000 IU and Gr II– 20 000 IU) during 3 months. The physical examination and all laboratory, instrumental results were measured at baseline and 3 months following the treatment. Results were analyzed with IBM SPSS Statistics. Significance level $P<0.05$ was considered.
Results
The mean of 3 months after add metformin XR and vitamin D3 on BMI and HbA_1C level was lowered by 0.77% and 0.81% each in two groups. On comparing with the baseline the mean deference of 25(OH)D after combination therapy were increase mean 52.5% in Gr I and 63.8% in Gr II. After adjustment, higher serum levels 25(OH)D were associated with decreased hazard for NT-proBNP (102.11$\pm$3.14 pg/ml) and LV mass index overall (101$\pm$ 22) driven by a significant association with HFpEF (increase mean LVEF (71.32$\pm$8.89%) for 1.2 time).
Conclusions
Particularly the association between vitamin D deficiency and comorbid diseses: prediabetes, obesity in women with HFpEF. During the war in Ukraine, there is a probable deepening hypovitaminosis D. Increased NT-proBNP, HbA_1C, BMI and LV mass index were associated with vitamin D deficiency. The insufficiency and deficiency vitamin D negatively influenced ejection fraction in females with prediabetes.

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EP562

The use of subcutaneous instead of intravenous insulin in a hypothyroid and diabetic patient with hypertriglyceridemia-induced pancreatitis - a case report

Kurt Bryan Tolentino[1], Abigail Kristine Juat[2], Trisha Gia Mae Viernes[2] & Monica Therese Cating-Cabral[2]
[1]St. Luke's Medical Center - Global City, Endocrinology, Taguig, Philippines; [2]St. Luke's Medical Center - Global City, Taguig, Philippines

Hypertriglyceridemia is a rare cause of acute pancreatitis occurring 1-35% of patients. Management of hypertriglyceridemia includes the use of intravenous insulin, however, requires close monitoring of capillary blood glucose every 1-2 hours and might warrant ICU admission, increasing the financial burden of patients. This case report explores the use of subcutaneous long-acting insulin, instead of intravenous insulin, on top of conventional therapy and Levothyroxine supplementation in a 47 year-old hypothyroid and diabetic female newly-diagnosed with severe hypertriglyceridemia. The patient initially came in for a 2-day history of new onset epigastric pain radiating to the back, aggravated by eating. Due to persistence, sought consult in the emergency room. Vital signs were stable. Workup done showed microcytic hypochromic anemia, leukocytosis with neutrophilic predominance (Hemoglobin 10.1 g/dl, Hematocrit 28.3%, WBC 11840 mm^3, 84% neutrophils, 10% leukocytes, Platelets 266,000 mm^3, MCV 58 fL, MCHC 36%), elevated CRP 48 mg/l, elevated ESR 24 mm/hr, elevated TSH 32.556 uIU/ml, low FT4 and FT3 of 0.76 ng/dl and 1.14 pg/ml respectively, normal transaminases (ALT 11 U/l, AST 12 U/l), normal bilirubin (total 0.2 mg/dl, direct 0.02 mg/dl, indirect 0.18 mg/dl), normal alkaline phosphatase (82 U/l), albumin (3.5 g/dl), elevated HbA1c 9.5%, normal ionized calcium (1.11 mmol/l), creatinine 0.74 mg/dl, BUN 6 mg/dl, potassium 3.6mEq/l, chloride (99 mEq/l), low sodium (131.4mEq/l), bicarbonate (19.9 mEq/l). Lipase was 4.1x elevated (222 U/l). Triglycerides and VLDL were elevated at 5177 mg/dl and 1035.4 mg/dl respectively. Capillary blood glucose was 237. ABG done showed a pH 7.42, pCO2 33, HCO3 21.4 O2 sat 96%, and a lactate of 1. BISAP score was 0. She was initially hydrated with 125 ml/hr of D5NSS, given Hyoscine N-Butylbromide for pain control, and placed on NPO. Since the patient had limited funds, the use of subcutaneous long acting insulin of approximately 0.2units/kg/day was given (15 units Glargine). The gastroenterologist also cleared the patient to be started on Levothyroxine 100 mg once daily (~1.76 mg/kg/d) and Fenofibrate 160 mg once daily. Serial monitoring of triglycerides was done noting a decreased trend of 1634 mg/dl on the 2nd day, 989 mg/dl on the 3st day, and 651 mg/dl on the 5th day. VLDL was also decreasing to 326.8 mg/dl on the 2nd day, 197.8 mg/dl on the 3st day, and 130.2 mg/dl on the 5th day. The patient was sent home well. Severe hypertriglyceridemia should still be considered in all patients with acute pancreatitis. Subcutaneous instead of intravenous insulin can be considered as a treatment modality in patients with hypertriglyceridemia-induced pancreatitis on top of conventional therapy.

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EP563

Prevalence of metabolic and cardiovascular diseases in Hidradenitis Suppurativa

Malek Cherif[1], Rim Chaabouni[1], Lina Bessaâd[1], Abdel Mouhaymen Missaoui[2], Fatma Hammami[1], Emna Bahloul[1], Nabila Rekik[2] & Hamida Turki[1]
[1]Hedi Chaker University Hospital, Dermatology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Endocrinology, Sfax, Tunisia

Introduction & Objective
Hidradenitis Suppurativa (HS), or Verneuil's disease, is a chronic suppurative inflammatory condition. This study aims to determinate the association between HS and metabolic diseases.
Materials and Methods
We conducted a retrospective study between January 2012 and December 2022 enrolling all cases of HS in our dermatology department.
Results
Over 11 years, we collected 77 cases. The average age was 39 years, with a sex ratio M/F of 4.1. Regarding lifestyle habits, 74% of patients were sedentary, and 66,2% were active smokers. The average Body Mass Index (BMI) was 26.38$\pm$4,44 [15-38.4]. Overweight and obesity were observed in 32.5% and 20.8% of patients, respectively. In our sample, 10 patients (13%) had previously diagnosed diabetes mellitus (DM), and 5 others (6.5%) were newly identified with prediabetes (fasting blood glucose between 1.1 and 1.25 g/l). Furthermore, six patients had a history of dyslipidemia (7.8%). The lipid profile indicated elevated triglyceride levels (above 1.50 g/l) in 8 cases (10.4%), elevated total cholesterol levels (above 2 g/l) in 4 cases (5.2%), and low HDL-cholesterol levels (below 0.4 g/l) in one case. Finally, 4 patients were diagnosed with hypertension (HT) (5.2%), and only one exhibited coronary insufficiency, undergoing revascularization (1.3%).
Conclusions
The significant prevalence of obesity and overweight in our HS series aligns with existing literature suggesting an association between these two conditions. Indeed, adipose tissue can release pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6, which are implicated in the pathophysiology of the dermatosis. For this reason, weight reduction is an essential non-pharmacological therapeutic approach in the management of HS. A literature review conducted in 2021 revealed that the prevalence of DM among HS patients is estimated to be between 7,1% and 20,8%. Similarly, the risk of dyslipidemia, hypertriglyceridemia, and low HDL levels is 1,4 to 4 times higher in the HS population compared to the control group. In addition, obesity and tobacco use are risk factors for HT and major adverse cardiovascular events (MACE). According to a literature review, patients with HS have a significantly higher prevalence of HT with adjusted odds ratios ranging from 1,2 to 2,1. In a cohort study, the adjusted incident risk of MACE among patients with HS is 1,5 times that of control individuals. In summary, metabolic and cardiovascular diseases constitute a cluster of comorbidities associated with HS, contributing to an increase in morbidity and mortality related to this chronic dermatosis.

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EP570

Assessment of left ventricular systolic function in obesity

Cvetanka Volkanovska Ilijevska[1], Valentina Andova[2], valentina Velkoska Nakova[3], Marija Zivkovic Hristova[1] & Ljubica Georgievska Ismail[4]
[1]University Clinic of Endocrinology, diabetes and metabolic disorders, Medical Faculty, Ss. Cyril and Methodius University in Skopje, RN Macedonia, Skopje, Macedonia; [2]University Clinic of Cardiology, Medical Faculty, Ss. Cyril and Methodius University in Skopje, RN Macedonia, Skopje, Macedonia; [3]Faculty of Medical Sciences, Goce Delcev University, Internal medicine, stip, Macedonia; [4]University Clinic of Cardiology, Medical Faculty, Ss. Cyril and Methodius University in Skopje, RN Macedonia, skopje

Aims
Identifying the left ventricular systolic disfunction in obesity is crucial, due to its ability to predict cardiovascular morbidity. LV systolic function is traditionally assessed with the volumetric parameter LV ejection fraction (LVEF). However, normal values for LVEF in all categories of obesity are published in the literature. Furthermore, guidelines for the biomarkers of heart failure, NT-proBNP and BNP, in the obese population remain unclear. Given the restricted BNP and LVEF use, there is a need to use parameters with proven predictability for the occurrence of heart failure in obesity. This research aimed to explore left ventricular systolic function in obese and overweight subjects.
Methods
A total of 126 subjects aged 45,0 ± 9,6 years, were categorized in 4 groups: Group 1 – overweight (BMI 25-29.9 kg/m^2); Group 2 – class I obesity (BMI 30-34.9 kg/m^2); group 3-class II obesity (BMI 35–39.9 kg/m^2) and group 4-class III obesity (BMI $>$ 40 kg/m^2). The conventional functional parameters of the LV and myocardial deformation by 2D speckel tracking echocardiography were assessed.
Results
In 74 % of the subjects the duration of overweight/obesity was over 10 years. Arterial hypertension, dyslipidemia and diabetes mellitus were present in 54.8%, 53.2%, 19.8% of subjects respectively. The echocardiographic indices of systolic function were preserved: LVEF (67.2% ± 7.4), indexed cardiac output (37.5 ± 10.3 ml/m2) and indexed minute volume (3.1 ± 2.4 l/min/m2). An average value of the peak mitral annular descend velocity, estimated by Tissue Doppler (s'TDI), was reduced (7.5 ± 1.5 cm/s). The highest classes of obesity had insignificantly lowest values. The mean values of global longitudinal strain (GLS) and global radial strain (GRS) were within reference and mean value of global circumferential strain (GCS) was below the reference range. Subjects with the most severe obesity had the lowest GLS and GCS values (-19.8% and -13.4%, respectively). Significant differences were seen in GLS and GCS between class III and overweight individuals (GLS% $P = 0.002$ and GCS% $P = 0.033$). The GRS% values of the class III obese participants were higher than those of the other groups; nevertheless, no statistically significant differences were found between the groups ($P = 0.448$).
Conclusion
The importance of myocardial deformation assessment is emphasized in context of the identification of subclinical LV dysfunction in obesity

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EP580

Homozygous familial hypercholesterolemia with resistance to Inclisiran (siRNA PCSK9i) – a case report

Mélina Michel, Hela Walha & Mohammed Barigou
Centre hospitalier universitaire vaudois, service d'endocrinologie, diabétologie et métabolisme, Lausanne, Switzerland

Introduction
Homozygous familial hypercholesterolemia (HoFH) is a rare inherited autosomal dominant disease (1/20000 Individuals) involving germline mutations in the LDL metabolism pathways (LDL receptor/PCSK9/APOB/IDLRAP) that results in very high levels of LDLc, usually $>$ 10 mmol/l, and premature cardiovascular disease. The EAS guidelines recommend the use of PCSK9 inhibitors (PCSK9i) as a third line therapy in HoFH, however they report no precision regarding the effect of monoclonal antibodies (MAB) vs small interfering RNA (siRNA) in this specific situation. Here we report a case of patient with HoFH and resistance to Inclisiran a siRNA PCSK9i.
Case series
Mrs M, 28-year-old woman, is a 4th of 6 siblings from a consanguineous (first degree cousins) marriage. She had a diagnosis of HoFH at the age of 10 with a baseline LDLc of 13.6 mmol/l (mutation LDLr: NM:000527.5:c.[(694 + 1_695-1)_(940 + 1_941-1)del]mat;[(694 + 1_695-1)_(940 + 1_941-1)del]pat). Despite an initiation of simvastatin and ezetimibe at a young age, LDLc remained very high due to adherence issues. Since 2023 we decided to conduct a stepped approach to treat her HoFH. We reinitiated rosuvastatin 40 mg plus ezetimibe 10 mg resulting in significant decrease of LDLc to 8.7 mmol/l. We then added inclisiran as a third line therapy for adherence purposes. However, LDLc decrease was insufficient: LDLc 7.5 mmol/l (additional 14% decrease) one month after the second injection. We then added bempedoic acid 180 mg and cholestyramine 3g/day, resulting in 16% additional decrease in LDLc (6.3 mmol/l). To better impact LDLc we decided to switch from inclisiran to evolocumab (MAB PCSK9i) since October 2023. In-fact, the patient's brother carrying the same mutation at homozygous state, showed a spectacular response to evolocumab 280 mg every 15 days, with LDLc decreasing from 9 mmol/l to 4.8 mmol/l (46% decrease).
Discussion
This case corroborates the recent results of Orion 5 Study reporting a non-significant decrease of LDLc with inclisiran compared to placebo in HoFH despite a potent effect on circulating PCSK9[1]. Real world data with monoclonal antibodies inhibiting PCSK9 in HoFH showed an excellent response (-57% of additional decrease in LDLc at 24 months) when added to other lipid lowering therapies[2].
Conclusion
in HoFH patients, the third line therapy after maximum statin/ezetimibe combination should be MAB PCSK9i, inclisiran showing poor efficacy in this context. Mechanisms explaining this discrepancy should be elucidated and future guidelines should precise this specificity.
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EP584

A novel lipoprotein lipase mutation in familial chylomicronemia syndrome – two case reports

Telma Moreno[1,2], Sara Ribeiro[1,2], João Freixo[3], Sílvia Pinhão[4], Flora Correia[4] & Elisabete Rodrigues[1,2]
[1]Unidade Local de Saúde São João, Endocrinology, Porto, Portugal; [2]Universidade do Porto, Faculty of Medicine, Porto, Portugal; [3]Instituto de Investigação e Inovação em Saúde (i3S), Center for Predictive and Preventive Genetics, Porto, Portugal; [4]Unidade Local de Saúde São João, Nutrition, Porto, Portugal

Introduction
Familial chylomicronemia syndrome (FCS) is a rare inherited disorder of lipoprotein metabolism leading to severe hypertriglyceridemia and increased risk for acute pancreatitis. Mutations in the lipoprotein lipase (*LPL*) gene account for the majority of cases of monogenic chylomicronemia.
Methods
We report the cases of two white males with a novel homozygous mutation in position 332 of the *LPL* gene.
Results
The patients are siblings from a consanguineous marriage and presented the same homozygous mutation in the *LPL* gene identified as c.995C $>$ G [p.(Thr332Ser)]. This variant has not been previously described and was deemed a variant of uncertain significance (VUS). According to the clinical manifestations and genetic findings on both patients, the diagnosis of FCS was established. Both patients were diagnosed during childhood at 14-years-old with severe hypertriglyceridemia and have a previous history of recurrent acute pancreatitis (8 episodes in one sibling and 2 episodes in the other). One patient developed diabetes mellitus secondary to pancreatic disease. Dietary modification plays a key role on management of FCS and severe restriction of dietary fat to $<$20 grams per day is recommended. Therapeutic resistance to routine triglyceride-lowering medication is a hallmark of FCS and the patients currently have triglyceride levels ranging from 1217-2920 mg/dl, under fenofibrate and omega-3 fatty acids therapy. Treatment with apolipoprotein C-III inhibitor volanesorsen is under consideration.
Conclusions
We describe a novel *LPL* mutation related to familial chylomicronemia syndrome. Even though it was considered a variant of uncertain significance in light of current knowledge, the mutation appears to be pathogenic according to clinical characteristics, causing severe hypertriglyceridemia with increased risk of acute relapsing pancreatitis.

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EP594

Munchausen syndrome in endocrinology: about two case reports of factitious hypoglycemia

Benabdelatif Katia[1], Aicha Lachkhem[1], Abdelkader Yahi[1], Redhouane Longo[2], Ould Kablia Samia[1] & Bensalah Meriem[1]
[1]Endocrinology department, Central Military Hospital, Algiers, Algeria.; [2]Endocrinology department, Regional university Military Hopsital of Oran, Algeria.

Introduction
The Munchausen syndrome, also known as factitious disorder, involves a compulsion to simulate illness or trauma. Individuals may go as far as taking medication or inflicting harm on their bodies to evoke compassion. The aim of this report is to illustrate the example of factitious hypoglycemia, one of the most common forms of factitious disorders in the endocrine-metabolic field, accounting for 4-11% of all non-diabetic hypoglycemias.
Observation
Case 1: A young women aged 23 years old, with a personal history of polycystic ovary syndrome and endometriosis, and a family history of a husband with type 1 diabetes mellitus on insulin therapy, was admitted for investigation of multiple hypoglycemic episodes which manifested by adrenergic and neuroglycopenic signs. The clinical examination found an overweight patient, with no signs of adrenal deficiency, the presence of several bruises related to injections on both arms. During her hospital stay, she presented a spontaneous hypoglycemia at 0.34 g/l on capillary blood, confirmed by a venous test at 0.33 g/l. Additional testing performed at that time revealed an inappropriately elevated level of insulin (38 uui/ml) and a low plasma C-peptide level (0.2 ng/ml). A qualitative serum and urinary sulfonylurea panel was negative, confirming the artificial origin of hypoglycemia. After psychological evaluation, she denied taking any glucose lowering agents, but she admitted to have taken blood thinner accidentally, which resulted in a hemorrhage. In light of these findings, a psychiatric evaluation was established which revealed an anxious, distressed patient with narcissistic personality traits. She was referred to a psychiatrist for follow-up. Case 2: 16-year-old young female, with no personal medical history, with a family history of diabetes mellitus in both her father and her maternal grandmother, treated with oral antidiabetic drugs and insulin respectively. She was admitted into the department of endocrinology to explore multiple severe hypoglycemic episodes (0.2-0.5 g/l) with adrenergic and neuroglycopenic symptoms. During her hospitalization, we did not objectify any hypoglycemic episodes on either capillary or venous tests. Oral glucose tolerance test was normal. The patient vehemently denied taking any hypoglycemic medication or having any affecting problem. After a psychological evaluation, she admitted to secretly taking insulin and oral antidiabetic drugs.
Conclusion
Factitious hypoglycemia is a real diagnostic challenge. Collaboration between endocrinologists, psychologists and psychiatrists is necessary for establishing this diagnosis and for follow-up.

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EP615

Improvement of glycemic control after initiation of enteral nutrition through percutaneous endoscopic gastrostomy (PEG)

Andrea Fernández Valero & Silvia Alonso Gallardo
Hospital Costa del Sol, Marbella, Spain

We present the case of an 83-year-old woman with a medical history of moderate-severe Alzheimer's disease, which made her dependent. Despite this, she was able to communicate and go out in a wheelchair. Over the last 6 months, she experienced decreased intake and lost more than 10% of her body weight. In addition, she was diagnosed in 2006 with latent autoimmune diabetes of adults (LADA), treated initially with oral antidiabetic agents but later on, it was necessary to switch to insulin therapy and glucose monitoring. She presented difficult glycemic control with episodes of hypoglycemia due to refusal to eat after administration of rapid-acting insulin, even requiring emergency services care for severe hypoglycemia in some of these episodes. Thus, the family began to skip insulin doses due to fear of new hypoglycemic events. The sensor discharge data were TAR 50%, TIR 41%, TBR 9% (very low 1%). In mid-2023, the patient was transferred to the emergency room due to poor general condition and impaired level of consciousness. Blood test revealed a glycemia of 560 mg/dl, metabolic acidosis, and positive urine ketone bodies, leading to a diagnosis of diabetic ketoacidosis and intensive fluid therapy and intravenous insulin perfusion were initiated. Once stabilized, she was admitted to the unit. On the hospital ward, intakes continued to be erratic, again presenting severe hypoglycemias that led to a reduction in insulin doses and subsequently resulted in hyperglycemia of >300 mg/dl when adequate intakes were taken. Finally, it was decided that the most appropriate approach was to initiate enteral nutrition by PEG, as this would improve nutritional status by guaranteeing adequate caloric intake and hydration, along with a fixed carbohydrate intake, enabling the administration of a consistent insulin dose at all times. After initiation of enteral feeding, there was a significant improvement in glycemic control, with flatter curves and no severe hypoglycemia, presenting a TAR 36%, TIR 63% and TBR 1% (very low 0%).
Conclusion
The treatment of insulinopenic diabetes can be challenging due to the varying amount of insulin needed based on carbohydrate consumption. This can be especially difficult for patients with irregular eating habits, such as those with advanced dementia. In these cases, establishing enteral nutrition through PEG may be an option, as long as the risks and benefits are carefully considered, and it is appropriately indicated. This approach will not only help manage diabetes but also ensure proper nutritional status.

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EP618

Hemoglobin Wayne as a cause for falsely high HbA1C in pregnancy

Nwe Aung[1], Amina Al-Qaysi[2] & Chitrabhanu Ballav[1]
[1]Buckinghamshire NHS Trust, Diabetes and Endocrinology, Aylesbury, United Kingdom; [2]Buckinghamshire NHS Trust, Endocrinology & Diabetes, Aylesbury, United Kingdom

Introduction
Diagnosis of Gestational Diabetes Mellitus (GDM) is with 75-g 2-hour Oral Glucose Tolerance Test (OGTT) at presentation and at 24 to 28 weeks when the first OGTT is normal. Although HbA1C is not recommended as a diagnostic test for GDM, this was used instead of OGTT during the Covid pandemic in the United Kingdom. Hemoglobin Wayne (Hb Wayne) is a rare variant of hemoglobin which may produce falsely high HbA1C level in some assays. We report a patient who was a carrier for Hb Wayne who presented with high HbA1C in pregnancy although her fructosamine and capillary blood glucose levels were in reference range.
Case report
A 30-year-old non-diabetic primigravida with family history of Type 2 diabetes and BMI of 24 kg/m^2 was screened for Gestational Diabetes Mellitus (GDM) at 14 weeks gestation using HbA1C instead of OGTT. Her HbA1c level at presentation was 89 mmol/mol (less than 42), although her capillary blood glucose levels were within euglycemic ranges, and fructosamine level was 257 umol/l (less than 330). Her Glutamate Decarboxylase and Islet autoantibodies were not raised. The fetal growth scans were within satisfactory parameters throughout pregnancy. She remained on diet and lifestyle with home monitoring of capillary blood glucose levels until the third trimester when she required treatment with metformin. She had elective Caesarean session at 39 weeks for personal preference, delivering a healthy baby (birth weight of 3.025 kg). In the postnatal period, her capillary blood glucose levels remained within euglycemic ranges after discontinuing Metformin. Her HbA1C remained high at 86mmol/mol with fructosamine level of 257 umol/l without treatment. She was found to be a carrier of Hb Wayne on haemoglobinopathy screening. This alpha chain variant heterozygous state is likely to have caused the falsely high HbA1C.
Conclusion
We report falsely high HbA1C in early pregnancy from Hb Wayne which may lead to overdiagnosis if used to screen for GDM instead of OGTT. Strategies to overcome this may include hemoglobinopathy screening and fructosamine level when HbA1C is high despite euglycemia on capillary blood glucose monitoring.

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EP622

Sometimes It's Lupus – A Case of Hydroxychloroquine-Induced Hypoglycemia

Gustavo Rodrigues[1,2], Alice Monsanto[1], Tânia Carvalho[1], Cristina Ribeiro[1], Sofia Gouveia[1], Dircea Rodrigues[1,2] & Isabel Paiva[1]
[1]Centro Hospitalar Universitário de Coimbra, Endocrinology, Coimbra, Portugal; [2]Faculdade de Medicina da Universidade de Coimbra, Portugal

Introduction
Therapy with hydroxychloroquine (HCQ) and chloroquine (CQ) constitutes a rare but documented cause of hypoglycemia in non-diabetic adults. The physiopathological mechanism is not fully understood, and symptoms may appear several years after starting treatment. In this paper, we describe the clinical presentation and investigation of a case of hypoglycemia attributed to HCQ therapy.

Clinical Case
A 60-year-old female patient was referred for an Endocrinology consultation due to recurring symptomatic hypoglycemia (headache, tremors, nausea) documented by capillary blood glucose measurement at home. The patient had a history of Systemic Lupus Erythematosus with nephropathy, treated with HCQ, mycophenolate mofetil, and prednisolone, with no history of diabetes mellitus or insulin or sulfonylurea therapy. The patient underwent a 72 h-fasting test, which induced symptomatic hypoglycemia at 24 hours (48 mg/dl, confirmed by laboratory assay) without biochemically evident hyperinsulinism (Insulin 0.6 umol/l, C-peptide 0.3 ng/l). The remaining etiological study was negative: laboratory testing for adrenal function was normal (ACTH, Cortisol within normal range). Sulfonylurea dosing was negative, IGF-1, IGF2, and anti-insulin antibody levels were within normal limits. β-hydroxybutyrate levels were slightly elevated (1.10 mmol/ml). Thoracic and abdominal CT scan did not reveal morphological changes, most notably in the pancreas; 18F-FDOPA PET scan did not show areas of increased radionuclide uptake. Given the absence of aetiologically suggestive biochemical or structural findings, as well as the existence of reported cases of hypoglycemia secondary to HCQ therapy, a decision was made to discontinue the drug. To date (approximately 5 months), there has been complete absence of symptoms, with no recurrence of hypoglycemia.
Conclusion
Although a rare condition, hypoglycemia due to HCQ therapy should be considered as a possible aetiology in patients with proven hypoglycemia under this therapy.

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EP634

Improvement of cardiovascular risk estimated by the SCORE2-Diabetes calculator in patients with type 2 diabetes treated with extended release metformin

Francisco Javier Martinez Martin[1,2], Agnieszka Kuzior[2], Claudia Arnas-Leon[2,3], Ana Delia Santana-Suarez[2], Paula Maria Fernandez-Trujillo-Comenge[3], Jennifer Maria Perez-Rivero[4], Alba Hernandez-Lazaro[5], Ricardo Jose de Leon-Durango[3], Borja Santana Ojeda[3] & Inmaculada Molinero-Marcos[3]
[1]Hospital Universitario de Gran Canaria Doctor Negrin, Outpatient Hypertension Clinic, Las Palmas de Gran Canaria, Spain; [2]Hospitales Universitarios San Roque, Endocrinologia y Nutricion, Las Palmas de Gran Canaria, Spain; [3]Hospital Universitario de Gran Canaria Doctor Negrin, Endocrinologia y Nutricion, Las Palmas de Gran Canaria, Spain; [4]Centro de Salud de Escaleritas, Medicina Familiar y Comunitaria, Las Palmas de Gran Canaria, Spain; [5]Hospital Universitari Parc Tauli, Endocrinologia i Nutricio, Sabadell, Spain

Introduction and Objectives
Extended-release (ER) metformin may reduce the gastrointestinal adverse effects of conventional metformin, increasing compliance, adherence and persistence. In mid 2022, a single-pill combination (SPC) containing 50 mg sitagliptin plus 1000 mg ER metformin was released in Spain, while monocomponent ER metformin is still unavailable. We rechallenged patients with T2DM labelled as metformin-intolerant and treated with a DPP4i with the mentioned SPC in order to assess its tolerability. With the recent availability (mid 2023) of the cardiovascular risk calculator SCORE2-Diabetes we retrospectively calculated the cardiovascular risk of our patients at baseline and after 3-4 months on treatment with this SPC.
Patients and Methods
Consecutive patients with T2DM patients, HbA1c $>7\%$ and GFR (CKD-EPI) $>$ 45 mL/min/1.73m^2 labelled as metformin-intolerant due to gastrointestinal symptoms, and treated with a DPP4i (with or without additional hypoglycemic medication) were switched to the 50 mg sitagliptin plus 1000 mg ER metformin SPC, taking 1 pill daily in the first month and afterwards 2 pills if the tolerance was good. Additional antidiabetic medication, if any, was unchanged; however in many patients lifestyle, antihypertensive and cholesterol-lowering medication were adjusted. Tolerance data were obtained by questionnaire in the follow-up visit. Data are given as mean $\pm$ sd. The calculations were done by intention to treat. All patients included gave informed consent. The SCORE2-Diabetes calculator was obtained at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10361012/bin/appendix_2.xlsx
Results
We calculated the CV risk by SCORE2-Diabetes in 58 patients (39 women, age 53 $\pm$ 8 years, 8 $\pm$ 3 years since the diagnosis of T2DM), of which 47 tolerated 2 tablets of metformin ER + sitagliptin (1000/50 mg); 6 tolerated 1 tablet and 5 did not tolerate any dose. The baseline CV risk (major event in the next 10 years) was estimated as 12.7 $\pm$ 2.2%; 6 patients were classified as intermediate risk, 39 as high risk and 13 as very high risk patients. After 3-4 months of treatment the CV risk was reduced to 10.4 $\pm$ 1.9% ($P<0.001$); 23 patients were classified as intermediate risk, 29 as high risk and 6 as very high risk patients ($P<0.001$).
Conclusions
A large majority of the patients with T2DM labelled as metformin-intolerant did tolerate the ER metformin plus sitagliptin SPC. Their cardiovascular risk was significantly reduced. The study intervention only added metformin ER as an antidiabetic drug, but in many of the patients there were additional interventions in lifestyle, antihypertensive and cholesterol-lowering drugs. Therefore, the changes in cardiovascular risk must be considered as multifactorial.

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EP635

Continuous glucose monitoring (CGM) satisfaction in patient with Type 1 Diabetes (T1DM), An audit of Irish population attending Diabetes outpatient clinic

Hurmat Walli[1], Derek O'Keefe[2], Donal O'Shea[1] & Catriona Jennings[2]
[1]St. Vincent's University Hospital, Ireland; [2]University of Galway, Galway, Ireland

Aims
- To audit CGM satisfaction in adult patients with T1DM, in Irish outpatient setting.
- To compare CGM satisfaction of patients attending public vs private setup.
- To compare CGM satisfaction of patients to perception of Diabetes Educators regarding CGM satisfaction of their patients.

Methods
This audit is a cross-sectional survey, conducted from April 2023 to June 2023, using a validated questionnaire; The Glucose Monitoring Satisfaction Survey (GMSS)[1]. Total 114 patients with T1DM, attending Diabetes Outpatients Clinic in St. Vincent's University Hospital and St Vincent's Private Hospital participated in the survey and completed the questionnaire. 8 Diabetes Educators (7 Diabetes Specialist Nurses and 1 Dietician), also completed the GMSS to express their perception of device satisfaction of their patients with T1DM using CGM. Participants were also invited to make any additional comments they have, to have qualitative data.
Results
All patients with T1DM were found to have high overall device satisfaction (M = 4.07, SD 0.66787). No statistically significant difference was observed among CGM satisfaction of patients attending public vs private setups (t (96) = -0.088, ρ = 0.381). Diabetes Educators also perceived high device satisfaction of their patients and comparison with CGM satisfaction of patients did not yield any statistically significant difference (t (102) = 0.311 ρ = 0.756).
Conclusion
High device satisfaction was found in patients with T1DM attending Diabetes clinic in St. Vincent's university and St. Vincent's private hospital. Diabetes Educators also perceive that their patients are satisfied with their device use.
Keywords: Type 1 Diabetes, CGM satisfaction, QoL, Adults, Diabetes Educators
Reference
1. Development of a New Measure for Assessing Glucose Monitoring Device-Related Treatment Satisfaction and Quality of Life. Diabetes Technology & Therapeutics. 2015;17(9):657-63.

Table 1. CGM satisfaction of patients with T1DM.

	Mean	Count	Maximum	Minimum	Standard Deviation
Emotoinal Burden	4.10	114	5.00	1.75	.89
Behavioral Burden	4.31	114	5.00	2.50	65
Trust	3.72	114	5.00	1.00	1.02
total	4.07	114	5.00	2.20	.66

Table 2. Comparison of CGM satisfaction of patients attending Public Vs Private outpatient services.

	Group Statistics				
	Hospital name	N	Mean	Std. Deviation	Std. Error Mean
total	St. Vincents University Hosital (public)	44	4.0000	.64476	.09720
	St. Vincents Private Hosital	58	4.1161	.67035	.08802

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EP639

Real-world effectiveness of dapagliflozin and sitagliptin fixed-dose combination in indian patients with type 2 diabetes: a retrospective analysis of electronic medical records stratified by BMI

Rajiv Kovil[1], Rajesh Deshmane[2], Prakadeesh Bharathi B[3], Prachi Ahire[3], Vinay Kudrigikar[3], Shruti Dharmadhikari[3], Chintan Khandhedia[3], Neeraj Markandeywar[3], Amey Mane[3] & Suyog Mehta[3]
[1]Kovil's Diabetes Care Centre, Mumbai, India; [2]Shree Mahalaxmi DIATONE Institute, Kolhapur, India; [3]Sun Pharma Laboratories Ltd, Mumbai

Introduction and Objective
Escalating prevalence of type 2 diabetes mellitus (T2D) in India presents a significant health challenge. Dapagliflozin and sitagliptin are important treatments for achieving glycaemic control in patients with T2D. Dapagliflozin promotes weight loss benefiting overweight and obese patients, while sitagliptin enhances incretin hormone activity with modest weight loss. This is a BMI-stratified analysis of electronic medical record (EMR) based real world, retrospective study assessing effectiveness of dapagliflozin + sitagliptin FDC in patients with T2D.
Methods
In this study, data of adult patients (age $\geq$18 years) of either gender with T2D having HbA1c $\geq$7% at baseline were included. Patients who were prescribed dapagliflozin + sitagliptin FDC in any visit other than baseline visit on EMR platform were included. Patients on insulin or other injectable antidiabetic medication were excluded. Primary endpoint was mean change in HbA1c from baseline to 3 months in patients with HbA1c $\geq$ 8% at baseline. This is a BMI Stratified-analysis of primary outcome.
Results
Total 3112 patients fulfilled selection criteria, of which 838 patients were eligible for primary endpoint. Mean HbA1c at baseline was 9.29% which reduced to 7.98% at end of 3 months with reduction of -1.31% ($P<0.001$). Patients were stratified per BMI ($n=466$): Group 1 (Normal: 18.50-22.99 kg/m^2; $n=41$), Group 2 (Overweight:23.00-24.99 kg/m^2, $n=64$), and Group 3 (Obese: $\geq$25.00 kg/m^2; $n=361$). Significant reduction in HbA1c from baseline to 3 months in all BMI groups was seen; Group 1: 9.26% to 7.90% [change -1.36%]; Group 2: 9.34% to 7.90% [-1.44%]; Group 3: 9.19% to 7.97% [-1.22%] ($P<0.001$ for all comparisons). Fasting and Postprandial blood glucose (FBG and PPBG) reduced significantly in all BMI strata. FBG changes -Group 1: 165.21 to 139.78 [-25.43 mg/dl; $n=35$], Group 2: 162.85 to 124.73 [-38.12 mg/dl; $n=56$], Group 3: 163.91 to 134.17 [-29.74 mg/dl; $n=303$]. PPBG changes -Group 1: 248.24 to 200.69 (Change -47.55 mg/dl; $n=34$), Group 2: 231.96 to 188.74 (-43.22 mg/dl; $n=51$), Group 3: 244.22 to 197.97 (-46.25 mg/dl; $n=249$) ($P<0.001$ for all comparisons) . In patients with BMI $>$23 kg/m^2;, weight reduced from 74.2 to 73.6 kg [change -0.6] at 3 months ($n=649$) and 73.76 to 73.12 kg [-0.64 kg] at 6 months ($n=334$). In patients with BMI $>$25 kg/m^2;, weight reduced from 76.31 to 75.65 kg [-0.66 kg] at 3 months ($n=537$) and 75.92 to 75.12 [-0.8 kg] at 6 months ($n=273$) ($P<0.0001$ for all changes).
Conclusions
Dapagliflozin + sitagliptin FDC demonstrated significant improvement in HbA1c reduction in patients with T2DM and higher HbA1c across BMI groups suggesting it as an effective therapeutic option in patients with varying BMI.

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EP642

Predictors of glycemic control monitoring in diabetic pregnant women from 449 patients

Rakia Bachir Moctar, Bensbaa Salma, Essabah Nassim, El Aziz Siham & Asma Chadli
CHU Ibn Rochd, Casablanca, Morocco, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Casablanca, Morocco

Introduction
Diabetic pregnancy is a high-risk pregnancy, hence the importance of perfect glycemic control. The objective of this study is to assess glycemic control in pregnant women as well as the factors involved.
Patients and methods
Retrospective study, including 449 patients with diabetic pregnancies followed at the Endocrinology-Diabetology department between January 2016 and January 2022. To do this work, we used SPSS software.
Results
The study included 449 patients with a mean age of 32 years, 19.82% had type 1 diabetes, 39.64% had type 2 diabetes and 40.53% had gestational diabetes. The mean preconception HbA1c was 8.5%. For treatment, 62.47% of patients were on insulin and 37.53% on hygienic and dietary rules. Physical activity was practiced in 58.12% of patients, 41.88% of patients were sedentary. 5.8% are on a free diet and consume fast sugars. Glycemic control was perfect in 49.32% of patients while it was insufficient in 50.68%. A significant relationship was found between glycemic control and adherence to treatment ($P<0.05$) as well as the type of diabetes ($P<0.02$).
Discussion and conclusion
It has been established that optimized management, including perfect glycemic control, reduces the risks associated with pregnancy, several factors intervene as demonstrated in our study, namely: eating habits and the type of diabetes.

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EP648

The Relationship between Precocious/Early Puberty and Obesity with Metabolic Abnormalities: A Comprehensive Review

Ashraf Soliman, Nada Alaaraj, Fawzia Alyafei, Noor Hamed & Shayma Mohamed
Hamad General Hospital, Pediatric Endocrinology, Doha, Qatar

The Relationship between Precocious/Early Puberty and Obesity with Metabolic Abnormalities: A Comprehensive Review
Introduction
The impact of pubertal timing on the development of obesity and metabolic abnormalities has been the subject of extensive research with variable outcomes.
Objective
We systematically reviewed studies (Medline, Pubmed, Google scholar, and Web of Science) 2000 until March 2023 evaluating the relation between early puberty and occurrence of obesity and metabolic abnormalities including T2DM.
Results
12 studies were examined and analyzed. The Gothenburg Osteoporosis and Obesity Determinants study followed 579 subjects. Early pubertal onset predicted central fat mass distribution, while high prepubertal BMI strongly predicted subcutaneous obese phenotype. A twin cohort analysis revealed strong heritability estimates for age at onset of pubertal growth spurt, and adult height. These traits were associated with childhood BMI and early adulthood stature due to shared genetic factors. A Finnish cohorts supported strong genetic etiology in the correlation between early puberty and higher childhood BMI especially in girls. A meta-analysis (34 studies) demonstrated that early menarche correlated with increased adult BMI, while late menarche correlated with decreased BMI. Another meta-analysis (28 studies) found that earlier age at menarche was associated with a higher risk of T2DM even after adjusting for adiposity. A Swedish study of 30,697 men demonstrated that earlier pubertal onset was linked to a higher risk of early diabetes, and early need for insulin therapy even after BMI adjustments. Late puberty correlated with reduced diabetes risk. Analysis of the Nurses' Health Study cohorts revealed that early menarche was associated with increased risk of type 2 diabetes. Adiposity partly mediated this association. A meta-analysis of 28 observational studies ($n=1,228,306$) identified that without adjustment for adult adiposity, T2DM/IGT risk was lower per year later onset of menarche and higher for early vs later menarche. In a UK Biobank study indicated that both in women and men separately, earlier puberty timing was associated with higher risks for angina, hypertension and T2D. A study in Brazil involving 8,075 women demonstrated that early menarche ($<$11 years) was linked to a higher risk of diabetes, even after controlling for socio-demographic factors and maternal diabetes.
Conclusion
Collectively, early puberty appears to contribute to an increased risk of obesity and T2DM in both men and women, often mediated by factors such as childhood BMI and genetic predisposition. Monitoring and early diagnosing these conditions are important for successful management.

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EP649

Prevalence of Metabolic Syndrome Components and High Atherogenic Index in Obese Nondiabetic Children

Ashraf Soliman, Noor Hamed, Fawzia Alyafei, Nada Alaaraj & Shayma Mohamed
Hamad General Hospital, Pediatric Endocrinology, Doha, Qatar

This study aimed to explore the prevalence of distinct Metabolic Syndrome (MetS) components and plasma AIP among obese children and adolescents, and

to evaluate their anthropometric measures in comparison to their parents, thereby considering genetic and environmental influences.
Methodology
Anthropometric and biochemical profiles of 91 randomly selected obese children and young adolescents (mean age: 10.5 ± 2.7 years) were meticulously analyzed. This cohort attended the Pediatric Clinic of Hamad Medical Center (HGH) in Doha (Qatar) between January 2018 and December 2020. Recorded data encompassed age, gender, weight, height, body mass index (BMI), systolic and diastolic blood pressures, as well as key biochemical parameters such as lipid profile, glycated hemoglobin (A1C), and alanine transferase (ALT) levels, which were subsequently compared to age-matched normative values.
Results
Among mothers, 44% were overweight (BMI $>25 <$ 30 kg/m^2), while 52.7% were obese (BMI $>$ 30 kg/m^2; range 24.5 - 51.5 kg/m^2). Similarly, 18% of fathers were overweight, while 64% were obese (range 21.5 - 51.2 kg/m^2). A significant correlation emerged between the BMI of obese children and young adolescents and their maternal BMI (r: 0.34, $P=0.01$), although not with paternal BMI. Obese children exhibited heightened prevalence rates of dyslipidemia, dysglycemia, and non-alcoholic fatty liver disease (NAFLD). Applying modified adult MetS criteria, MetS was evident in 30.2% of this obese cohort, with 76.7% displaying elevated AIP.
Discussion and Conclusion
The 30% prevalence of MetS among our obese, nondiabetic children and young adolescents underscores the pressing need for early detection and nationwide preventive strategies. Moreover, the notable 76.7% occurrence of high AIP emphasizes the augmented risk of future cardiovascular diseases (CVDs), necessitating early interventions to normalize atherogenic lipemia. The strong relationship between parental overweight and child obesity underscores the complex interplay between genetic predisposition and environmental factors.
Recommendations
studies suggest that interventions aimed at reducing dietary carbohydrate intake and promoting weight loss may hold potential in mitigating atherogenic dyslipidemia and its associated cardiovascular risks.

Prevalence (%) of different metabolic components in obese children.

Obese children and young adolescents($n=91$)	Prevalence
AIC > 5.7%	21%
Fasting blood glucose >5.6 mmol/l	32%
Low Hb < 11g/l	10%
LDL > 2.9 mmol/l	16.2%
HDL < 1.1 mmol/l	40%
Triglycerides > 1.7 mmol/l	18.6%
Cholesterol > 4.5 mmol/l	32.6%
Atherogenic index of plasma > 0.23	76.7%
Pre-hypertension BP >85th percentile	16.2%
Hypertension BP >95th percentile	11.2%
ALT > 35 IU/l	12%
Vitamin D < 50 nmol/l	78.50%

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EP650

Impact of obesity and diabetes in colorectal cancer
Wafa Khemiri, Myriam Ayari, Mtir Maha, Abdelaali Imen, Douggui Hedi & Taieb Jomni
FSI hospital, Internal Medecine, Tunisia

Background
Colorectal cancer is the world's third most common cancer. The prognosis is mainly determined by the stage of the tumor, but several other factors related to the patient, such as co-morbidities, may also have an impact on the disease course. The aim of our study was to assess the prognostic value of diabetes and obesity in colorectal cancer.
Methods
We conducted a retrospective study including patients diagnosed with primary colon or rectal cancer, over an 8-year period [January 2014-June 2022]. Patients were compared according to the presence or absence of diabetes and obesity, that was defined by a body mass index (BMI) greater than 30 kg/m^2. Data were entered and analyzed via SPSS 26 software. Prognostic analysis was performed using the Kaplan Meier method.
Results
A total of 83 patients were included, with a mean age at disease diagnosis of 60 ± 12 years and a sex ratio M/F = 1.96. Liberkhunian adenocarcinoma was the dominant histological type (90%). Eleven patients had metastatic disease at diagnosis, with the majority classified as TNM stage 2 and 3 (25% and 47% respectively). Twenty-three patients had diabetes (28%). Thirty-one patients were obese (31%). The cancer was in the rectum in 30% of the cases and in the colon in 70%. For treatment, 24% of patients received neoadjuvant chemotherapy (24%), 74 patients underwent surgery (89%), with urgent surgery in 20% of the cases, and 60% required adjuvant chemotherapy. In a univariate study, diabetes was significantly associated with an age of cancer's discovery greater than 50 years ($P=0.018$). The presence of pulmonary metastases was higher in diabetic patients, without a significant difference ($P=0.06$). In terms of endoscopic characteristics, patients with a BMI greater than 25 kg/m^2 were more likely to have a stenosing and circumferential tumour, with a difference at the limit of signification ($P=0.05$ and $P=0.06$ respectively). Comparing Kaplan-Meier survival curves, there was no significant difference in survival in diabetic patients (log rank test = 0.86) and also in obese patients (log rank test = 0.72).
Conclusion
Diabetes and obesity are known as risk factors for colorectal cancer and could influence tumor characteristics, but they do not appear to impact prognosis in our study.

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EP651

Eating habits in obese children: a comparative study
Rym Ben Othman, Salma ABADLIA[1,1], Ramla Mizouri, Berriche Olfa, Emna Talbi, Syrine Trabelsi & Henda Jamoussi
National Institute of Nutrition and Food Technology, tunis

Introduction
Childhood obesity rates have globally increased in the last five decade. It is well known that eating habits are a crucial contributing factor. Our study aimed to understand the impact of dietary habits on this global issue.
Methods
It was a comparative study including 50 obese children (G1) and 35 normal-weight children (G2) aged between 6 and 13 years old. Our study was conducted in the outpatient department of Bechir-Hamza Children's Hospital of Tunis, Tunisia from December 26, 2016 to February 1, 2017. Obesity was determined by World Health Organization growth charts sex-specific Body Mass Index for age.
Results
The average age was 8.9 ± 3 years for G1 and 8.1 ± 3 years for G2 ($P=0.22$). G1 were mainly females (64%). We noted that G1 had significantly an earlier food diversification during the first year of life (5.11 months with a minimum of 2 months vs 5.8 with a minimum of 3, $P=0.05$). During childhood, the majority of participants had 3 meals per day (G1: 95% vs G2: 97%, $P=0.86$). Nevertheless, 60% of meals were consumed in front of TV for G1 vs 40% for G2 ($P<0.01$). Eating disorders were noted in G1 as following: 8% prandial hyperphagia, 26% binge-eating disorder, 26% night-eating syndrome and 28% bulimia. Furthermore, nearly all obese children (98%) reported the intake of snacks.
Conclusion
These findings highlight the importance of addressing not only the nutritional aspects but also the behavioral and psychological dimensions of eating habits to combat the increasing prevalence of childhood obesity.

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EP652

Comparative analysis of nutritional status in obese and non-obese children
Rym Ben Othman, Salma Abadlia, Ramla Mizouri, Olfa Berriche, Emna Talbi, Rihab Yamoun, Amal Salem & Henda Jamoussi
National Institute of Nutrition and Food Technology, tunis

Introduction
Childhood obesity is a growing public health concern worldwide, necessitating a comprehensive understanding of the nutritional disparities between obese and non-obese children. This study presents a comparative analysis aiming to elucidate the distinctive nutritional profiles in these two groups
Methods
We undertook a comparative study involving 50 obese children (G1) and 35 normal-weight children (G2) aged 6 to 13 years. The research was conducted at the outpatient department of Bechir-Hamza Children's Hospital in Tunis, Tunisia, from December 26, 2016, to February 1, 2017. Obesity was determined by World Health Organization growth charts sex-specific Body Mass Index for age.
Results
The average ages for G1 and G2 were 8.9 ± 3 years and 8.1 ± 3 years, respectively ($P=0.22$). Among G1, two-thirds (64%) were female. We observed that G1 had a significantly higher consumption of white bread (94% vs 80%, $P=0.04$) as well as cheese (50% vs 20%, $P<0.01$) for breakfast. Additionally, lunchtime

consumption showed a higher prevalence of sodas in G1 compared to G2 (86% vs 37%, $P<0.01$). Furthermore, the average daily caloric intake was significantly higher in G1 (2646±320 vs 1792±340 Kcal/j, $P<0.01$). The diet of G1 was characterized not only by hypercaloric content but also by a lower fiber intake (G1: 19 g fiber/day vs G2: 32.9 g fiber/day, $P=0.01$). No significant difference was noted between the two groups regarding the intake of water-soluble vitamins. However, for fat-soluble vitamins, G1 had a significantly higher vitamin E intake (42 mg/day vs 26 mg/day, $P<0.01$). In terms of trace elements, iron intake was similar in both groups, whereas zinc intake was significantly greater in G1 (54 mg/day vs 20 mg/day, $P<0.01$). As for minerals, magnesium and sodium intake were comparable in both groups ($P=0.74$, $P=0.12$, respectively), while a significant higher intake of phosphorus, potassium and calcium was noted in G1 ($P<0.01$, $P<0.01$, $P<0.01$, respectively).

Conclusion

These findings underscore the importance of targeted interventions and public health initiatives to address and modify dietary behaviors among obese children.

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EP653

Is Freeze-dried Superfood Kale Supplementation Healthier than Common Green Peas? Outcomes of a Cross-Over Trial

Dara Aldisi[1], Shaun Sabico[2], Amani Alfarraj[1] & Al-Daghri Nasser[2]
[1]King Saud University, College of Applied Medical Colleges, Riyadh, Saudi Arabia; [2]King, Biochemistry, College of Science, Riyadh, Saudi Arabia

Kale (Brassica oleracea species) is considered a functional food whose macronutrient and phytochemical contents are considered beneficial and as such widely considered as a superfood. In the present 6-week cross-over trial with a 2-week washout period we compared the beneficial effects of freeze-dried kale over peas among Arab women with obesity. A total of 124 Saudi women with obesity were allocated to receive either freeze-dried kale ($n=62$) or freeze-dried peas ($n=62$) given in the form of 3-gram sachets thrice daily for two weeks followed by a 2-week washout period and a cross-over of 4 weeks. Anthropometric measurements, glucose, lipids and markers of gut barrier function were assessed at baseline and post-intervention. Participants who took kale supplementation first resulted in significant weight reduction ($P=0.02$) which was not observed among those who took peas first. Participants receiving pea supplementation first experienced a significant decline in Hba1c ($P=0.005$) and CD14 ($P=0.03$), but C-peptide increased ($P=0.05$). Crossover analysis revealed significant carryover effects in most variables with non-significant combined treatment effects. Among the variables with no carryover effect with significant combined treatment effect include HbA1c which was in favor of the pea group ($P=0.005$) and C-peptide modestly in favor of the kale group ($P=0.05$). While both freeze dried kale and pea supplementation appear beneficial, supplementation of freeze-dried pea appears to be more effective in terms of acute glycemic control than kale. The study demonstrates that common by less-hyped vegetables such as pea maybe equally, if not more beneficial than those categorized as superfoods such as kale.

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EP654

Assessment of motor activity of patients undergoing medical rehabilitation

Valeriia Vasileva & Larisa Marchenkova
Federal State Budgetary Institution "National Medical Research Center of Rehabilitation and Balneology" of the Ministry of Health of the Russian Federation, Department of Somatic Rehabilitation of Reproductive Health and Active Longevity, Moscow, Russian Federation

Introduction

Problem of evaluation of the motor activity patients undergoing medical rehabilitation and sanatorium treatment remains relevant, including obesity.

Aim.

To study the nature and degree of disorders of muscle strength, motor and coordination functions in patients undergoing medical rehabilitation and sanatorium treatment.

Material And Methods

Single cross-sectional study included 160 patients aged 40 to 65 years with normal and overweight. The complex of the study included: functional tests and assess muscle strength and balance.

Results

In patients with obesity, compared with persons with normal body weight of the same age, significantly ($P< 0.05$) lower indicators of muscle strength of the right and left arms, strength of the abdominal and back muscles, lower endurance of the abdominal muscles and back muscles and longer time to complete the "Get up and walk" test. Also, in obesity, it turned out to be significantly less time to maintain balance in the 'Stand on one leg' tests on the right and left legs with open eyes. A statistically significant direct relationship was found between the level of back muscle strength ($\gamma = –0.82$, $P=0.0038$) and body weight. A significant relationship was also found between the level of endurance of the back muscles to physical activity and BMI, $\gamma = -0.79$, $P=0.01$. At the same time, there was no relationship between age and the level of endurance of the back muscles to physical activity ($\gamma = 0.107$, $P=0.36$).

Discussion

In patients undergoing medical rehabilitation and health resort treatment, obesity is associated with a decrease in muscle strength and motor activity.

Conclusion

In patients with obesity at the age of 40–65 years, compared with persons with normal body weight of the same age and gender, there is a statistically significant decrease in the muscle strength of the arms, abdomen and back, a longer time to complete the "Get up" test and walk', as well as deterioration in the function of static balance according to the results of the 'Stand on one leg' test.

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EP655

Bidirectional association between fat mass and 25-hydroxyvitamin D in male with type 2 diabetes mellitus

Iryna Kostitska[1], Tetiana Fostun[2], Nadiia Zherdova[3], Oleg Voloshyn[1] & Olga Zhurakivska[1]
[1]Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine; [2]Communal Non-commercial Enterprise "Bogorodchanska Central Hospital", Ivano-Frankivsk, Ukraine; [3]Centre of Innovative Medical Technologies, Kyiv, Ukraine

Introduction

To date, there was evidence for an association between lower serum 25(OH)D levels and higher prevalence of obesity in individuals with type 2 diabetes mellitus (DM). Vitamin D status is inversely associated with the prevalence of obesity in patients with insulin resistance syndrome. Actually, no study that has been specifically performed to investigate the association between vitamin D levels and all the parameters of body composition in obese males with type 2 DM in Ukraine.

Aim of the study

was detect 25-hydroxyvitamin D (25(OH)D) level in obese male with type 2 DM depending on fat mass (FM).

Materials and methods

A total of 31 males with type 2 diabetes have been examined and divided into II groups according to body mass index (BMI): I group ($n=15$) overweight subjects (BMI 26.0-29.9 kg/m^2) and II group ($n=16$) male with obesity (BMI $\geq$ 30.0 kg/m^2). The participants were on average 54.6±6.9 years, type 2 diabetes duration of 12.2± 7.6 years, mean value of glycated hemoglobin (HbA_1C) – 7.7±1,1%. BMI was calculated by a ratio of body weight (in kilograms) and square of height (in meters), expressed in kg/m^2. Body composition parameters (FM, fat free mass (FFM), body cell mass (BCM), total body water (TBW)) were measured by electrical bioimpedance analysis. Serum level of 25(OH)D was detected by electrochemiluminescent method (Roche Diagnostics, Germany) and cobas test system.

Results

Analysis of 25(OH)D level depending on BMI showed revealed the highest level 25(OH)D in male with overweight (28.5±7.3 ng/ml), while the lowest level were in male group II (14.8 ±8.2 ng/ml). Male with type 2 DM of II group have a higher FM level than patients of I group (35.8±6.8 kg vs 31.2±1.9; $P<0.001$). Univariate analysis showed significant differences in FFM(II group: 68.5±9.7 kg vs I group: 50.2±1.8 kg, $P<0.01$); BCM (II group: 41.1±5.5 kg vs I group: 33.2±1.1 kg, $P<0.01$); TBW (group: 52.7±6.3 kg vs I group: 40.4±5.9 kg, $P<0.01$) between II and I groups. The highest correlation between the 25(OH)D levels and FM was observed in patients with obesity ($r= -0.26$; $P<0.01$), and significantly and negatively correlated with BMI ($P<0.001$) and HbA_1C ($P<0.01$).

Conclusion

This study confirms that obesity in males with type 2 DM is associated with vitamin D deficiency and it shows detected significant influence FM on the progression lower serum vitamin D.

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EP656

Psycho-emotional status in patients with metabolic syndrome

Olga Moskalenko & Eduard Vilyamovich Kasparov
Federal Research Center «Krasnoyarsk Science Center» of the Siberian Branch of the Russian Academy of Sciences, KSC SB RAS, Krasnoyarsk, Russian Federation

Metabolic syndrome (MS) is a widespread clinical syndrome, the incidence of which is increasing annually in both developing and developed countries. The prevalence of MS among the working population is quite high (20-25%) and tends to increase. The presence of MS increases the risk of developing type II diabetes and cardiovascular diseases, and anxiety and depression are considered as independent risk factors for the development of MS. It has also been found that the prevalence of anxiety is approximately 10% higher among the group of patients with MS compared to those without MS.

Purpose

to study the psycho-emotional status in patients with metabolic syndrome.

Methods

This study was conducted at the clinic of the Scientific Research Institute of Medical Problems of the North. Inclusion criteria: age (20-60 years); absence of mental, infectious and chronic somatic diseases in the stage of decompensation. All patients were divided into 2 groups: 1) group No. 1 - 76 patients with MS, 2) group No. 2 - 42 practically healthy volunteers who had no concomitant diseases and were not obese. The patients were examined and anthropometric parameters were determined: waist circumference (cm), body weight (kg), BMI (kg/m^2;). The assessment of quality of life (QOL) was determined using the questionnaire «SF-36». The assessment of the psycho-emotional status of patients was carried out using a questionnaire: HADS.

Results

in the course of our study, we found that according to the SF-36 questionnaire, QOL indicators were statistically significantly different in the group of patients with MS relative to the group of patients without MS. Thus, indicators of the level of quality of life are significantly higher in healthy individuals than in obese patients. The differences in all groups are significant ($P \leq 0.05$). It was also found that the average level of parameters on the scale 'physical functioning' decreased by 19.7% ($P < 0.05$), 'role functioning' by 35.2% ($P < 0.05$), 'general health' by 15, 1% ($P < 0.05$), 'vitality' by 18% ($P < 0.05$), 'emotional functioning' by 53.1% ($P < 0.05$). The assessment of the level of anxiety and depression in patients with MS corresponded to a subclinically expressed level, and the level of depression exceeded the indicator in group No. 2 by 19.3%. The level of quality of life in obese patients is significantly lower than in healthy individuals.

Conclusion

The results obtained show that the patterns established in this study should be taken into account when carrying out preventive measures among patients with MS.

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EP657

Environmental factors on childhood obesity: a comparative study

Ben Othman Rym[1], Abadlia Salma[2], Mizouri Ramla[1], Berriche Olfa[1], Talbi Emna[1], Yamoun Rihab[3] & Salem Amal[4]
[1]National Institute of Nutrition and Food Technology, Nutrition A, tunis; [2]Faculty of Medicine of Tunis, Tunis, Tunisia; [3]National Institute of Nutrition and Food Technology, Outpatient department, tunis; [4]National Institute of Nutrition and Food Technology, Nutrition C, tunis

Introduction

Childhood obesity is a major global health problem that has reached alarming levels. We conducted our study to determine the influence of environmental factors on this international scourge.

Methods

It was a comparative study involving 50 obese children (G1) and 35 normal-weight children (G2) aged between 6 and 13 years old. Our study was conducted in the outpatient department of Bechir-Hamza Children's Hospital of Tunis, Tunisia from December 26, 2022 to February 1, 2023. Obesity was determined by WHO growth charts sex-specific BMI for age

Results

We included 85 participants with a mean age of 8.9 ± 3 years for G1 and 8.03 ± 3 for G2 ($P = 0.22$). Obese participants were predominately females (64%). No significant difference in educational levels between G1 and G2 was found ($P = 0.41$), nor in those of their parents ($P = 0.8$). While a tendency for working mothers to have obese children was noted, the association wasn't significant (G1: 48% vs G2: 35%, $P = 0.23$). Besides, socio-economic status was comparable between the two groups ($P = 0.53$). Both G1 and G2 lived mostly in urban areas (G1: 66% vs G2: 68%, $P = 0.7$). Furthermore, G1 and G2 had comparable TV-watching time ($P = 0.06$). However, almost all participants of G1 used cell phones (98%) vs 85% for G2 ($P = 0.03$). In addition, the daily duration of mobile phone use was significantly higher in G1 than in G2 ($P < 0.01$).

Conclusion

These findings emphasize the complex link between environmental factors and childhood obesity, highlighting the need for targeted interventions in addressing this public health challenge

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EP658

Impact of maternal factors on childhood obesity

Ben Othman Rym[1], Abadlia Salma[2], Mizouri Ramla[1], Berriche Olfa[1], Talbi Emna[1], Ghamgui Wissal[3] & Jamoussi Henda[1]
[1]National Institute of Nutrition and Food Technology, Nutrition A, tunis; [2]Faculty of Medicine of Tunis, Tunis, Tunisia; [3]National Institute of Nutrition and Food Technology, Outpatient department, tunis

Introduction

Childhood obesity is influenced by various factors. Maternal health plays a crucial role in this public concern. We carried out our study aiming to uncover key insights into this relationship.

Methods

It was comparative study in the outpatient department of Bechir-Hamza Children's Hospital of Tunis, Tunisia, from December 26, 2022 to February 1, 2023. The study included 50 obese children (G1) and 35 normal-weight children (G2) aged between 6 and 13 years old. World Health Organization growth charts sex-specific Body Mass Index (BMI) for age were used to define obesity.

Results

The average age of participants was 8.9 ± 3 years for G1 and 8.03 ± 3 for G2 ($P = 0.22$). The majority of G1 were females (64%). Maternal pre-pregnancy BMI of G1 was significantly higher than that of G2 (29.9 ± 5 kg vs 27.4 ± 4, $P = 0.02$). Pregnancy was complicated by gestational diabetes in 32% of cases for G1 vs 11.4% for G2 ($P < 0.01$). In addition, average maternal weight gain during pregnancy was significantly greater for G1 (15.6 ± 8 kg vs 8.13 ± 3 k g, $P < 0.01$). Moreover, macrosomic infants were more likely to develop childhood obesity (46% of G1 were born macrosomic vs 14.3%, $P < 0.001$). We also noticed that G1 exhibited lower rates of breastfeeding compared to G2 (80% vs 94.3%, $P = 0.04$). It's interesting to also note that the average duration of breastfeeding was shorter for G1 (6.2 months vs 9.9 months, $P = 0.04$).

Conclusion

These findings highlight the significant link between maternal health and childhood obesity, emphasizing the need for targeted interventions.

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EP659

Hyponatremia in patients receiving total enteral nutrition (TEN): the importance of appropriate treatment

Cristina Serrano Valles[1], Emilia Gómez Hoyos[2], Ana Ortolá Buigues[2], Rebeca Jiménez Sahagún[2], Susana García Calvo[3], Juan Jose Lopez Gómez[2], Beatriz Torres Torres[2], Esther Delgado García[2] & Daniel de Luis Román[2]
[1]Hospital General de Segovia (HGSE), Servicio de Endocrinología y Nutrición, Segovia, Spain; [2]Hospital Clínico Universitario de Valladolid., Servicio de Endocrinología y Nutrición, Valladolid, Spain; [3]Complejo Asistencial de Palencia. Hospital Rio Carrión, Servicio de Endocrinología y Nutrición, Palencia, Spain

Introduction

Hyponatremia is the most frequent disturbance in hospitalized patients. The appropriate treatment of non-severe hyponatremia according to the clinical guidelines is essential to achieve an effective response defined as eunatremia (Serum sodium >135 mmol/l). The aim of this study was to know the relationship between appropriate treatment and effective response in patients with enteral tube feeding (TEN).

Methods

An observational, prospective study during 24 months. The study was designed in non-critically hyponatremic patients receiving TEN and presenting hyponatremia. Data collected included sex, age, clinical volemia, type of treatment and serum sodium levels before, 72 hours and one week after started treatment.

Results

87 patients were included, 62,1% males, age 76 (IR 67–84) years. 8,0% were hypovolemic, 86,0% were euvolemic and 6,0% were hypervolemic. 39 patients

(44,8%) received appropriate treatment, in 100% hypovolemic, 83,3% euvolemic and 100% hypervolemic patients. Eunatremia was reached by 74%: 5,1% of hypervolemic; 64,1% of euvolemic patients and 5,1% in hypovolemic patients. The percentage of patients achieving eunatremia following one week was 38,4% and the median of time between hyponatremia diagnostic and the start of treatment was 3,0 [RIQ 3,9-14,0] days.
Conclusion
The appropriate treatment was established in almost half of the hyponatremic patients with TEN. An effective response was achieved in the majority of patients within a week of the beginning treatment.

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EP660

Evaluating Unhealthy dietary habits: A Study on Fast Food and Sugary Beverage Consumption Among Teachers in Southern Tunisia

Ahmed Trigui[1], Houda Ben Ayed[2], Mariem Ben Hmida[1], Mouna Baklouti[2], Mondher Kassis[1] & Sourour Yaich[3]
[1]Habib Bourguiba University Hospital, Preventive Medicine and Hospital Hygiene Department, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Preventive Medicine and Hospital Hygiene Department, Sfax, Tunisia; [3]Hedi Chaker University Hospital, Preventive and Community Medicine Department, Sfax, Tunisia

Introduction
Unhealthy dietary habits, such as the consumption of fast food and carbonated beverages, are associated with various health risks. Given their significant role in society, teachers are a group of particular interest in the context of health-related concerns. This study aimed to assess the prevalence of fast food and carbonated beverage consumption among teachers and to explore the influencing factors of these habits.
Methods
This cross-sectional study was conducted among a randomized sample of public-school teachers at all educational levels, including primary, middle, and high schools, within Sfax Governorate in Southern Tunisia during the period March-April 2021.
Results
Among the 525 teachers, 80.8% ($n=424$) were of urban origin. The sex ratio was 1.23. The median age of teachers was 48 years, ranging from 20 to 68 years. We noted that 101 teachers (19.2%) were obese. Regarding weight perception, suboptimal adherence to healthy weight perception was observed among 70.9% of teachers ($n=372$). In terms of dietary habits, 20.2% ($n=106$) reported consuming fast food or carbonated beverages more than twice a week, while 52.2% ($n=274$) consumed fruits or vegetables daily. A significantly higher prevalence of fast food or carbonated beverage consumption was observed among teachers with post-university educational level compared to those with university educational level (34% vs 19.5%; $P=0.02$). Multivariate analysis showed that age (Adjusted odds ratio ORA) = 0.96; 95% confidence interval (CI) [0.93, 0.98]; $P=0.01$) and female gender (AOR = 0.44; 95%CI [0.27, 0.7]; $P=0.01$) were independently associated with a lower prevalence of fast food or carbonated beverage consumption. Additionally, fast food or carbonated beverage consumption was independently associated with higher alcohol consumption (AOR = 2.16; 95%CI [1.06, 4.4]; $P=0.03$) and pasta consumption (AOR = 1.73; 95%CI [1.1, 2.7]; $P=0.01$).
Conclusion
This study highlighted the prevalence of fast food and carbonated beverage consumption among teachers and identified significant associated factors. These findings underscore the need for targeted interventions to promote healthier dietary habits, especially among teachers at specific risk.

Keywords: Unhealthy Dietary Habits/Fast Food Consumption/Sugary Beverage Consumption/Teachers' Health/Southern Tunisia Study

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EP661

Effect of low muscle mass on total mortality related to metabolic disease in patients with chronic kidney disease in US adults

Dong Sun Kim & Jung Hwan Park
Hanyang University College of Medicine, Department of Internal Medicine, Seoul, Korea, Rep. of South

Background
Sarcopenia is associated with mortality in patients with chronic kidney disease (CKD). However, the extent to which sarcopenia contributes to this risk, either independently or in conjunction with metabolic abnormalities and frailty, remains unclear. Therefore, this study aimed to explore the associations among sarcopenia, frailty, central obesity, metabolic abnormalities, cardiovascular risks, and mortality.
Methods
This study used data from the National Health and Nutrition Examination Survey (NHANES) 1999–2006 and 2011–2018. Low muscle mass was defined as Appendicular Skeletal Mass Index <7 kg/m^2 in men or <5.5 kg/m^2 in women. The follow-up duration was from the first anthropometric and clinical measurements to death or the last follow-up (December 31, 2019).
Results
This study enrolled 2072 patients with CKD. Low muscle mass was associated with a significantly reduced risk of metabolic abnormalities. Conversely, central obesity was associated with a significant increase in the risk of metabolic abnormalities and frailty. Notably, although low muscle mass was associated with an elevated mortality risk, central obesity did not show a significant association. Subsequent analysis using propensity score matching showed similar results. Furthermore, mediation analysis indicated that the effect of low muscle mass on mortality was mediated directly through frailty and metabolic abnormalities. Despite the inverse relationship between low muscle mass and metabolic abnormalities, low muscle mass is directly associated with an increased risk of all-cause mortality.
Conclusion
Low muscle mass may play a direct role in the pathogenesis of mortality in patients with CKD, independent of metabolic abnormalities and frailty.

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EP662

Eating behavior patterns, metabolic parameters, and circulating levels of oxytocin in patientswith obesity: a prospective pilot study

Giorgia Maria Baldazzi, Davide Masi, Chandra Massetti, Maria Letizia Spizzichini, Fiammetta Cipriani, Elena Colonnello, Maria Ignazia Curreli, Mikiko Watanabe, Stefania Mariani, Lucio Gnessi & Carla Lubrano
Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy

Introduction
Obesity is a chronic disease, significantly influenced by maladaptive eating patterns. Oxytocin (OT), recognized for its central role in regulating energy metabolism and eating behavior, represents a potential link in understanding this intricate relationship.
Objective
This study aimed to investigate the potential association between circulating levels of OT and maladaptive eating behaviors, assessed through the Eating Behaviors Assessment for Obesity (EBA-O) questionnaire, in correlation with clinical, anthropometric, metabolic and body composition parameters in a population with obesity.
Materials and Methods
Our prospective, observational study was conducted at the Highly Specialized Center for the Treatment of Obesity at La Sapienza University of Rome. The cohort included adult individuals with obesity. Comprehensive evaluations included anthropometric analysis, body composition analysis by bioimpedance analysis, complete biochemical and hormonal profile, measurement of plasma OT concentration by ELISA, and an in-depth assessment of dysfunctional eating behavior using the EBA-O questionnaire.
Results
21 participants (16 females, 5 males) with a mean age of 45.67 ± 15.07 years, a mean BMI of 40.89 ± 8.02 kg/m^2;, and a mean plasma OT concentration of 1365.61 ± 438.03 pg/ml were enrolled. Interesting associations emerged, demonstrating significant correlations between various dysfunctional eating behaviors. Specifically, individuals exhibiting food addiction tendencies often had concomitant manifestations in multiple EBA-O domains ($P<0.05$), excluding night eating. Lower waist-to-hip ratios were observed in individuals exhibiting food addiction. In addition, the Receiver Operating Characteristic (ROC) analysis demonstrated that OT levels below 1312.55 pg/ml were predictive of food addiction, displaying a sensitivity of 100% and a specificity of 62.5%. The presence of night eating was correlated with elevated lipid profiles - triglycerides ($P<0.001$) , total cholesterol ($P=0.05$), and TG/HDL ratio ($P=0.02$) - while hyperphagic behaviors were correlated with increased hepatic steatosis index (HSI) ($P=0.05$). Positive correlations were established between circulating OT levels and BMI ($r=43$; $P<0.05$), HOMA-IR ($r=0.55$; $P=0.014$), HSI ($r=0.46$; $P=0.049$), and estradiol in the female population ($r=0.72$; $P=0.002$).
Conclusions
This study highlights the complex interaction of maladaptive eating traits assessed through the EBA-O, showing associations and predictive potential, particularly in identifying markers of food addiction. Further in-depth clinical investigations are essential to validate the utility of EBA-O and circulating OT as diagnostic markers of dysfunctional eating behaviors in the context of obesity.

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EP663

Exploring the Genetic Landscape of Obesity: A Family Report of a Genetic Variant of BBS10 Gene

Leandro Augusto Silva[1,2], Gonçalo Varela Cunha[1,2], Rui Pina[2], Benilde Barbosa[2,3], José Pereira de Moura[2,3] & Lèlita Santos[2,3]
[1]Portuguese Institute of Oncology of Coimbra Francisco Gentil; [2]Local Health Unit of Coimbra; [3]Faculty of Medicine of University of Coimbra

Introduction
Bardet-Biedl Syndrome is a rare autosomal recessive disease characterized by defects in multiple organ systems, presenting with diverse clinical manifestations such as retinopathy, polydactyly, obesity, intellectual developmental disorders, hypogonadism, renal dysfunction, among others.
Clinical Case 1
49-years-old female, case index, followed multidisciplinary since the age of three due to progressive night blindness from generalized retinal dystrophy, learning difficulties, primary amenorrhea and polycystic ovary syndrome, epilepsy, metabolic syndrome (grade 2 obesity, grade 1 hypertension, dyslipidemia), chronic kidney disease and musculoskeletal alterations (macrocephaly, short stature, and scoliosis). It is worth highlighting parental consanguinity. Given the phenotype clinically suggestive of Bardet-Biedl Syndrome, a whole exome sequencing was performed revealing the genetic variant c.1542del p.(Asp515IIefs*9), in apparent homozygosity, of the *BBS10* gene, classified as likely pathogenic, confirming the diagnosis.
Clinical Case 2
45-years-old male, brother of case index, followed since childhood for retinal dystrophy with progressive bilateral night blindness, intellectual developmental disorder, metabolic syndrome (grade 3 obesity, dyslipidemia, type 2 diabetes under insulinotherapy), chronic kidney disease, moderate unilateral sensorineural deafness requiring hearing aid and musculoskeletal alterations (scoliosis and macrocephaly). As in the index case, the patient was advised in a medical genetics' consultation and the same genetic variant was identified, confirming the genetic diagnosis of Bardet-Biedl Syndrome.
Clinical Case 3
36-years-old male patient, first cousin of the above-mentioned individuals, also followed since childhood for bilateral retinal dystrophy, intellectual developmental disorder, cryptorchidism treated with orchidopexy in childhood, grade 1 obesity and arterial hypertension. Additionally, post-axial bilateral polydactyly in the feet. Given the similar phenotype, genetics consultation was performed and the same genetic variant was identified in homozygosity. Genetic counseling for the family was provided.
Conclusion
This report presents three cases of Bardet-Biedl Syndrome within a family, detailing the associated diagnosis process, emphasizing the role of identifying a clinical phenotype and guiding genetic studies. The cases underscore the importance of early recognition of characteristic phenotypes where obesity is a key element, often overlooked, limiting proper patient management.

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EP664

The impact of weight and BMI on prostate cancer severity through PSA levels - real-world data from a Romanian center

Theodor Mustata[1], Dan Jinga[2], Ioana Lazar[2] & Simona Fica[1,3]
[1]Carol Davila University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania; [2]Neolife Medical Center, Oncology, Bucharest, Romania; [3]Elias Emergency University Hospital, Endocrinology, Bucharest, Romania

Introduction
Prostate cancer is the second most frequent malignancy in men, with more than 1.4 million new cases diagnosed in 2020[1]. Obesity, on the other hand, has reached epidemic proportions, with 59% of adults living with overweight or obesity in Europe[2]. Our aim was asses the impact of weight and BMI on prostate cancer (PCa) severity, reflected in PSA levels.
Methods
We analyzed 225 patients diagnosed with PCa between August 2001 and May 2022 through transrectal prostate biopsy and referred to the Oncology Department of Neolife Medical Center in Bucharest, Romania. Weight, BMI and PSA levels were noted at diagnosis. Lining up with the NCCN risk stratification[3], we divided the patients into two PSA groups: <20 ng/ml and ≥ 20 ng/ml.
Results
Obesity was seen in 71 (31.6%) patients. Median PSA level (IQR) was 12.8 (29.4) ng/ml. 143 (63.6%) patients had PSA <20 ng/ml, while 82 (36.4%) ≥ 20 mg/ml. Binary logistic regression analysis was performed to asses the effects of weight on the risk of having PSA levels >20 ng/ml. An increase in weight was associated with a decreased likelihood of having PSA >20 ng/ml (OR $=$ 0.974, 95% CI: 0.954 – 0.994, $P=0.011$). Similarly, binary logistic regression analysis was performed to asses the effects of BMI on the risk of having PSA levels >20 ng/ml. An increase in BMI was associated with a decreased likelihood of having PSA >20 ng/ml (OR $=$ 0.925, 95% CI: 0.864 – 0.989, $P=0.023$). There was a good capacity of weight (AUROC $=$ 0.604, 95% CI: 0.527 – 0.682, $P=0.009$; cut-off $=$ 81.5 kg, Se $=$ 57.3%, S$P=60.8$%) and BMI (AUROC $=$ 0.583, 95% CI: 0.505 – 0.661, $P=0.038$; cut-off $=$ 24.7 kg/m^2, Se $=$ 32.9%, S$P=81.1$%) to predict the presence of PSA levels >20 ng/ml.
Discussions
It is known that the hemodilution and lower testosterone levels in patients with obesity are associated with lower PSA levels. Ultimately, obesity could delay PCa diagnosis through lower PSA levels.
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EP665

Predictive factors of Cardiovascular and metabolic complications of obesity:About 502 cases

imane HASBI[1], Nassim Essabah Haraj[2], Siham El Aziz[2] & Asma Chadli[2]
[1]Ibn Rochd University Hospital, Endocrinology and Metabolic Diseases Department, Casablanca, Morocco; [2]Ibn Rochd University Hospital, Endocrinology and Metabolic Diseases, Casablanca, Morocco

Introduction
Obesity, a multifactorial chronic disease resulting from the interplay of genetic and environmental factors, is associated with numerous complications that can impact both vital and functional prognosis. The aim of our study was to analyze the epidemiological, clinical, and paraclinical characteristics of cardiovascular and metabolic complications related to obesity while identifying associated predictive factors.
Patients and methods
In this retrospective study, 502 obese patients were included, recruited from the Endocrinology Department of Ibn Rochd University Hospital in Casablanca. A clinical evaluation including anthropometric parameters and a biological assessment was conducted. The statistical analysis was performed using the SPSS software, version 25.
Results
The average age of our patients was 51.7 ± 3 years, with a clear female predominance (83.5%). The mean body mass index (BMI) was 35.2 kg/m^2, and the mean waist circumference (WC) was 113.8 cm. Notably, 88.4% of patients had at least one obesity-related complication, with an average of 4.5 complications per patient. Metabolic complications were predominant (88.6%), including 79.3% with diabetes, 66.5% with dyslipidemia, and 7.8% with hyperuricemia. Cardiovascular complications were present in 37.4%, dominated by hypertension (90.5%), followed by coronary insufficiency (7.4%), heart failure (6.2%), and myocardial infarction (5.6%) . Age and waist circumference (WC), but not gender and BMI, were identified as predictive factors for metabolic complications. However, cardiovascular complications were significantly correlated with age, BMI, and waist circumference.
Conclusion
Obesity is associated with a range of complications that impact quality of life and pose a threat to vital prognosis. Understanding the predictive factors for these complications allows for anticipation and early intervention, thereby reducing the morbidity and mortality associated with obesity.

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EP666

Monogenic obesity prevalence and response to bariatric surgery in a cohort of Emirati patients

Tanveer Ashraf[1], Budour AlKaf[1], Saradalekshmi Radha[1], Esphie Fojas[1], Amal Baqer[1], Rayan Khaled[1], Sara Suliman[2], Matthew Allum[2] & Nader Lessan[1]
[1]Imperial College London Diabetes Centre, Research Institute, Abu Dhabi, United Arab Emirates; [2]Imperial College London Diabetes Centre, Diabetes & Endocrinology, Abu Dhabi, United Arab Emirates

Introduction
We have previously shown good short-term but variable long-term weight loss outcomes of bariatric surgery (BS) in a cohort of obese patients with MC4R deficiency. This study aims to elucidate the epidemiological landscape of Monogenic Obesity (MO) and quantify bariatric surgery's effectiveness in weight reduction among Emirati patients with severe obesity.
Methods
We selected a group of patients with extreme obesity (>50 kg/m^2) from our prospective BS cohort for genetic testing (MO genes including LEPR, PCSK1, POMC, MC4R and *BDNF*. Combined Annotation-Dependent Depletion (CADD) and Sorting Intolerant From Tolerant (SIFT) tools were used to measure variant deleteriousness. Relevant linked information including anthropometry, type (and number) of bariatric surgery, diabetes status and glycosylated haemoglobin were available from prospectively conducted questionnaires and patient records. Patients confirmed to have mutations (cases) with complete follow-up data ($n=14$) were compared to controls who were tested and in whom no mutations were found ($n=35$); relevant comparisons were made over 2 years (baseline, median of 3-, 6-, and 12-months post-surgery).
Results
The bariatric surgery cohort included 1089 patients (56% were males); 828 had recorded information on the type and number of surgeries (mean age of 38.6 ± 11.3 years). Diabetes status was identified as T2DM (64), IFG (54), IGT (17) and IFG+ IGT (15). 129 (42%) patients were NGT; 41 patients had unrecorded diabetes status. 84 patients (11 %) underwent multiple (79 with two) surgeries. 190 morbidly obese patients (age 40.0 ± 5.1 years; BMI 54.73 ± 10.49 kg/m^2) were selected and genotyped. 29 mutations (15.2 %, $n=26$) were found, of which four were novel polymorphisms of the UCP2 and MC4R genes. Baseline HbA1c was 6.02 ± 1.25%. Compared to baseline, there were significant decreases in HbA1c, total weight and BMI at all time points over 24 months. The largest drop in weight occurred at 3 months post-surgery (172.10 ± 31.31 to 119.05 ± 17.70 kg). There was a reduction in HbA1c to 5.14 ± 0.45 twelve months post-surgery. Percentage and excess weight loss were significantly less, compared to baseline, at all time points when comparing the cohort with mutations with controls without mutations.
Discussion
The prevalence of monogenic obesity is high (15.2% in our cohort, including four novel mutations) in patients with extreme obesity (BMI >50 kg/m^2) undergoing bariatric surgery. Overall, the response to BS is acceptable but less than a comparator group without MO.

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EP667

Osteocalcin: relation to glucose metabolism in young women with obesity

Piterschi Carolina[1], Vudu Stela[2], Rizov Cristina[2] & Lorina Vudu[1]
[1]'Nicolae Testemitanu' State University of Medicine and Pharmacy, Laboratory of Endocrinology, Chisinau, Moldova; [2]'Nicolae Testemitanu' State University of Medicine and Pharmacy, Department of Endocrinology, Chisinau, Moldova

Introduction
Osteocalcin is a bone-specific hormone also involved in regulation of glucose and fat mass metabolism. It regulates energy expenditure by acting on adipocytes and pancreatic islet cells. The aim of the present study was to examine the relation between serum osteocalcin and glucose metabolism in young women with obesity.
Material and methods
A total of 66 healthy women were included in the analysis. Data on body mass index (BMI), waist circumference (WC), serum osteocalcin, fasting plasma glucose (FPG) and insulin levels were collected. Insulin sensitivity was estimated by homeostasis model assessment for insulin resistance (HOMA-IR = [glucose (mmol/l) × insulin (mIU/l)]) and by quantitative insulin sensitivity check index (QUICKI index = 1/[log (insulin in mIU/l) + log (glucose in mmol/l)]). All measurements were done in the morning after an 8-h overnight fast.
Results
The participants of the study were classified according to their weight status, 36 women with obesity (BMI ≥30 kg/m^2, WHO) and 30 normal weight women (BMI $\leq$ 25 kg/m^2). The mean age was 33.1 ± 5.9 years and was similar in both groups. Serum osteocalcin was significantly lower in women with obesity than in normal weight women (8.9 ± 4.1 vs 13.8 ± 6.9 ng/ml, $P=0.009$). Insulin resistance was detected by HOMA-IR in 55.5% and by the QUICKI index in 68.2% in women with obesity and no cases of insulin resistance in normal weight women. Serum osteocalcin was inversely associated with BMI ($P=0.02$), waist circumference ($P=0.021$), FPG ($P=0.003$) and fasting insulin ($P=0.004$). Moreover, osteocalcin was inversely associated to HOMA-IR ($P=0.028$) and QUICKI index ($P=0.020$).
Conclusion
These results suggests that serum osteocalcin concentration was significantly lower and inversely associated with blood markers of glucose metabolism, insulin secretion, insulin resistance and adiposity in young women with obesity.

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EP668

Evolution of metabolic-associated fatty liver desase measured by fibroscan and biopsy in patients with morbid obesity undergoing bariatric surgery

Miguel Damas-Fuentes[1], Victor Simon-Frapolli[1], Marta Generoso-Piñar[1], José María Pinazo-Bandera[2], Francisco José Tinahones Madueño[1] & Lourdes Garrido Sánchez[1]
[1], Endocrinology and Nutrition; [2], Hepatology

Introduction
Metabolic dysfunction-associated fatty liver disease (MAFLD) is present in a high percentage of obese patients undergoing bariatric surgery (BS), being an effective strategy for the remission of MAFLD. A significant proportion of patients still have steatohepatitis even after considerable weight loss and metabolic improvements. Liver biopsy remains the definitive test to classify a patient with steatohepatitis, but it is an invasive test. The use of non-invasive techniques such as Fibroscan would avoid the limitations and risks that biopsy can cause in this group of patients.
Objective
To evaluate the effect of CB on the improvement of steatohepatitis in patients with morbid obesity (MO), classified according to type 2 diabetes (T2D).
Material and Methods
Patients with morbid obesity and steatohepatitis undergoing CB and classified according to T2D (non-T2D vs T2D). Liver biopsy was performed during BC in order to determine the status of steatohepatitis or fibrosis. Patients underwent Fibroscan before surgery and one year after. Clinical, anthropometric and biochemical variables were measured and liver fibrosis scores (FLI, NFS, APRI, FIB4, Hepamet) were calculated.
Results
Previous BMI (49 kg/m^2) and the average weight (135 kg.), as well as the liver biopsy result were similar in the two cohorts studied, diabetics and non-diabetics. Likewise, BMI (33) and average weight (91) were similar one year after surgery in both groups. Fibroscan was equally similar in both groups, prior to the surgical intervention, reflecting a significant improvement, especially in the non-diabetics, but also in the diabetics, after surgery.
Conclusions
The impact of bariatric surgery improving different parameters associated with metabolic syndrome, achieving regression of most serious stages of MAFLD and remission of T2D in a high percentage of patients, makes it as a valid metabolic therapy, especially in cases of severe obesity.

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EP669

Pre-surgical Factors and Their Influence on Therapeutic Response to Bariatric Surgery

Alice Monsanto[1], Tânia Carvalho[1], Gustavo Rodrigues[1], Mara Ventura[1,2,3], Dírcea Rodrigues[1,2] & Isabel Paiva[1]
[1]Hospitais da Universidade de Coimbra - Unidade de Saúde Local de Coimbra, Endocrinology, Diabetes and Metabolism, Coimbra, Portugal; [2]Faculdade de Medicina – Universidade de Coimbra; [3]Faculdade de Ciências da Saúde - Universidade da Beira Interior

Introduction
Bariatric surgery continues to stand as the most effective therapeutic intervention in treating severe obesity. However, a portion of patients experiences less satisfactory outcomes, diminishing the overall beneficial impact of this intervention. Identifying predictive factors for unsatisfactory responses to bariatric surgery could represent a crucial step in evaluating candidates, enabling the establishment of personalized care.
Methods
Retrospective cohort study, including patients submitted to bariatric surgery (gastric bypass or vertical gastrectomy) between January 2016 and December 2020. Initial suboptimal clinical response/insufficient weight loss (IWL) assessed based on the criteria of Total Weight Loss (TWL) at nadir <20% and Excess Weight Loss (EWL) at nadir <50%. Late post-operative clinical deterioration/significant weight regain (WR) evaluated by weight gain ≥10 kg compared to the nadir weight. Follow-up over 36 to 60 months. The relationship between IWL and WR was assessed, considering preoperative factors: comorbidities (cardiovascular and psychiatric),

anthropometric characteristics, and pharmacology. The statistical evaluation was conducted using the chi-square test, t-test, Mann-Whitney U test.
Results
98 patients were evaluated, 52% undergoing gastric bypass, 79.6% having a preoperative BMI $\geq$ 40 kg/m^2. The prevalence of cardiovascular comorbidities was: 50% hypertension, 51% dyslipidemia and 24.5% diabetes mellitus. Postoperative follow-up was conducted for up to 60 months in 55.1% of the patients. At the nadir weight, TWL was 31.9$\pm$8.6%, and EWL was 63.6$\pm$18.8%. Insufficient weight loss occurred in 11.2 to 18.4% of patients, and weight regain occurred in 34.7%, median increase of 13.6 (10; 22.6) kg. The following relationships were observed: IWL and dyslipidemia (P=0.03), type of surgery (P=0.017), and use of antiepileptics (P=0.001); WR with preoperative BMI (P=0.005), diagnosis of psychiatric disease (P=0.020), use of antidepressants (P=0.007), and use of antiepileptics (P=0.005). The relationship between the initial suboptimal clinical response and the remission of comorbidities in the postoperative period was assessed. A lower remission rate of diabetes in patients with IWL relationship was observed (P=0.037).
Conclusions
The initial suboptimal clinical response was found to be influenced by the type of surgery, the preexistence of a dyslipidemia diagnosis, and the use of antiepileptic medications. On the other hand, late postoperative clinical deterioration was mainly influenced by psychiatric disease and the use of antidepressants and antiepileptic medications. It was also observed that the occurrence of an initial suboptimal clinical response may impact the rate of remission of diabetes, reinforcing the importance of weight loss in the course of metabolic diseases.

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EP670

Weight variation in diabetic women during and after pregnancy

Chaima Sdiri, Haifa Abdesselem, Emna Bornaz, Mariem Cheikhrouhou, Fatma Boukhayatia, Asma Ben Brahim, Rim Yahyaoui, Kamilia Ounaissa & Chiraz Amrouche
National Institute of Nutrition, Department of Nutritional Diseases (D), Tunis, Tunisia

Background
According to several previous studies, breastfeeding offers mothers an opportunity to lose weight and improve their metabolic profiles. The aim of the present study was to investigate weight variation in a population of postpartum diabetic women.
Methods
We conducted a prospective descriptive study in pregnant women treated for pregestational diabetes and followed at the Department of Nutritional Diseases «D» of the National Institute of Nutrition of Tunis. Women's weight was monitored during pregnancy and two months postpartum. A dietary survey was carried out by the department's dietician. Women who had an abortion or had been lost to follow-up were excluded from the study.
Results
We collected 51 diabetic patients with a mean age of 35.4$\pm$4 years [ext:23-44]. Most patients had type 2 diabetes (80%). Before pregnancy, the average body mass index (BMI) was 28.3$\pm$4.7 kg/m^2;. Pre-pregnancy obesity and pre-obesity affected 26% and 48% of the population, respectively. The average weight gain during pregnancy was 9.6$\pm$3.5 kg [ext:5-20]. This weight gain was 27.7$\pm$3.6 kg/m^2; for exclusive breastfeeding, 28$\pm$5.2 kg/m^2; for partial breastfeeding and 30.9$\pm$6.6 kg/m^2; for formula feeding. We noted that weight loss was correlated with breastfeeding pattern (P=0.015). When asked about their knowledge of the nutritional needs of breastfeeding women, 48% of patients had no idea of the nutritional requirements of breastfeeding women. By analyzing patients' dietary intake, women who exclusively breastfed their babies had a more high-calorie energy intake (63% of cases) than women who did not breastfed (38% of cases) or who partially breastfed (2% of cases) their babies (P<0.001). In addition, all patients were not physically active during pregnancy or after childbirth.
Conclusion
We can conclude that breastfeeding is associated with weight loss, but this remains modest in our sedentary diabetic patients. Nutrition education is the cornerstone of care for postpartum patients.

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EP671

Perceived obesity among patients with type 2 diabetes in albania

Dorina Ylli[1,2], Arbi Mulhaxhia[1], Sigi Mehalla[1], Violeta Hoxha[2], Klodiana Poshi[1,2], Marjeta Kermaj[2] & Agron Ylli[1,2]
[1] University of Medicine Tirana, Tirana, Albania; [2]Mother Teresa University Hospital Center, Endocrinology, Tirana, Albania

Background
This study seeks to assess the precision of obesity perception among patients diagnosed with type 2 diabetes (DMT2), acknowledging obesity as a pivotal modifiable risk factor crucial for diabetes prevention. Furthermore, it is important to unveil and analyze the factors that contribute to the misperceptions of obesity within DM patients.
Methods
This study aims to investigate a cohort of consecutive patients treated at the Endocrinology Unit of Mother Teresa University Hospital Center in Tirana during the period from September to November 2023. A questionnaire was used to collect subjective information as weight perception, lifestyle factors, and glycemic knowledge. Complementary objective measures were extracted from medical records, such as Body Mass Index (BMI), Hemoglobin A1c (HbA1c) levels, High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), and Triglyceride levels.
Results
In our cohort of 59 participants, 59.32% had diabetes. 74.30% of the DM patients had a misperception of their weight classification. The mean age was 56.2$\pm$15 years. Among patients with misperception, 65.3% perceive themselves as overweight but were obese, 19.23% perceive themselves as normal weight but were overweight or obese, and 15.38% perceive themselves as underweight but were normal weight. Despite this misperception, a strong correlation exists between their self-reported weight and the real weight. DM patients with misperception mainly attribute the cause of their obesity to the administration of multiple medications (31.71%), followed by lack of movement (27.23%), diabetes (22.76%), overeating (13.62%), and genetic factors (4.66%). In contrast, patients with accurate perceptions primarily attribute obesity to overeating (65.75%).
Conclusions
The study reveals a notable prevalence of body misperceptions (74.30%) regarding weight classification among DM patients, emphasizing the need for targeted interventions to improve awareness. Various factors identifying as the causes of obesity among patients with DM underscore the importance of tailored education and counseling for effective diabetes management.

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EP672

Impact of cakut syndrome and UTI on pediatric BMI

Svitlana Suchok, Oleksandr Yakymenko & Nitin Gupta
National Pirogov Memorial Medical University, Vinnytsya, Pediatric Surgery, Vinnytsia

Background
Several recent studies suggest that continuous low-dose antibiotics prophylaxis used in VUR may affect the growth of children. Guidos P.J. *et al*. (2018) found a significant increase in BMI in children who had prior antibiotic usage. CAKUT syndrome involves both the kidney and urinary tract and generally is associated with antibiotic therapy among pediatric patients and metabolism of waste products.
Aim
We aimed to evaluate the impact of congenital genitourinary defects (CAKUT syndrome) on BMI in pediatric patients compared to patients without structural pathology.
Materials and methods
We prospectively enrolled 49 pediatric patients admitted to the surgical and nephrological departments from June 1 to November 31, 2023. All patients were divided into two groups: study group (n=27) – CAKUT syndrome (VUR, PKD, horseshoe kidney, renal agenesis/hypoplasia, etc.) and prior/current episodes of CAP; control group (n=22) – UTI, without CAKUT (proved by US, VCUG or CT). All patients underwent complete work-up including clinical examination, evaluation of BMI according to WHO standards(underweight, healthy weight, overweight, obese, renal function tests (creatinine, urine, GFR), and imaging studies (US and/or VCUG/CT). Written informed consent was obtained from the parents. P<0,05 was considered significant.
Results
In the study group, 7.4% of patients were obese; 14.8% - overweight; 51.8% -healthy weight; 26% -underweight. BMI distribution in the control group: 4.5% -obese; 4.5% -overweight, 72.7% -healthy weight; 18.3% -underweight. We observed no significant risk of obesity (OR=1.68; 95% CI 0.1422 to 19.8541; P=0.06805), being overweight (OR=3.6522; 95% CI 0.3774 to 35.3435; P=0.2633) or underweight (OR=1.575; 95% CI =0.3948 to 6.2839; P=0.5199) among children with CAKUT syndrome comparing to their peers without congenital defects of urinary system.
Conclusion
CAKUT syndrome does not affect pediatric BMI. There is the same risk of being obese, overweight, or underweight among children with and without congenital defects of urinary system and UTI.

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EP673

Anthropometric profile in asthma

Mehrez Achwak[1], Chaima Jemai[1], Tesnim Farhat[2], Khouloud Chaabi[3], Hichem Aouina[3], Zohra Hadj ali[1], Yosra Htira[1] & Faika Ben Mami[1]
[1]The national institut of nutrition of Tunis, Department C, Tunisia; [2]Nutrition studies university, Tunisia; [3]Charles Nicole Hospital, Pneumology Department, Tunisia

Introduction
Asthma is a multifactorial disease, resulting from the interaction of genetic, environmental, behavioral and social factors. These components can play a role in disease onset, progression and control. More specifically, one of the factors that could influence asthma control is obesity. The aim of this study was to analyze the anthropometric profile and body composition of a population with asthma.
Methods
Descriptive cross-sectional study over 6 weeks, involving 40 patients followed up at the pulmonology outpatient clinic. Patients included in the study had their weight, height and BMI measured. Body composition was studied using a professional bioelectrical impedance meter.
Results
The population comprised 32 women and 8 men, with a mean age of 46.15 ± 14.13 years. Mean weight was 75.9 ± 12.6 kg with a mean BMI of 29.1 ± 5.7 kg/m^2;. Three quarters of the study population were overweight: 27.5% were overweight, 30% were obese class 1 and 17.5% were obese class 2. Regarding the results of the body composition study: mean body fat was 34.96 ± 10%; mean fat mass was 27.56 ± 10.76 kg; mean lean mass was 48.92 ± 6.65 kg and bone mass was 2.38 ± 0.30 kg. Mean visceral fat was 8.88 ± 4.07 kg. Poor asthma control was associated with higher fat mass, but p was not significant.
Conclusion
Obesity is among the key factors contributing to poor asthma control. By adopting a multidisciplinary approach involving dieticians and physiologists, it is possible to optimize clinical outcomes and provide patients with comprehensive management to facilitate the adoption and maintenance of good dietary habits, by providing specialized and personalized support.

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EP674

Nutritional deficiencies in obese patients

Benzineb Sara[1], Imane Motaib[2], Saloua Elamari[2], Soukaina Laidi[1] & Marouan Fatima[2]
[1]Cheikh Khalifa Bin Zayd Al Nahyan Hospital-University Mohamed VI of Health Sciences, Endocrinology, Casablanca, Morocco; [2]Cheikh Khalifa Bin Zayd Al Nahyan Hospital-University Mohamed VI of Health Sciences, Endocrinology, Casablanca

Introduction
Nutritional deficiencies are a lesser-known complication of obesity despite their frequency. The aim of this study was to identify nutritional deficiencies in obese patients.
Materials and methods
This was a prospective study, which included all patients with a BMI greater than 30 kg/m^2 followed up in the endocrinology department of the Cheikh Khalifa Ibn Zaid Hospital in Casablanca, Morocco. The study began in January 2023. For each patient, we collected anthropometric data, evaluated the dietary survey, traced vitamins and elements such as vitamin D, folic acid, ferritinemia and albuminemia.
Results
The preliminary results of the dietary survey of the 20 patients showed insufficient consumption of fruits (13.3%), vegetables (6.7%) and dairy products by 26.7%, with consumption of foods with a high caloric value but of low nutritional quality, reduced physical activity, and a prevalence deficiencies of 33%, of which 46% were vitamin D deficient, 33% vitamin D deficient, 46% iron deficiency, 6.7% hypoalbuminemia and hypoalbuminemia and 6.7% folic acid deficiency.
Discussion
Our study highlighted the high prevalence of nutritional nutritional deficiencies in obese patients, which can be explained by the poor nutritional quality of meals, and repetitive restrictive diets.

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EP675

A study of nutritional profile in a population with asthma

Mehrez Achwak[1], Chaima Jemai[1], Tesnim Farhat[2], Khouloud Chaabi[3], Hichem Aouina[3], Zohra Hadj Ali[1], Yosra Htira[1] & Ben Mami Faika[1]
[1]The national institut of nutrition of Tunis, Department C, Tunisia; [2]Nutrition studies university, Tunisia; [3]Charles Nicole Hospital, Tunisia

Introduction
The influence of diet on asthma outcomes is of growing interest. The aim of our work is to assess the nutritional intake of a population of patients followed for asthma.
Methods
This was a cross-sectional descriptive study conducted over a 2-month period. It concerned all asthma patients who presented to the consultation for follow-up of their disease, having benefited from an interrogation, a somatic examination and a dietary survey.
Results
The study involved 40 asthmatic patients with a mean age of 46.15 ± 14.13 years and a sex ratio of 0.25. Mean weight was 75.9 ± 12.6 kg with a mean BMI of 29.1 ± 5.7 kg/m^2;. Mean spontaneous caloric intake was 1938.20 ± 753.35 kcal/day, with 67.5% of the study population having a caloric intake in excess of their mean energy requirement estimated by calculating basal metabolic rate and physical activity level at 1714.54 ± 420.30 kcal/day. Average daily carbohydrate intake was 246.84 ± 110.43 g/day, as 29.22 ± 8.90% of total energy intake (TEI). Protein intake was 75.50 ± 31.77 g/day, as 15.63 ± 4.35% of TEA. Fat intake was 62.56 ± 31.08 g/day, as 51.43 ± 10.07% of TEA. Ten percent of the population had higher protein and fat intakes than established recommendations. While 22.5% of the population had a carbohydrate intake higher than recommended. Average fiber intake was 22.61 ± 8.42 g/day. In terms of daily water consumption, 60% of the population consumed less than 1.5 l.
Conclusion
The results of our study highlight worrying eating habits. It is vital to make asthma patients aware of the importance of a balanced diet and a healthy lifestyle, in order to minimize the risks associated with obesity and improve asthma control.

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EP676

Differences in the nutritional status and cardiac function between type 2-diabetes and non diabetes patients with heart failure

Carlos Manuel Alzás Teomiro, Ana María Moyano Sánchez, Mireia Isabel García Ramírez, Concepción Muñoz Jiménez, Ángel Rebollo Román & Aura D. Herrera Martínez
Reina Sofía University Hospital, Endocrinology and Nutrition

Backround and objectives
Heart failure (HF) has a rising incidence and is one of the most prevalent diseases worldwide. The number of patients with type 2 diabetes (T2DM) with heart failure is very high. Serum NT-proBNP and systolic ejection fraction correlate with the severity and prognosis of this condition. The nutritional evaluation of patients with HF, who usually have normal weight, overweight or obesity, has acquired a novel approach due to the incorporation of novel techniques (bioelectrical impedance, nutritional ultrasonography), and functional tests. The main objective is to evaluate the relation between nutritional parameters and clinical outcomes in patients with HF and check the possible differences in the ones affected with T2DM.
Methods
Patients with at least one hospital admission during the previous year were included. Anthropometric, biochemical, ultrasound, cardiac and functional tests were collected. Statistical analysis was performed with SSPS v.24.
Results
Thirty-eight patients were included (72.2% males). 44.4% patients of the sample presented diabetes at the moment of inclusion (100% T2DM). During the previous 12 months, patients affected with T2DM required more hospital admissions due to heart failure when compared to the ones without T2DM. Mean systolic ejection fraction measured by echocardiogram in T2DM patients was lower than the ones with no T2DM (39.5 vs 34.9%, $P > 0.05$), and serum NT-proBNP levels were higher (4950.13 vs 9513.37, $P > 0.05$). T2DM patients of the sample tended to have a higher lean mass and lower fat mass percentage measured by bioelectrical impedance than the no T2DM, and showed a higher phase angle (5.47 vs 4. 93º, $P > 0.05$). T2DM also presented lower results in hand grip dynamometer in both dominant and non-dominant arms. Nutritional biochemical parameters showed that T2DM patients had a better control of LDL colesterol and trglycerides than no T2DM patients.
Conclusions
T2DM is associated with worse clinical outcomes in patients with heart failure. Routine nutritional evaluation and early nutrition intervention, if required, should be implemented in order to improve the clinical outcome in these patients. Prospective, interventional studies should be performed.

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EP747

Regulation of Kv2 potassium channel expression in pancreatic β cells in a rat metabolic syndrome model induced by arsenic and sucrose

Alberto Aguirre Ponce[1], Juan Pablo Pánico[2], Marcia Hiriart[1] & Myrian Velasco Torres[1]
[1]Instituto de Fisiología Celular, Neurociencia Cognitiva, Ciudad de México, Mexico; [2]Institute of Biomedical Research, Ciudad de México, Mexico

Metabolic syndrome (MS) is a group of signs that increase the risk of developing cardiovascular diseases and type 2 diabetes mellitus (DM2). MS includes at least 3 of these signs: central obesity, dyslipidemia, hypertension, fasting glucose disorders, and insulin resistance. The consumption of sugar drinks, a high-calorie diet, a sedentary lifestyle, and environmental pollutants such as arsenic increase the risk of developing MS. Arsenic affects beta-cell function and insulin secretion. This study aimed to evaluate the effect of SM induced by the additive effect of sucrose and arsenic on the expression Kv2 potassium channels (Kv2.1 and Kv2.2) in pancreatic islets. Male Wistar rats were treated with water (C), 20% sucrose (S), 50 mg/l sodium arsenite (A), or both (A + S) in drinking water for 8 weeks. We assessed the abundance of proteins by Western blot and expression genes for Kv2 channels by real-time qPCR. Previous work in our laboratory showed that S, A, and A + S groups developed hyperinsulinemia. However, only group A showed a reduction in Kv2 potassium current. In this work, we observed that the arsenic treatment decreased the abundance of the Kv2.1 channel but not of the Kv2.2 channel. However, the *Kcnb1* gene expression didn't change. Interestingly, there were no changes when the animals were treated with sucrose and arsenic. In conclusion, arsenic produces hyperinsulinemia through the abundance of proteins for the Kv2.1 channel.

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EP748

Moringa oleifera and hypoglycemia: the causal link!

Talbi Dounia, Sebbar Ghizlane, Rifai Kaoutar, Hinde Iraqi & Gharbi Mohamed El Hassan
Ibn Sina University Hospital, Endocrinology, Morocco

Introduction
Moringa oleifera (MO) (also known as 'drumstick') is a tree belonging to the family Moringaceae, genus Moringa, originally native from the Himalayans but currently cultivated in many tropical and subtropical regions around the world. It has been used as a food source and for traditional medicine purposes due to possible antihyperglycemic, antioxidant, anti-inflammatory, and lipid regulating properties, and have been reported earlier by different scientific groups using animal models.
Case Report
44 year old patient, chronic haemoldialysis since 2017 for nephropathy of undetermined aetiology. Has been reporting hypoglycemia at 0.4 g/l for 3 months, with no disturbance of consciousness. His history includes regular intake of moringa leaves, coinciding with the onset of hypoglycemia. The Hypoglycemia assessment was negative, and the abdomino-pelvic CT scan did not reveal a pancreatic mass. The evolution was marked by the disappearance of hypoglycemia after moringa was stopped.
Discussion and Conclusion
The tree Moringa oleifera (MO) MO has been used in traditional medicine for the treatment of various conditions and, more recently, has been proposed to be of benefit in numerous diseases including cardiovascular, diabetes, cancer, neurological, gastroenterological, and inflammatory. MO aqueous leaf extract has been shown to inhibit the activity of α-glucosidase, pancreatic α-amylase, and intestinal sucrose, contributing to antihyperglycemic properties. These inhibitory effects are possible thanks to phenols, flavonoids, and tannins present in MO. A delay in carbohydrate digestion, caused by the inhibition of these enzymes, leads to a reduction in post-prandial hyperglycemia and hemoglobin A1C (HbA1C). These inhibitory effects of flavonoids, including quercetin and kaempferol, have been biochemically explained due to an increase in the number of hydroxyl groups on the B ring, and to the presence of a 2,3-double bond. In addition, these compounds have been studied regarding protective and regenerative properties on pancreatic beta-cells, augmenting insulin production and release. However, the hypoglycemic effects of MO on humans are not as clear given the scarce number of human studies, together with a diverse range of methodologies and MO doses. Therefore, more structured studies are needed to clarify if MO has an effect on insulin levels or activity.

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EP769

Audit on initial assessment of hyponatraemia in hospitalised patients and it's subsequent outcome

Kavinga Kalhari Kobawaka Gamage[1], Rachel Livingstone[2], Natasha Steven[2], Sophie Edwards[2], Daniel Slack[2] & Neil McGowan[2]
[1]Sheffield Teaching Hospitals NHS Foundation Trust; [2]NHS Greater Glasgow and Clyde

Introduction
Hyponatraemia is the commonest electrolyte disturbance encountered in the clinical practice. However, its initial evaluation is commonly found inadequate. We conducted a retrospective audit on evaluation of inpatient hyponatraemia in a large district general hospital.
Study methodology
Retrospective data of patients admitting with or who developed moderate to severe hyponatraemia during the hospital stay were collected over 4 week's period (1st to 28th of July 2023). Out of them, 84 randomly selected patients' clinical records were assessed regarding initial evaluation.
Results
Eighty-four cases with moderate to severe hyponatraemia were identified and included in the study. 38 (45.2%) were male and 55 (65.4) % were above 65 years old. Patients with age range from 27 years to 92 years were included. 68 (80.9%) had hyponatraemia on admission while rest had hospital acquired hyponatraemia. Severe hyponatraemia was found only in 3 (3.5%), while the rest had moderate hyponatraemia. Serum osmolality, urine osmolality and urine sodium were documented in 26(30.9%), 12 (14.2%), 9 (10.7%) respectively. 16 (19%) had hypotonic hyponatraemia, however volume status was documented only in 11 out of the above 19 patients and only 4 had fluid balance charts maintained. Out of the patients with hypotonic hyponatraemia 9 (56%) had their cortisol levels done and hypothyroidism was excluded in 10 (62.5%) despite the unavailability of rest of the investigations such as urine osmolality or urine sodium. Out of the 3 patients with severe hyponatraemia, only one had osmolality studies available. 14(16%) of hyponatraemic patients succumbed to death during the same admission.
Conclusions
Hyponatraemia is a frequently occurring condition associated with high mortality rates. However, it is evident that the initial evaluation remains insufficient despite the widespread availability of guidelines. Therefore, it is necessary to take steps to improve the initial investigation process.

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EP777

Unpredicted diagnosis of type 1 diabetes after delivery

Mohamed Khairi Arous, Najla Bchir, Anaam Ben Chedida, Chadia Zouaoui & Haroun Ouertani
The Military Hospital of Tunis, Endocrinology, Tunis, Tunisia

Introduction
Gestational diabetes mellitus (GDM) is a common and increasing complication, concerning 2–17% of pregnancies [1]. This glucose intolerance often resolves after delivery, and rarely becomes permanent type 2 diabetes, exceptionally type 1 diabetes (T1D). We present a case of a patient with GDM, which unexpectedly revealed T1D.
Case report
A 33-year-old woman consulted for GDM. Her family medical history includes hypothyroidism in her maternal aunt and psoriasis in her daughter. Our patient has had two COVID-19 infections. During her first pregnancy, she had gestational hypertension but no history of GDM or macrosomia. Prior to her pregnancy, the patient had a BMI of 30.8 kg/m^2;. Her GDM was diagnosed at 26 weeks' amenorrhoea through systematic screening. The patient had no previous carbohydrate assessment. Dietary management was sufficient to achieve glycemic targets for the rest of the pregnancy. Maximum weight was 82 kg. Five months after delivery, our patient lost 5 kilograms in 2 weeks. The glycemic cycle was between 0.86-2.02 g/l and HbA1C at 8.1%. The patient benefited from a basal insulin regime as she was breastfeeding. The evolution was marked by an increase in glycemia with the appearance of a polyurea-polydipsic syndrome despite insulin therapy, reaching a plateau of 2.5-3 g/l. Diabetes antibodies were requested (after 9 months postpartum), and were positive: Anti-GAD65 = 18.84 IU/ml, anti-IA2 = 88 IU/ml confirming T1D.
Discussion and conclusion
Our patient presented with a picture typical for T2DM. T1DM was unlikely given the good response to dietary management. The predictive factors for T1DM in patients with GDM are the presence of diabetes-related autoantibodies, which is the main factor, age < 30 years, the need for insulin treatment, and multiparity. The familiar history of autoimmunity should raise the possibility of T1D, even

with such an atypical metabolic phenotype. Some studies have assessed phenotypic traits associated with autoimmunity among women with gestational diabetes: a lower BMI, a lower waist measurement, a lower weight gain during pregnancy, which was the case of our patient, and lower fasting insulin levels. Most studies identified an increased risk for many autoimmune diseases among patients with COVID-19. The explanation for our patient would be a partial and slowly progressive autoimmune destruction of pancreatic β cells, during pregnancy. In fact, many autoimmune diseases go into remission during pregnancy secondary to natural immune tolerance.

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EP778

The influence of age on the morpho-constitutional characteristics of urolithiasis in diabetic patients in southern tunisia

Ines Mezghani, Aida Elleuch, Mouna Turki & Fatma Ayedi
Habib Bourguiba University Hospital, Laboratory of biochemistry, Sfax, Tunisia

Background-Aim
Urolithiasis is a frequent and recurrent pathology. Diabetes has a very important role in the formation of kidney stones. The objective of our study was to study the influence of age on the morpho-constitutional characteristics of urolithiasis in diabetic patients in southern Tunisia.
Methods
This is a mono-centric retrospective and descriptive study of urinary lithiasis cases in diabetic patients. The lithiasis were identified by the morpho-constitutional study, they were collected in the Laboratory of biochemistry, during the period from January 2011 to December 2020. We were interested in diabetic patients over the age of 18. To study the influence of age, we subdivided our diabetic lithiasis patients into 2 groups: Group1 (G1): group of diabetic lithiasis patients with an age less than 59 years. Group 2 (G2): group of diabetic lithiasis patients having an age more than or equal to 60 years.
Results
Our study involved 76 stones which represents 7.08% of all urinary stones analyzed during the study period. Our patients were aged from 33 to 85 years. Sex ratio = 2.16. Nephritic colic was the most common discovery circumstance (44.8% for G1and 61.3% for G2). Renal localization was the most frequent (58.6% for G1 and 58.1% for G2) followed by the ureter(37.9% for G1and 29% for G2). The notion of recurrence was present in 31% of G1 patients and 38.7%of G2 patients. The constitutional study of the calculi showed that oxalocalcic lithiasis was the major component of the calculi for the two groups:the C1 monohydrate type was the most frequent in 36.7% and 42.9% of the cases (respectively for G1 and G2), followed by the mixed type (C1 + C2):10% and 14.3% (respectively for G1 and G2) and the dihydrate type C2 (3.3 and 3.6% respectively for G1 and G2). Purine lithiasis represented by pure purines (6.7% and 25% respectively for G1 and G2) and mixed purines (23.3% and 14.3% respectively for G1 and G2), followed by phosphocalcium lithiasis (20% for G1and no patient for G2). The difference by age was not significant for the different stone types.
Conclusions
The influence of age on the morpho-constitutional characteristics of urolithiasis in diabetic patients in southern Tunisia were comparable to those reported in many countries. The modifications are generally due to the expression of nutritional disorders and metabolic modifications linked to cellular aging

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EP779

Not all ketosis is type 1 diabetes - think of flatbush

Sarah Craus[1], Abigail Mula[1] & David Coppini[2]
[1]Mater Dei Hospital, Malta; [2]University Hospitals Dorset NHS Trust

A 35 year old otherwise healthy gentleman from Togo, was referred to our clinic with new onset diabetes and a glycated haemoglobin (Hba1c) of 119mmol/mol (13.1%). He initially presented to his general practitioner with polyuria and polydipsia, and 5 kg of weight loss. He denied any change in bowel habit and had no recent illnesses. Both parents had Type 2 Diabetes Mellitus (T2D). Initial blood tests revealed a blood glucose of 22.84 mmol/l, with positive ketones (1.2 mmol/l). Urinalysis showed glycosuria (1000 mg/dl) but was negative for nitrites and white cells. Renal, liver and thyroid function tests were all within normal limits. In addition, the patient had mild metabolic acidosis (Table 1). The markedly elevated blood glucose levels in association with ketoacidosis strongly suggested a diagnosis of Type 1 Diabetes Mellitus (T1D). The patient was admitted to the diabetes ward and treated with a fixed rate insulin infusion as per diabetic ketoacidosis (DKA) protocol. There was a fairly rapid improvement in both hyperglycaemia and ketonaemia within a few hours. Anti-glutamic acid (GAD), anti-insulinoma antigen 2 antibodies (IA2) and anti-insulin antibodies were all negative. The next day, the patient was discharged on a basal bolus regime of glargine and aspart after review by the inpatient diabetes team. The patient continues with regular clinic reviews. His glucose levels continued to improve with incremental insulin dose reductions and he remains on low dose metformin (500 mg daily), with normalisation of his Hba1c after 6 months.
Conclusions
A rapid response to insulin, negative testing for type 1 autoimmunity, in a young gentleman of African origin, suggested a diagnosis of ketosis prone/Flatbush diabetes was most likely. The aetiology of ketone-prone diabetes remains unknown. Further studies may help future therapies. A diagnosis of ketosis prone diabetes should always be borne in mind in patients of African ethnicity presenting with new onset diabetes and ketosis. Misdiagnosing patients with KPD as T1D can lead unnecessary treatment with long-term insulin therapy, with all its implications (e.g. hypoglycaemia, occupational impact).

Table 1 Initial investigations

	On admission	Reference range
Glucose	22.84	
Creatinine (umol/l)	48	59-104
Urea (mmol/l)	5.4	1.7-8.3
Sodium (mmol/l)	130	135-145
Potassium (mmol/l)	4.07	3.5-5.1
Hba1c (mmol/mol)	119	28-46
Venous Blood Gases		
pH	7.34	7.35-7.45
pCO2 (kPa)	5.5	5.1-5.6
pO2 (kPa)	6.2	10.5-13.5
Lactate (mmol/l)	1.3	<2
HCO3- (mEq/l)	23.6	18-22
Chest X-Ray	Normal	
Electrocardiogram (ECG)	Normal sinus rhythm at 95bpm	

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EP781

Bacteriological and mycological profile of necrotizing otitis externa in diabetics

El Omri Malika[1], Jemli S[1], Bellakhdher Mouna[1], Meherzi Abir[1], Houas Jihene[1], Ghammem Monia[1], Ach Taieb[2], Kermani Wassim[1] & Abdelkefi Mohamed[1]
[1]ENT Department Farhat Hached Hospital, Sousse, Tunisia; [2]Endocrinology Department Farhat Hached Hospital, Sousse, Tunisia

Introduction
Necrotizing otitis externa (NOE) is a rare but serious condition which is mainly seen in diabetics. This condition has a poor prognosis, due to the complexity of the terrain in which it occurs. The aim of our work is to study the clinical, paraclinical and therapeutic data of NOE.
Material and methods
This is a retrospective study covering 64 cases followed and treated in our ENT department over a period of 12 years between 2000 and 2022.
Results
Our serie includes 29 women and 33 men, with an average age of 67 years, 90% of our patients were diabetic. The bacteriological sample isolated *Pseudomonas aeruginosa* in 54% of cases. Culture was negative in 19 samples; among the latter, 10 cases had a mycotic origin. The temporal computed tomography scan performed for all patients was in favor of NOE in 22 cases and showed an extension of the infection in 29 cases. Fluoroquinolone was prescribed in all cases associated with a Cephalosporine 3rd generation (C3G) in 58 cases, and a C3G with Metronidazole in 6 cases. The treatment was revised in 15 patients, 9 patients had fungal involvement, 4 patients developed resistance to Ceftazidine and 2 cases were allergic to Ceftazidine. The total duration of antibiotic treatment was on average 54.43 days. Healing was achieved in 98.4%.
Conclusion
The bacteriological profile of NOE in diabetic patients a is predominated by the presence of *Pseudomonas aeruginosa* and characterized by the emergence of mycotic infections nowadays.

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EP783

Type 1 diabetes: Diagnosis rectified years after treatment with oral hypoglycemic drugs

Mohamed Khairi Arous, Najla Bchir, Roua Mankai, Anaam Ben Chedida, Chadia Zouaoui & Haroun Ouertani
The Military Hospital of Tunis

Introduction
Type 1 diabetes (T1D) is a progressive autoimmune disease, the diagnosis is obvious in classic forms. However, misleading forms are possible, sometimes leading to inappropriate treatment. We report the case of two type 1 diabetic patients who were treated for years with oral hypoglycemic drugs.
Case report
Patient 1: Mr. M, aged 34, with a family medical history of type 2 diabetes (T2D), was diagnosed with diabetes revealed by a polyurea-polydipsic syndrome (PPS), 8 years ago, without acute decompensation. He was treated with oral dual therapy: glimiperide 2 mg and metformin. He recently consulted for unintentional weight loss of 3 Kg in 3 months with non-controlled diabetes: fasting plasma glucose (FPG) = 10 mmol/l, glycated hemoglobin (HbA1C) = 10.7%. Biology showed peptide C = 1.06 ng/ml, anti-GAD65 antibodies were negative but anti-AI2 antibodies were positive at 28 IU/ml ($^n < 8$), confirming autoimmune T1D. Patient 2: Mr. N, aged 34, with no previous medical history, was diagnosed with diabetes revealed by PPS with no weight loss or acute decompensation. His BMI was 25.05 kg/m^2; and biology showed an HbA1C = 12%. The patient received oral dual therapy: glimepiride 2 mg/d and metformin. At 6-month follow-up, PPS disappeared and HbA1C fell to 6.7%. The patient described occasional hypoglycemia, leading us to decrease the dose of glimiperide to 1 mg/day. HbA1C has remained stable at around 7.5-8.5% for 5 years, then rose sharply to 12%, associated with weight loss. Increasing the dose of glimepiride was ineffective. We asked for anti-GAD65 antibodies, which were markedly positive at 1625 IU/ml ($^n < 10$), thus indicating T1D.
Discussion and conclusion
T1D is easy to diagnose in the presence of abrupt onset, inaugural ketosis, and young age, especially in the presence of autoimmune stigmata. The absence of these elements makes T1D unlikely. The diagnosis was more diverted by the clinical-biological improvement with oral hypoglycemic drugs for years, classically incompatible with T1D. This equilibrium would be explained by the autoimmune destruction, slowly progressive and incomplete, of the beta cells of the islets of Langerhans. This persistent insulin secretory capacity, enabled good glycemic balance to be achieved for a while. Reascension of glycemic parameters reflected an utter decline in pancreatic beta cells. Although T2D is increasingly seen at a younger age, the diagnosis of diabetes at an age <35 should raise the possibility of T1D.

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EP784

Hyperuricemia predictive factors among type 2 diabetes mellitus patients

Wafa Ben Hilel, Ramla Mizouri, Skander Msolly, Faten Mahjoub, Rym Ben Othman, Nadia Ben Amor, Olfa Berriche & Jamoussi Henda
National Institute of Nutrition, Tunis, Tunisia

As type 2 diabetes mellitus (T2DM) is a metabolic disorder, it frequently poses challenges for patients in metabolizing uric acid, resulting in hyperuricemia (HUA). In this study, our objective is to investigate the risk factors of HUA among T2DM patients.
Method
Patients with T2DM who were attended in the National Institute of Nutrition in Tunis, Tunisia, between August and November 2023 were included in this retrospective observational study. Diagnosing HUA was based on sound diagnostic criteria (i.e. SUA of greater or equal to 420 mmol/l and 360 mmol/l for male and female respectively). Patients younger than 18 years old, effected by another type of diabetes, pregnant women, patients undergoing urate-lowering therapy or taking medications that affect blood uric acid levels, suffering from a serious liver or kidney damage or chronic heart failure were not included in the study.
Results
A total of 131 T2DM patients were included: 23 in the HUA group and 108 in the non-HUA group. In simpler terms, the prevalence of HUA among patients with T2DM was 17.5%. The mean ages of the non-HUA group and the HUA group were 60.3 ± 9.5 and 66.3 ± 9.5 respectively. the sex ratios (female/male) were respectively 1.8 and 1.3. The average diabetes duration of the non-HUA group and the HUA group was 13.5 ± 5.5 and 15.1 ± 6 respectively. Participants with HUA were older and more likely to have hypertension ($P < 0.01$). Additionally, there were higher values of body mass index, creatinine, triglycerides and gamma-glutamyl transferase (GGT) in the HUA group compered to non-HUA group ($P < 0.5$) but lower values of high-Density Lipoprotein cholesterol (HDLc) ($P < 0.05$). Findings did not reveal any notable difference in other indicators including sex, diabetes complications, diabetes duration, HbA1C, total cholesterol, low-Density Lipoprotein cholesterol (LDLc), aminotransferases (SGAT, SGPT) and albumin between HUA group and non-HUA group ($P > 0.05$).
Conclusion
Our study indicates HUA occurrence among patients with T2DM and establishes independent risk factors associated with HUA, suggesting promising potential for early detection and diagnosis of HUA in T2DM patients.

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EP785

Involvement of social networks in the education of young people with type 1 diabetes

Sofia Ouhessaine, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy-University Hassan II-Casablanca-Morocco

Introduction
Diabetes is one of the most complex chronic health conditions of our time. Daily management of the disease as well as its acute and chronic complications requires a certain level of education; social media could play a role in disseminating appropriate information.
Objectives of the study
Evaluated the involvement of social media in the education of young people with type 1 diabetes.
Material and methods
Descriptive cross-sectional study, carried out at the endocrinology department-diabetology at Ibn Rochd University Hospital of Casablanca, of interest to young type 1 diabetics followed at the transition consultation. Results: Our study included 54 patients. The average age was 16.2 years with a female predominance of 62%. The duration of diabetes was 7.93 ± 4.02 years. Mean HBA1c = $11.19 \pm 2.12\%$). 95% of our patients said they go to social media looking for information about their illness. The most searched subjects were: complications of diabetes in 67%, therapeutic perspectives in 45%, the pathophysiology of diabetes in 35%, diabetes and physical activity in 40%, the impact of diabetes on fertility in 16%. Our patients judged that the information acquired on social networks was useful in 89%.
Conclusions
Social media is widely used nowadays, and provides a valuable digital education tool providing an opportunity for medical staff to support diabetic patients by disseminating useful and authentic knowledge and information related to diabetes management and of its complications.

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EP788

Twists and turns of diabetology – immune checkpoint inhibitor-mediated diabetes

Ana Majic Tengg[1] & Tanja Palaversa[2]
[1]Clinical Hospital Dubrava, Department of Endocrinology, Diabetes, Metabolic Diseases and Clinical Pharmacology, Zagreb, Croatia; [2]Levanger Hospital, Department of Medicine, Levanger, Norway

Introduction
Immune checkpoint inhibitors (ICIs) have revolutionized oncological treatment and substantially improved a prognosis for patients with advanced malignancy. ICIs inhibit the immunological pathways controlling T-cell activation or anergy. The most frequently used classes of ICIs are those that targeted and inhibit cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), programmed cell death receptor 1 (PD-1) or its ligand PD-L1. The initiation of ICIs therapy is often associated with immune-related adverse events that can lead to destruction and permanent loss of function of various tissues, including the endocrine glands, with the thyroid gland being the most commonly affected. The overall incidence of ICI-induced diabetes mellitus ranges from 0.4% to 2%, resembling type 1 diabetes. It is characterized by the acute onset of hyperglycaemia with severe

insulin deficiency and diabetic ketoacidosis very frequent at diagnosis. Autoantibodies and HLA genotypes associated with type 1 diabetes are often present. The standard treatment mode is a multiple insulin injection regimen.
Case presentation
A 71-year-old woman was admitted to the emergency department due to hyperglycaemic hyperosmolar syndrome, metabolic acidosis, and diarrhoea. Prior to admission, she had received eight cycles of nivolumab therapy for metastatic skin melanoma, and had been on glucocorticoid therapy for more than 10 years due to seropositive rheumatoid arthritis. She had no history of diabetes. Upon assessment, she was found to have severe hyperglycaemia [plasma glucose level of 55.2 mmol/l (993.6 mg/dl)] with positive urine ketones, acute renal insufficiency (urea level of 17.0 mmol/l, creatinine level of 269 umol/l), and hyperkalaemia (potassium level of 6.6 mmol/l). HbA1c was 9.4% (79 mmol/mol). She was treated per standard-of-care fluid resuscitation and insulin infusion protocols, and discharged as fully recovered to the outpatient diabetes clinic with basal insulin, a DPP-4 inhibitor, and repaglinide. During the follow-up visit, the glycaemic control was unsatisfactory with high glycaemic variability, and ICI-induced diabetes was suspected. Additional laboratory examinations showed immeasurable C-peptide level of < 0.02 nmol/l (normal range: 0.27 – 1.28) while GAD, ICA, and IA-2 autoantibodies were negative. A multiple insulin injection regimen was initiated, and glycaemic control significantly improved.
Conclusions
ICI-related diabetes is a rare but often life-threatening condition. As the increasing number of patients will be exposed to ICIs, healthcare professionals and patients should be aware of ICI-mediated endocrinopathies, with the regular monitoring of plasma glucose level being a part of comprehensive care for all patients treated with ICIs.

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EP790

Prevalence and characteristics of chronic obliterating arteritis of the lower limbs in a population of patients with type 2 diabetes

Nesrine Dhieb, Chaima Jemai, Maryam Cheikhrouhou, Chaima Sdiri, Zohra Hadj Ali, Olfa Lajili, Yosra Htira & Faika Ben mami
National Institute of Nutrition, Department C, Tunis, Tunisia

Introduction
Chronic obliterating arteritis of the lower limbs is common in patients with type 2 diabetes (T2D). Our aim was to determine the prevalence and characteristics in a tunisian population.
Methods
This was a cross-sectional study including 100 patients with T2D hospitalized in department C of the national institute of nutrition of Tunis. For each patient, we carried out a physical examination, we measured the systolic pressure index (SPI) and we retrieved biological parameters from medical records.
Results
Average age was 57.20 ± 8.48 years. Women made up 74% of the population. 29% were smokers. Diabetes mean duration was 14.79 ± 4.55 years. All patients were treated with insulin. The majority (70%) were on NPH insulin. Median BMI was 30.46 kg/m^2; with extremes of 22.5 and 38.28 kg/m^2. Mean HbA1C was 10,33% with extremes of 8 and 12%. Ischemic coronary artery disease and stroke was frequent by 10% and 3% respectively. The mean IPS was 0.86 ± 0.12, with extremes of 0.4 and 1. The median value was 0.8. 18% of our population had chronic obliterating arteritis of the lower limbs. It was predominant in men (66.6%). All of these patients had hypercholesterolemia. Associated factors were smoking ($P = 0.03$), BMI ($P = 0.008$) and diabetic peripheral neuropathy ($P < 0.001$).
Conclusion
Chronic obliterating arteritis of the lower limbs constitutes a risk factor for the development of diabetic foot ulcers. Early screening, smoking cessation and weight reduction to prevent this complication of reserved prognosis.

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EP791

Management of chronic diseases in elderly diabetics

Mouna Elleuch, Wissal Ghamgui, Dhouha Ben Salah, Lilia Affes, Mouna Mnif, Ftama Mnif, Nadia Charfi, Feten Hadj Kacem, Nabila Rekike & Mohammed Abid
Hedi Chaker Hospital, Sfax, Tunisia

Introduction
Tunisia is a country classified as high cardiovascular risk with a population tending towards aging and the appearance of chronic diseases.
Objective
Analyze the management of chronic diseases in elderly subjects with type 2 diabetes (T2DM)
Material and methods
This is a retrospective study of T2D patients hospitalized in the endocrinology-diabetology department of Hedi Chaker Sfax University Hospital between January and March 2023.
Results
We included 50 patients, with a median age of 69.5. The sex ratio (F/M) = 1.7. The associated diseases were hypertension (74%) and hyperlipidemia (70%). The average number of tablets was 6.75 ± 3 tablets/day. For diabetes, the treatment regimen includes oral antidiabetics (OADs) exclusively in 52% of cases, insulin in 26% of cases and mixed treatment in 22% of cases. Only 12% met the glycated hemoglobin targets (mean HbA1c = 10.81 ± 2.74). For hypertension, 68% were on ACE inhibitors, 34% on calcium channel blockers, 20% on diuretics and 18% on ARA2. Hypertension was uncontrolled in 68% of patients. For dyslipidemia, 68% of patients were placed on statins. LDL targets were not achieved in 76% of diabetic patients.
Discussion
We deduce that the elderly in Tunisia require intensification of education on hygienic and dietary rules and encouragement for the prescription of medicinal combinations.

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EP792

Interrelation of TNF-α concentrations with the onset and progression of diabetic complications

Elvira Ibragimova[1], Talat Saatov[1], Timur Alimov[1,2], Sanobar Irgasheva[1,3], Tokhir Ishankhodjaev[1], Gulnora Artykbaeva[1], Nigora Maksutova[4], Abdunabi Tashtemirov[1] & Zulaykho Shamansurova[1,5]
[1]Institute of Biophysics and Biochemistry, Mirzo Ulugbek National University of Uzbekistan, Tashkent, Uzbekistan; [2]Republican Specialized Scientific Practical Medical Center of Hematology and Blood Transfusion, Uzbekistan Public Healthcare Ministry, Tashkent, Uzbekistan; [3]Alfraganus University, Tashkent, Uzbekistan; [4]Ya. Kh. Turakulov Center for Scientific and Clinical Study of Endocrinology, Uzbekistan Public Healthcare Ministry, Tashkent, Uzbekistan; [5]Central Asian University, Tashkent, Uzbekistan

As a cytokine, TNF-α plays a role of key anti-inflammatory mediator involved in the onset and progression of insulin resistance and type 2 diabetes mellitus. TNF-α is known to inhibit insulin-stimulated of auto-phosphorylation of insulin receptors by tyrosine kinase; as the result, insulin sensitivity decreases in its turn resulting in insulin resistance and glucose transport damage. TNF-α is a trigger in the onset of obesity, diabetes mellitus and its complications. Studies on concentrations of TNF-α in peripheral blood are of high importance in assessment of extent in type 2 diabetes mellitus progression.
Materials and methods
68 patients with type 2 diabetes mellitus, 50 persons with diabetic neuropathy of various degrees and 18 persons without any 2DM complications among them, were examined. Non-diabetics were included into the control group. ELISA was used to determine TNF-α concentrations in the blood serum of the examinees.
Results
Determination of TNF-α concentrations in blood serum of the examinees demonstrated their significant increase as compared to those in the non-diabetics (3.05 ± 0.44 vs 1.1 ± 0.05 pg/ml). In patients with moderate diabetic neuropathy, the serum concentrations of TNF-α turned out significantly lower than those in patients with severe disease (3.62 ± 0.89 vs 7.13 ± 1.14 pg/ml). Thus, paralleling disorders in carbohydrate and lipid metabolism in 2DM, concentrations of TNF-α in blood serum of the patients were found to be in direct dependence with the disease severity.

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EP793

Comparative study on concentrations of TNF-α upon type 2 diabetes mellitus and neurodegenerative diseases

Elvira Ibragimova[1], Talat Saatov[1], Dilnoza Saidova[1,2], Timur Alimov[1,3], Zafar Ibragimov[1], Gulnora Artykbaeva[1], Abdunabi Tashtemirov[1], Zulaykho Shamansurova[1,4] & Tokhir Ishankhodjaev[1]
[1]Institute of Biophysics and Biochemistry under Mirzo Ulugbek National University of Uzbekistan, Tashkent, Uzbekistan; [2]Ya.Kh. Turakulov Center

for Scientific and Clinical Study of Endocrinology, Uzbekistan Public Healthcare Ministry, Tashkent, Uzbekistan; [3]Republican Specialized Scientific Practical Medical Center of Hematology and Blood Transfusion, Uzbekistan Public Healthcare Ministry, Tashkent, Uzbekistan; [4]Central Asian University, Tashkent, Uzbekistan

Damages of the central and peripheral nervous systems as peripheral neuropathy and encephalopathy of mixed vascular and metabolic genesis, respectively, are known to take place in diabetes mellitus, ultimately resulting in progressing decline of cognitive function and development of dementia. Findings of many studies demonstrated interrelation between increases in the TNF-α concentrations and onset of inflammation, tumor processes and a number of metabolic, autoimmune and neurodegenerative disorders. The work was initiated to compare the TNF-α concentrations in the blood of serum of patients with type 2 diabetes mellitus and neurodegenerative disorders.
Methods and materials
115 persons were included into the experimental group, 50 patients with diabetic neuropathy, 50 patients with vascular dementia and 15 patients with Alzheimer's disease among them. The control group included the non-diabetics and those without cognitive disorders. Concentrations of TNF-α in blood serum were measured using ELISA.
Results
Our findings demonstrated significant increases in concentrations of the cytokine both in patients with type 2 diabetes mellitus and those with Alzheimer's disease, in contrast to the non-diabetics and people with normal cognitive function. Type 2 diabetes mellitus complications including diabetic neuropathy progressed, the TNF-α concentrations were found to significantly increased in blood serum of patients; the concentrations of the cytokine being significantly higher than those in patients with neurodegenerative disorder. This could be the evidence for the more severe effect of inflammatory load on an organism upon progression of type 2 diabetes mellitus. Comparison of the TNF-α concentrations in blood serum of patients with vascular dementia of various severities helped find significant differences ($P<0.05$) in the parameter. The disease progresses, concentrations of the cytokine increase twice. Comparison of the TNF-α concentrations in blood serum of patients with vascular dementia and in those with Alzheimer's disease demonstrated no significant differences ($P>0.05$). Thus, comparison of TNF-α concentrations in groups of patients under study as compared to healthy subjects demonstrated significant increases in the concentrations of the cytokine in both patients with type 2 diabetes mellitus and those with neurodegenerative disease.

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EP797

An extream case of malabsorption in a patient with type 1 diabetes and celiac disease

Dorsaf Ben Salem, Chaima Jemai, Yasmine Fakhfekh, Yosra Ben Hmida, Chaima Sdiri, Mohamed Bacha, Sami Fitouri, Olfa Lajili, Zohra Hadj Ali, Yosra Htira & Faika Ben Mami
National institute of nutrition of Tunis, C

Introduction
Type 1 diabetes and celiac disease are two autoimmune pathologies that frequently coexist. This association implies specific nutritional management whose application by the patient is not always simple. We report An extream case of malabsorption in a patient with type 1 diabetes and celiac disease.
Case presentation
This was the case of a 34-year-old with type 1 diabetes (T1D), celiac disease and vitiligo evolving since 13, 7 and 2 years respectively. She reported poor socio-economic conditions and no compliance with insulin therapy and gluten-free diet. Her weight and height were of 52.4 kg and 154 cm respectively, i.e. a BMI of 22.1 kg/m^2. On impedancemetry, her body composition was characterized by a fat mass of 29.2%. Her total energy intake was hypocaloric (TEI) (1931.6 cal/d), hypoglucidic (2.8 g/kg/d), hypolipidic (0.73 g/kg/d) and hypoprotidic (0.85 g/kg/d), according to WHO recommendation. Likewise, her diet was rich in high glycemic index carbohydrates (15.5% of TEI) and sodium (2195 mg/d), and poor in fiber (21.5 g/d), B12 vitamin (1.78 µg/d), calcium (617 mg/d), iron (7.6 mg/d) and potassium (2020 mg/d). Her diabetes was uncontrolled (HbA1C = 9.1%) and complicated by pathologic microalbuminuria (36.4 mg/24H) put on ACE inhibitors. She had no hypoglycemia. Her celiac disease was complicated by a malabsorption syndrom: She had chronic hypocalcemia (2.24 mmol/l) and chronic hypovitaminosis D, complicated with secondary hyperparathyroidism with Looser Milkman streaks on her pelvis x-ray, well tolerated microcytic hypochromic anemia (9.8 g/dl) due to iron deficiency (Ferritinemia = 6.65 ng/ml) and chronic hypolkaliemia (3.6 mmol/l). Liver test and TSH were normal. She was put on gluten-free diet and supplementation (calcium carbonate 500 mg 2 times a day, Ergocalciférol 2000UI/d, ferrous sulfate 80 mg 2 times a day, potassium chloride 600 mg/d and B 12 vitamin an injection of 1000 µg each month).
Conclusion
Managing the case of our patient was challenging. Multiple supplementation effectiveness is discussed given the risk of interaction between micronutrients. Likewise, their bioavailability is not guaranteed given the intestinal lesions of celiac disease. Total adherence to free-gluten diet remains the cornerstone of the treatment.

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EP798

Prevalence of depression in type 2 diabetic patients and its impact on glycemic control

Rym Ben othman[1], Syrine Trabelsi[2], Yasmine Jallouli[3], Ramla Mizouri[1], Yosra Ben Hmida[2], Olfa Berrich[1] & Henda Jammousi[1]
[1]National Institute of Nutrition and Food Technology, Department A; [2]National Institute of Nutrition and Food Technology, C, Tunis; [3]National Institute of Nutrition and Food Technology

Introduction
Depression and type 2 diabetes are often associated, but until now their exact relationship has remained unclear. The aim of our work was to evaluate the prevalence of depression in type 2 diabetic subjects and to determine its impact on glycemic control.
Methods
This was a descriptive cross-sectional study conducted in the National Institute of Nutrition. We included 400 type 2 diabetic patients. To assess depression, we used the Hospital Anxiety And Depression Scale (HADS). A score of 11 or above was considered positive.
Results
The mean age of our patients was 59.19 ± 8.81 years. Female predominance was noted (67.5%). The mean age of diabetes was 13.31 ± 7.9 years, with a mean HbA1c of 10.03 ± 2.03% and fasting plasma glucose of 11.26 ± 4.81 mmol/l. The majority of patients had good medication compliance (82.3%), with 13.75% not accepting their diabetes. Obesity was present in 44.5% of subjects. The prevalence of depression was 36.8%. The presence of this psychological disorder was positively associated with female gender ($P<0.001$), obesity ($P=0.004$), diabetes duration ($P=0.012$), diabetes acceptance ($P=0.02$), diabetic retinopathy ($P=0.02$), peripheral neuropathy ($P=0.001$) and vegetative neuropathy ($P=0.03$).
Conclusion
The large number of diabetic patients with definite depression calls for systematic screening of all diabetics for this psychiatric disorder, for better management and quality of life.

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EP801

Ramadan fasting prohibition among muslim individuals with diabetes: exploring cultural impacts on self-esteem

Abdel Mouhaymen Missaoui, Fatma Mnif, Siddiqa Soomauroo, Souhir Maalej, Rihab Khochtali, Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Department of Endocrinology, Sfax

Background and Aim
Besides its religious aspect, Ramadan Fasting (RF) represents a significant cultural affirmation practice for Muslim patients with diabetes. Despite the health risks related to this ritual, many Muslims with diabetes continue to fast against medical advice. This study aims to analyze the effect of RF contraindication on the self-esteem of Muslim patients with diabetes.
Methods
We conducted a cross-sectional study involving 25 Muslim patients with diabetes referred to the Department of endocrinology of Hedi Chaker University Hospital, Sfax, Tunisia, two months before Ramadan 2021. We stratified the fasting-related risk according to the 2021 IDF-DAR score. Rosenberg's self-esteem scale (RSES) was administrated immediately after announcing the medical decision about the possibility of fasting.
Results
The mean age was 58.7 ± 12.6 years, with a female predominance (78.3%). Hypertension (52.2%) and dyslipidemia (47.8%) were the leading comorbidities.

The mean duration of the evolution of diabetes was 10.9 ± 8.4 years, with an average A1C of 9.1 ± 1.7%. The mean 2021 IDF-DAR score was 5.5 ± 4 points. We stratified our patients into three risk categories:
- Low-risk patients (34.8%) who were allowed to fast.
- Moderate-risk patients (26.1%) who were discouraged from fasting.
- High-risk patients (39.1%) with a strict medical prohibition to fast.

The mean RSES was 30.7 ± 3.4 points. Lower self-esteem scores were recorded in the high-risk category (77.8%) compared with the moderate (50%) and the low-risk groups (50%). Higher self-esteem rates were observed in patients with low risk (50%), unlike those with moderate (12.5%) and high (0.0%) fasting-related risk ($P = 0.08$).

Discussion

The imposition of restrictions on certain community and cultural practices in response to medical considerations possesses the potential to exert a profound influence on the self-esteem and social integration of individuals grappling with diabetes. Recognizing the intricate interplay between health-related constraints and cultural identity underscores the imperative for healthcare providers to adeptly navigate the provision of culturally safe, patient-centered care. This nuanced approach ensures a holistic and sustainable health outcome for individuals navigating the intersection of medical considerations and cultural identity.

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EP802

Ophthalmological complications in patients with diabetes and chronic kidney disease: a single center cohort study

Abdel Mouhaymen Missaoui, Fatma Mnif, Siddiqa Soomauroo, Hamdi Frikha, Souhir Maalej, Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Department of Endocrinology, Sfax

Background and Aim

Multiple studies support that chronic glycemic imbalance has deleterious effects on microcirculation. It is the central physiopathological factor in the development of chronic kidney disease (CKD) and several ophthalmologic complications in patients with type 2 diabetes mellitus (T2DM). This study aims to assess the peculiarities of eye complications in patients with diabetes and CKD.

Methods

We conducted a descriptive study including 88 patients suffering from T2DM and CKD who were admitted to the inpatient unit of the Endocrinology department of Hedi Chaker University Hospital between 2019 and 2020. Medical charts were reviewed retrospectively to identify the clinical, biochemical, and ophthalmological findings.

Results

The mean age was 68.7 ± 10.9 years old, with a male predominance (52.3%). A family history of diabetes (84.1%), hypertension (61.4%), and CKD (12.5%) were frequently reported. The average diabetes evolution was 13 ± 9 years. A glycemic imbalance was recorded in 80.2%. The mean A1C was 9.68 ± 2.5% in this population. The leading comorbidities were dyslipidemia (94.0%), hypertension (86.4%), and obesity (35.7%). The mean glomerular filtration rate (GFR) was 32.2 ± 13.81 ml/min. Patients who had reached advanced stages of CKD represent 43.2%. Macroalbuminuria was encountered in 52.2%. The main ophthalmologic conditions were diabetic retinopathy (DR) and cataracts, respectively, observed in 53.3% and 11.1% of cases. Glaucoma and hypertensive retinopathy were also reported in 2.8% of patients. DR was non-proliferative in 29.7%. Intravitreal hemorrhage and maculopathy complicated the course of DR in 2.7% of patients. Panretinal photocoagulation was performed in 27%. Cecity affected 4.3% of our sample.

Discussion

DR represents a vision-threatening complication that may increase the risk of functional impairment and dependence in patients with CKD. Screening for this condition with a specialized annual eye exam is recommended. Optimal control of glycemic profile, blood pressure, and lipid parameters are efficient measures that could prevent the onset and the progression of this disease.

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EP804

Assessment of the diabetes mellitus prevalence dynamics in the republic of belarus

Olga Salko[1], Marina Shchaveleva[2] & Tatsiana Mokhort[3,4,4]
[1]Republican Center for Medical Rehabilitation and Balneotherapy, Minsk, Belarus; [2]Minsk City Clinical Endocrinological Center, Minsk, Belarus; [3]Belarusian State Medical University, Minsk, Belarus; [4]Belarusian State Medical University, Endocrinology, Minsk, Belarus

Objective

To assess the dynamics of Diabetes Mellitus (DM) prevalence in the Republic of Belarus in the period from 1993 to 2023.

Materials and Methods

There were the data from the Ministry of Health official statistics in the Republic of Belarus used for the analysis

Results

In the Republic of Belarus, since 1993, there has been a steady increase in the prevalence of types 1 DM and type 2 DM. The total prevalence of type 1 DM increased from 185.30 to 847.6 per 100,000 population, in the absence of an increase in primary incidence. These data indicate that the availability of insulin and self-monitoring tools have a positive impact on the life expectancy of this category of patients. The total prevalence of type 2 DM increased 7.8 times - from 510.99 to 3981.3 per 100,000 population. The marked increase in the incidence of type 2 DM is the result of active detection of the disease in risk groups and popularisation in the media in accordance with the State program. The estimated prevalence rate of DM in the Central European region, including the Republic of Belarus, should be 5-7% of the population. The World Health Organization and the International Diabetes Federation have determined that by 2030, DM should be detected in 80% of sufferers with these desease. When taking the calculated indicator of the number of patients with DM from the general population of a approximately 6% at the beginning of 2024, there are 3,889,395 patients with DM in the Republic of Belarus, which is 4.1%.

Conclusion

It is necessary to intensify measures to identify type 2 DM through further screening and expansion of risk groups, as well as increased popularisation in the media.

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EP805

Mean platelets volume and diabetic retinopathy in patients with diabetes mellitus

Hadhemi Belhassen[1,1], Mizouri Ramla, Siwar Saoudi, faten mahjoub, Chaima Sdiri, Nadia Ben Amor, Olfa Berriche & Jamoussi Henda
National Institute of Nutrition, A, Tunis, Tunisia

Introduction

Mean platelet volume (MPV) is an indicator of the average size and activity of platelets. Higher levels of MPV are encountered in conditions with increased production in response to increased destruction of platelets. Some studies suggest an association between impaired platelet function and vascular complications in patients with diabetes mellitus. The aim of our study is to prove this association.

Methods

Descriptive cross-sectional study conducted over 4 months in ward A of The National Institute of Nutrition Tunis which included patients with diabetes mellitus.

Results

Sixty patients were included of whom 41 were women and 19 men. The characteristics of the patients were: age: 50 ± 16.46 years, 44 patients with type 2 diabetes mellitus and 16 with type 1 diabetes mellitus, 20% were treated with oral medication, 35% with human insulin and 13% with insulin analogs, HbA1C: 10.2% ± 1.8. Mean values for MPV in patients with diabetic retinopathy, without diabetic retinopathy were 10.97 ± 0.74 fL and 11.01 ± 0.9fL, respectively. There was no statistically significant correlation between MPV and the development of diabetic retinopathy ($P = 0.751$).

Conclusion

Although MPV can be a predictor of the platelets' high activity in diabetes mellitus, other risk factors of micro or macroangiopathy must be taken into consideration while monitoring the disease progression.

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EP807

Characteristics of diabetes in a group of tunisian women at procreative age

Chaima Sdiri, Haifa Abdesselem, Emna Bornaz, Nesrine Dhieb, Fatma Boukhayatia, yahyaoui rim, Ben Brahim Asma, Kamilia Ounaissa & Chiraz Amrouche
National Institute of Nutrition, Department of Nutritional Diseases (D), Tunis, Tunisia

Background
Type 1 diabetes (T1DM) affects young women of childbearing age. Type 2 diabetes (T2DM) is also increasingly affecting this age group due to obesity increase. The aim of this study was to determine the characteristics of diabetes affecting a group of women at procreative age.
Methods
We conducted a descriptive cross-sectional study among pregnant women followed for pre-gestational diabetes at the Department of Nutritional Diseases « D » of the National Institute of Nutrition of Tunis, between January and December 2023.
Results
We included 100 diabetic patients with a mean age of 34.12 ± 4.9 years [ext:23-44 years]. The level of education was primary, secondary and high in 34%, 43% and 23%, respectively. Most patients (82%) had T2DM. The mean duration of diabetes was 13.61 ± 7.36 years for T1DM and 3.61 ± 2.92 years for T2DM. Before pregnancy, about the half of patients (51%) were treated with metformin and 21.6% with insulin (among them, 21.6% were treated with insulin analogs). At the first diabetes consultation in pregnancy, the mean glycated hemoglobin (A1c) was 7.8 ± 1.6% with extremes from 5.9% to 12%. More than the half of the patients (57%) had an A1c level higher than 7%. Hypoglycemic episodes were reported by 22% of patients. Diabetic retinopathy affected 39% of T1DM and 6% of T2DM. Diabetic nephropathy affected 12% of T1DM. However, none of the T2DM had this complication. Hypertension, dyslipidemia, anemia and hypothyroidism affected 3%,6%,3%,7% of patients, respectively. The prevalence of planned pregnancies was 28% in the T1DM group and 11% in the T2DM group. Pregnancy planning was associated with: the university level of education ($P=0.026$), the presence of microangiopathic complications before pregnancy ($P=0.036$) and pre-gestational treatment with insulin analogs ($P=0.004$).
Conclusion
The preconception consultation is essential in the management of the futur pregnant diabetic women to anticipate and prevent maternal and fetal complications. Then, educating women about the benefits of this consultation is essential.

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EP808

Effect of habit modification on the likelihood of hospitalization with complications of patients with diabetes during the covid-19 pandemic social isolation

Liana Jashi[1,2], Tamar Peshkova[3], Nestan Bostoganashvili[4], Tamar Sharashenidze[2] & Koba Kamashidze[5]
[1]Avicena-Batumi Medical University, Georgia, Medicine, Batumi, Georgia; [2]David Aghmashenebeli University Of Georgia, Medicine, T'bilisi, Georgia; [3]Batumi Shota Rustaveli state University, Medicine, Batumi, Georgia; [4]Tbilisi Heart and Vaskular Clinic, Medicine, T'bilisi, Georgia; [5]University of Georgia, Medicine, T'bilisi, Georgia

Habits play an essential role in the treatment of chronic diseases. The main complaints of patients during isolation were sleep disturbance, eating patterns, increased tobacco and alcohol consumption, and reduced physical activity. The aim of the study is to examine the change in habits during social isolation during the COVID-19 pandemic as a predictor of the rate of hospitalizations with diabetes-related complications to determine the odds of impact.
Results
A retrospective cross-sectional study was conducted in Georgia from September 2022 to March 2023. 65 people participated in the survey—752 patients with early diabetes mellitus. Stenting/heart bypass during isolation increased the likelihood of hospitalization with sweet (OR = 3.3. CI 95% (1.16-9.71) $P=0.03$) and fatty (OR = 1.3 CI 95% (1.3-16.9) $P=0.018$) food. increase in consumption when quitting cigarette smoking (OR = 0, 103 CI 95% (0.11-1.0) $P=0.05$), protein diet (OR = 6,62. CI 95% (1.67-17.5) $P=0,000$) and physical activity up to 4-6 hours per week reduced (OR = 3,7. CI 95% (1.78-15.7), $P=0,000$). The probability of hospitalization for diabetic foot during isolation decreased with smoking cessation (OR = 0.108. CI 95% (0.011-1.034) $P=0.05$), increased with increased cigarette consumption (OR = 0.05. CI 95% (0.4-0.692) $P=0.025$), fatty foods (OR = 6.02. CI 95% (2.85-18.7) $P=0.000$) and hypodynamics (OR = 10.9. CI 95% (4.963-21.5) $P=0.000$). The probability of hospitalization for stroke was increased by insomnia (OR = 5.8. CI 95% (1.36-24.7) $P=0.017$), obesity (OR = 5.9. CI 95% (1.59-22.4) $P=0.008$) and intake increase in sugary food (OR) = 6.7. CI 95% (1.47-23.9) $P=0.014$).
Conclusion
Thus, changing habits (food, sleep, tobacco use, physical activity) during the COVID-19 pandemic was one of the critical predictors of the development of complications associated with diabetes mellitus, which significantly increased the likelihood of hospitalization of patients.

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EP810

Association between microalbuminuria and thyroid gland function in patients with diabetes type 2 and diabetic nephropathy

Alina Urbanovych, Andriana Vereshchynska & Fedir Laniush
Danylo Halytsky Lviv National Medical University, Endocrinology, Lviv

Background and aims
Diabetes type 2 (DT2) is a chronic condition that damages the whole metabolism. It has a growing incidence and is recognized as epidemic of 21st century. One of the most common complications of DT2 is diabetic nephropathy (DN). It is caused by persistent hyperglycemia and kidney damage. Microalbuminuria is one of the most important hallmarks of DN. Besides, it increases a risk of cardiovascular and neurological complications. Microalbuminuria is defined as albumin/creatinin ratio (ACR) 30-300 mg/g or daily albumin excretion 30-300 mg/24 h. DT2 is often accompanied by thyroid dysfunction. According to literature reviews, microalbuminuria is associated with thyroid function disorders. Our research aimed to study structure and function of thyroid gland in patients with DT2 and microalbuminuria.
Materials and methods
our study included 87 individuals (mean age – 57.1 ± 0.86 years; mean ACR – 139 ± 5.5 mg/g) with DT2 and no history of thyroid gland disorders. All participants had HbA1c level below 8.0% and did not change glucose-lowering agents during the study. Thyrotropin-stimulating hormone (TSH), free T4 (fT4), free T3 (fT3), thyroid-peroxidase antibodies (anti-TPO) levels were obtained as well as thyroid gland ultrasound.
Results
TSH (mean level 2.75 ± 0,34) positively correlated with ACR ($r=0.09$, $P<0.05$). FT4 (14.32 ± 1.09) and fT3 (2.37 ± 0.18) levels negatively correlated with ACR ($r=$ -0.22, $P<0.05$ and $r=$ -0.17, $P<0.05$ respectively), whereas Anti-TPO level (57.26 ± 6.84) positively correlated with ACR ($r=0.09$, $P<0.05$). Total thyroid gland volume (17.72 ± 1.39 ml) positively correlated with ACR ($r=0.05$, $P<0.05$).
Conclusion
our study demonstrates a strong association between thyroid and renal function. Patients with DN more often have hypothyroidism, positive anti-TPO, and greater total thyroid volume. Effective treatment of hypothyroidism in these patients can improve clinical outcomes of DT2 and microalbuminuria.

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EP811

Severe diabetic ketoacidosis following methamphetamine ingestion

Bethany Laquidara
Summa Health/Akron City Hospital, Internal Medicine, Akron, United States

Introduction
Diabetic ketoacidosis (DKA) can occur when the body is in an insulin-deficient state, which results in an inability to suppress lipolysis and thus ketone production[1]. Certain recreational drugs, particularly cocaine, have been found to increase the risk of developing DKA[2]. What is less clearly defined is whether methamphetamines act as a DKA-precipitant. This case depicts a patient with insulin-dependent diabetes and negative autoantibodies who was found to have severe DKA following methamphetamine ingestion.
Case Description
A 54-year-old male with a past medical history of insulin-dependent diabetes and polysubstance use disorder presented to the emergency department for altered mental status (AMS). History unable to be obtained secondary to AMS. Physical exam was notable for tachypnea, diffuse abdominal tenderness, and profound confusion. Initial work-up revealed severe DKA and hyperkalemia. Toxicology screen was positive for amphetamines and THC. Head imaging was

unremarkable. The patient was treated with regular insulin and bicarbonate drips, intravenous calcium, and fluids. Autoantibodies associated with type 1 diabetes were negative and C-peptide was low, suggesting a diagnosis of type 2 diabetes with depletion of pancreatic islet cells. The patient's DKA and hyperkalemia resolved with the above therapies. His hospital course was complicated by ongoing AMS and heavy oral secretions due to a lung abscess. This necessitated intubation and ultimately a tracheostomy. The patient was ultimately discharged to a long-term acute care facility.

Discussion

This case demonstrates severe DKA in a patient with insulin-dependent diabetes with negative autoantibodies following methamphetamine ingestion. While research on the interplay between methamphetamine use and DKA is scarce, one study examined autopsy and toxicology case files for the presence of methamphetamine in post-mortem blood samples[1]. They found a significantly increased rate of DKA in patients with insulin-dependent diabetes who use methamphetamine (66.7%) compared to patients with insulin-dependent diabetes alone (6%). While cause and effect cannot be established by that study or this patient case, further investigation into the role of methamphetamine as a possible precipitator for DKA is warranted.

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EP812

Foot care knowledge and practices of diabetic patients

Mouna Elleuch, Maryam Cheikhrouhou, Dhouha Ben salah, Khouloud Boujelbene, Yasmine Abdelkafi, Souhir Maalej, Fatma Mnif, Nadia Charfi, Mouna Mnif, Faten Hadj kacem, Mohamed Abid & Nabila Rekik
Tunisia

Introduction

Diabetic foot is a significant public health issue, and its management remains challenging, emphasizing the importance of prevention through the screening of high-risk feet and educating diabetic patients about preventive care.

Objectives

To assess, using a questionnaire, the knowledge and practices of diabetic patients regarding diabetic foot care and to determine the level of podiatric risk in our diabetic patients according to the International Working Group of the Diabetic Foot (IWGDF) classification.

Methods

We conducted a cross-sectional observational study with 60 diabetic patients hospitalized for uncontrolled diabetes at the Endocrinology Department of CHU Hedi Chaker in Sfax. Each patient underwent an interview, a physical examination, and a questionnaire on foot care knowledge and practices.

Results

The mean age of our patients was 52 ± 13.68 years, with a male-to-female ratio of 0.53. The average duration of diabetes was 12.5 ± 5.9 years. Clinical examination of the feet revealed skin dryness in 63.3% of cases. The knowledge level was poor in 28.3% of cases, satisfactory in 43.3% of cases, and good in 28.3% of cases, with a significant association with the educational level ($P < 0.001$) and diabetes type ($P = 0.012$). The practice level was poor in 26.7% of cases, satisfactory in 48.3% of cases, and good in 25% of cases, with a significant association with the educational level ($P = 0.03$) and diabetes type ($P = 0.036$). In our study population, the podiatric risk level was high in 18.3% of cases, with a significant association with knowledge level ($P = 0.029$) and practice level ($P = 0.019$).

Conclusion

These results underscore the need to enhance therapeutic education regarding diabetic foot care to improve adherence to foot care among diabetic patients, thereby contributing to better prevention.

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EP813

Clinical characteristics and complications of gestational diabetes mellitus: a single center spanish experience

Ana Paola Leon Ocando, Oliver Quintero Rodríguez, Selena Rodríguez Fernández, Kevin Díaz Gorrin & Itziar Aznar Ondoño
Hospital Universitario de Canarias, Endocrinology and nutrition, San Cristóbal de La Laguna, Spain

Introduction

Pregnancy involves distinct metabolic stages, initially characterized by maternal anabolism, followed by a catabolic phase driven by placental lactogen and various cytokines, leading to varying degrees of insulin resistance. DM is the most common metabolic disorder linked to pregnancy.

Objective

The study aimed to detail the clinical characteristics, obstetric complications, and neonatal outcomes of patients with GDM and their children.

Materials and Methods

This cross-sectional study utilized accidental sampling of 50 patients diagnosed with GDM (diagnosed in the 2nd or 3rd trimester, with no prior DM history), who were treated in our Hospital's Endocrinology and Nutrition clinic in 2022.

Results

The average age is 35.44 years. 68% were overweight or obese before pregnancy, and 16% had a history of GDM in previous pregnancies. 76% have a family history (of first or second degree) of T2DM. Regarding glycemic control, achieved through capillary glucometry, 60% was managed with dietary measures and physical activity, while the remaining 40% required insulin. 38% of the patients and their children lost follow-up so these results are unknown, however, during labor, 14% experienced complications, and 48% had normal vaginal deliveries. Concerning neonatal outcomes, 2% experienced hypoglycemia, another 2% were preterm, and 58% had no immediate complications. In the postpartum period, 10% of mothers showed carbohydrate intolerance, but DM was ruled out.

Conclusion

According to the literature, GDM is predominantly observed in individuals with a history of overweight or obesity and those with a family history of T2DM. While most cases are manageable through hygienic-dietary measures, a significant portion of patients require insulin therapy to maintain euglycemia throughout the pregnancy. It is important to note, however, that some patients may not adhere strictly to the recommended dietary guidelines. Furthermore, the incidence of complications during delivery and for the newborn is likely higher than reported in this study. This discrepancy can be attributed to the loss of patient follow-up, which is a notable limitation of this research.

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EP816

Characteristics of phenotypes in patients with diabetes mellitus type 2 and myocardial infarction

Yanina Saienko[1] & Borys Mankovsky[2]
[1]State Institution "Scientific and Practical Medical Center of Pediatric Cardiology and Cardiac Surgery of the Ministry of Health of Ukraine", Department of Cardiovascular Diabetology, Kyiv, Ukraine; [2]D.F. Chebotarev Institute of Gerontology of the National Academy of the Medical sciences of Ukraine, Kyiv, Ukraine

Cardiovascular (CV) diseases are the main cause of death in patients with diabetes mellitus. The different phenotypes can predispose to those disease in people with diabetes.

Aim

to identify phenotypic features in patients with type 2 diabetes mellitus (T2DM) and their impact on the development of myocardial infarction (MI).

Materials and methods

We examined 231 patients with T2DM with and without MI. The average age of patients was 61.57 ± 0.89 years, the duration of diabetes was 8.61 ± 0.56 years. The average level of HbA1c was 7.78 ± 0.12%, systolic blood pressure - 134.92 ± 1.04, diastolic blood pressure - 81.95 ± 0.68 mm Hg. Depending on the presence or absence of MI patients with T2DM were alienated into 2 groups. The number of patients with T2DM and MI was 59, and 172 without MI. For all patients were calculated BMI, creatinine level, albuminuria and the ratio of albumin to creatinine in the urine to diagnose chronic kidney disease (CKD). All patients received antidiabetic, antihypertensive and statin therapy. We analyzed the effect of age, BMI, duration of T2DM, HbA1c and CKD on the development of MI in patients with T2DM.

Results

Patients with T2DM without MI were significantly younger, their age was 62 [53-69] years, the duration of diabetes was significantly less than 6 [2-11] years, in compared to patients with T2DM with MI, where the age was 65 [61-72] years, and the duration of diabetes was 10 [2-17.5] years. BMI was significantly higher in the group of patients with T2DM without MI and amounted to 32 [28.1-36.2] kg/m^2, while in patients with T2DM with MI was 30 [28-34.3] kg/m^2. The level of HbA1c

in the groups of patients with T2DM with or without MI did not differ significantly. The risk factor of CKD III – IV was present in 21 of 172 patients without a history of MI and in 31 of 59 patients with MI and T2DM. The odds ratio for developing a heart attack in the presence of CKD was OR = 2,242 [1,21 - 4,125], $P=0,008$.
Conclusion
we identified the influence of age, duration of diabetes mellitus on the development of MI in patients with T2DM.

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EP817

Disease perception in patients with type 2 diabetes

Ben Hamida Yosra[1], Htira Yosra[1], Fitouri Sami[2], Trabelsi Syrine[1], Jallouli yesmine[1], Hadj Ali Zohra[1], Jemai, Chaima[1,1] & Ben Mami Faika[1]
[1]Institut De Nutrition, Tunis, Tunisia; [2]Institut De Nutrition, therapeutic dietetics and nutritional diseases 'C', Tunis, Tunisia

Background
The aim of the study was to describe patients' cognitive and emotional representations of type 2 diabetes.
Methods
We conducted a cross-sectional study of 50 adults with type 2 diabetes hospitalized in November 2023 in ward C at the National Institute of Nutrition and Food Technology. We used the translated and validated Arabic version of the Brief Illness Perception Questionnaire. Data were analysed using SPSS 26.
Results
The mean age of patients was 57 years. the ratio females-to-males was around 1.5. Diabetes had been present for more than 10 years in 66% ($n=33$) of participants, and was unbalanced in 92% ($n=46$). Patients treated with insulin therapy alone accounted for 50% ($n=25$). Degenerative complications were present in 88% ($n=44$) of cases, with microangiopathic complications predominating 84% ($n=42$). The first five items of the questionnaire concerned cognitive perception of the disease. Of those questioned, 6% ($n=3$) had answered that diabetes is a disease that severely affects life and 78% ($n=39$) thought that the disease would last a lifetime. 2% ($n=1$) of patients thought they could totally control their diabetes, 6% ($n=4$) felt that treatment was not helpful at all and 10% ($n=5$) had very severe symptoms. Items 6 and 8 described the emotional aspects of the disease so that 24% ($n=12$) of patients felt extremely worried about the disease and 14% ($n=7$) said they were extremely emotionally affected by it. In item 7, we measured the degree of understanding of the disease, as 4% ($n=24$) of participants felt they could understand their disease very well and identified the three main causes cited in order, namely acute psychological stress (68% $n=34$), followed by dietary errors 48%(% $n=24$) and heredity 12% ($n=6$). The mean score was 49.6, with extremes ranging from 24 to 72. Half the participants had a score of 50 or more.
Conclusion and recommandations
Most patients have a negative perception of their diabetic condition. We recommend that family and friends become more involved, as they can provide essential support for lifestyle changes and treatment compliance.

Key words: type 2 diabetes – Tunisia – perception – life-experience

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EP818

Diabetic type 1 adolescents and physical activities: Between recommendations and obstacles

Sofia Ouhessaine, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy-University Hassan II-Casablanca-Morocco

Introduction
Physical activity helps improve physical performance and glycemic balance in type 1 diabetics. Furthermore, these patients encounter obstacles to accessing a normal sporting life and therefore its benefits.
Objectives of the study
To evaluate the practice of physical activity (PA) among T1D people, their knowledge in terms of therapeutic adaptation and the obstacles facing its practice.
Material and methods
Descriptive cross-sectional study including adolescent T1D patients followed at the consultation in the endocrinology-diabetology department at Ibn Rochd University Hospital. During an interview, patients responded to a questionnaire consisting mainly of closed questions.
Results
Our study included 225 patients. The mean age was 16.9 years (14–18 years). The average HbA1c was 9.2%. Among our patients, 46% practiced regular sports activity as part of the school program, and only 19% practiced PA outside of school. Our patients had benefited from therapeutic education on PA in 23%. Our patients were reluctant to exercise by choice in 44% due to fear of hypoglycemia. Concerning treatment adaptations, the majority of patients resorted to reducing the doses of rapid insulin. Blood glucose self-monitoring was only ensured in 18% of patients. Hypoglycemia was found in 45% of cases, including 4% severe hypoglycemia. The occurrence of hyperglycemia was less frequent.
Conclusion
Our study showed the need for therapeutic education and patient support for better self-management of treatment, given that glycemic variations represent the main obstacle.

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EP821

Assessment of nurses' knowledge levels of diabetic foot care management

Ben Salah Dhoha, Khouloud Boujelben, Hamdi Frikha, Mouna Elleuch, Younes Derbel, Faten Hadjkacem, Fatma Mnif, Nadia Charfi, Mouna Mnif, Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Department of Endocrinology

Introduction
The diabetic foot represents a major public health problem worldwide, as it exposes patients with diabetes mellitus to a high prevalence of ulceration and amputation, with potential repercussions on patients' quality of life and even the society through its economic impact. Health care personnel, particularly nurses, play a crucial role in the management and prevention of diabetic foot disease. The aim of our study was to assess nuses'Knowledge levels of diabetic foot care management.
Patients and methods
A cross sectional and descriptive study was performed between September and November 2021. Knowledge levels were assessed by referring to a questionnaire based on International Working Group on the Diabetic Foot (IWGDF) recommendations, designed to evaluate the knowledge of 50 randomly selected nurses working in different departments caring for diabetic foot.
Results
Mean age was 30,9 years (25-58 years). Forty five were female (90 %) with a sex ratio of 0.11. Forty percent of nurses had between 5 and 10 years of professional experience in their current departments. Thirty-four percent of our population were aware that patients with diabetes mellitus are considered to be at high risk of ulceration, particularly when they present peripheral neuropathy or arteritis. Only 10 % of the nurses knew that the foot at risk should be examined regularly. Fourt two percent of nurses know that patients with diabetes mellitus should monitor their foot temperature one a day. Half of our population recognized that patients with diabetes mellitus should avoid applying moisturizing cream into interdigital spaces of foot.
Conclusion
At the end of our study, we demonstrated the existence of gaps in the theoretical knowledge of diabetic foot care management among nurses, which underlines the importance of better planning of continuing education of health care personnel, as well as multidisciplinary management.
Patients and methods

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EP824

Survey to understand gaps in diabetes patient education resources and to identify potential lifestyle-modifying services

Banshi Saboo[1], Manoj Chawla[2], Rishi Shukla[3], Debasis Basu[4], Blessy Saju[5], Rahul Iyer[5], Amarnath Sugumaran[5] & Senthilnathan Mohanasundaram[5]

[1]Dia Care – Diabetes Care and Hormone Clinic, Ahmedabad, India; [2]Lina Diabetes Care Center, Mumbai, India; [3]Regency Hospital, Kanpur, India; [4]Apollo Multispecialty Hospital, Kolkata, India; [5]Cipla Ltd., Medical Affairs, Mumbai, India

Introduction & Objective
A vital but often disregarded pillar of diabetes management is effective patient education. The objective of this survey was to identify gaps in the existing patient education resources & to understand which patient services can help boost adherence to requisite lifestyle & therapy.
Methods
A cross-sectional study was conducted between January & March 2023, involving clinicians managing type 2 diabetes mellitus across India. Responses were collected, with prior informed consent, using a structured digital questionnaire. Data was analysed & expressed as descriptive statistics.
Results
This survey involved 903 clinicians pan India, of whom ~70% belonged to 30-50 years age group, had postgraduate degree in medicine & had private consulting practice. Clinicians opined that besides in-clinic counselling; 'physical counselling' (60%) & 'initial physical counselling followed-up on virtual platform' (35%) were the most effective. When enquired about the major gaps in existing patient education content, clinicians chose- 'content not being tailored as per regional/local preferences' (55%), 'lack of content simplicity' (54%) & 'quality of content' (39%). Most clinicians (84%) rated availability of patient education content in regional languages to be important/very important. The key challenges observed by clinicians in the existing dietary education resources were 'diet charts not tailored to local region' (48%), 'content unavailability in regional languages' (46%) & 'lack of qualified dietitians' (40%). Most clinicians mentioned that complimentary services were extremely/very useful {lab tests (86%), dietitian (83%) & gym (64%)} in helping to increase patient adherence to lifestyle & therapy.
Conclusion
This survey reveals that for patient education resources-quality, regional customization, simplification & availability in regional languages are important requisites. Furthermore, complimentary services including dietitian, gym & lab tests may help improve patient adherence to lifestyle & therapy.

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EP827

Comparative analysis of clinical, bioelectrical and ultrasound characteristics in a cohort of post-critical patients after severe pneumonia covid-19, according to serum vitamin d levels

Víctor José Simón Frapolli[1,2], Miguel Damas Fuentes[1], Isabel Vegas Aguilar[1], José Manuel García Almeida[1] & Francisco Tinahones Madueño[1,2]
[1]Hospital Universitario Virgen de la Victoria, Endocrinology and Nutrition, Málaga, Spain; [2]BIONAND, Málaga, Spain

Introduction
Vitamin D deficiency is a common health problem worldwide, particularly in elderly patients. Vitamin D is considered a key hormone in mineral and bone metabolism, as well as in functions such as the regulation of cell proliferation and differentiation, its immunoregulatory activity, its effect on the cardiovascular system and its neuroprotective and anti-ageing effects, among others. Hypovitaminosis D has been linked in multiple studies to a higher incidence and severity of COVID-19 infection, as well as to increased mortality. It is also involved in muscle function, maintaining strength and physical performance, and there is evidence to support the association between vitamin D deficiency and an increased risk of sarcopenia, frailty and sarcopenic obesity. The aim of this study is to compare different clinical, bioelectrical and ultrasound characteristics according to serum vitamin D levels in a cohort of patients after having been admitted to the ICU for severe SARS-COV2 pneumonia.
Methods
Vitamin D levels, in no case supplemented, as well as other demographic, anthropometric, ultrasound, bioelectric, analytical and hospital stay-related variables were collected in a cohort of 29 patients 15 days after hospital discharge following admission to the ICU for severe SARS-COV2 pneumonia. These variables were then compared according to serum vitamin D levels. For this purpose, patients were classified into 3 categories according to vitamin D levels ($\leq$20 ng/ml, 20-29.99 ng/ml, $\geq$30 ng/ml).
Results
Statistically significant differences were observed in the degree of obesity according to BMI ($P=0.037$) and age ($P=0.032$) as a function of serum vitamin D concentration, while a trend towards statistical significance was observed in other variables such as skeletal muscle mass (SMM)/kg. No differences were observed in other variables such as sex, diabetes, sarcopenia, sarcopenic obesity, malnutrition (according to GLIM criteria), ultrasound or bioelectrical variables. In the correlation analysis, vitamin D levels correlated significantly positively with albumin levels ($r=0.499$, $P=0,022$).
Conclusion
Vitamin D only shows a significant positive correlation with albumin levels. In our cohort, only the degree of obesity and age showed statistically significant differences according to vitamin D levels, but no differences were found in other clinical, bioelectrical and ultrasound parameters.

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EP828

Polymedication in the elderly

Yesmine Jallouli[1], Rym Ben Othman[2], Syrine Trabelsi[3], Yosra Ben Hmida[3], Ramla Mizouri[3], Olfa Berriche[3], Henda Jamoussi[3] & Faten Mahjoub[3]
[1]Tunis, dapartment A, tunis; [2]Tunisia, dapartment A, tunis, Tunisia; [3]National Institue Of Nutrition and food technology, dapartment A, tunis

Introduction
Polymedication is a major problem affecting an increasing number of patients, particularly the elderly which can be deleterious in terms of quality of life, morbidity and mortality.
Objective
The aim of the present study was to determine the prevalence of polymedication in elderly diabetic patients.
Methods
This was a descriptive cross-sectional study conducted at the Institut National de Nutrition in 2023 in diabetic patients aged over 70. Polymedication was defined as taking more than five tablets per day.
Results
We enrolled 70 diabetic patients. The mean age of the population was 73 ± 2.4 years, with females predominating (65.1%). Diabetes was poorly controlled in 73.77% of patients, with a mean glycated hemoglobin of $10.54\%\pm2.16$. Diabetes was complicated by retinopathy in 61% of cases. Comorbidities were dominated by hypertension and dyslipidemia in 84.1% and 85.7% of patients respectively. Polymedication concerned 64% of the study population. Statins were the most prescribed pharmaceutical class (78.2%), followed by antihypertensive drugs (69.7%), oral antidiabetics 51.2%)
Conclusion
Polymedication was common among elderly diabetic subjects. This may increase the risk of drug interactions and poor compliance.

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EP836

Perception of the risk of developing type 2 diabetes among women with gestational diabetes

Mouna Elleuch, Younes Derbel, Hamdi Frikha, Dhoha Ben Salah, Kouloud Boujelben, Fatma Mnif, Mouna Mnif, Nadia Charfi, Faten Haj Kacem Akid, Mohamed Abid & Nabila Rekik Majdoub
Hedi Chaker University Hospital, Endocrinology

Introduction
Gestational diabetes poses a significant public health challenge in Tunisia and various regions globally, affecting approximately 1 in 6 pregnant women. While it typically resolves post-delivery, about 20% of individuals with gestational diabetes (GD) develop Type 2 Diabetes (T2D) within five to ten years thereafter. Recognizing this heightened risk is crucial for prompt adoption of preventive measures. This study aimed to evaluate the perception of the risk of developing T2D among women with GD.
Methods
A cross-sectional study conducted at the Obstetric Gynecology Department at Hedi Chaker Hospital in Sfax. We assessed socio-demographic characteristics, educational backgrounds, and familial history of diabetes among participants. Health risk perception was measured using the RPS-DD instrument.
Results
The study included 130 patients with GD. Results revealed that the majority of participants were aged over 30, possessed a high school education (36%), and half reported one or more family members with a history of diabetes. The majority of patients (59,7%) were at their third pregnancy. The findings indicated that the perception of future health risk was moderate (mean score 2,4/4). Specifically, the perception of developing Type 2 diabetes over the next ten years subsequent to gestational diabetes was relatively average; notably, 49% perceived virtually no

risk of developing diabetes in this timeframe. Additionally, patients showed an average perception of the impact of lifestyle measures on the subsequent risk of developing TD2 (5,5/11 on RPS-DD scale).
Conclusion
In this study, women with gestational diabetes exhibited an average perception and knowledge of the risk to their future health. Consequently, enhancing health risk perception is essential for promoting preventive measures among individuals with gestational diabetes.

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EP840

Vitamin B12 and B9 deficiency in type 2 diabetes: Diabetic nephropathy risk assessment

Youssef Gharbi, Bchir Najla, Salma Salhi, Annam Benchhida, Dorra Dorraelguiche, Zouaoui Chadia & Haroun Ouertani
Military Hospital of Tunis, Endocrinology, Tunis, Tunisia

Introduction
Diabetic nephropathy (DN) is a major complication of diabetes and may be fatal at an end stage kidney disease. Several mechanisms lead to the basic lesion of DN (thickening of the glomerular basement membrane) including oxidative stress, inflammation and hyperhomocysteinemia. Being coenzymes of homocysteine metabolism, a deficiency in vitamin B12 and B9 will cause an accumulation of circulating homocysteine. Our objective was to evaluate the association between the deficiency of these vitamins and DN in type 2 diabetics.
Methods
It was a cross-sectional study that included 100 type 2 diabetic patients. Vitamin B12 deficiency was defined by a level $<$ 203 pg/ml. Vitamin B9 deficiency was certain for a level $<$ 3 ng/ml and possible for a level between 3 and 6 ng/ml. DN was considered in the presence of albuminuria $>$ 30 mg/24 h or a Glomerular Filtration Rate $<$60 ml/min
Results
In our population, 40% of patients had positive albuminuria and 11% had renal failure of all stages. In total, 43% of patients had DN. It was significantly associated to diabetic retinopathy ($P=0.015$) and diabetic neuropathy ($P=0.039$). The average vitamin B12 level was 220.62 pg/ml for patients with DN vs 209.43 pg/ml for those without DN. Vitamin B12 deficiency was not significantly associated to DN ($P=0.420$). The average vitamin B9 level was 8.83 ng/ml for patients with DN and slightly higher at 9.05 ng/ml for those without DN but with no significant association between possible vitamin B9 deficiency and DN ($P=0.796$).
Conclusion
Our study didn't show an association between vitamin B12 and B9 deficiency and DN. However, given the multitude of studies on the subject, more in-depth studies would be necessary to confirm the absence of this association.

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EP841

Nutrients intake and gastrointestinal disorders in type 2 Diabetics

Hana Ben jemâa, Berriche Olfa, Rym Ben Othman, Amel Gamoudi, Emna Talbi & Jamoussi Henda
National Institute of Nutrition, A, Tunis, Tunisia

Introduction
Micronutrient deficiencies can contribute to the development or exacerbation of gastrointestinal disorders especially in type 2 diabetic patients. The aim of our study was to determine the effect micronutrient status on gastrointestinal symptoms in diabetic patients.
Methods
We conducted a retrospective descriptive study. We included 115 type 2 diabetics patients. A dietary survey was conducted for each patient to determine nutrient intake. We used the screening micronutrient deficiencies questionnaire (DDM) ''B'' related to digestive disorders and validated by the European Institute of Dietetics and Micronutrition (IEDM). The patients were classified into 3 groups depending on their score results: high, medium, low scores.
Results
The patients' median age was 57.93$\pm$7.48 years. The majority of the participants were women (67.8%), resulting in a sex ratio of 2.1. The majority of the patients are sedentary (73%). The majority of diabetic patients (58.3%) had high blood pressure. Sixty percent had dyslipidemia. The average duration of type 2 diabetes among patients was 10.94$\pm$7.33 years. Microvascular and macrovascular complications were found in 54,8% and 20% of the patients, respectively. High, medium, and low scores were noted in 23,5%; 40,8% and 35,7% of the patients, respectively, using the DDM B. We found negative associations between DDM B score and fiber intake ($P<0,001$). No significant associations were found between micronutrient intake and the DDM score.
Conclusion
Understanding the relation between gastrointestinal health and nutrition is essential for developing effective strategies for both preventing and managing these conditions.

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EP842

What about breastfeeding in diabetic women?

Chaima Sdiri, Haifa Abdesselem, Emna Bornaz, Mariem Cheikhrouhou, Fatma Boukhayatia, Asma Ben Brahim, Rim Yahyaoui, Kamilia Ounaissa & Chiraz Amrouche
National Institute of Nutrition, Department of Nutritional Diseases (D), Tunis, Tunisia

Background
Breastfeeding offers short- and long-term health benefits to mothers and their infants. In the literature, many studies suggest that diabetic women breastfed their babies less than non-diabetic women. The aim of our study was to determine the breastfeeding rates in a group of diabetic women.
Methods
It was a prospective descriptive study conducted in pregnant women followed for pregestational diabetes at the Department of Nutritional Diseases « D » of the National Institute of Nutrition of Tunis. Women included in this study were contacted by telephone one week after delivery and they consulted at two and six months postpartum. Women who had an abortion or had been lost to follow-up were excluded from the study.
Results
We included 102 diabetic patients with a mean age of 35.12$\pm$4.8 years [ext:23-44]. Most patients had type 2 diabetes (82%). The mean duration of diabetes was 4.37$\pm$3.87 years. Twenty-four patients were excluded from the study. Most patients (73%) had given birth by caesarean section. Preterm delivery was noted in 14% of the cases. To one week after delivery, 40% of patients breastfed exclusively, 42% breastfed and bottle-fed, while 18% used formula milk only. After 2 months of childbirth, breast-feeding was noted in 77% of patients; it was exclusive in 44% of cases and partial in 33%. After six months of childbirth, only 10% of babies were exclusively breastfed, while the half were formula-fed. Hospitalization of the newborn in neonatology was the main obstacle to initiate breastfeeding, according to the patients included in the study (41%). Twenty-two patients considered the quantity of breast milk produced insufficient to cover the needs of the newborn. During hospitalization in the maternity ward, 30% of women were educated about breastfeeding techniques.
Conclusion
Our study highlighted the low rate of breastfeeding among diabetic women. Boosting education for diabetics on the importance of breastfeeding could improve this rate.

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EP843

Prevalence of undernutrition among elderly diabetics in hospitals

Yesmine Jallouli, Rym Ben Othman, Syrine Trabelsi, Ramla Mizouri, Olfa Berriche, Faten Mahjoub & Henda Jamoussi
National Institue of Nutrition and Food Technology, Dapartment A, Tunis

Objective
To estimate the prevalence of undernutrition among elderly diabetic patients in hospital.
Patients and methods
Descriptive cross-sectional study enrolling 100 patients aged $\geq$ 70 years who were hospitalized in ward A of the National Institute of Nutrition in Tunis. The diagnosis of undernutrition was established according to the criteria proposed by HAS 2021.
Results
The mean age of included patients was 73 y$\pm$2.4 years with a female prevalence (65.1%). The mean HbA1c level was 10.54%$\pm$2.16%. The majority of patients were on insulin therapy (84.9%). Mean weight was 71.9$\pm$5.5 kg, corresponding to a mean BMI of 28.75$\pm$4.51 kg/m^2. Among elderly diabetics, 14% had a BMI

< 22. The overall prevalence of undernutrition was estimated at 49%. Sarcopenia was present in 42% of patients, of whom 31% had reduced muscle strength, 9% had reduced muscle mass and 2% had both reduced strength and muscle mass.
Conclusion
Nutritional screening is essential for all diabetic seniors, regardless of their calorie intake and BMI.

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EP845

Cardiovascular risk in type 1 diabetes

Marwa El Arem, Bilel Ben Amor, Hanene Sayadi, Inès Khochteli, Ekram Hajji, Héla Marmouch, Sana Abid & Ines Bayar
Hospital Fatouma Bourguiba, Endocrinology

Objectives
The aim of our work is to evaluate the prevalence of cardiovascular risk factors in type 1 diabetics aged between 10 and 20 years.
Patients and methods
Retrospective study including 54 type 1 diabetic patients, followed at the endocrinology department of Fatouma Bourguiba hospital of Monastir during the year 2023.
Results
The mean age was 34.3 ±1.33 years with a female predominance (sex ratio=F/H) =2. they were all poorly balanced with a mean HbA1C=10.7±2.7%. the mean BMI was 22.8 ± 3.7 kg/m^2, with overweight observed in 12.9% and no patient was obese. the prevalence of smoking and hypertension were 16.4% and 7.3% respectively. The lipid profile showed LDL>1 g/l in 31% and hypoHDL-haemia in 31.4%. Diabetic nephropathy was found in 20% of patients, only one of whom had stage 4 renal failure. Diabetic retinopathy was found in 38.2%, half of whom had proliferative DR. Cardiovascular problems were mainly ischaemic heart disease (10.9%). Only one patient suffered a stroke.
Conclusion
These results suggest that after a decade of evolution, a diabetic accumulates several cardiovascular risk factors. This underlines the importance of comprehensive management of glycaemic control and other cardiovascular risk factors to improve cardiovascular morbidity.

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EP847

Unveiling the diabetes dilemma: a comprehensive analysis of type 2 diabetes complications in tunisia

Souhir Maalej, Fatma Mnif, Siddiqa Soomauroo, Abdel Mouhaymen Missaoui, Dhouha Ben Salah, Khouloud Boujelben, Mouna Mnif, Nadia Charfi, Faten Hadjkacem, Mouna Elleuch, Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Endocrinology, Sfax

Background
Diabetes mellitus is a global chronic health challenge, and Tunisia is witnessing a concerning surge in the prevalence of type 2 diabetes (T2D). According to the IDF 2021, diabetes affects 10.8% of adults in Tunisia, equivalent to 869,400 cases among a total adult population of 8,046,400.
Materials and Methods
A retrospective descriptive study was conducted to gather data on diabetic patients with chronic complications. The study encompassed patients hospitalized in the Endocrinology Department of Hedi Chaker University Hospital in Sfax from January 1 to December 31, 2022. The research focused on the epidemioclinical and therapeutic profiles of complicated diabetic disease.
Results
The study comprised 114 patients, with 64 (56.1%) males and 50 (43.9%) females, resulting in a sex ratio of 1.28. The average age at hospitalization was 65.38±10.17 years, ranging from 41 to 87 years. The mean BMI was 28.8±6.2 kg/m^2;, with females exhibiting a higher average (32.2±6.5 kg/m^2;) compared to males (26.3±4.7 kg/m^2;). Dyslipidemia was the predominant risk factor (86.8%), followed by hypertension (74.6%), obesity (32.5%), and smoking (21.1%). The average diabetes duration was 12.87±8.38 years. Treatment modalities included exclusive use of oral antidiabetic drugs (OAD) for 61.4%, insulin for 17.5%, and a combination of OAD and insulin for 14.9%. Diabetic nephropathy was identified in 67.54% of patients, while diabetic retinopathy and neuropathy were present in 33.3% and 52.6%, respectively. Among the 90 patients with cardiovascular involvement, coronary insufficiency was the predominant macroangiopathy (59.7%), followed by heart failure, peripheral arterial disease, and stroke (10.5%).
Conclusion
Type 2 diabetes is linked to a wide array of complications, categorized as macrovascular and microvascular. This study illuminates the pervasive complications of type 2 diabetes, emphasizing the necessity for comprehensive management strategies addressing both macrovascular and microvascular aspects. A deep understanding of the epidemiology and treatment patterns of diabetic complications is vital for enhancing patient outcomes and preventing long-term complications.
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EP848

Quality of life assessment in patients with diabetic foot

Malak Iggar, Haraj Nassim Essabah, El Aziz Siham & Chadli Asma
CHU Ibn Rochd, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
Diabetic foot represents a daunting complication of diabetes, compromising the patient's functional prognosis and leading to a deterioration in the quality of life.
Objectives
To assess the quality of life of diabetic patients with diabetic foot and analyze the factors associated with a decline in quality of life.
Patients and methods
An observational, analytical, and prospective study involving 58 patients hospitalized in the Department of Endocrinology and Metabolic Diseases. The patient's quality of life was assessed using the SF36 score, and factors related to poor quality of life were analyzed using SPSS software.
Results
The average age of our patients was 52.5 years, with a male predominance in 59.5% of cases. The average duration of diabetes was 14.2 years, and that of foot ulcers was 3 months. Overall, the quality of life was low in all eight SF-36 subscales: physical functioning (mea n=45%); role limitations due to physical health (mea n=32%); role limitations due to emotional problems (mea n=33%); emotional well-being (mea n=52%); social functioning (mea n=37.45%); pain (mea n=55%); general health (mea n=35.6%), and vitality (mea n=35%). The presence of pain, ulcer recurrence, peripheral arterial disease (PAD), and a longer duration of ulcer evolution were associated with a poorer quality of life (p: 0.05).
Conclusion
Diabetic foot represents an economic and psychosocial burden, resulting in a significant deterioration in the quality of life for patients. Psychological support and better pain management are necessary to alleviate this burden.

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EP850

Wolfram syndrom: a case report

Marwa El Arem[1], Hamza Elfekih[2], Fatma Ben Abdessalem[2], Koussay Ach[2], Yosra Hasni[2] & Molka Chadli Chaieb[2]
[1]Hospital Fatouma Bourguiba, endocrinology; [2]Farhat Hached University Hospital Sousse, Endocrinology

Wolfram syndrome is a rare, autosomal recessive entity characterized by several progressive neurodegenerative manifestations.
Observation
We report the case of a 27-year-old patient from a Consanguineous marriage, followed for hypogonadism with delayed puberty and insulin-requiring diabetes since the age of 13 with negative autoantibodies. His diabetes is complicated after 5 years of a mainly vegetative neuropathy with neurogenic bladder complicated by bilateral ureterohydronephrosis with intermittent catheterization, unfelt hypoglycemia and gastroparesis. The diagnosis of central diabetes insipidus was made after 13 years of progression of diabetes mellitus in the face of no improvement in the polyuropolydipsic syndrome despite glycemic control. This diagnosis was confirmed by a fluid restriction test and an hypothalamic pituitary MRI. Faced with this association, and the presence of a bilateral decline in visual acuity, Wolfram syndrome was suspected. An ophthalmological examination was completed which showed bilateral optical atrophy with minimal diabetic retinopathy. The ENT examination showed bilateral sensorineural hearing loss.

Conclusion
The clinical picture of Wolfram syndrome is quite rich and variable. This heterogenicity is a cause of diagnostic delay and the appearance of quite serious complications.

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EP852

Assessment of vitamin d status and depression grade in patients with diabetes mellitus type 2 in chronic stress conditions

Maryna Bobryk[1], Viktoriia Yerokhovych[1], Dmytro Malyi[2] & Iuliia Komisarenko[1]
[1]Bogomoletz National Medical University, Endocrinology, Kyiv, Ukraine; [2]Bogomoletz National Medical University, Dentistry, Institute of Post-graduate Education, Kyiv, Ukraine

Introduction
Ukrainian population is facing many challenges of war including chronic stress, D deficit, often unavailability of medical care. In these conditions some diagnostic disadvantages of Diabetes Mellitus type 2 (DM 2) patients' status are also observed[1]. According to Ukrainian Consensus on Diagnosis and Management of Vitamin D Deficiency in Adults, approximately 20% of Ukrainian population has Vit D deficit (VDD) and 27% Vit D insufficiency (VDI)[2].
Aim of the study
To evaluate 25-hydroxyvitamin D level in DM 2 patients with different severity of depression.
Methods
121 DM 2 patients aged 19-75 years were examined. We studied the level of 25 hydroxycholecalciferol (25-OH D) using Chemiluminescent immunoassay. Diagnosis of VDD and VDI were made according to Clinical Practice in the Prevention, Diagnosis and Treatment of Vitamin D Deficiency: A Central and Eastern European Expert Consensus Statement[3]. Grade of depression was evaluated with Depression, Anxiety and Stress Scale, DASS 21. There were 5 grades of depression: Normal, Mild, Moderate, Severe, Extreme.
Results
Distribution of patients according to the severity of depression: 6 patients had no symptoms of depression, 24 patients had Mild, 43 Moderate, 42 Severe and 6 Extreme grade of depression. We observed inverse relationship between 25-OH D level and Depression grade in DM 2 patients, from 28.05 ± 2.6 ng/ml (correspond to VDI) in Mild depression to 9.5 ± 0.4 ng/ml (correspond to VDD) in Extreme depression ($P < 0{,}001$); inverse relationship between 25-OH D level and Body Mass index (BMI) (rSpearman = -0.304, $P = 0.001$).
Conclusion
In chronic stress patients with DM 2 need treatment with vitamin D and consultation of psychologist.
Keywords 25-OH D, Vit D deficit, Vit D insufficiency, Depression, Diabetes Mellitus, DASS21
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EP853

Pubertal development in young type 1 diabetic patients: about 121 patients

Younes Boukaidi Laghzaoui, Nassim Essabah Haraj, Siham El Aziz & Asmaa Chadli
CHU Ibn Rochd, Endocrinology, Diabetology and Metabolic Diseases, Casablanca, Morocco

Introduction
Pubertal development is controlled by a series of hormones produced by the hypothalamus, pituitary and sex glands. In people with type 1 diabetes, blood glucose levels can affect the production of these hormones and, consequently, affect the pubertal development, inducing pubertal delay. The aim of this study is to describe the impact of diabetes and its various parameters on pubertal development in young type 1 diabetic patients.
Patients and Methods
This is a cross-sectional, descriptive, analytical study about 121 cases conducted in the Endocrinology Department of CHU Ibn Rochd in Casablanca, from January 1, 2019 to December 31, 2022. We included young type 1 diabetic patients aged between 14 and 20 years, whose diabetes diagnosis was more than 6 months old. The Tanner score was used to assess puberty in patients. Statistical analysis was performed using the SPSS 20 program.
Results
We recruited 121 patients with a mean age of 16.78, 58% female and 42% male. The duration of diabetes ranged from 1 to 14 years, with an average of 5.63 years. HbA1c ranged from 6.4% to 17.6%, with an average of 12.1%. Only 5% of patients were balanced, with HbA1c $<7.5\%$. In our study, the prevalence of delayed puberty was 21% (26 patients). We noted no significant relationship between toxic habits, duration of diabetes, regularity of follow-up, type of insulin therapy regimen, glycemic imbalance, total basal dose, frequency of hypoglycemic episodes, BMI and pubertal delay.
Conclusions
The prevalence of delayed puberty is high among diabetic patients in developing countries, and can be explained by various socio-economic factors: poor access to healthcare, poor diet and poor balance… Our results suggest that the occurrence of delayed puberty was not related to socio-demographic or diabetes-related factors.

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EP854

Diabetic Mastopathy- a diagnostic dilemma

Hanaan Ashraf & Andrabi Basharat
University Hospital Sussex, Endocrinology, United Kingdom

Introduction
Diabetic mastopathy (DM) is a rare benign fibroinflammatory disease of the breast with the prevalence of 0.6–13%· seen in long standing Type 1 diabetes who may have other diabetes related complications. Its also been described in patients with type II diabetes, autoimmune diseases such as Hashimoto's thyroiditis. The term lymphocytic mastopathy in used interchanged due to the histopathology and for patients without diabetes. It presents in men and women presents as a solitary mass or bilateral disease. Both the clinical features and the imaging characteristics of DM can mimic those of invasive breast cancer. Lymphocytic mastitis with or without diabetes mellitus may represent a lymphoepithelial lesion of the MALT-type which is considered to bear a prelymphomatous potential. Diagnosis is complex, and biopsy of the lesion is often necessary to establish a proper lesion classification. Here, we report a case of Diabetic mastopathy.
Clinical Presentation
31 years old type 1 diabetic woman G1P1 presenting with right painless breast lump for 3 weeks duration. She has no other comorbidities other than long standing Type 1 DM and has been on Insulin Aspidra + Lantus. She is 11 months postpartum and stopped breastfeeding 4 months ago. On clinical examination she appeared normal built, normal general Physical examination; breast examination right subaeroelar hard mobile painless irregular nodule of 2 cm, no skin or nipple changes or lymphadenopaty. She was evaluated with bloods and usg breast. The Usg breast showed dense glandular tissue with 2 cm subaereolar lump appeared benign in nature. She was reviewed after 6 weeks for a repeat scan which showed 3 cm right ill defined mass with low echogenecity. She had a core biopsy which reported lymphocytic infiltration and fibrosis compatible with the diagnosis of diabetic mastopathy.
Discussion
Diabetic mastopathy is a rare benign breast lesion. It poses a clinical dilemma due to similarities of presentation with breast malignancy it can lead to additional investigations and surgery. Dm is seen with other diabetic complications such as neuropathy, retinopathy or nephropaty. Although our patient had long standing type 1 diabetes she did not have any other related diabetic complications. It can be diagnosed with the help of radiological imaging but as it may mimic invasive cancer. Core-needle biopsy remains to be a gold standard. In difficult cases complementary imaging methods such as ultrasound, mammography, and MRI should be used. This is important to confirm the diagnosis and to avoid any risk of missing early breast cancer. DM patient can be managed symptomatically and excision is not necessary in asymptomatic patients.

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EP855

Nutrition for diabetic patients and oral health

Yesmine Jallouli, Zohra Hadj Ali, Sami Fitouri, Syrine Trabelsi, Olfa Lajili, Imen Hedfi, Chaima Jemai, Yosra Htira & Faika Ben Mami
National Institue Of Nutrition and food technology, dapartment C, tunis

Introduction
Diabetes is a chronic pathology with multivisceral repercussions, and the oral cavity is no exception. Oral disorders in diabetic patients are frequent and varied, negatively influencing their oral quality of life.
Objective
The aim of our work was to determine the link between the diet of the diabetic subject and oral health.
Methods
This was a descriptive cross-sectional study conducted at INNTA among 30 diabetic inpatients. Data were collected on the basis of a pre-established questionnaire, a biological check-up, a 24-hour dietary survey, a frequency survey and dietary habits.
Results
We enrolled 30 diabetic patients. The sex ratio F/H was 0.6. The mean age of our population was 45.94 ± 14.52 years. Type 2 diabetes predominated (67%) and was poorly controlled in 97% of patients, 50% of whom were treated with insulin. The average age of diabetes was 11.37 ± 9 years. According to the analytical study, there was a significant correlation between mucosal inflammation and diabetic nephropathy, as well as between periodontitis and diabetic retinopathy. Iron, calcium and chromium deficiency was significantly correlated with the number of decayed and decayed teeth. Gingival inflammation was significantly correlated with excess intake of simple sugar and thiamine.
Conclusion
Oral pathologies are an integral part of the complications of diabetes, which must be managed early to preserve patients' oral quality of life.

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EP856

Prediction of glycemic imbalance during ramadan in non-fasting diabetic patients using artificial intelligence-based machine learning

Zaynab Hifdi[1], Imane Motaib[1], Saloua Elamari[1], Soukaina Laidi[1] & Marouan Fatima[1]
[1]Cheikh Khalifa Bin Zayed Al Nahyan Hospital, Casablanca, Morocco

Introduction
During Ramadan, the daily lifestyle undergoes changes that influence the glycemic balance of both fasting and non-fasting diabetic patients. The aim of this study is to predict glycemic imbalance during Ramadan in non-fasting diabetic patients using Machine learning models.
Methods
This is a prospective study which included all non-fasting diabetic patients during the month of Ramadan and followed at the endocrinology department of the Sheikh Khalifa University Hospital in Casablanca. We collected anthropometric and metabolic parameters during three consultations (before, during and after Ramadan). To predict imbalance, we trained artificial intelligence models based on Machine Learning using the collected data. Finally, we ran several simulations with the best-performing model, using the variables that proved to be the main predictors of poor glycemic control.
Results
We included 154 patients. The prevalence of poor glycemic control among patients was 52.6%. The Extra Tree Classifier was the best-performing model for predicting imbalance (accuracy $= 0.87$, AUC $= 0.87$). The most significant variables for predicting imbalance were: baseline caloric intake and its evolution, female sex, baseline weight, evolution of BMI and waist circumference, and total cholesterol level after Ramadan.
Conclusion
The clinical use of our results will enable us to target risk factors in order to improve glycemic control in non-fasting diabetics.

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EP857

Screening for obliterating arteriopathy of the lower limbs in type 2 diabetics using the systolic pressure index

Ramla Mizouri, Berriche Olfa, Rym Ben Othman, Nadia Ben Amor & Jamoussi Henda
Institut De Nutrition, Tunis, Tunisia

Introduction
Lower limb arterial disease (PAAD) is a serious complication of diabetes and is particularly common in patients at high cardiovascular risk. Its management in diabetic patients is a major public health problem, with sometimes tragic consequences for the patient. The objective of our work was to detect PAD in type 2 diabetics.
Materials and Methods
This was a descriptive cross-sectional study involving 122 type 2 diabetics hospitalized at the National Institute of Nutrition. Systolic pressure index (SPI) was measured using a Spengler pocket Doppler. Obliterative arteriopathy of the lower limbs is defined by a systolic pressure index less than 0.9 or more or less significant arterial incompressibility (mediacalcosis) by an ABI greater than 1.3.
Results
The average age of our patients was 52.4 ± 7.3 years with a sex ratio of 0.96. The duration of diabetes was 11.07 ± 3.3 years. The majority of patients (78.7%) were on insulin therapy. The average HBA1c was 9.8%. The average BMI of our population was 28.18 kg/m^2. More than a third (35.2%) of our patients were smokers and 39.8% were sedentary. Hyper-LDLemia type dyslipidemia was found in 56.2% of patients. Arterial hypertension was present in 45.1% of patients. Macroangiopathic complications were dominated by ATCD of stroke (5.7%) and MI (4.9%). The ABI was less than 0.9 in 38.5% of cases and greater than 1.3 in 3.3% of cases, of which more than half of the cases (58%) were asymptomatic.
Conclusion
Obliterating arteriopathy of the lower limbs (PAAD) is a frequent and serious complication in diabetic patients. Which underlines the interest of an effective preventive approach and early detection.

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EP858

Risk factors in persons with diabetes who underwent major and minor lower limb amputations during 2010-2016

Susanna Valland[1], Netaniel Philipson[2] & Trine Elisabeth Finnes[1,3]
[1]Hospital Innlandet, Norway; [2]University of Oslo, Faculty of medicine, Norway; [3]University of Oslo, Norway

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EP860

Primary hyperparathyroidism: analysis of 132 cases

Mohamed Abderrahmane Ahmed Ebett, Chadli Asma, El Aziz Siham & Haraj N.EEE
University Hospital Center Ibn Rochd - Casablanca, Casablanca, Morocco

Introduction
Primary hyperparathyroidism, common in the general population with a prevalence of 1 to 6 per 1000, is caused by an overproduction of parathyroid hormone, often due to a benign adenoma of the parathyroid glands.
Objectives
The study aims to analyze the correlation between the clinical manifestations of hyperparathyroidism and abnormalities detected through ultrasound, scintigraphy, and computed tomography (CT).
Methods
A study of 132 patients at Ibn Rochd Hospital, Casablanca, from January 1988 to October 2023, focused on the epidemiological, clinical, paraclinical, and therapeutic aspects of primary hyperparathyroidism. The goal was to promote early diagnosis, relying on imaging data for detecting adenomas and parathyroid nodules.
Results
The study shows an average age of 53.4 years with a notable female predominance (85.93%). The analyses reveal a high average blood calcium level of 114.93 mg/l and an increased average phosphorus level of 22.20 mg/l. The average parathormone (PTH) level is high, at 830.56 pg/ml. Regarding symptoms and complications, 71.87% of patients suffer from bone pain, and 23.43% have renal lithiasis. Ultrasound revealed parathyroid adenomas in 64.06% of patients, while scintigraphy showed hyperfixation in 85.93% of them. CT results indicate that 64% of cases are due to parathyroid adenomas, with 6.25% representing hyperplasia and 1% parathyroid carcinomas. Additionally, 67% of patients have hypovitaminosis D.

Conclusion
These results indicate a significant prevalence of clinical manifestations and paraclinical findings typical of primary hyperparathyroidism. They highlight the importance of early screening and management to prevent complications, especially bone disease and nephrolithiasis. Focusing on correcting hypovitaminosis D could also be an important aspect of treatment for these patients. Surgery remains the standard treatment for removing the responsible adenomas.

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EP861

Hypomagnesemia in type 2 diabetics and its impact on glycemiccontrol and diabetes chronic complications

Yosra Hasni[1], Jihen Ben Abdallah[2], Hamza Elfekih[1], Oumayma Zarrouk[1], Saoussen Mrad[2], Asma Maalal[2], Chaima Boughzala[2], Nassim Ben Hadj Slama[1] & Molka Chadli Chaieb[1]
[1]University Hospital of Farhat Hached, Endocrinology Departement, Sousse; [2]University Hospital of Farhat Hached, Biochemistry Laboratory, sousse

Introduction
Several studies have incriminated hypomagnesemia in the pathophysiology of diabetes, as the prevalence of this deficit in type 2 diabetics is high, and as it is correlated with glycemic control and chronic diabetic complications.
Aims
Studying the prevalence of hypomagnesemia in type 2 diabetics and assessing its impact on quality of life, glycemic control and chronic diabetic complications. Patients and methods: We conducted a descriptive cross-sectional study over a period from November 01, 2022 to January 31, 2023, including type 2 diabetic patients followed at the endocrinology department of CHU FARHAT HACHED. Data were collected from careful questioning, physical examination and medical records. Missing biological parameters were performed at the biochemistry laboratory of CHU FARHAT HACHED.
Results
We included 190 type 2 diabetics (sex ratio M/F 1.09), with a mean age of 60 $\pm$ 9.9 years and a mean diabetes duration of 11.9 $\pm$ 9.1 years. Diabetic retinopathy was present in 43.5% of our subjects. Diabetic nephropathy and diabetic peripheral neuropathy were present in 33% and 23.6% of patients respectively. 15.3% of our population had a coronary syndrome and 14.2% had a history of stroke or transient ischemic attack. Hypomagnesemia was present in 45.3% of our population, with a mean magnesemia of 0.74 $\pm$ 0.09 mmol/l. It was statistically correlated with fasting blood glucose ($P=0.004$, OR = 2.27) and HbA1c ($P=0.047$, OR = 1.53); for a FPG >8.95 mmol/l and for HbA1c values $>$ 8.25%, the prevalence of hypomagnesemia increases significantly. However, we found no correlation between magnesium and quality of life, nor with chronic diabetic complications.
Conclusion
Hypomagnesemia is a frequent biological abnormality in type 2 diabetics and is significantly correlated with glycemic control. Therefore, its screening in these patients is recommended for possible supplementation.

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EP862

Impact of age on healthcare costs in type 2 diabetes patients with chronic complications: a retrospective study

Souhir Maalej, Fatma Mnif, Hamdi Frikha, Yesmine Elloumi, Khouloud Boujelben, Dhouha Ben Salah, Faten Hadj Kacem, Nadia Charfi, Mouna Mnif, Mouna Elleuch, Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Endocrinology, Sfax

Introduction
Type 2 diabetes (T2D) is a globally expanding disease with severe consequences. Cardiovascular and renal complications are concerning, leading to high costs for individuals and healthcare systems. Evaluating these costs is crucial to guide health policies and identify factors influencing these expenditures.
Materials and Methods
A retrospective descriptive study was conducted to collect data on diabetic patients with chronic complications. The study included patients hospitalized in the Endocrinology Department of Hedi Chaker University Hospital in Sfax from January 1 to December 31, 2022. The research focused on the impact of age on the expenses of managing complicated diabetes.
Results
The study involved 114 patients, with a sex ratio of 1.28. The average age of our population of T2D patients with chronic complications was 65 years, ranging from 41 to 87 years. In our study, 67.54% of patients were found to have diabetic nephropathy, while diabetic retinopathy and neuropathy were observed in 33.3% and 52.6% of cases, respectively. Among the 90 patients exhibiting cardiovascular involvement, the prevalent macroangiopathy was coronary insufficiency (59.7%), followed by heart failure, peripheral arterial disease, and stroke (10.5%). The average cost per patient was approximately 2,246.46 TND or 713.16 USD for an average hospitalization duration of 7 days. The difference in the average cost of care between patients under 65 and those 65 or older was statistically significant (2773.50 vs 1804.42 TND, $P=0.043$). This finding indicates that patients under 65 have higher care costs than those 65 or older. Table IV provides a detailed analysis of the variations in overall cost between the two age groups based on the different components of this cost. Specifically, advancing age correlated with a decrease in expenses related to cardiovascular, radiological, and medical treatment, with significant correlation coefficients of $r=-0.208$, $r=-0.245$, $r=-0.094$, respectively. Interestingly, age showed a positive correlation with expenses for biological explorations, with a correlation coefficient of $r=0.273$ and a P-value less than 0.001, potentially aiding in alleviating the financial burden and enhancing patient outcomes.
Conclusion
This emphasizes that aging itself, beyond managing classic risk factors, can significantly contribute to the onset of diabetes-related complications. The study's results highlight the importance of closely monitoring elderly diabetic patients, even if they have adequate control of their cardiovascular risk factors, to prevent and manage these complications.

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EP865

Impact of the use of continuous subcutaneous insulin infusion versus multiple daily insulin injections in adults with type 1 diabetes mellitus

Irene Zayas Aguilar[1], Cristian Jesús Lucena Morales[1], Almudena Lara Barea[1], María de los Ángeles Cutilla Muñoz[1] & Isabel María Torres Barea[1]
[1]Hospital Universitario Puerta del Mar, Endocrinology and Nutrition Department, Cádiz, Spain

Objective
The aim of this study is to assess the impact of continuous subcutaneous insulin infusion (CSII) via a pump for patients with type 1 diabetes mellitus (DM1) on blood glucose and metabolic control.
Materials and methods
A descriptive study was performed in a cohort of patients with DM1, showing blood glucose measurements at one month, six months and one year after implantation of the CSII. In addition, we performed an intra-subject before-after study comparing the parameters with multiple daily insulin injections (MDI) and the use of CSII one month and six months after its implementation.
Results
The study included 34 patients with DM1 (70% women), the mean age was 34.38 años (28.22-40.54) years and the average time to progression of DM1 19.97 years (15.19-24.76). After one month of treatment the glucometric report a Time In Range (TIR) of 76.71% (73.02-80.41), Time Below Range (TBR) 1.93% (1.33-2.52) and Time Above Range (TAR) 21.00% (17.15-24.85); the Glucose Management Indicator (GMI) was 6.77% (6.64-6.91). At six months treatment we highlight: TIR 79.00% (76.29-81.71), TBR 2.10% (1.47-2.72), TAR 18.84% (16.23-21.45), GMI 6.74% (6.64-6.84); with a glycated hemoglobin (A1C) of 7.01% (6.72-7.30). At one year: TIR 80.65 % (78.14-83.15), GMI 6.69 %, (6.55-6.83). In the before-after study ($n=24$; 62.5% women) a significant improvement is observed one month after the use of the insulin pump with respect to MDI treatment: TIR (77.50 vs 55.62; $P<0.001$), TAR (20.55 vs 40.50; $P<0.001$), TBR (1.95 vs 3.87; $P=0.038$), GMI (6.78 vs 7.35; $P=0.003$) and coefficient of variation (CV) (29.93 vs 35.38; $P=0.01$). After six months of treatment, improvements were also observed in TIR (79.41%; $P<0.001$), TAR (18.68%; $P<0.001$), TBR (1.91%; $P=0.034$), CV (30.70%; $P=0.08$) and GMI (6.73%; $P=0.02$).
Conclusions
In the descriptive study, a TIR $>70\%$ was observed with the use of CSII at one month, six months and one year after treatment. In the before and after study, we observed an improvement in glucometric parameters (TIR, TBR, TAR, GMI, CV).

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EP866

Evaluation of salt consumption in patients with type 2 diabetes

Rym Ben othmen[1], Emna Talbi[2], Nesrine Dhieb[1], Ramla Mizouri[1], Brahim Khalfa[2], Maryam Naifar[1], Rahma Mahjoub[2], Olfa Berriche[1] & Henda Jamoussi[1]
[1]National Institute of Nutrition and Technology, Deparment A, Tunis, Tunisia; [2]Zouhair Kallel Institute of Nutrition and Food Technology, Clinical Biology Laboratory, Tunis, Tunisia

Introduction
The World Health Organization recommends a daily salt intake of no more than 5 grams per day to prevent complications associated with excessive sodium intake. The aim of our study was to screen type 2 diabetic patients for excessive salt consumption using the Exsel Test.
Methods
This was a cross-sectional study including 106 type 2 diabetic patients which took place in department A of the National Institute of Nutrition and Food Technology in Tunis. The duration of the study was 6 months.
Results
The mean age was 55.46 ± 7.51 years. The sex ratio was 0.85. Hypertension was present in 49% of our patients. The mean BMI was 29.68 ± 5.92 kg/m^2. The majority of the population was obese. The mean waist circumference was 97.47 ± 14.18 cm. In our population, 28 patients (26.4%) had a positive Exsel Test. The majority of patients (68.8%) had a daily bread consumption of 240 g. Exsel Test was associated with waist circumference ($P=0.001$). We found a significant difference in BMI ($P=0.001$) between patients who had a positive exsel test and those who had a negative exsel test. In our study, the exsel test was associated with the frequency of consumption of salted cheese ($P=0.001$), preserves ($P=0.005$), oleaginous ($P=0.01$), variants ($P=0.005$) and sauces ($P=0.03$).
Conclusions
The ExSel test is easier to administer than other methods. Using this questionnaire offers a simple and practical way of identifying excessive salt consumers.

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EP867

Diabetes self-management skills in patients considering Ramadan fasting: Sfax pre-Ramadan education workshops experience

Abdel Mouhaymen Missaoui, Fatma Mnif, Siddiqa Soomauroo, Khouloud Boujelben, Souhir Maalej, Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Department of Endocrinology, Sfax

Background and Aim
Ramadan-specific diabetes education (RDE) is fundamental to achieving safe fasting. During RDE sessions, healthcare providers should perform a risk assessment based on the patient's medical status and his glycemic self-managing competence. This study aims to appraise the educational skills of diabetic patients intending to fast.
Methods
We conducted a cross-sectional descriptive study including 35 diabetic patients who attended the RDE workshops organized by our Endocrinology and Diabetology Department in April 2021. We evaluated the patient educational background by applying self-administered questionnaires.
Results
The mean age was 58.5 ± 12 years, with a female predominance (73.9%). Most of the participants were receiving insulin therapy (56.5%). Some of them attended the workshops accompanied by a supportive family member (28.6%). Poor glycemic control was reported in 47.8%. The attendees had appropriate comprehension of the effects of their anti-diabetic agents in 60.9%. They featured solid dietary managing skills in 52.0%. Hypoglycemic events were more easily recognized and managed than hyperglycemic episodes (91.3% vs 56.5%). Barely 39.1% of patients could discern their specific glycemic targets. However, only 26.1% were performing regular self-monitoring of blood glucose (SMBG). Hypoglycemia, acute illness, and hyperglycemia were considered as indications to break the fast in 88.6%, 74.3%, and 28.6%, respectively.
Discussion
RDE programs should bring individualized knowledge on risk stratification, SMBG, diet, exercise, and physical activity for patients with diabetes. Healthcare providers are responsible for removing misconceptions and adjusting medications in patients considering fasting. Better recognition of circumstances requiring breaking the fast could avoid serious complications linked to food and water restriction during Ramadan. Several studies have demonstrated the clear benefits of these personalized programs on glycaemic control, weight loss, and the reduction of the risk of hypoglycemia, even in higher-risk individuals.

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EP870

Factors affecting the level of therapeutic literacy in patients with type 2 diabetes

Mouna Elleuch, Insaf Nasri, Wissal Ghamgui, Khouloud Boujelbene, Mnif Mouna, Fatma Mnif, Dhouha Ben Salah, Charfi Nadia, Mohammed Abid, Feten Hadj Kacem & Nabila Rekike
Hedi Chaker Hospital, Endocrinology and Diabetology Department, Sfax, Tunisia

Background
Despite the significant rewards offered by diabetes education, programs are underused with a significant proportion of patients choosing not to attend.
Aim
The aim of this study is to identify the factors that determine the level of knowledge of diabetic patients about their disease.
Methods
Our study involved 61 type 2 diabetic patients followed at the endocrinology department of the university hospital or followed at the city basic health centre.
Results
Only 24.6% of our patients had knowledge of ETP programmes. Only one patient was a member of a diabetes association. Ignorance of the existence of such associations (31.1%) or lack of motivation to participate (26.2%) explained non-adherence in the remaining patients. In our series, socioeconomic status influenced the level of discipline and knowledge of the disease, and more than 45% of the population studied had a low socioeconomic status. Furthermore, it was shown that well-off patients recognized the origin of type 2 diabetes 8 times more than poor patients (OR = 8, $P=0.037$). Our study showed a significant association between a good level of therapeutic literacy and occupation, in particular being a female employee ($P=0.02$), the level of school education (university) and the socio-economic level ($P=0.037$). We confirmed the significant influence of patients' occupational status, educational level and socioeconomic level on their TPE level. There was a significant correlation between the objective assessment of patients' level of TVE and the use of new telecommunication technologies (0.316).
Conclusion
therapeutic education programs should be adapted to the needs of people in precarious socio-economic situations, taking into account their socio-demographic situation, level of education, etc.

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EP872

Immunotherapy induced endocrinopathies: "pembrolizumab-induced pancreatitis presenting as diabetic ketoacidosis with concurrent hyperthyroidism-related atrial fibrillation"

Mohsin Mukhtar, Irbaz Nazir, Mirza Aftab & Colm McGurk
St. Luke's General Hospital, Kilkenny, Ireland

In this report, we discuss the case of a 77-year-old male with no previous history of diabetes or thyroid disease, undergoing pembrolizumab treatment for malignant melanoma. He presented to the emergency department in diabetic ketoacidosis (DKA) and shock after five days of vomiting, unable to eat or drink. Laboratory findings indicated severe metabolic disturbances, including high blood glucose and amylase levels, consistent with pembrolizumab-induced pancreatitis and subsequent pancreatic insufficiency leading to DKA. Additionally, the patient developed new-onset rapid atrial fibrillation and a thyroid profile indicative of hyperthyroidism, presumably secondary to the immunotherapy. He was successfully managed with a DKA protocol and intensive care, highlighting the complexity of treating immune checkpoint inhibitor-induced endocrine complications and the importance of a multidisciplinary approach in such cases

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EP886

Physical exercise as a sustainability tool in men affected with metabolic syndrome-related late-onset central hypogonadism: role of endocrine-metabolic and neurovegetative outcomes

Luca Giovanelli[1], Biagio Cangiano[1,2], Silvia Federici[1,2], Daniela Lucini[1,3] & Marco Bonomi[1,2]
[1]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy; [2]Istituto Auxologico Italiano, IRCCS, Department of Endocrine and Metabolic Medicine, Milan, Italy; [3]Istituto Auxologico Italiano, IRCCS, Exercise Medicine Unit, Milan, Italy

Background
Late-onset central hypogonadism (LOH), whose prevalence is high among dysmetabolic males, impairs quality of life and increases cardiovascular risk. Although lifestyle modification is the first-line therapeutic strategy, it often fails in clinical practice, probably due to socio-cultural, economic and organisational barriers, as well as the lack of effective and sustainable intervention programs.
Aim
To delineate sustainable physical exercise programs and to assess the effects of such programs mainly on endocrine-metabolic and neurovegetative outcomes in a cohort of men with metabolic syndrome-related central LOH.
Methods
18-80-year-old men, consecutively referred to IRCCS Istituto Auxologico Italiano due to dysmetabolic central LOH, will be enrolled in this prospective study. Participants will undergo a structured and personalised exercise program (accompanied by an adequate nutrition program). After 6 months they will be subdivided into two groups, according to the weekly physical activity volume actually performed (above or below 600 MET·minutes/week). Changes in endocrine-metabolic and neurovegetative outcomes (e.g., gonadal axis function, glucose and lipid profile, body composition, cardiac autonomic regulation (CAR)) will be compared between the two groups. In particular, Autonomic Nervous System Index (ANSI), being extracted from the autoregressive spectral analysis of heart rate variability by combining the three most informative variables, will be used for non-invasive assessment of CAR[1]. Besides, genetic investigations will be performed to explore the potential role of genetic predisposition in the development of dysmetabolic LOH.
Preliminary results and discussion
Seven patients have been hitherto enrolled. As expected, they presented low percentages of fat free mass in the face of increased fat mass, and low SHBG levels. An impairment in both autonomic function (ANSI) was observed in comparison with reference populations from other studies. This is the first study assessing neurovegetative control by means of ANSI in hypogonadal men. Indeed, obesity/insulin resistance is associated with neurovegetative dysfunction, and lifestyle interventions have been shown to improve CAR in dysmetabolic patients. In this context, it will be interesting to explore the possible crosstalk between metabolic syndrome-related hypogonadism, autonomic dysfunction, and physical exercise. Notably, exercise prescription requires the clear definition of modality, intensity, frequency, duration and progression of exercise, tailored on patient's clinical conditions and goals. Intervention programs should be sustainable in economic and organisational terms, with a view to embedding behavioural changes in patient's everyday life.
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EP898

Management of hypertriglyceridemia-induced pancreatitis - case series

Furhana Hussein[1], Gideon Mlawa[2], Ayan Mohammed[2], Syeda Anika Mahtab[2], Man-Yan Cheung[2], Ali Akram[3], Mariana Dram[2], Mahamud Bashir[2] & Agne Jovaisaite[2]
[1]Queen's Hospital, Endocrinology and Diabetes/Acute Medicine, London, United Kingdom; [2]Queen's Hospital, London, United Kingdom; [3]Queen's Hospital, Endocrine and Diabetes, Romford, United Kingdom

Background
Acute pancreatitis is both a medical and surgical emergency. Common causes of acute pancreatitis include gallstones and alcohol. Hypertriglyceridemia-induced pancreatitis is rare (1-4%); here we discuss management of 5 cases of hypertriglyceridemia-induced pancreatitis.
Case-1
37-year-old female presented to A&E with epigastric pain radiating to back and vomiting. Blood test showed raised amylase, triglyceride 81.6 and cholesterol 6.1. CT-Abdomen showed acute pancreatitis. She was treated conservatively with insulin sliding-scale and intravenous antibiotics. She was discharged on atorvastatin and fenofibrate.
Case-2
45-year-old male presented with abdominal pain radiating to back. Bloods showed raised triglycerides 43.1 and cholesterol 5.1. CT-Abdomen showed acute-on-chronic pancreatitis. Treated conservatively with insulin sliding-scale and kept nil-by-mouth initially.
Case-3
28-year-old female presented with acute generalised crampy abdominal pain and vomiting. Medical history included Type2 Diabetes Mellitus and high BMI. Blood test showed raised triglycerides 71.26. CT-Abdomen showed acute pancreatitis. Managed conservatively with an insulin sliding-scale and discharged on atorvastatin and fenofibrate.
Case-4
42-year-old male was admitted with abdominal pain, diarrhoea and vomiting. Blood showed raised triglycerides 40. CT-Abdomen showed acute pancreatitis. Treated with insulin sliding-scale and analgesia. He clinically improved and discharged with atorvastatin, fenofibrate and lifestyle advice.
Case-5
38-year-old male was admitted with left-upper-quadrant abdominal pain radiating to back and vomiting. Medical history included Type2 Diabetes Mellitus, hypercholesteremia and hypertriglyceridemia (non-compliant with medication). Blood showed raised amylase 378, triglycerides 28.77 and hyperglycaemia of 17. CT-Abdomen showed acute pancreatitis and treated conservatively with insulin sliding-scale and analgesia. Discharged on atorvastatin, fenofibrate and lifestyle advice.
Discussion
Hypertriglyceridemia is an increasing cause of acute pancreatitis and is associated with high morbidity and mortality risk. Hypertriglyceridemia-induced pancreatitis is caused by the hydrolysis of excessive triglyceride-rich lipoproteins releasing high concentrations of free-fatty-acids that cause inflammation of the pancreas. This case series describes initial management is conservative with insulin infusion, intravenous fluids and analgesia. Plasmapheresis is considered in severe pancreatitis where above measures have failed. Contrast-enhanced CT is important to look at severity, presence of gallstones and necrotizing pancreatitis.
Conclusion
Hypertriglyceridemia-induced acute pancreatitis is a rare but a well-established cause of acute pancreatitis. It is important to check lipid profile when a patient presents with acute pancreatitis as it is often associated with greater clinical severity and rate of complications. Early diagnosis with correct treatment will help prevent complications. It is important to advice on lifestyle changes and start on medications such as fenofibrate to help lower serum triglyceride levels.
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EP906

Inflammatory and nutritional profile of elderly people hemodialyzed

Faten Mahjoub, Ramla Mizouri, Nadia Ben Amor, Rym Ben Othman & Jamoussi Henda
Institut De Nutrition, Tunis, Tunisia

Introduction
Protein-energy malnutrition appears frequently and early in course of chronic renal failure and represents a determining element of the morbidity and mortality. The objective of this study was to evaluate spontaneous food intake and to study the inflammatory profile of elderly people on hemodialysis.
Materials and methods
This cross-sectional and descriptive study involved 40 elderly hemodialysis subjects. All patients underwent a complete clinical examination and a biological assessment with a dosage of C-Reactive protein and a dietary survey by 3 day recording.
Results
The average age of the population was 71 ± 5.9 years. Evaluation of contributions energy consumption of patients showed an average daily intake of 25.3 ± 12.3 kcal/kg of ideal weight/d. The average total energy intake of patients on the day of dialysis and non-dialysis was respectively 29.7 ± 17.7 kcal/kg and 20.9 ± 6.9 kcal/kg with a statistically significant difference ($P = 0.001$). The ration Average protein content was 0.99 ± 0.57 g/kg on the non-dialysis day. It was decreasing statistically significantly ($P = 0.005$) on the non-dialysis day at 0.73 ± 0.28 g/kg. The mean CRP of the study population was 12.3 ± 4.2 mg/l. He exists a positive and statistically significant correlation between the rate of CRP and weight ($r = 0.41$; $P < 0.05$). The analytical study showed no positive association between CRP level and the following factors: age, gender, creatinine clearance and type of nephropathy.
Conclusion
Protein-energy malnutrition is a common pathological situation and serious in elderly hemodialysis patients who may be life-threatening. The development of a Tunisian nutritional guide intended for the elderly hemodialysis is imperative.
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EP907

Mixed hypertriglyceridemia: a therapeutic challenge!

Ahmed Boukhalfa, Hanane Boualam, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Mohamed VI University Hospital Center, Marrakech, Morocco, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Introduction
Severe mixed hypertriglyceridemia (SMH) is a highly heterogeneous group of dyslipidemias, both phenotypically and mechanistically (1). The primary origin is dominated by familial combined hyperlipidemia; the most frequent genetic cause. The major concern is the development of acute pancreatitis. We report the case of a patient with mixed hypertriglyceridemia to illustrate the therapeutic difficulties encountered in managing.
Clinical case
Forty-eight years-old patient, type 2 diabetic, hypertensive, followed for mixed hypertriglyceridemia with hepatic steatosis. Initially put on a hypocaloric and hypolipidic diet with a combination of fenofibrates and statins, discontinued because of cholestatic hepatitis. Examination: bilateral corneal arc with xanthomas of the hands and left gluteal region. Lipid profile: total cholesterol: 5.53 g/l HDL-C: 0.4 g/l, TG: 14.2 g/l. Normal lipasemia. Cardiovascular workup showed concentric LVH. Indication for LDL apheresis was made, but the patient's lipid profile showed an incomplete response and fluctuated. Over the course of the last 3 sessions, the patient experienced malaise, hypotension and bradycardia, which led to suspension of LDL-apheresis. Given the improvement in liver function, treatment with fenofibrate 160 mg and pravastatin 40 mg, supplemented with omega-3 fatty acids, was reintroduced with good results.
Discussion and conclusion
Hypertriglyceridemia (HTG) is a common condition, most often caused by multiple, interrelated factors. Genetic hypertriglyceridemias are apparently uncommon. (2). Mixed HTG increases the risk of cardiovascular and cerebral events, and is frequently associated with metabolic syndrome. Acute pancreatitis is an extremely serious complication, and should be avoided in all cases of severe HTG. HTG accounts for 1-10% of all AP etiologies (3). Genetic diagnosis has precise indications. In our patient, after eliminating secondary causes, an essential mixed dyslipidemia was suggested. Fibrates and statins can trigger toxicity or worsen already impaired liver function, so they should be discontinued (4). LDL-apheresis is a better therapeutic alternative, especially in emergency situations (5), despite its limited cost and availability. Family screening is essential for children, and for women of childbearing age planning a pregnancy (1).

Keywords: Hypertriglyceridemia, pancreatitis, apheresis, statins, fibrates, genetics.

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EP910

Plasmapheresis as treatment for hyperlipidemic severe pancreatitis

Zineb Ait Si Ali, Neima Hassan, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Centre Hospitalo-Universitaire Mohammed VI Marrakech, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction
Plasmapheresis is an extracorporeal blood purification method that removes potentially harmful macromolecules (molecular weight L15 - 50 kDa) from the blood. Pancreatitis is a potentially fatal complication of hypertriglyceridemia. The current mainstay of treatment for hypertriglyceridemia associated with pancreatitis includes heparin, insulin and lipid-lowering agents. Experience with plasmapheresis is limited. We report here our experience of using plasmapheresis in the treatment of a patient with severe acute pancreatitis induced by major hypertriglyceridemia.
Case report
A 40-year-old female patient with no specific pathological history, including no known dyslipidemia, diabetes, thyreopathy or nephropathy. Admitted to intensive care for grade E pancreatitis, revealed by a sharp pain in the epigastric region, radiating to the back associated with nausea and vomiting, evolving 3 days prior to her admission. Clinical examination revealed a conscious patient, hypotension to 84/60 mmhg, tachycardia to 105 bpm, polypneac to 30 cpm, distended abdomen with diffuse abdominal sensibility. No cutaneous xanthoma or eruptive xanthomatosis were found. On workup: WBC: 3100 hb: 10.7 plq: 362000 Triglycerides: 21.48 g/l Total cholesterol: 3.9 g/l PT: 87% Urea: 1.34 Creatinine: 55.13 mg/l GFR calculated at 9.11 ml/mn Natremia: 124mmol/l K: 5.12 mmol/l Calcemia: 49.88 mg/l Albumin 31g/l Calcemia corrected: 60 mg/l rechecked 48 h later at 84.89 mg/l CRP: 670 mg/l lipase 31.99ui/l. Abdominal CT: grade E pancreatitis with multiple fluid collections around the pancreas and important ascite. The patient underwent 2 sessions of plasmapheresis and 2 sessions of hemodialysis. The clinical and paraclinical outcome was favorable, with a control triglyceridemia of 4.55 g/l and improvement of renal function.
Discussion and conclusion
Betteridge *et al*, were the first to perform apheresis to lower triglyceride concentrations in 1978. Since then, plasmapheresis has become a therapeutic tool for major hypertriglyceridemia. Studies currently available have demonstrated that apheresis treatment is effective in rapidly and significantly lowering triglyceride concentrations. Most studies have shown that plasmapheresis generally reduces triglyceride levels by 60-70% in a single session. Relief of acute pancreatitis symptoms after one to three sessions of plasmapheresis has been reported. In addition, several studies have noted that a maximum reduction in morbidity and mortality can be achieved when plasmapheresis is used as early as possible.

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EP925

Proteolytic cleavage of insulin receptor in the skeletal muscle of a wistar rat model of metabolic syndrome

Wendy Priscila Alcantar Villasana[1], Juan Pablo Pánico[2] & Marcia Hiriart[1]
[1]Instituto de Fisiología Celular, Neurociencia Cognitiva, Ciudad de México, Mexico; [2]Instituto de Investigaciones Biomédicas, Medicina Genómica y Toxicología Ambiental, Ciudad de México, Mexico

Extracellular proteolytic cleavage of insulin receptor (IR) and the generation of soluble insulin receptor (sIR) is a response of the liver and fat associated with physiological conditions and metabolic alterations mainly related to hyperinsulinemia. However, cleavage of this receptor has not been analyzed in skeletal muscle, a central tissue in insulin-mediated glucose homeostasis. This study aimed to analyze the insulin receptor subunits in the gastrocnemius and soleus muscles in a model of male young Wistar rats of metabolic syndrome induced by sucrose 20% in drinking water for 8 weeks. Using quantitative western blot analysis, we found the presence of at least 7 protein bands when using an antibody against the alpha subunit under reducing and non-reducing conditions. The band with the highest molecular weight in non-reducing conditions, which appears close to 315 kDa, possibly corresponds to the intact insulin receptor, whose abundance is not altered in our model. A greater abundance of the 157 kDa and 60 kDa fragments in non-reducing conditions and 25 kDa in reducing conditions was found in the treated animals compared to the control group. An additional 48 kDa fragment was found in the soleus muscle under non-reducing conditions, whose presence could be related to the metabolic differences between both muscles. A subsequent *in silico* analysis suggested that the fragments obtained through western blot may correspond to fragments resulting from proteolysis mediated by membrane proteases families (ADAM, MMP, calpains) that have been implicated in the past in the generation of IR soluble ectodomain. These findings suggest the shedding of IR from skeletal muscle in a hyperinsulinemic state characteristic of our metabolic syndrome model.

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EP938

Characteristics of obese patients with a body mass index (BMI) of > 50 who opted for metabolic/bariatric surgery

Bunzo Matsuura, Hironobu Nakaguchi, Hidenori Senba, Ayumi Kanamoto, Masumi Miyazaki, Akihito Shiomi, Teruki Miyake, Shinya Furukawa & Yoichi Hiasa
Ehime University Graduate School of Medicine, Toon, Japan

Aim
The basis of treatment for obesity is diet and exercise therapy. Since 2006 at our hospital, lifestyle modification, such as diet and exercise, for obese patients has been provided through a team approach with a physician, dietician, nurse, physical therapist and psychologist. From 2016, a surgeon and anesthesiologist were added to the team for metabolic/bariatric surgery. The aim of this study is to clarify the characteristics of patients with a BMI of 50 or more who opted for metabolic/bariatric surgery (laparoscopic sleeve gastrectomy: LSG).
Patients & Methods
Of 40 patients who were received LSG between January 2017 and December 2021, 9 were in the super-obese (S) group with a BMI of 50 or more and 31 were in the obese (C) group with a BMI of 30 to less than 50. The preoperative weight loss rate, postoperative weight loss rate, postoperative body composition change rate, and postoperative rebound rate were compared.

Results
The male/female ratio in group S vs group C was 6/3 vs 13/18, mean age (years) was 42 vs 45, diabetes mellitus/other complication was 3/6 vs 21/10, mean preoperative weight (kg) was 160 vs 108, mean BMI was 57 vs 40. The preoperative weight loss rate (%) was 10.0 vs 5.6, 6-month postoperative weight loss rate (%) was 20.0 vs 16.4, and 1-year postoperative weight loss rate (%) was 21.6 vs 17.3. There was no difference in diabetes complete remission rate. There was a significant less postoperative weight rebound rate in group S than that in group C.
Conclusions
The surgical treatment was required in patients with very high obesity, with or without diabetes mellitus, and even if preoperative weight loss of 10% or more was achieved.

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EP939

Screening and quantification of hepatic steatosis in obese patients using the controlled attenuation parameter (CAP)

Ahmed Mohamed Nefzi, Cherif Dhouha, Kahlaoui Fatma, Dabbebi Habiba, Yacoub Haythem, Hassine Hajer, Kchir Hela & Maamouri Nadia
RABTA Hospital, Hepato-gastroenterology "B", Tunis, Tunisia

Introduction
Liver steatosis currently represents a hepatic manifestation of metabolic syndrome. It occurs more frequently in patients with obesity, and liver biopsy remains the gold standard for the positive diagnosis of this condition. In recent decades, the positive diagnosis of hepatic steatosis has increasingly relied on non-invasive methods such as Controlled Attenuation Parameter (CAP). The objective of this study was to investigate the prevalence of hepatic steatosis diagnosed via CAP among obese patients and to determine the factors associated with the occurrence of moderate to severe steatosis in this group.
Methods
This is a retrospective, single-center, descriptive study including all obese patients undergoing screening for hepatic steatosis via CAP integrated into the Fibroscan Echosens 502 device. We collected age, various medical histories, anthropometric measurements, and CAP values. Obesity and its different classes were defined according to the World Health Organization recommendations. The different degrees of hepatic steatosis were defined as follows: Absence of steatosis (S0): CA$P < 294$ dB/m, Mild steatosis (S1): CA$P < 310$ dB/m, Moderate steatosis (S2): CA$P < 331$ dB/m, Severe steatosis (S3): CAP≥ 331 dB/m.
Results
Our population included 94 patients with an average age of 53.42 ± 11.4 years, ranging from 28 to 81 years, and a gender ratio of 0.3. Various medical histories were distributed as follows: Type 2 diabetes (29%), hypertension (23.7%), dyslipidemia (20.4%), hypothyroidism (7.5%), and obstructive sleep apnea syndrome (OSA) (1.1%). The mean BMI was 35.72 ± 4.8 kg/m^2, ranging from 30 to 54.5 kg/m^2. We observed hepatic steatosis in 50% of patients ($n=47$). The mean CAP value was 290.22 ± 60 dB/m, ranging from 109 to 400 dB/m. The different degrees of hepatic steatosis were distributed as follows: S1 (14.9%), S2 (29.8%), S3 (55.3%). In univariate analysis, factors associated with the occurrence of moderate to severe steatosis (S2-S3) were male gender ($P=0.028$), associated dyslipidemia ($P=0.047$), and BMI ≥ 35 kg/m^2 ($P=0.037$). In multivariate analysis, male gender and BMI ≥ 35 kg/m^2 were independently associated with the occurrence of moderate to severe steatosis in obese patients, with respective P-values of 0.02 and 0.03, and odds ratios of 3.47 and 2.68.
Conclusion
Our study suggests a notable prevalence of hepatic steatosis in obese patients, with greater severity in males with Class II and III obesity.

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EP940

Study of patients referred for obesity to a nutrition consultation

Jose Antonio Ariza Jimenez[1], Maria del Carmen Vázquez Alférez[1] & Jorge Marín Martín[2]
[1]Hospital la Merced, Endocrinology and Nutrition, Osuna (Sevilla), Spain; [2]Hospital la Merced, Internal Medicine, Osuna (Sevilla), Spain

Introduction
Changes in dietary habits coupled with sedentary lifestyles have led to a true pandemic of obesity. This situation has also been observed in the new nutrition consultation at La Merced Hospital in Osuna (Seville), where, after 6 months of operation, 88.9% of the patients were referred due to obesity.
Objective
To analyze the profile of patients referred for obesity to the nutrition consultation at La Merced Hospital, as well as the sources of these referrals.
Materials and Methods
An observational descriptive study was conducted. Patients referred for obesity to the Nutrition Consultation at La Merced Hospital from August 1 to December 31, 2023, were recorded. The age, gender, and body mass index (BMI) of the patients were analyzed, along with the specialty making the referral. The official referral criteria were BMI >40 or 35 kg/m^2 with at least two comorbidities (diabetes, hypertension, dyslipidemia, or sleep apnea syndrome).
Results
A total of 137 patients referred for obesity were attended. 86 were females (62.77%), and 51 were males (37.23%). The mean age was 53 years (14-80), with the mean age for males being 52.33 years and for females 52.51 years. The mean BMI was 41.50 kg/m^2, with males at 41.92 kg/m^2 and females at 41.23 kg/m^2. Internal Medicine referred a total of 48 patients, followed by Traumatology with 32 patients, Pneumology with 24 patients, Surgery with 12 patients, Primary Care with 11 patients, Cardiology with 4 patients, Digestive with 2 patients, and Rheumatology, Anesthesia, Neurosurgery, and Rehabilitation with 1 patient each.
Conclusions
Obesity dominates most of the activity in the new nutrition consultation at La Merced Hospital. More women than men have been referred (62.77% vs 37.23%). The specialty that has referred more patients to the nutrition consultation for obesity is Internal Medicine, followed by Traumatology and Pneumology.

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EP941

Metabolic syndrome: assessment of the role of biochemical indicators in diagnostics

Olga Moskalenko & Eduard Vilyamovich Kasparov
Federal Research Center «Krasnoyarsk Science Center» of the Siberian Branch of the Russian Academy of Sciences, Russian Federation

Metabolic syndrome (MS) is a pressing problem of modern medicine. The prevalence of MS has a worldwide tendency to increase and depends on many factors, which explains the difficulty in diagnosis, prevention programs and treatment of this pathology. It has been established that MS has a multifactorial etiology, in which psycho-social factors, genetic and environmental factors are important. At the subclinical stage, functional and biochemical changes associated with MS are reversible and with proper treatment, the severity of MS manifestations can be reduced. MS is defined as a combination of 3 of 5 conditions: central obesity, decreased cholesterol, high-density lipoprotein, increased triglycerides and blood glucose, arterial hypertension. Purpose of the study: to evaluate individual biochemical parameters in the development of metabolic syndrome.
Materials and methods
The main study group included 76 patients with MS and 41 people without MS, practically healthy volunteers (control group), comparable in age and gender to the main group. Blood plasma was studied: glucose levels were measured using the glucose oxidase method; The lipid profile was assessed (total cholesterol, total cholesterol, TG, NEFA, FL). Insulin was determined by enzyme immunoassay using the DRG test system. All study participants signed an informed consent approved by the ethics committee. Statistical data processing was carried out using application packages 'STATISTICA 10.0'.
Results
When analyzing the results obtained, an increase in the values of the insulin resistance index - HOMA-IR was revealed. This coefficient has the greatest diagnostic value and has received wide practical application. Calculation of HOMA-IR revealed an almost 2-fold increase in this indicator in patients with MS ($P<0.05$), which is a predictor of the risk of developing diabetes and cardiovascular diseases. The level of NEFA in patients with MS was increased in 95% of cases and was almost 2 times higher than normal values. Also, in patients with MS there was an increase in the levels of insulin and glucose in the blood compared to the control group ($P<0.05$). In patients with MS, the levels of total cholesterol and FL were normal, falling within the range of threshold values.
Conclusion
Thus, there is no doubt that early diagnosis of MS is important and currently the most effective strategy in preventing the progression of metabolic disorders is lifestyle correction (diet changes, weight loss, regular physical activity) in combination with pharmacotherapy or without drug treatment.

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EP942

Enhancing nutritional assessment in tunisian children: development and validation of an arabic version of the quesca nutritional questionnaire

Ben Othman Rym, Amorri Amani, Salma Abadlia, Ben Zina Baya, Ben Mansour Nadia, Kasraoui Sabeh, Gamoudi Amel & Jamoussi Henda
National Institute of Nutrition and Food Technology, Tunis

Introduction
Unhealthy eating behaviors are common in children. Therefore, assessing children nutritional knowledge is crucial. The QuesCA, a validated French tool, serves this purpose. Our study aimed to develop and validate an Arabic version of QuesCA.
Methods
We conducted a multicenter cross-sectional study from December 2021 to June 2022. Our study was conducted at the National Center for School and University Medicine in Tunis and five randomly selected nurseries in Ariana governorate. Six hundred children aged from 9 to 15 years were included.
Results
Our study was conducted in two phases. The first phase focused on the development and validation of the Arabic version. Initially, two independent forward translations were conducted. One by a committee of Tunisian nutrition experts (focus group), and the second by a sworn translator. The focus group reviewed the obtained Arabic versions, identifying errors, detecting divergences, and adapting them to Tunisian specificities. Subsequently, a French national proficient in both French and literary Arabic performed a backward translation of the questionnaire. Using the Delphi procedure, the focus group compared the back-translation with the original version, producing thus a consensus translation deemed suitable for children in Tunisia. After the Delphi procedure, we sought opinions from primary and secondary school teachers regarding the obtained Arabic version. Then, a pre-test was conducted on 30 randomly selected students aged 9 to 15 in a primary school in Gabes governorate using the Arabic version. Ultimately, we obtained a final translated Arabic version through the development and revision process by the focus group. The second phase aimed to evaluate the reliability and validity of the finalized Arabic version. The 600 participants were debriefed for phrasing or comprehension issues, with noted comments and questions. Post-questionnaire, participants received correct answers and nutritional education sessions. For the reliability analysis, the global Cronbach's alpha was 0.3, below the threshold (0.7). Despite recalculations after removing items with low correlations, the alpha value remained below the threshold. Thus, we decided to keep the questionnaire unchanged with the same number of items. After reliability analysis, validity analysis was tested. Construct validity was not assessed given the single-item representation of each questionnaire theme, while content validity was thoroughly evaluated by the focus group.
Conclusion
Our study developed a validated Arabic version of the QuesCA questionnaire. Challenges, like a low reliability coefficient, emphasize the need for further research to refine the questionnaire

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EP944

Sexuality in obese and pre-obese women: a descriptive cross-sectional study

Kouloud Boujelben[1], Mohamed Khairi Arous[1], Fatma Mnif[1], Dhouha Ben Salah[1], Mouna Elleuch[1], Rim Djebbi[2], Faten Haj Kacem[1], Nadia Charfi[1], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik[1]
[1]Hedi Chaker Hospital, Endocrinology, Sfax, Tunisia; [2]Faculty of Medecine of Sfax, Sfax, Tunisia

Introduction
Obesity is a global pandemic with adverse health implications, notably impacting quality of life, including sexuality. There is growing evidence that obesity adversely affects sexuality, not only in males but also in females. The objective of our study was to ascertain the influence of obesity on various phases and aspects of sexual activity
Methods
We conducted a descriptive cross-sectional study involving women who engaged in sexual intercourse within the past four weeks and whose body mass index exceeds 25 kg/m^2;. For the assessment of sexual function, we utilized the Arabic version of the Female Sexual Function Index (arFSFI), where a score below 23 indicates female sexual dysfunction. All patients provided oral informed consent freely and voluntarily
Results
The study included 50 overweight and obese women, with a mean age of 38.5 $\pm$ 9.45. The average duration of marriage/cohabitation was 11.8 years. The majority of women were educated (88%). More than two-thirds of participants (78%) were obese, and 22% were overweight. Most women (80%) were in the reproductive age group, 6% had primary or secondary amenorrhea, and 14% were menopausal. The mean BMI was 37 $\pm$ 8.7 kg/m^2;. The average Female Sexual Function Index (FSFI) score was 27.4 $\pm$ 6.2. We observed that 12% had sexual dysfunction, 42% had a lack of desire, and 24% experienced pain during sexual intercourse.
Discussion and conclusion
The rate of women experiencing sexual dysfunction is lower than that reported in the literature. This could be explained by the difficulty women in our context face in discussing their sexuality in general and their discomfort in particular. The lack of desire may be associated with a negative perception of body image. Our study emphasizes the need to raise awareness and educate healthcare professionals working with obese women on sexual health, in order to detect dysfunctions and improve the quality of life for patients.

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EP945

Epidemiological profile of chronic renal disease in obese people: prospective study in avicenna military hospital - marrakech

El Jadi Hamza[1] & Hicham Baizri[2]
[1]Avicenna Military Hospital, Endocrinology and metabolic diseases, marrakech, Morocco; [2]Avicenna Military Hospital, Endocrinology and metabolic diseases, Marrakech, Morocco

Obesity is accompanied by chronic diseases including cardiometabolic diseases. Obesity is also an independent factor of renal risk that deserves to be taken into account. The aims of our work were to determine the prevalence of chronic kidney disease related to obesity independently of all other usual risk factors and to describe its epidemiological characteristics in our population. We conducted a prospective descriptive and analytic study over a period of 12 months in 38 patients over 18 years of age, with a BMI $>$ 30 Kg/m^2 and without diabetes, hypertension, or other apparent cause chronic kidney disease, collected at the consulting service of the Military Hospital Avicenna of Marrakech. The average age of our patients was 38 years with a female predominance (sex ratio (m/w) of 0.80). The average BMI was 35.35 kg/m^2;, the average TT was 98.61 cm with android obesity in 88.2% of men and 85.7% of women. Dyslipidemia was found in 68.42% of patients, hyperuricemia in 18.42%, microalbuminuria in 13.15%, macroalbuminuria in 7.89% and hematuria in 2.6%. Glomerular hyperfiltration was present in 13.15% of cases and no patient had a GFR $<$ 60 ml/min/1.73m^2. The prevalence of chronic kidney disease among obese people in our population was 10.5%. Older obese patients with high BMI, hypertriglyceridemia, hypercholesterolemia, and hyperLDLemia were the most affected, with statistically significant differences between the 2 groups of patients with and without chronic kidney disease ($P < 0.05$). The results of our study warn of the need for cost-effective and well-adapted prevention measures to reverse the growing epidemic of obesity in the world.

Keywords
Obesity - Chronic kidney disease - Epidemiology - Risk factors
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EP946

The controlled attenuation parameter (CAP) and metabolic syndrome: is there a link?

Meriam Dalhoum[1], Olfa Berriche[1], Rim Ben Othmen[1], Emna Talbi[2], Raja Tlili[3], Sahar Hamza[3], Amel Gammoudi[1], Awatef Kacem[2], Lamia Kallel[3] & Henda Jamoussi[1]
[1]National Institute of Nutrition in Tunis, Human Obesity Research Unit, Tunis, Tunisia; [2]National Institute of Nutrition in Tunis, Biochemistry Laboratory, Tunis, Tunisia; [3]Mahmoud El Matri Hospital, Ariana, Tunis, Gastroenterology Department, Tunis, Tunisia

Introduction
The prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing worldwide. Since its earliest descriptions, NAFLD has been associated with the metabolic syndrome and its components.
Objective
To assess the relationship between Controlled Attenuation Parameter (CAP) values and the various components of metabolic syndrome.
Materials and methods
We carried out a longitudinal study including 161 patients with non-alcoholic fatty liver detected by a fibroscan using the CAP function (threshold $>$ 248 dB/m

for M and XL probes) and followed up for obesity at the Human Obesity Research Unit of the National Institute of Nutrition in Tunis. They were interviewed, anthropometrically measured (weight, height, body mass index (BMI), waist circumference (WC)) and biologically assessed.
Results
The mean age of our population was 49.23 ± 11.15 years. Patients were divided into 143 women (88.8%) and 18 men (11.2%). Mean BMI was 41.14 ± 6.37 kg/m^2; and mean WC was 119.21 ± 14.82 cm. Among our patients, 59 (36.6%) had diabetes, 66 (41%) were hypertensive, 63 (39.1%) had hypertriglyceridemia and 90 (55.9%) had hypo-HDL cholesterol. The prevalence of metabolic syndrome in our patients was 57.9% and the severity of hepatic steatosis increased significantly with the prevalence of metabolic syndrome ($P < 0.001$). In univariate analysis, there was a statistically significant positive linear relationship between CAP and the majority of metabolic syndrome parameters except hypoHDL cholesterol, CAP values were significantly higher in patients with diabetes, hypertension and hypertriglyceridemia respectively (respectively $P = 0.004$; $P = 0.02$ and $P = 0.016$ respectively).
Conclusion
Our study shows that there is a significant correlation between CAP values and the various parameters of the metabolic syndrome, which thus favors the onset of hepatic steatosis in obese patients, justifying comprehensive management targeting all risk factors.

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EP947

Changes in sex hormone levels after bariatric surgery and its association with weight loss in morbidly obese patients

Vindya Wellala[1], Udai Wijethunga[2], Dr. Udith Bulugahapitiya[3], Anuradha Jayasuriya[2] & Hasani Karunarathna[4]
[1]University Hospital Coventry & Warwickshire, United Kingdom; [2]Colombo South Teaching Hospital - Kalubowila, Dehiwala-Mount Lavinia, Sri Lanka; [3]National Hospital of Sri Lanka, Colombo, Sri Lanka; [4]University of Colombo, Colombo, Sri Lanka

Introduction
Bariatric surgery has become an essential option for long-term weight loss in morbidly obese population.
Objective
This study was aimed at investigating the effects of bariatric surgery on sex hormone levels and potential hormonal changes associated with significant weight loss in a cohort of 49 patients with obesity.
Methodology
Forty-nine patients with obesity, scheduled for bariatric surgery in Colombo South Teaching Hospital, Sri Lanka were enrolled in this prospective study. Preoperative assessments included demographic information and anthropometric measurements. The baseline sex hormones, including follicular stimulating hormone (FSH), luteinizing hormone (LH, testosterone), Sex Hormone Binding Globulin (SHBG), and symptomatology related to hypogonadism, were collected. Postoperative follow-ups were conducted at regular intervals to evaluate weight changes and hormonal profiles.
Results
Thirty-one females and 19 males were analysed. The mean weight before surgery among females were 124 kg (SD = 16.7), and males were 129.1 kg (SD = 19.6). The prevalence of Polycystic Ovary Syndrome (PCOS) in females was 64.5% ($n = 20$). The prevalence of obesityrelated hypogonadism was 64% ($n = 11$) among males. The average weight loss by 12 months after surgery was 40.2 kg (95% CI 36.7–43.63, $P < 0.05$) in females, and males had an average weight reduction of 39.2 kg (95% CI 33.00–45.54, $P < 0.05$). The Sex hormone binding globulin (SHBG) level was significantly increased in males 63.9% from baseline (95CI; 40.9-86.5: $P < 0.05$) and females in 50.5% from the baseline (95%; 61.75-121.3; $P < 0.05$) at the end of 12 months after surgery. It was positively correlated with weight loss, percentage of total fat loss and waist circumference reduction in both males and females. Total testosterone increased significantly in men at the end of 12 months 6.4 nmol/l (95%C; I4.2-7.6: $P < 0.05$. Total testosterone levels showed a significant positive correlation with weight loss parameters in males. There was no significant correlation found in gonadotrophin levels or oestrogen levels in males or females. The free androgen index improved in females at the end of 12 months, but no significant change was seen in males. These changes led to the resolution of PCOS in 72.4% of the female population. And obesityrelated male hypogonadism led to a resolution of 84.3%.
Conclusions
There was significant improvement in SHBG following bariatric surgery in males and females. The remarkable rate of resolution of PCOS and male obesity-related hypogonadism after bariatric surgery provides strong evidence supporting a causal role of obesity and adipose tissue dysfunction in the development of gonadal dysfunction in severely obese subjects.

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EP948

Factors associated with the risk of developing eating disorders in young doctors

Faten Haj Kacem Akid, Hana Charfi, mouna elleuch, Dhoha Ben Salah, Fatma Mnif, Nadia Charfi, Mouna Mnif, Mohamed Abid & Nabila Rekik Majdoub
Hedi Chaker Hospital, Sfax, Tunisia

Introduction
Young doctors in training are considered a population at risk for developing eating disorders. These disorders have multifactorial origins and require early and rapid screening, often utilizing the SCOFF questionnaire. Our aim is to screen and identify factors associated with the development of eating disorders among medical residents.
Materials and Methods
This is a cross-sectional, descriptive, and analytical study involving 70 medical residents working at Hedi Chaker University Hospital in Sfax over a 2-month period: November and December 2023. A self-administered questionnaire was distributed to our population using the Google Forms application.
Results
The average age of our population was 28 years, with a clear female predominance and a sex ratio of 0.55. Eating disorders were present in 27% of our population. Within our sample, 10% of medical residents had a history of psychiatric disorders, especially depression, and 79% used psychoactive substances, particularly coffee. Among participants, 56% engaged in weight control methods, especially through dietary habits and exercise. Psycho-affective consequences were observed, with 20% of the studied population showing symptoms of anxiety, and 10% exhibiting depressive symptoms. Among the factors studied, the use of weight control methods, the use of psychoactive substances, and anxiety were significantly associated with the risk of developing an eating disorder (P-value less than 0.05). Other factors were investigated, but they were not significantly related to the risk of eating disorders, such as gender, marital status, socioeconomic status, and depression.
Conclusion
The results of our study underscore the importance of screening for eating disorders in young doctors undergoing training. Additionally, socio-cultural, clinical, and psychological factors were associated with the risk of developing eating disorders in our population.

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EP949

Prediction of body fat percentage: development and validation of new anthropometric equations

Hadda Meroua Hani[1], Bennouar Salam[2], Kerrouche Asma[1] & Abdi Samia[2]
[1]Departement of Pharmacy, Faculty of Medecine, University SAAD DAHLEB, Blida; [2]Central Laboratory of Clinical Biology, University Hospital Center of Blida, Blida

Introduction
Obesity is a public health concern, several evidence have linked excess body fat to various metabolic disorders such as type 2 diabetes. In clinical practice, body mass index (BMI) is the most commonly used anthropometric index to define overweight and obesity given its simplicity and affordability. However, it has many limitations that are now widely recognized. Indeed, BMI is unable to compartmentalize body weight. Moreover, its cut-off values for the diagnosis of overweight and obesity set by the World Health Organization (WHO) are also advised, regardless of age, gender or physical activity level.
Aim
The aim of this study was to test the validity of existing equations, retrieved from the literature, in the Algerian adult population. To develop, and validate, new predictive equations for body fat percentage (%BF) using simple and easy-to-measure anthropometric parameters.
Methods
This is a cross-sectional study including 877 Algerian adults who underwent a body composition assessment by the direct segmental multi-frequency bioelectrical impedance technique (Inbody770). Participants were randomly divided into two groups: the development group ($n = 577$) and the validation

group ($n=300$). To develop the equations, multiple linear regression models were analyzed. The predictive performance of the developed equations was compared with the direct technique. The following validation tests were used: Student's t-test for paired samples, correlation, and BlandeAltman diagram. Diagnostic accuracy has also been assessed.

Results

Four existing equations were tested, and all showed statically significant bias. Four new equations were developed; all had satisfactory predictive performance, with a correlation coefficient ranging from 0.72 to 0.94 in men and 0.87 to 0.93 in women. The best-fitting equation was based on body mass index, waist-to-hip ratio, and chest circumference. The diagnostic accuracy of this equation was 96.7% in men and 95.3% in women.

Conclusion

The newly developed equations based on anthropometric parameters can serve as a simple tool for the accurate prediction of BF% in adult subjects, at both individual and epidemiological levels.

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EP951

Hypogonadism in men with type 2 diabetes: a close look at anthropometric insights

Anis Grassa, Manel Jemel, Salma Salhi, Brahim Khalfa, Marwa Chiboub, Emna Talbi, Hager Kandara & Ines Kammoun
National Institute of Nutrition and Food Technologies, Zouheir Kallel

Introduction

Obesity and hypogonadism (HG) are two conditions frequently observed in people with type 2 diabetes (T2D). The complex relationship between obesity and hormonal imbalances, particularly hypogonadism, remains a key area of interest in understanding the overall health profile of men with T2D.

Methods

In this cross-sectional study involving 250 men with T2D undergoing diabetes consultations, comprehensive clinical examinations were carried out, including measurements of weight, height, and waist circumference(Wc). Testosterone levels, specifically Free Testosterone (FT) and Bioavailable Testosterone (BT), were determined using the Vermeulen formula[1]. Hypogonadism was defined by meeting one of the following criteria: Total Testosterone (TT) below 231 ng/dl, FT below 6.5 ng/dl, or BT below 150 ng/dl. We defined two groups: (HG) hypogonadic patient and (non-HG) for non hypogonadic patients. Antropometric indices were compared in the two groups.

Results

The median age (IQR) of men with HG was 59 years [56-64], with a prevalence of 27.2% ($n=68$). In comparison to the non-HG group, patients with HG had a higher average weight (84.9 ± 14.3 vs 82.7 ± 11.7 kg; $P=0.192$), as well as a higher BMI (28.3 ± 4.5 vs 27.9 ± 3.8; P 0.492). The mean WC was also higher in the HG group (98.3 ± 10.3 cm vs 97.3 ± 8.9; P 0.481), as well as android fat distribution (65.7% vs 67.0%; P 0.471). Although obesity was higher in the HG patients (35.8% vs 26.7%), this difference was not significant ($P=0.162$). A significant inverse correlation was found between weight and the levels of TT (r: -0.313, $P<10^{-3}$), FT (r: -0.141, $P=0.030$, and BT (r: -0.134, $P=0.036$). In a multivariate analysis, considering age, glycemic control, and inflammatory status, weight emerged as an independent risk factor for HG in men with T2D. Indeed, each kilogram of weight was associated with a 1.05 times increased risk of HG (adjusted Odds Ratio = 1.05; 95% confidence interval = [1.01-1.08]; $P=0.006$).

Conclusion

These findings underscore the significant role of weight as an independent risk factor for HG in men with T2D, even after adjusting for other relevant variables. Further research and interventions targeting weight control may contribute to improved hormonal health outcomes in this patient population.

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EP952

Managing childhood obesity: teleconsultation as good as routine care

Bharat Saboo[1], Aniket Inamdar[2], Shweta Saboo[3], Dhruvi Hasnani[4] & Vipul Chavda[5]
[1]Prayas Diabetes Center, Metabolic health, Indore, India; [2]Samarpan clinic, Omerga, India; [3]Prayas Diabetes Center, Indore, India; [4]Rudraksha Institute of Medical Sciences, Ahmedabad, India; [5]Rudraksha institute of medical sciences, Ahmedabad, India

We all know that care delivery can become too much exhaustive and regular follow-up by patients in not maintained in India due to various reasons. This study aimed to compare the long-term effects of tele consultation (TC) and routine care (RC) on the weight status of children with obesity. Patients aged 5-14 years from the OPD, India were assigned to either TC or RC for 6 months after completing a standard obesity treatment programme during the period of march 2022 to July 2022. They were followed up for an average of 1 year. The study included 32 children (TC, $n=16$ and RC, $n=16$) with a mean (SD) age of 12.8 (3.5) years and a BMI SDS of 3.8 (0.4). There was no significant difference in BMI SDS change between the groups during the study ($P=0.7$) or at 1.5 years after the first clinic visit, TC = - 0.54 and RC = 0.57 BMI SDS units ($P=0.7$). Gender did not affect the results. The groups also did not differ in the average time spent by caregiver per patient during the study ($P=0.6$). All patients completed the follow-up. The study concluded that TC was as effective and efficient as RC in treating paediatric obesity and could provide more flexibility for patients and healthcare providers. Also in a resource crunched country like India it can be of a great help to provide optimum healthcare. More work in this area is needed.

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EP953

Effect of Macronutrient Intake on Tolerance to Chemotherapy in Breast Cancer Patients

Selma Mohsen[1], Berriche Olfa[1], Ben Mansour Hajer[2], Rym Ben Othman[1], Mehrez Achwak[1], Mezlini Amel[2] & Jamoussi Henda[1]
[1]National Institute of Nutrition, Service A, Tunis, Tunisia; [2]National Institute Salah Azaiez, Oncology, Tunis, Tunisia

Introduction

Macronutrient intake in cancer therapy is a controversial subject. Low protein intake could lead to malnutrition and cachexia. This can affect the response to chemotherapy. To date, there are no clinical studies to answer this question. The aim is to assess the influence of different macronutrient intakes in breast cancer patients on the digestive tolerance of chemotherapy.

Methods

This was a cross-sectional, descriptive study conducted over a 6-month period in patients with breast cancer undergoing chemotherapy. Macronutrient intakes were collected using a dietary survey and assessed according to ESPEN recommendations. A protein daily intake of less than 1.2 g/kg corresponds to an inadequate intake. Carbohydrate and fat intakes of over 55% and 30% respectively corresponded to excessive intakes. The digestive effects studied were vomiting, diarrhoea and constipation. The tolerance was assessed according to WHO grades ranging from 0 to 5. High grades 3 and 4 signified toxic grades.

Results

During this study 107 patients were enrolled. The mean age was 52.56 ± 9.75 years. The average of total energy intake was 2187 kcal/day. The intake was hypocaloric in almost 60% of cases. Insufficient protein intake was found in 35.5% of cases. Excessive fat intake was found in 84% of patients. And excessive intake of polyunsaturated fatty acids and cholesterol was noted in around 10% of cases. The digestive effects studied were: nausea/vomiting noted in 70% of cases, diarrhoea in 73% and constipation in 80% of cases. In multi-variate analysis, inadequate protein intake was associated with the severity of nausea/vomiting and diarrhoea, with respective P-values of 0.01 and 0.02. Carbohydrate intake was also associated with the severity of nausea/vomiting and diarrhoea, with respective ORs of 1.05 and 1.6 ($P=0.05$). Excessive cholesterol intake was identified as a risk factor for grade 3 and 4 of vomiting ($P=10$-3) and of constipation ($P=0.028$).

Conclusion

Tolerance of chemotherapy differs from one patient to another depending on nutritional status. A balanced diet is therefore essential in the treatment of breast cancer in order to improve efficacy and quality of life for patients.

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EP954

The obesity paradox in murine models of sepsis

Weronika Wasyluk[1], Marcin Czop[2] & Agnieszka Zwolak[1]
[1]Medical University of Lublin, Department of Internal Medicine and Internal Medicine in Nursing, Lublin, Poland; [2]Medical University of Lublin, Department of Clinical Genetics, Lublin, Poland

Introduction
Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. In sepsis, a phenomenon called obesity paradox has been described, which involves a reduction in mortality in patients with a body mass index allowing for the diagnosis of overweight and obesity. In the clinical context, the phenomenon is confirmed by current meta-analyses. The aim of the study is a systematic review and meta-analysis of studies on obesity paradox conducted on an animal model of sepsis.
Methods
A search was performed on PubMed for articles published up to December 31, 2023. Studies examining obesity-related mortality in a murine model of sepsis were selected.
Results
We identified 19 studies that reported sepsis mortality data from 36 experiments. Obesity was obtained in the diet-induced obesity model or in the leptin deficiency model. Sepsis was induced in the cecal ligation and puncture, cecal slurry injection, lipopolysaccharide injection or Staphylococcus aureus inoculation models. In the studies, obesity in the experimental groups (obesity model) was, depending on the study, higher or lower than in the control groups. Nine studies using the same obesity model (diet-induced obesity) and sepsis model (cecal ligation and puncture) were selected for meta-analysis. There was no statistically significant difference between animals receiving a high-fat diet and animals from the control group receiving a standard diet ($P=0.5716$). The statistical regression analysis showed that a higher age at the time of introduction of a high-fat diet ($P<0.001$) and a longer duration of feeding with a high-fat diet ($P<0.001$) reduce mortality, while a higher age ($P<0.001$) at the time of sepsis induction increases mortality. In the above model, the regression coefficient R^2 is 0.86 ($P<0.001$).
Conclusions
The results indicate the role of study protocol in the obtained results. The age of the animals at particular stages of the study and the duration of use of the high-fat diet may be important for the obtained results. Further research is necessary to confirm and better understand this phenomenon.

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EP955

Comparative study of body mass index and percentage of body fat in the definition of obesity

Hadda Meroua Hani[1], Bennouar Salam[2], Kerrouche Asma[1] & Abdi Samia[2]
[1]Departement of Pharmacy, Faculty of Medecine, University SAAD DAHLEB, Blida; [2]Central Laboratory of Clinical Biology, University Hospital Center of Blida, Blida

Introduction
Body Mass Index (BMI) is recommended by the World Health Organization (WHO) for assessing weight due to its simplicity, reliability, and accessibility. However, as highlighted in several studies, it does not accurately reflect body fat and does not account for physiological changes in body composition that occur during different periods of life, or across sexes.Aim: Our study aimed to determine the prevalence of underweight, overweight, and obesity according to both definitions – BMI and Percentage of Body Fat (PBF) measured by bioelectrical impedance analysis.
Methods
This is a retrospective cross-sectional study on a population of 877 Algerian volunteers who underwent a body composition assessment using multifrequency segmental direct bioelectrical impedance analysis (MSD-BIA). WHO cutoffs were used for the definition of underweight, overweight, and obesity. The comparison was made using the Pearson chi-squared test.
Results
Statistical analysis revealed numerous discrepancies between the two definitions. Indeed, 38.9% of women had a high PBF while being classified as underweight according to BMI (<18.5 kg/m^2;). 48.4% and 80.6% of men and women, respectively, had a high PBF while being considered normal weight according to BMI (18.5-25 kg/m^2). 12% of men and 0.7% of women classified as overweight according to BMI (25-30 kg/m^2) had a normal PBF. Additionally, 1.7% of men classified as obese according to BMI (>30 kg/m^2) had a low PBF.
Conclusion
Obesity has become a major health problem. The use of BMI alone appears ineffective in our population; therefore, a direct measurement of body composition is desirable to establish a correct diagnosis and act quickly to prevent potential impacts and complications, especially metabolic and cardiovascular.

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EP956

Effects of depression, anxiety and quality of life on mid-term weight loss after sleeve gastrectomy

Faten Mahjoub, Abir El Amri, Ramla Mizouri, Nadia Ben Amor, Saida Boumefteh & Jamoussi Henda
Institut De Nutrition, Tunis, Tunisia

Introduction
Obesity is a leading cause of morbidity and mortality globally, with significant physical and psychological repercussions. The aim of our study was to assess anxiety-depressive symptoms and health-related quality of life at the mid-term following bariatric surgery and to determinate their effect on mid-term weight loss.
Methods
We conducted a descriptive longitudinal study at the obesity research unit of the National Institute of Nutrition and Food Technology in Tunis on 30 obese patients who had undergone sleeve-gastrectomy with a medical follow-up of at least 5 years. Anxiety and depressive disorders were screened using the Hospital Anxiety and Depression scale (HAD), which includes 14 items. Seven questions related to anxiety and seven others to depression. The outcome of sleeve gastrectomy and changes in quality of life over the mid-term were assessed using the BAROS (Bariatric analysis and reporting outcome system) evaluation scale.
Results
The mean age of our patients was 43 ± 9.5 years. In the mid-term post-sleeve gastrectomy period, the prevalence of anxiety was 87% (6 patients had mild anxiety, 16 patients had moderate anxiety and 4 patients had severe anxiety) and the prevalence of depression was 60% (6 patients had mild depression, 8 patients had moderate depression and 4 patients had severe depression). The association between depression and weight loss at 2 and 5 years after sleeve gastrectomy was statistically significant, the more severe the depression the less weight loss ($r=-0.45$, $P=0.01$), ($r=0.48$, $P=0.007$) respectively. No statistically significant association was found between anxiety and loss of excess weight in the mediumterm post sleeve gastrectomy. Calculation of the overall BAROS score showed that 20 patients had a score >3, so surgery resulted in a good or very good outcome in 66% of patients. Analysis of the relationship between the global score and the percentage of excess weight lost at 5 years showed an excellent correlation between these two data ($P=0.01$).
Conclusion
The presence of depressive disorders after sleeve gastrectomy significantly predicted attenuated post-surgical weight loss. It is important to consider and treat these disorders, as they are important factors in a patient's quality of life.

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EP959

Ketogenic diet (KD) as a nutritional therapeutical option for women suffering from polycystic ovary syndrome

Tamta Sharadze[1,2], Teona Nutsubidze[3] & Tekle Bakhtadze[3]
[1]National Institute of Endocrinology Georgia, Tbilisi, Georgia; [2]National Institute of Endocrinology Georgia, Endocrinoly, Tbilisi, Georgia; [3]National Institute of Endocrinology Georgia, T, Georgia

The ketogenic diet (KD) has been extensively studied as a potential therapeutic approach for various conditions, including Polycystic Ovary Syndrome (PCOS) in women. We describe a 29-year-old overweight woman with PCOS. Clinically, she presented with hirsutism, acne, and pink stretch marks in the hip and abdomen areas, no significant menstrual cycle disturbances were reported. Patient underwent a 12-week KD regimen. Initially, her body mass index (BMI) was 33.5, with a weight of 87.9 kg. After the diet, she experienced a significant weight loss of 12.2 kg, reducing her weight to 75.7 kg and her BMI to 28.8. Remarkably, patient's hormonal profile showed considerable improvement. Patient at the beginning of the study had a HOMA-IR 3.7 confirming insulin resistance. At the end of the study, a significant decrease was observed in glucose (pre 98 mg/dl vs post 92 mg/dl) and insulin (pre 15.2 uIU/ml vs post 10,78 uIU/ml) and consequently in the HOMA-IR (pre 3,7 vs post 2.4). Luteinizing Hormone (LH) to Follicle-Stimulating Hormone (FSH) ratio, which was reversed at the study's outset (2.42), normalized post-diet (1.44). There was a decrease in free testosterone levels (from 4.6 pg/ml to 3.71 pg/ml) and Dehydroepiandrosterone Sulfate (DHEA-S) levels (from 5.02 µg/ml to 4.07 µg/ml). Additionally, there was an increase in estradiol (from 73.4 pg/ml to 82.6 pg/ml) and progesterone levels (from 0.21 ng/ml to 0.32 ng/ml). The patient's Ferriman Gallwey Score showed a minor decrease (from 11.3 to 10.5), indicating a slight improvement in symptoms. KD is an effective option for women with PCOS to manage weight and hormonal imbalances. Further research is needed on its long-term sustainability and potential side effects, as this short-term study reported no adverse effects.

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EP963

Immune checkpoint inhibitor-associated diabetes mellitus

Joana Vinhais, Beatriz R. Pereira, David Veríssimo, Catarina Ivo, Ana Cláudia Martins, João Nunes e Silva, Dolores Passos, Luís Lopes, João Jácome de Castro & Mafalda Marcelino
Hospital das Forças Armadas, Serviço de Endocrinologia, Lisbon, Portugal

Introduction
The immune checkpoint inhibitors (ICI) are increasingly being used in the treatment of several malignancies. ICI are monoclonal antibodies that inhibit immune checkpoints, thus stimulating the action of the immune cells to attack the tumour cells. The overstimulation of the immune system can lead to several endocrinopathies, such as autoimmune diabetes, known as ICI-associated diabetes mellitus (ICIDM).
Case Report
In September 2023, a 62-year-old male presented to the emergency department with diabetic ketoacidosis (DKA). He had no prior diagnosis of diabetes mellitus. The patient was diagnosed with clear cell renal cell carcinoma in November 2022 and underwent right nephrectomy in January 2023. In May 2023 there were detected pulmonary metastases, initiating immunotherapy with nivolumab and ipilimumab one month after, which led us to suspect of autoimmune diabetes secondary to ICI. In admission, the patient presented with polyuria, polydipsia, and loss of 3 kg in the past week, and a biochemical evaluation that revealed DKA with a glycemia of 590 mg/dl, a ketonemia of 6.2mmol/l, and arterial pH of 7.303. The autoimmunity study with anti-GAD, anti-ICA, anti-insulin and anti-IA2 was negative, the C-peptide was low (0.26 ng/ml) and the HbA1C was 6.5%. Abdominopelvic CT was performed and did not show neoplastic lesions or sins of pancreatitis. Furthermore, the study of other endocrinopathies potentially associated with ICI was negative. Glycaemic control was achieved with insulin perfusion followed by intensive insulin therapy. The patient was then discharged, monitored with a continuous glucose monitoring device and under intensive insulin therapy, which he currently maintains, with good control of glycaemic profile.
Discussion
ICIDM presents as an acute symptomatic and severe hyperglycaemia with a high prevalence of DKA (in approximately 70% of the cases), a near-normal HbA1C and an undetectable C-peptide, suggesting a rapid progression of beta-cell destruction. In this case report, approximately 3 months after starting an ICI, the patient presented with DKA, a HbA1C of 6.5%, and a low C-peptide which indicated rapid progression to insulin insufficiency. Roughly 60% of the cases of ICIDM described in the literature doŕt have diabetes autoantibodies, as occurred in this case report. In accordance with other endocrinopathies associated with ICI, ICIDM requires lifelong treatment with the deficient hormone, in this case insulin.
Conclusion
This case report is in line with other case studies available in literature and not only alert us to this unusual diagnosis, but also for the need to screen these patients for endocrinopathies associated with ICI.

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EP965

Identification of etiology in non-diabetic hypoglycemia in resource poor settings: experience from a tertiary care center in sri lanka

Shahini Winson Gnanathayalan[1], Isuru Jayawardana[2], Nethrani Pathirana[3], Sharmika Sivageethan[4], Beminahennadige Fernando[4], Vinitharann Varunanantharajah[4], t g Athukorala[4], Uditha Bulugahapitiya[4], manilka Sumanatilleke[4] & Prasad Katulanda[4]
[1]National Hospital Sri Lanka, Diabetes and Endocrinology, Colombo, Sri Lanka; [2]National Hospital Sri Lanka, Diabetes and Endocrinology, COLOMBO, Sri Lanka; [3]National Hospital Sri Lanka, Colombo, Sri Lanka; [4]National Hospital Sri Lanka, COLOMBO, Sri Lanka

Background
Non-Diabetic Hypoglycemia is a rare entity in Endocrinology. After the confirmation of hypoglycemia with Whipple's triad and excluding drug induced hypoglycemia, identification of underlying etiology using appropriate and targeted investigations is fundamental to institute specific management. It is challenging in resource poor settings due to unavailability and high cost of some investigations such as insulin autoantibodies and insulin-like growth factr-2 (IGF-2) level.
Methods
We retrospectively analyzed 11 patients who were diagnosed with non-diabetic hypoglycemia in 2023, in a tertiary care center in Sri Lanka
Results
Among the 11 patients, six patients, three and one were diagnosed with insulinoma, Insulin autoimmune syndrome (IAS) and nesidioblastosis respectively. Another one patient with neurofibromatosis type 1(NF-1) was diagnosed with non-islet cell tumor hypoglycemia (NICTH) due to metastatic gastrointestinal stromal tumor (GIST). Among patients with insulinoma, 2 had multifocal insulinoma in the background of MEN-1 syndrome and NF-1 respectively. Among cases of IAS, two were idiopathic and the other one was carbimazole induced. The patient with nesidioblastosis didn't have a history of gastric surgeries. Most patients had recurrent level-3 hypoglycemia. Timing of the symptoms, whether fasting or postprandial was not reliably helpful in differentiating between the etiologies because one patient with insulinoma had predominantly post-prandial hypoglycemia and two patients with IAS had almost fasting symptoms. All cases of insulinoma and nesidioblastosis had insulin/c-peptide ratio of less than one with insulin recovery after PEG precipitation of more than 70%, while all three patients with IAS had very high insulin levels with the ratio of much more than one and insulin recovery after PEG precipitation of less than 10%. The diagnosis of IAS was confirmed by the presence of insulin autoantibodies in all cases. The case of NICTH had hypo-insulinemic hypoglycemia with suppressed beta-hydroxy butyrate level, low IGF-1 and positive response to glucagon challenge test. IGF-2 level could not be performed.
Conclusion
This series highlights the challenges in identifying the cause of non-diabetic hypoglycemia especially in resource poor settings. The timing of hypoglycemia is not a good indicator to differentiate the etiologies. In the resource-limited settings where insulin autoantibodies cannot be done freely, insulin/c-peptide ratio with insulin recovery after PEG precipitation might be a good alternative to diagnose IAS. The diagnosis of NICTH can be made in a patient with malignancy having hypo-insulinemic hypoglycemia with suppressed ketogenesis, low IGF-1 and positive glucagon challenge test as IGF-2 assay is very expensive and not available in many settings.

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EP972

Immunotherapy-induced endocrinopathies: unraveling a clinical case of immune-mediated diabetes firstly and thyroid pathology secondly

Anastasiia Kriuchkova & Vladislav Evseev
Saint Petersburg, Saint Petersburg, Russian Federation

Immunotherapy, a cancer treatment leveraging the individual's immune system, has demonstrated its efficacy by eliciting responses from immune cells in and around tumors, notably tumor-infiltrating lymphocytes (TILs). The presence of TILs often correlates with more favorable outcomes in cancer cases. Immune-mediated adverse events (imAEs) accompany immunotherapy in 13.7-54% of patients, with the involvement of the endocrine system detected in nearly 10% of cases, representing a common form of imAEs. Despite the potential involvement of any secreting endocrine glands, immune-mediated thyroid dysfunction stands out as the most prevalent variant. A distinctive aspect of endocrine imAEs lies in the ability to safely continue immune therapy concurrently with replacement hormonal treatment. On the other hand, if these issues are discovered later, they may worsen and necessitate resuscitation or urgent care. Immune-mediated diabetes is a rare complication, with an incidence rate reported at only 0.1%. This report aims to describe a clinical case involving the primary development of diabetes during ongoing immunotherapy with pembrolizumab, coupled with the secondary development of thyroid gland pathology. The case involves a 51-year-old female diagnosed with Central cancer of the right intermediate bronchus (squamous cell carcinoma), stage IIB (pT2bN1(1/30) cM0). Since June 13, 2023, the patient has been undergoing adjuvant immunotherapy with pembrolizumab. Her medical history includes prior observation by an endocrinologist due to nodal formations in the thyroid gland without thyroid disfunction. After completing 4 th cycles of immunotherapy, she noticed a sudden and significant change in her health condition, characterized by a strong thirst and a dry mouth. Immediate medical check revealed elevated blood glucose levels up to 17 mmol/l, glucosuria, acetone in urine (+++), glycated hemoglobin at 8.3%, C-peptide (fasting) at 1.16 μIU/ml, Insulin (fasting) at 1.16 μIU/ml, and TSH at 3.2 μIU/ml. The presence of absolute insulin deficiency did not raise any doubts, and the diagnosis of type 1 immune-mediated diabetes was established. Insulin therapy in a basal-bolus regimen was immediately initiated, complemented by continuous glucose monitoring. Subsequent blood monitoring indicated a decrease in TSH levels and an increase in free T3, signaling the initiation of thyroid tissue destruction amidst ongoing treatment. This case underscores the importance of timely identification and management of immune-related complications on such

therapy, shedding light on the unique challenges presented by the interplay between immunotherapy, endocrine function, and resultant adverse events.

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EP973

Alopecia universalis and epilepsy in a patient with type 1 diabetes

Jelena Andric, Anamarija Zrilic Vrkljan & Vlatka Pandzic Jaksic
Dubrava University Hospital, Department of Endocrinology, Diabetes and Metabolic diseases, Zagreb, Croatia

Background
Alopecia areata is a common non-endocrine manifestation in autoimmune polyendocrine syndromes (APS). Alopecia universalis is its most severe form with total loss of scalp and body hair. Several attempts at classifications for multiple combinations of autoimmune disorders in APS were proposed. Type 1 diabetes is associated with epilepsy due to glycemic extremes and microvascular damage, but a shared etiology mediated by anti-glutamic acid decarboxylase antibodies (anti-GAD) was also recognized.
Case presentation
A 38-year-old patient was admitted to our clinic with severe diabetic ketoacidosis. A few days before he had generalized seizure attack. Besides being shaved and mostly white beard, he had no scalp, no eyebrows, eyelashes, and any other body hair. He was diagnosed with alopecia universalis at the age of 3, epilepsy at the age of 9, and type 1 diabetes at the age of 18 years. Laboratory studies showed undetectable C-peptide, very high HbA1c, elevated anti-GAD, normal thyroid peroxidase antibodies, thyroid hormones, calcium, and basal cortisol. Low compliance with insulin, diet and anti-seizure therapy was presumed. The mental impairment after recurrent seizures together with probable permanent psychological changes made the control of his diabetes extremely difficult.
Conclusion
The typical successive occurrence from the very early age suggests a probable common autoimmune etiology of his disorders. Thyroid and adrenal autoimmunity are still absent which is not typical for known APS. Immunotherapy in such longstanding diseases would probably lack effectiveness, but early recognition and intervention - potentially even preventive - might provide an opportunity for avoiding the development of such a severe clinical presentation.

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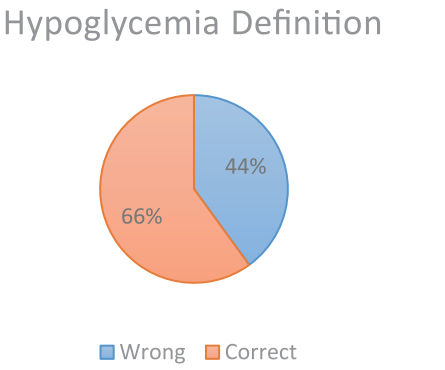
EP981

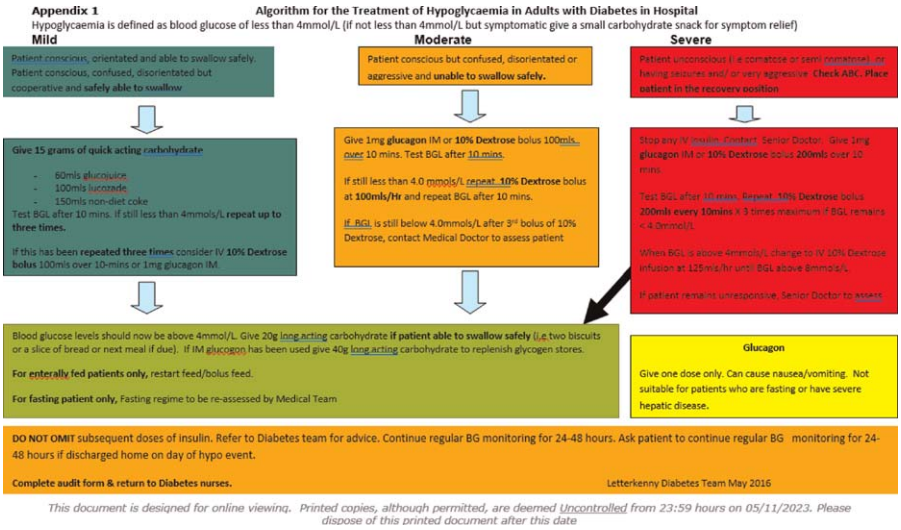
Healthcare staff awareness of hypoglycemia among in patients in a model 3 hospital university hospital

Azhar Al-Shaibany[1], Marketa Vyskocilova[2] & Rowa Abdulla[2]
[1]Letterkenny University Hospital, Endocrinology, Letterkenny, Ireland; [2]Letterkenny University Hospital, Letterkenny, Ireland

Background
Hypoglycemia is defined as a blood sugar less than 4mmol/l. It is defined clinically in the presence of Whipple's triad, characterized by signs and symptoms of hypoglycemia, low plasma glucose and reversal of symptoms on correction of hypoglycemia. Inpatients prevalence of hypoglycemia ranges from 3.5% to 10.5% with the majority of patients affected having diabetes and receiving insulin therapy[1]. Hypoglycemia is one of the side effects of intensive glycemic control and between 20-25% of in patients with diabetes will experience hypoglycemia during hospital stay[2]. Hypoglycemia's is also associated with poorer outcomes and reduced quality of life in patients living with diabetes[2]. Patients are at increased risk of hypoglycemia, especially those prescribed glucose lowering drugs like insulin and sulfonylurea. Around 25% of patients who are admitted to hospitals take glycemic lowering medications. Inpatient hypoglycemia increases morbidity, mortality, prolonged hospital stay, and increases hospital 30 day readmission rates and also increases the cost of treatment[3]. Mortally among inpatients with hypoglycemia are high as 6.5%, compared to 3.8% in those who do not experience hypoglycemia4. Therefore, it is important that healthcare workers are knowledgeable in the recognition and treatment of hypoglycemia[4].
Aims and Objectives
This audit aimed to assess the knowledge of healthcare staff (nonconsultant) hospital doctors and nurses of the local hypoglycemia management protocol among inpatients in our hospital.
Guidelines
Our local protocol for the treatment of hypoglycemia present in every ward.
Methods
Over a two week period between the dates off 10/10/2023 and 25/10/2023 a best of five questionnaires was administered at random to 60 non consultant hospital doctors and nurses. These questionnaires were collected in common areas such ED, Wards, ICU, CCU in relation to definitions, treatment and prevention of hypoglycemia were gathered under observation and analyzed against the hospital policy to determine awareness of the local policy.
Results

Q1





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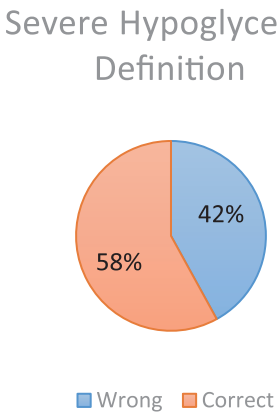

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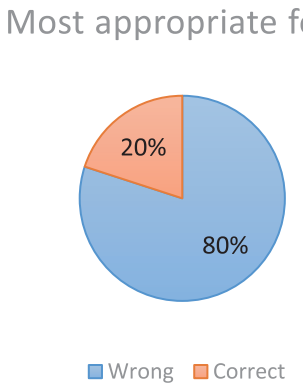
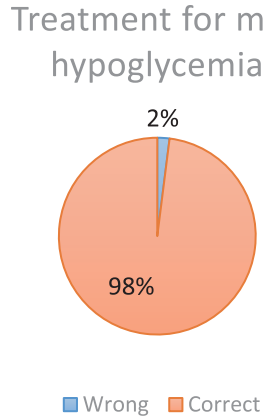


Q4:



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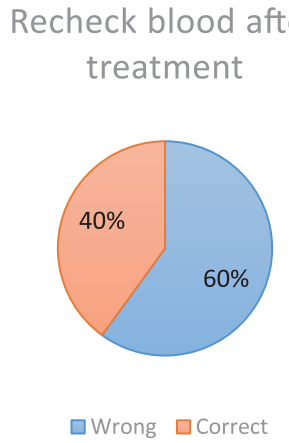

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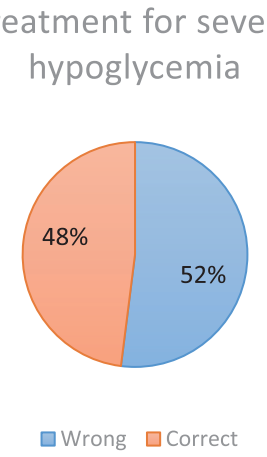


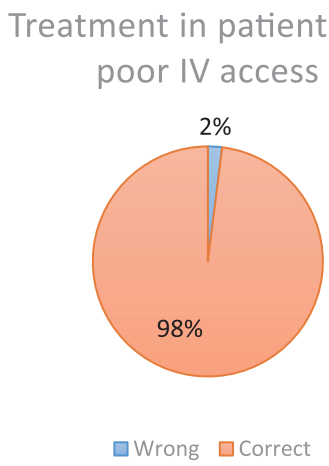
Conclusion

To sum up, our audit findings highlight a concerning lack of awareness regarding hypoglycemia management. This knowledge gap significantly affect patient safety, as timely and appropriate intervention is critical in preventing severe consequences. The results suggests the need for increased education and training of healthcare providers, to improve their understanding of hypoglycemia and how to manage it effectively. This can significantly lead to better outcomes and an enhanced quality of patient's life.

Recommendations

- Regular training programs.
- Use visual aids and handouts.
- Regular audits.

Q7:



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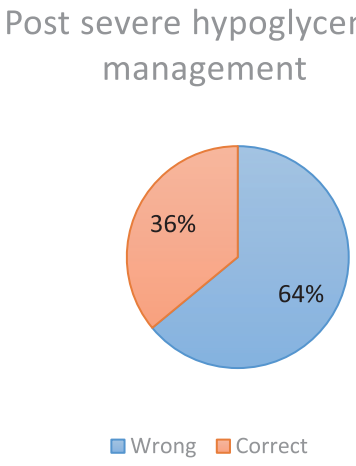

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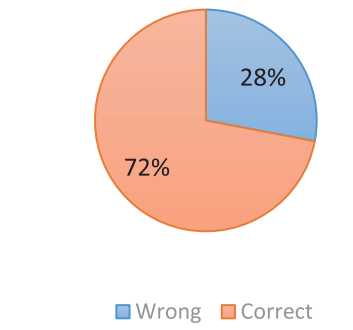

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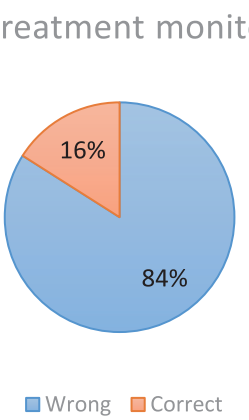

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EP982

Pathways to diagnosis and missed opportunities in newly diagnosed T2DM with NAFLD

Supriyo Mukherjee[1], Bishnupriya Mukherjee[1], Anjali Goswami[1], Chun Shing Kwok[2] & Anne Phillips[3]
[1]Research Centre for Diabetes Hypertension and Obesity, Medicine, Samastipur, India; [2]Cardiology Registrar, University Hospitals of North Midlands NHS Trust, Newcastle, United Kingdom; [3]Faculty of Health Education and Life Sciences, Department of Post-Qualifying Healthcare Practice, Birmingham City University, Birmingham, United Kingdom

Introduction & Objective
This poster shows various pathways for patients who were recently diagnosed with T2DM and NAFLD in North Bihar, India. It also analyses trajectories as well as missed opportunities and earlier intervention possibilities.
Methods
The study was conducted at RCDHO in Samastipur, Bihar. A total of 148 participants were enrolled and data was obtained from questionnaires and analysis of healthcare records.
Results
In the healthcare sector, the journey towards well-being often diverges into three distinct pathways, each steering individuals towards different outcomes. On the favourable pathways, those who seek consultations from highly skilled and MBBS qualified doctors experience a streamlined process of diagnosis and optimal management of their health concerns. The expertise of these healthcare professionals ensures early and effective identification of issues, paving the way for timely and targeted interventions. Contrastingly, the unfavourable pathways are fraught with impediments that hinder the trajectory towards health improvement. Delays often ensue when individuals opt for non-specialist consultations, leading to a protraction in the diagnostic and management phases. Financial difficulties become an additional roadblock, impeding access to necessary healthcare services. Late referrals to health professionals exacerbate the situation, further complicating the path to recovery. Within this intricate web of healthcare dynamics, missed opportunities emerge as a critical concern. The lack of awareness about health issues and the absence of awareness-based screening contribute to a failure in early detection. Limited availability of specialized care and diagnostic tools further impedes progress, while inadequate knowledge among healthcare providers adds a layer of complexity to the situation. The domino effect continues with low timely referrals and economic constraints, collectively creating missed opportunities for individuals to attain optimal health outcomes. Addressing these multifaceted challenges is paramount to fostering a healthcare system that ensures equitable access, early intervention, and improved overall well-being for all.
Conclusion
Critical improvements in healthcare necessitate a multifaceted approach. Strengthening systems of referral is essential for seamless patient transitions between care levels. Concurrently, enhancing health literacy empowers individuals to make informed decisions, fostering a proactive approach to well-being. Investing in healthcare infrastructure ensures sufficient resources for diagnosis and treatment, while comprehensive training for healthcare providers equips them to navigate evolving healthcare demands effectively. A poignant priority lies in raising awareness and broadening access for the early diagnosis and treatment of Type 2 Diabetes Mellitus

(T2DM) with Non-Alcoholic Fatty Liver Disease (NAFLD), addressing a pressing need for proactive management and improved health outcomes.

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EP985

Management of the diabetic foot: experience of the diabetology department of the army central hospital. about 282 cases

Imane el ghebir, Hani Meriem, Rehaimia Amina & Ait Abderrahmane Samir
Army Central Hospital, Diabetology, Algiers, Algeria

Introduction
The diabetic foot is a public health problem. It can cause serious complications leading to amputation.
Aim
To determine the clinical, biological, therapeutic and evolutionary characteristics of the diabetic foot.
Patients and Methods
Prospective descriptive study conducted at the HCA Diabetology Department, over a period of 36 months. Inclusion of all hospitalized or followed up patients in consultation for a diabetic foot. The total number of patients was 281.
Results
The average age of patients was 61.82 years. The majority of them (74%) were males of which, 94% had T2DM. The median age of diabetes was 15 years. A diabetic foot ulcer was the reason for the initial discovery of diabetes in 4.7% of the patients. Over 65% of the patients were on insulin. One or more degenerative complications were noted in 94.8% of them. 25.4% of the patients had at least one history of amputation. The right foot was affected in 52.3% of the cases. The median consultation time at the diabetology department was 30 days. Infected diabetic feet accounted for 54.9% of the cases. The most frequent entry portal for foot infections was inter-toe intertrigos in 31% of cases, followed by trauma in 25.51% and the plantar neuropathic ulcer in 24.13%. Dermo-hypodermatitis was the most frequent type of infection, representing 86.2% of the cases. The average duration of antibiotic therapy for infected feet was 14.73 days. Osteitis was present in 87.6% of patients with infected feet; they were treated medically in 69.2% of cases. 16% of patients underwent minor amputation. Median hospital stay was 22 days, with extremes ranging from 7 to 101 days. Median time to definitive healing was 30 days.
Conclusion
The diabetic foot is a public health problem because of the risk of wounds progressing to amputation. Proper education of diabetic patients and early multidisciplinary medical care can improve prognosis and prevent recurrence.

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EP986

Characteristics of type 2 diabetes evolving for more than 10 years in a tunisian population

Nesrine Dhieb, Chaima Jemai, Mariem Cheikhrouhou, Chaima Sdiri, Sami Fitouri, Yosra Htira, Zohra Hadj Ali, Imen Hedfi, Olfa Lajili & Faika Ben Mami
National institute of nutrition of Tunis, C

Introduction
Diabetes mellitus is a chronic disease. Long-standing diabetes increases the prevalence of degenerative complications. The aim of our study was to determine the clinical and biological characteristics of a population of type 2 diabetic patients whose diabetes had been evolving for more than 10 years.
Methods
This was a descriptive cross-sectional study about 100 type 2 diabetic patients hospitalized in the national institute of nutrition of Tunis. For each patient, we carried out an interview and physical examination, we assessed anthropometric parameters and we examinated the feet. Then we graded the podiatric risk for each patient. Creatinine clearance was calculated using the CKD-EPI formula.
Results
The mean age was 57.20 ± 8.48 years. Sex ratio was 0.35. 29% of patients were smokers. Median weight was 91 kg with extremes of 65 and 110 kg. The median BMI was 30.46 kg/m^2; with extremes of 22.50 and 38.28 kg/m^2. The mean duration of diabetes was 14.79 ± 4.55 years. All patients were on insulintherapy. The majority of patients (70%) were on NPH insulin. The mean HbA1C was 10.33%. Mean creatinine clearance was 93.16 ± 19.19 ml/l/1.73 m^2. The respective frequencies of diabetic neuropathy, diabetic retinopathy and diabetic nephropathy were 30%, 55% and 46%. Macroangiopathy was present in 35% of cases (coronary artery disease (10%), stroke (3%), obliterative arteriopathy of the lower limbs (18%). Podiatric risk was null for the majority of the population (55%). Frequencies of podiatric risks of 1, 2 and 3 were 55%, 25%, 18% and 2% respectively. Factors significantly associated to poditric risk was smoking ($P=0.026$), BMI ($P<0.001$), Hypertension ($P=0.038$) and diabetic nephropathy ($P<0.001$).
Conclusion
The duration of diabetes exceeding 10 years was characterised by a high prevalence of degenerative complications. Rigorous early management of diabetes and comorbidities is essential to prevent complications.

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EP987

Glucometric comparison in DM1 patients after implantation of continuous glucose monitoring

Elena Martínez Silla, Enrique Redondo Torres, Javier García Sánchez, Raúl Rodríguez Juárez, Miguel Quesada Charneco & Pablo-José López-Ibarra Lozano
San Cecilio Clinical University Hospital, Endocrinology and Nutrition, Granada, Spain

Introduction and Objectives
Continuous glucose monitoring (CGM) has demonstrated benefits in the prevention of hypoglycemia in patients with type 1 diabetes mellitus (DM1) vs flash monitoring (CGM). Our aim was to analyze the clinical characteristics, indication and glucometric changes in patients using MFG after CGM implantation.
Material and methods
Retrospective observational study of 13 patients under follow-up for DM1 in Endocrinology consultations at the Hospital Universitario Clínico San Cecilio with suboptimal glycemic control using MFG who underwent implantation of MG (Dexcom G6). Demographic variables related to the disease and its complications and glucose monitoring parameters before and after implantation of the Dexcom G6 system were studied.
Results
7 women and 6 men were evaluated. Mean age 40 ± 14.1 years, mean time of diabetes evolution 16.9 ± 11.1 years. Mean BMI 24.7 ± 3.27. 2 kg/m^2. Only 2 patients had microangiopathic complications. The mean time of use of MFG was 2.5 years and of MG 7.8 months. In 12 patients, the indication for CGM was frequent hypoglycemia, the remaining case being due to skin reaction. After the indication for CGM, HbA1c (6.9 vs 6.4%, $P=0.039$), time below range (7.4 vs 2.5, $P=0.001$) and coefficient of variation (37.5 vs 32.8, $P=0.004$) decreased significantly. There were no significant changes in time in range or time in hyperglycemia.
Conclusions
In our study, the use of GCM compared to previous MFG use is related to better glycemic control in patients with DM1 in terms of HbA1c, with reduced time in hypoglycemia and coefficient of variation. GCM systems may be useful in the management of the DM1 patient with a tendency to hypoglycemia and wide glycemic variability.

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EP988

Unraveling syndromic diabetes in the context of h syndrome - a rare genetic entity with multisystemic manifestations - case report

Souhir Maalej, Fatma Mnif, Siddiqa Soomauroo, Abdel Mouhaymen Missaoui, Mouna Mnif, Dhouha Ben Salah, Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Endocrinology, Sfax

Introduction
The H syndrome, an autosomal recessive genodermatosis, is characterized by cutaneous and systemic manifestations resulting from mutations in the SLC29A3 gene (10q22.2), leading to histiocytic infiltration of multiple organs. This study presents a new observation of H syndrome.
Observation
We report the case of a 33-year-old patient, born of consanguineous parents, with a history of diabetes diagnosed at the age of 28 and treated with oral antidiabetic drugs (OAD). Hospitalized for an acidocetotic decompensation associated with acute pyelonephritis and an abscess of the anal margin, she exhibited poorly controlled diabetes (HbA1c = 11.7%) under OAD. Clinical examination revealed a pronounced dysmorphic syndrome, characterized by bilateral, symmetrical, hyperpigmented, and thickened plaques present for five years, with hypertrichosis. These lesions were observed not only on the inner thighs but also in the pubic and lumbar regions. The patient also presented buttock lipodystrophy, swelling with hyperpigmentation of the labia majora, camptodactyly, hallux valgus, and dental deformity. Erythematous, annular, and figurate lesions, slightly keratotic without atrophy, were present on the cheeks and nose. Dermoscopy revealed multiple telangiectasias forming a reticulated network. A 4mm punch biopsy showed a lymphocytic and histiocytic infiltrate, with positive immunohistochemistry for CD68. The patient had a short stature (1.53m) of familial origin, hepatomegaly associated with bicytopenia (leukoneutropenia and

hypochromic microcytic anemia at 5.8 g/dl), elevated ferritin levels (273.3 ng/ml), and low serum iron (2.1 umol/l) persisting even after sepsis resolution. An osteomedullary biopsy revealed grade 2 medullary fibrosis, excluding neoplastic infiltration. The diagnosis of H syndrome was confirmed through histological and immunohistochemical examinations. Echocardiography was normal, and the patient was referred to an Ear, Nose, and Throat (ENT) specialist for hearing loss screening. Follow-up since insulin initiation demonstrated good glycemic control.
Conclusion
This case highlights the importance of considering H syndrome in diabetic patients with atypical cutaneous, hematological, and skeletal manifestations. The management of this complex condition requires a multidisciplinary approach involving specialists in dermatology, endocrinology, hematology, and genetics. This observation contributes to enhancing the understanding of the links between H syndrome and diabetes, emphasizing the need for a comprehensive evaluation for optimal management of this rare pathology.

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EP989

Frailty in elderly diabetics: frequency and associated factors

Maryam Cheikhrouhou, Kamilia Ounaissa, Nesrine Dhieb, Hana Ben jemaa, Mariem Naifar, Emna Bornaz, Haifa Abdesslem & Chiraz Amrouche
national nutrition institute, Department of Nutritional Diseases D, Tunisia

Introduction
The care of elderly people with diabetes depends on their clinical and functional state. The prognosis and therapeutic goals are impacted by the degree of fragility The aim of this study was to assess the level of frailty in a group of elderly diabetic subjects.
Methods
This was a cross-sectional study including twohundr edelderly type 2 diabetic patients. All of them were screened for the five Frieds'frailty criteria. A patient was considered frail if he presented three or more criteria out of five and pre-frail if he presented less than three criteria.
Results
The median age was 70 years (IIQ [72-76.75]). The mean diabetes duration of 16.5 ± 9.26 years. The frequencies of each of fields'criteria in descending order are physical inactivity (86.5%), decreased walking speed (62%), decreased muscles'strength (40.5%), asthenia (40.5%) and decreased muscle mass (11.6%). Frailty was diagnosed in 54% of patients. While 43.5% of subjects were pre-frail and only 2.5% were not frail. Factors associated with frailty were advancedage ($P=0.003$), female gender ($P=0.002$), poorly controled diabetes ($P=0.002$) and depression ($P<0.001$).
Conclusion
Prevention, early detection and management of frailty in elderly diabetics are of crucial importance to optimize diabetes management and mitigate its impact on the quality of life of these patients.

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EP991

MODY in pregnancy: a report of two clinical cases

Maria Salomé Serranito, Bruno Bouça, Inês Manique, Olga Gutu, Paula Bogalho, Nelson Cunha & José Silva-Nunes
Hospital Curry Cabral, Lisboa, Portugal

Introduction
Distinguishing between gestational diabetes and MODY (Maturity Onset Diabetes of the Young) during pregnancy is relevant for therapeutic approaches and potential maternal-fetal complications. However, performing genetic study for MODY in pregnant women is uncommon.
Aim
To describe 2 cases in which the hypothesis of MODY was considered during pregnancy. Case 1: Woman, 35 years old, G1P0A1, BMI 25 kg/m^2. At 5 weeks of gestation, she developed polyuria and polydipsia, prompting blood glucose measurement: glucose 293 mg/dl, A1C 9.3%. She started metformin 1.5 g/day. At the first Diabetes appointment, she demonstrated inadequate glycemic control. C-peptide was 3.9 ng/ml (reference range 1.1-4.4) and anti-GAD, and anti-IA2 antibodies were negative. Insulin therapy was initiated with progressive titration, and adequate glycemic control was achieved at 13 weeks. At the end of pregnancy, she was on metformin 2 g/day, detemir 28 U/day, and lispro 5U at dinner. Fetal macrosomia was identified without other ultrasound abnormalities. She underwent cesarean section at 38 weeks, with no complications; live birth with a weight of 4365 g, without malformations. She has maintained euglycemia without therapy in the 3 months postpartum. Due to a significant family history of Diabetes *mellitus* (DM), a genetic study for MODY was performed, revealing a result of uncertain significance - c.31A> G p.(Thr11Ala) in heterozygosity in the PDX1 gene (unreported variant). Case 2: Woman, 37 years old, G3P0, BMI 27 kg/m^2, diagnosed with DM in 2019, with no complications. Several maternal relatives with history of DM. She was referred to the Diabetes clinic for preconception assessment: HbA1C 5.6% on glargine 16U/day. Analytically: C-peptide 1.26ng/ml (reference range 1.1-4.4), anti-GAD and anti-IA2 antibodies were negative. At 12 weeks of gestation, she started prandial insulin, with no significant dosage increase since then. Currently, she is in the third trimester, with good glycemic control under glargine 24U and aspart 5U/day; fetal ultrasounds and echocardiogram without abnormalities. Genetic study for MODY revealed an inconclusive result - c.-152C>A in heterozygosity in the promoter region of the INS gene (reported variant).
Conclusion
In the described cases, the pre-existing DM/early diagnosis during pregnancy, the need for IT, significant family history of DM, and the exclusion of pancreatic autoimmunity, raised MODY suspicion. Pregnancy is associated with insulin resistance and may reveal pre-existing dysfunction in individuals with mutations associated with MODY. Genetic studies may provide a better understanding and classification of hyperglycemia during pregnancy.

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EP992

Flash glucose monitoring: is it having a real impact on our patients' quality of life?

Víctor Siles-Guerrero, Juan Manuel Guardia-Baena, Araceli Munoz-Garach & Martín López-de-la Torre Casares
Hospital Universitario Virgen de las Nieves, Servicio de Endocrinología y Nutrición, Granada, Spain

Introduction and Objectives
Despite the many known advantages of Flash Glucose Monitoring (FGM), very few studies have shown a real improvement in the patient's overall quality of life. Therefore, our aim is to assess, using the validated Diabetes Mellitus Specific Quality of Life Questionnaire: Spanish version (EsDQOL), whether these differences really exist in our population.
Methods
An observational, prospective study was conducted comparing quality of life in patients with T1D prior to FGM and after 6 months of its use in a cohort of 89 patients from 1 January 2021 to 31 December 2022 employing the EsDQOL questionnaire which measures four variables: satisfaction, impact, social concern and concern about diabetes. The total score ranges from 43 to 215, with a higher score corresponding to a poorer quality of life. Kolmogorov-Smirnov test, Student's *t*-test and Wilcoxon test were used.
Results
89 patients were studied with 63% of women with a mean age of 42 ± 14.1 years with 10.8 ± 8.3 years of T1D evolution obtaining an improvement ($P<0.05$) in quality of life comparing each of the 4 items separately and globally in the questionnaire (96 [63-125] vs 79 [58-101]).
Conclusions
In addition to the already known advantages in glycaemic control variables, we can conclude that the implementation of the FGM has led to an improvement in the quality of life of our patients with T1D, reducing their concerns about social and occupational aspects and about the future effects of diabetes while improving the impact and satisfaction with the treatment received.

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EP993

Cost of managing complicated diabetic patients in tunisia: a retrospective study in a hospital setting

Souhir Maalej, Fatma Mnif, Abdel Mouhaymen Missaoui, Siddiqa Soomauroo, Khouloud Boujelben, Mouna Mnif, Dhouha Ben Salah, Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Endocrinology, Sfax

Background
Diabetes mellitus presents a pervasive global health challenge, and Tunisia grapples with a concerning upswing in the prevalence of type 2 diabetes (T2D). Cardiovascular and renal complications stand out as prevalent and severe outcomes linked to T2D. Evaluating the costs associated with managing these complications in T2D patients is pivotal for improving care quality, optimizing resource allocation, and ultimately mitigating the escalating economic and social burden of this chronic disease.
Materials and Methods
We conducted a retrospective descriptive study to gather data on diabetic patients with chronic cardiovascular and renal complications. The study included patients hospitalized in the Endocrinology Department of Hedi Chaker University Hospital in Sfax from January 1 to December 31, 2022. The aim was to assess the

costs associated with managing cardiovascular and renal complications in our hospitalized patients.
Results
Our study comprised 114 patients, with cardiovascular and renal complications being the predominant category, affecting 53 individuals (46.5%). Cardiovascular complications alone were observed in 37 patients, constituting 32.5%, while renal complications alone were present in 24 patients, accounting for 21% of the sample. In our patient sample, the vast majority (93%) had social coverage, with 71% insured through the National Health Insurance Fund (64.9%) or the National Social Security Fund (6.1%). Additionally, 22% were considered indigent, benefitting from social coverage provided by the Ministry of Social Affairs. Only 7% of our study population lacked any social coverage. The average hospitalization duration was 7.2±4.5 days, with a minimum stay of 2 days and a maximum stay of 26 days. The overall direct cost of hospital management for cardiovascular and renal complications of diabetes in our population amounted to 256,096.18 TND, equivalent to 81,300.37 USD. This translated to an average cost per patient of approximately 2,246.46 TND, or 713.16 USD for an average hospitalization duration of 7 days. The daily cost was 320.92 TND or 101.88 USD. On a global scale, cardiovascular explorations represented the most significant portion of direct costs, encompassing 69.65% of the overall expenses. Conversely, glycemic monitoring was the least expensive, accounting for only 0.63% of the total costs.
Conclusion
Our comprehensive cost analysis of managing cardiovascular and renal complications in diabetic patients reveals significant economic implications. Optimizing healthcare strategies is imperative to alleviate the financial burden and enhance patient outcomes.

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EP994

Hypomagnesemia in type 2 diabetics and its impact on glycemiccontrol and diabetes chronic complications

Yosra Hasni, Oumayma Zarrouk, Hamza Elfekih, Nassim Ben Hadj Slama, Molka Chadli Chaieb & Koussay Ach
University Hospital of Farhat Hached, Endocrinology Departement, Sousse

Introduction
Several studies have incriminated hypomagnesemia in the pathophysiology of diabetes, as the prevalence of this deficit in type 2 diabetics is high, and as it is correlated with glycemic control and chronic diabetic complications.
Aims
Studying the prevalence of hypomagnesemia in type 2 diabetics and assessing its impact on quality of life, glycemic control and chronic diabetic complications. Patients and methods: We conducted a descriptive cross-sectional study over a period from November 01, 2022 to January 31, 2023, including type 2 diabetic patients followed at the endocrinology department of CHU FARHAT HACHED. Data were collected from careful questioning, physical examination and medical records. Missing biological parameters were performed at the biochemistry laboratory of CHU FARHAT HACHED.
Results
We included 190 type 2 diabetics (sex ratio M/F 1.09), with a mean age of 60±9.9 years and a mean diabetes duration of 11.9±9.1 years. Diabetic retinopathy was present in 43.5% of our subjects. Diabetic nephropathy and diabetic peripheral neuropathy were present in 33% and 23.6% of patients respectively. 15.3% of our population had a coronary syndrome and 14.2% had a history of stroke or transient ischemic attack. Hypomagnesemia was present in 45.3% of our population, with a mean magnesemia of 0.74±0.09 mmol/l. It was statistically correlated with fasting blood glucose ($P=0.004$, OR=2.27) and HbA1c ($P=0.047$, OR=1.53); for a FPG >8.95 mmol/l and for HbA1c values >8.25%, the prevalence of hypomagnesemia increases significantly. However, we found no correlation between magnesium and quality of life, nor with chronic diabetic complications.
Conclusion
Hypomagnesemia is a frequent biological abnormality in type 2 diabetics and is significantly correlated with glycemic control. Therefore, its screening in these patients is recommended for possible supplementation.

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EP995

Evaluation of glycemic balance in diabetic patients with mental disorders: about 68 cases

Bassiratou Hamza Maliki, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
CHU Ibn Rochd - Casablanca, Morocco, Casablanca, Morocco

Introduction
Mental disorders are frequent in diabetic patients and this makes care difficult.
Objective
Evaluate the repercussions of psychiatric pathologies on glycemic balance and complications of diabetes and show the need to detect them systematically and treat them in these subjects.
Patients and methods
Analytical retrospective study from 2016 to 2023 on 68 diabetic patients also with mental disorders hospitalized in the Endocrinology Service of the Ibn Rochd CHU of Casablanca, HBA1C and diabetes complications have been evaluated.
Results
The average age of our patients was 44 years, 44 DT1 and 24 DT2, sex ratio ½, the average duration of diabetes was 13.42 years (1-25 years), the average duration of evolution of psychiatric disorders 5.7 years (1-9 years), the average HBA1C 8.9 % (7.9- 12.4). Among our patients 20 (29.41%) have an emotional disorder, 16 (23.53%) had a driving disorder and 32 (47.05%) had an anxious disorder. The HBA1 was higher with depression. All patients had poor therapeutic observance both for the treatment of diabetes and for psychopathology, 40 patients (58.82%) had been hospitalized for diabetic ketosis, 14 (20.58%) in the aftermath of an acido ketose and 14 (20.58 %) for serious hypoglycemia. In our series: 14 patients (20.58%) had diabetic retinopathy, 18 (26.47%) had an albumin report on positive urinary creatinine, 32.35%($n=22$) had peripheral neuropathy. Low socio-economic status and mental disorders were associated with an elevation of HBA1C ($p\leq 0, 05$).
Conclusions
Psychiatric disorders in diabetic patients are associated with a glycemic imbalance and an increase in the risk of acute and degenerative complications.

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EP997

Precocious puberty and skyrocketing obesity rates among children: a contemporary clinical perspective on the co-occurrence

Teona Nutsubidze[1], Ketevani Obolashvili[1], Tekle Bakhtadze[1], Tamta Sharadze[1] & Mariami Bakhtadze[2]
[1]National Institute of Endocrinology, T'bilisi, Georgia, [2]Tbilisi State University, Tbilisi, Georgia

Introduction
Puberty is a crucial period, marking the transition from childhood to adulthood with significant physical and psychological changes. (1) In girls, when puberty begins before the age of eight, it is considered precocious. (2) While multiple factors influence individual differences in pubertal timing, the interactions between hormones and nutrition during critical growth periods, like puberty, are crucial. (3) Girls with a higher BMI experienced early menarche compared to those who did not have excess weight. (4) In recent years, there has been a global increase in both obesity rates among children and early pubertal maturation. (6,7,8,9) By analysing the correlation between precocious puberty in girls and their weight, the study aims to provide insights that contribute to the ongoing discourse on the intertwined rise of obesity and precocious puberty among children, offering valuable information on the dynamics over the past years.
Methods and Materials
A retrospective study was conducted on children aged 4-7 years with an established diagnosis: precocious puberty (PP). Data was obtained from medical records of children who visited the National Institute of Endocrinology, Georgia, during 2020-2023. BMI-for-age percentile was calculated based on CDC growth charts for children. (10)
Medical history of Children with congenital disease, type 1 diabetes, steroid intake history and malignancy was excluded.
Results
We analysed medical records for 165 patients aged 4-7 years, of whom 88 were girls and 22 were boys. 2021 - from 18 evaluated patients, 33.33% ($n=6$) had healthy weights, 33.33 ($n=6$) were overweight, 33.33% ($n=6$) were obese and 0% ($n=0$) had severe obesity. 2022 - from 39 evaluated patients, 23.07% ($n=9$) had healthy weights, 38.46% ($n=15$) were overweight, 23.07% ($n=9$) were obese and 15.38% ($n=6$) had severe obesity. 2023 - from 108 evaluated patients, 19.44% ($n=21$) had healthy weights, 25% ($n=27$) were overweight, 19.44% ($n=21$) were obese and 36.11% ($n=39$) had severe obesity.
Conclusios
Early sexual maturation can have an enormous impact on both the mental and physical. Children with PP often have more psychological difficulties than their non-PP peers. (11) Based on the findings, it is evident that there is a rapidly growing trend of two variables among children: Obesity and sexual precocity, prompting the need for more controlled studies. Our team intends to conduct further preclinical research into identifying the most effective dietary interventions for managing precocious puberty in obese children.

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EP1022

Environmental endocrine disruptors and obesity: what is the causal link?

Mennani fatima ezzahra[1], Hind Ouakrim[1], Sana Rafi[1], Ghizlane El Mghari[2] & Nawal El Ansari[2]
[1]Centre Hospitalo-Universitaire Mohammed VI Marrakech, Endocrinolgy, marrakech; [2]Centre Hospitalo-Universitaire Mohammed VI Marrakech, Endocrinolgy, Marrakech

Introduction
Endocrine disruptors are natural or chemical molecules capable of interfering with the endocrine system, as well as disrupting the signaling pathways of carbohydrate and lipid metabolism.
Materials and methods
This is a retrospective study of 85 patients with a BMI greater than 30 kg/m^2 followed in the endocrinology department of CHU Mohamed VI; we studied exposure to endocrine disruptors.
Results
85 patients were included, mean age 41.96 years, with a predominance of female sex. Mean BMI was 38.24 kg/m^2. 67 patients, 78.82% had been exposed to endocrine disruptors either via inhalation, ingestion or transdermal absorption. 69.41% of patients had been exposed to bisphenol A (plastic), 36.47% to alkyl phenols and phthalates (household products), 31.77% to organochlorines (pesticides), 12.94% to thiocyanates (active or passive smoking).
Discussion
Endocrine disruptors have the ability to interfere with hormone regulation by binding to membrane and nuclear receptors normally occupied by natural hormones; they mimic or disrupt the action of certain hormones on organs such as adipose tissue, pancreas and skeletal muscle. The Endocrine Society described the toxicity of endocrine disruptors; their effects on various diseases including obesity in 2015 they can act directly or indirectly as obesogens, by altering basal metabolic rate, by altering gut microbiota favoring food storage, and by altering hormonal control of appetite and satiety.
Conclusion
The rapid increase in the prevalence of obesity cannot be explained solely by overeating and a sedentary lifestyle. Endocrine disruptors can affect adipocyte differentiation and endocrine function, and disrupt metabolic processes.

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EP1023

Intentional insulin overdose in a type 2 diabetic patient and depressive disorder

Daniel Cosma[1], Cristina Alina Silaghi[2] & Horatiu Silaghi[3]
[1]Horezu City Hospital, Diabetes, Nutrition and Metabolic Diseases Outpatient Clinic, Horezu, Romania; [2]"Iuliu Hatieganu" University of Medicine and Pharmacy, Endocrinology Department, Cluj-Napoca, Romania; [3]"Iuliu Hatieganu" University of Medicine and Pharmacy, 5th Department of Surgery, Cluj-Napoca, Romania

Intentional insulin overdose in diabetic patients is a rare critical situation. The severity is due to numerous neurological complications, electrolyte disturbances, liver and lung damage or death. A 59-year old female, under treatment for depressive disorder, diagnosed with type 2 diabetes since 2016 and treated with glargine (20 IU/day), lispro (30 IU/day) insulin and Metformin (500 mg/day) was admitted to the Internal Medicine department via ER (emergency room) for repetitive episodes of severe hypoglycemia in the ER after administration of 280IU of glargine insulin. Found unconscious, dyspneic with a glycemic value (Gl) of 26 mg/dl, she was brought to the ER approximately 9 hours after overdose with a Gl of 97 mg/dl after 70 ml of 33% glucose. At admission: altered general status, Gl = 130 mg/dl, BP = 160/90 and QT prolongation. Labs exams revealed: Gl = 35.46 mg/dl, hyperamylasemia, hypokalemia and A1c = 5.96%. An infusion of 5% glucose was begun at 250 ml/h. The glucose infusion rhythm and concentration was adjusted according to the glycemic profile while trying to maintain values around 150 mg/dl. Hypokalemia was corrected by oral supplementation. Calcium and magnesium remained within normal limits during hospitalization but phosphorus could not be determined. Psychological and psychiatric consults revealed the trigger of the overdose (a health problem of a newborn grandson) and recommended hospitalization in a psychiatric facility, but the patient refused. The last hypoglycemic episode (Gl = 62 mg/dl) was registered 24h after admission. In the 4th day of hospitalization, the oral treatment with Metformin was resumed and she was discharged in the 5th day with only metformin and glargine insulin. Insulin overdose requires intensive and prolonged glycemic monitoring to prevent recurrent hypoglycemia due to an early cessation of i.v. therapy. The dose is not correlated with the severity of hypoglycemia but with a prolonged hypoglycemic risk higher than that deduced from the pharmacokinetics of insulin analogue administered. This case represents the first insulin overdose treated in our hospital.

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EP1046

Effect of hypoglycemics on lipid parameters in patients with diabetes mellitus and ischemic heart disease

Gulnora Artykbaeva & Talat Saatov
Institute of Biophysics and Biochemistry, Mirzo Ulugbek National University of Uzbekistan, lab of metabolomics, Tashkent, Uzbekistan

2 type diabetes mellitus (2DM) determines high risk of cardio-vascular disorders and pathologies of cardio-vascular system, to name arterial hypertension, ischemic heart disease and hypercholesterolemia. In addition, prolonged insufficient DM compensation results in onset of macrovascular complications eventually causing adverse effects. UKPDS findings demonstrated that intense glycemia control significantly reduced the risk of microvascular diabetic complications, but produced no significant effect on the macrovascular ones and total mortality. The conclusions confirm necessity for the complex control of glycemia, arterial pressure and blood lipids. In our study, patients received metformin as the first line therapy in 2DM. The work was initiated to study lipid profiles of the 2DM patients with IHD and its correction with metformin. We examined 38 2DM patients with IHD to analyze concentrations of triglycerides (TG), total cholesterol (TC), HDL C, LDL and VLDL. 20 donors were included in the control group. Lipid profile in 2DM is characterized with 'lipid triad' including increase in TG, reduction in HDL cholesterol and predominance of small dense particles of LDL. In diabetes, the latter prevail. Due to higher atherogenicity of the particles in question, the risk of atherogenicity is higher in the diabetics with the similar LDL C. The LDL levels were proved to be a risk factor for IHD. In our patients, levels of TG and TC were significantly increased, while those of LDL and VLDL were significantly reduced, as compared to the controls. In contrast, the HDL C was significantly reduced. Metformin therapy results in positive changes in the lipidogram. In the patients, TC significantly reduced, as compared to the pre-therapy values (219.6 ± 8.3 vs 2317 ± 10.7 mg%, $P < 0.05$). TG were found to decrease to 280.0 ± 34.1 mg%, as compared to the initial values (394.6 ± 29.0 mg%, $P < 0.001$). Post-therapy total sum of LDL and VLDL was reduced to 735.0 ± 48.3 mg% vs 948.2 ± 52.4 mg% ($P < 0.001$) before therapy. The therapy insignificantly increased HDL C concentrations (31.4 ± 5.03 vs 28.0 ± 2.7 mg%). Despite reduction in atherogenic lipids and increase in anti-atherogenic ones, all parameters under study were found not to reach the levels in the controls. Metformin significantly reduced atherogenic lipoproteins; the anti-atherogenic ones tended to increase. As in metformin therapy the parameters under study in our experiments did not reach the control values, it can be concluded that statins are necessary to be added to the hypoglycemics in therapy of the dislipidemia in DM.

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EP1047

Healthcare system and current treatment of type 2 diabetes in Uzbekistan

Jamolkhon Kayumov & Otabek Akhunbaev
Fergana Medical Institute of Public Health, Endocrinology, Fergana, Uzbekistan

Background
Diabetes mellitus (DM) is increasing because of urbanization, aging, growth in population, physical inactivity, and excess body weight. The management of diabetes is an important issue for Uzbekistan both from medical and socio-economic points of view due to the increase in the number of patients with type 2 diabetes (T2DM), resulting in disability and premature mortality. This study aims to summarize the recent status of diabetes care in Uzbekistan and to analyze the current treatment of diabetes in the Fergana region.
Materials and methods
To describe the current healthcare for DM in Uzbekistan, recommendations for diabetes treatment in Uzbekistan, reports from international organizations, and research papers were used. Besides, the treatment of T2DM in the Fergana region, 2022, was analyzed.
Results
In 2022, a total of 230,610 patients with DM, composed of 18,349 type 1 diabetes and 212,261 T2DM were registered in the National Registry of Diabetes. Among patients with T2DM in the Fergana region, monotherapy was the most common (71.0%),

followed by dual combination therapy of two anti-diabetic drugs (28.1%). Only 0.9% of the patients with T2DM received no medications. Among monotherapies of DM, insulin (25.3%) was the most common, followed by biguanides (23.4%), sulfonylureas (20.8%), and thiazolidinediones (1.5%). Among dual combination therapies, biguanides + sulfonylureas (24.5%) was the most common.
Conclusion
Insulin monotherapy, biguanides, sulfonylureas, and biguanides + sulfonylureas were the most common medications for T2DM in the Fergana region. Insulin monotherapy was the most common in the older age groups and patients with longer durations of T2DM.
Keywords: type 2 diabetes, prevalence, treatment, policy, Uzbekistan
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EP1049

Metformin-induced vitamin b12 deficiency and its impact on neurological health

Souhir Maalej[1], Nadia Charfi[1], Abdel Mouhaymen Missaoui, Siddiqa Soomauroo, Faten Hadjkacem, Mouna Elleuch[1], Mohamed Abid & Nabila Rekik
Hedi Chaker University Hospital, Endocrinology, Sfax, Tunisia

Introduction
Metformin, the primary treatment for type 2 diabetes, is renowned for its positive effects on carbohydrate metabolism, weight management, and vascular health. Despite these well-established benefits, prolonged use of metformin has been linked to potential adverse reactions, including a decrease in serum vitamin B12 levels and the development of anemia[1]. This case further emphasizes the complexities associated with metformin use by introducing an unusual yet consequential complication: severe neurological manifestations stemming from vitamin B12 deficiency.
Case Report
We present an intriguing case involving a 64-year-old woman managing type 2 diabetes through the extended use of insulin analogs, vildagliptin, and metformin. The patient exhibited a frontal syndrome, progressive gait instability, cognitive disruptions, frequent falls, and paroxysmal episodes associated with urinary incontinence. Thorough investigations, including normal imaging and a temporal artery biopsy excluding inflammatory origins, were conducted. The electroencephalogram revealed moderate diffuse cerebral distress with a metabolic component. Despite the absence of dietary deficiencies, gastric surgery, or Biermer's disease, a significant vitamin B12 deficiency was identified at 50 pg/ml. A meticulous examination uncovered a connection between extended metformin use and the observed vitamin B12 deficit. Following intramuscular vitamin B12 supplementation and discontinuation of metformin, despite the authors' suggestion to "search, treat the deficiency, and continue metformin"[2] we decided to discontinue it due to the absence of clear directives. The subsequent progress yielded positive outcomes, including symptom regression, the restoration of normal ambulation, and the resumption of daily activities, accompanied by the normalization of vitamin B12 levels.
Conclusion
This case highlights the critical importance of regular monitoring for individuals on metformin, especially those with identifiable risk factors, underscoring the potential for vitamin B12 deficiency. The intricate relationship between metformin and vitamin B12 deficiency necessitates continuous scrutiny and consideration in clinical practice. This emphasizes the need for heightened awareness and vigilance in managing complications related to diabetes.
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EP1050

The role of the hybrid closed loop subcutaneous insulin pump system in patients with weakness in the management of type 1 diabetes and complete failure to achieve satisfactory glycemic control

Christina Lymniati, Eleni Statiri, Anastasios Chatzinikolaou & Charalampos Tsentidis
General Hospital of Nikaia Piraeus 'Agios Panteleimon', Endocrinology, Diabetes and Metabolism, Nikaia, Greece

Introduction
The assessment of the glycemic regulation of patients with Type 1 Diabetes Mellitus is necessary, in order to design an individualized treatment plan, to control the complications resulting from hyper- or hypoglycemia. For this purpose, we use HbA1c, continuous glucose monitoring (CGM) with TIR (time in range), or blood glucose monitoring (BGM). However, none of the above, can be applied without the cooperation of the patient, which for various reasons, often becomes ineffective.
Case Presentation
We describe 4 cases of patients, who were implanted with a hybrid closed loop subcutaneous insulin pump system. The main problem was their unmanageable condition, resulting in many hospitalizations and poor glycemic control. Patient 1: 24 year old male with type 1 diabetes since the age of 7. HbA1C 10.3% Mental immaturity and learning disabilities. Frequent hospitalizations for DKA (at least 3 per 6 months). He did not take glucose measurements or administer insulin when he was with his friends because of embarrassment. Patient 2: 34 year old male with T1DM since the age of 14. HbA1c 14.4%. Middle school teacher. Many hospitalizations for DKA. He had a phobia of hypoglycemia, so he consciously aimed for glucose values >200. Concomitant medical conditions: Sensorimotor neuropathy and diabetic retinopathy. Patient 3. 32 year old male with type 1 diabetes since the age of 8. HbA1c 11.4%. He did not measure his blood sugar, neither he knew how to calculate carbohydrates. He is a professional driver for a courier company, and he eats irregular meals with many carbohydrates without preprandial insulin. Patient 4: 37 year old male with type 1 diabetes since the age of 9. HbA1c 10.2%. Sometimes anxious and depressed behavior. Cleaning worker on a garbage truck, almost impossible to take measurements or eat while working. Frequent hospitalizations with severe hypoglycemic episodes. Concomitant medical conditions: Arterial hypertension, hypertensive retinopathy, dyslipidemia.
Conclusion
The immediate result of the insulin pump placement, was the stability of glucose values and the avoidance of hospitalizations in all patients. Some of them managed TIR >45% within the first 3 months, without hypoglycemia. The placement of a hybrid closed loop system of subcutaneous insulin infusion, dramatically improved both their glycemic control and much more the general management of diabetes mellitus.
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EP1051

The influence of sitagliptin on metabolic parameters - importance and value in clinical practice

Ivan Lekić[1,2], Maja Antunović[2] & Tatjana Bačun[2,3]
[1]Health center Zagreb - Centar, Zagreb, Croatia; [2]Faculty of Medicine, Department of Internal Medicine, Osijek, Croatia; [3]Clinical Medical Center Osijek, Department of Internal Medicine - Endocrinology, Osijek, Croatia

Aim of the study
To examine the influence of sitagliptin in patients treated with a diabetic diet and metformin, on metabolic parameters and kidney function after three months of sitagliptin therapy.
Subjects and methods
35 patients (19 men and 16 women) were included in the study. Sitagliptin was introduced in patients on a diabetic diet and metformin with HbA1c≥6.5%. Fasting and postprandial plasma glucose value, HbA1c, cholesterol, HDL, LDL, triglycerides, kidney function (endogenous creatinine clearance (ECC)), 24-hour proteinuria and albuminuria, urea, creatinine, urates, height, body mass, body mass index were observed.
Results
Fasting glucose decreased by 1.52 mmol/l (14.85%), and postprandial by 3.42 mmol/l (26.10%, $P<0.001$), HbA1c decreased by 1.05% (12.35%, $P=0.001$). Total cholesterol concentration decreased by 7% ($P=0.07$), HDL increased by 0.89% ($P=0.31$), LDL decreased by 12.39% ($P=0.46$) and triglycerides by 1.2% ($P=0.74$). Median ECC remained unchanged ($P=0.59$), initial mean proteinuria was 140 and final 149 mg/dU ($P=0.4$), while mean 24-hour albuminuria decreased by 3 mg/dU ($P=0.07$). Urea concentration increased from initial 5.3 (SD 1.42) to 5.52 µmol/l (SD 1.31, $P=0.37$), creatinine concentration increased by 3.23% ($P=0.02$), which was statistically significant, and the concentration of urate was reduced by 0.43% ($P=0.66$). Furthermore, BMI was reduced by 2.3% ($P=0.18$).
Conclusion
After administration of sitagliptin, fasting and postprandial glucose concentrations were significantly reduced, as well as HbA1c. Changes in the concentration of cholesterol, HDL, LDL and triglycerides and body weight

were not statistically significant. The change in the concentration of urea, urate, ECC, proteinuria and albuminuria were not significant, while the slight increase in creatinine was statistically significant. The above indicates that sitagliptin is a metabolically neutral drug with a milder negative effect on renal function.

Key words: *Sitagliptin, Metformin, Diabetic nephropathy, Lipid metabolism*

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EP1053

Gliptin-associated bullous pemphigoid: about two cases

Lina Bessaad[1,1], Rim Chaabouni[1], Malek Cherif[1], Abdel Mouhaymen MISSAOUI[2], Mohamed Amine Fouad[1], Khadija Sellami[1], Fatma Hammami[1], Abderrahmen Masmoudi[1], Nabila Rekik[2] & Hamida Turki[1]

[1]Hedi Chaker University Hospital, Dermatology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Endocrinology, Sfax, Tunisia

Introduction & Objective

Bullous pemphigoid (BP) is a chronic immune-mediated blistering disease that mainly affects the elderly. This affection can be triggered by multiple factors such as drugs. Gliptins are one of the most incriminated drugs in the drug-induced bullous pemphigoid (DIBP). Our objective was to determine the characteristics of this pathology associated with the use of this medication through two cases of BP confirmed by histology and direct immunofluorescence.

Cases presentation

Two male patients aged 67 and 74 treated with linagliptin for type 2 diabetes mellitus consulted for a pruritic bullous dermatosis. The pruritus have been evolving for 1 month after the introduction of linagliptin in the first patient and after 1 year in the second patient with the appearance of bullous lesions after 3 and 1 months respectively. The clinical presentation was large, fluid-filled and tender blisters of different sizes with an erythematous base in both cases. These lesions were generalized with a predominant acral location. Mucosal involvment was present in one patient with post-bullous erosions on the inner side of the cheeks. The clinical diagnosis of BP was suspected and completed by histology and direct immunofluorescence. The interruption of linagliptin was indicated in both patients. One patient received systemic corticosteroid therapy (0.5 mg/kg/day) and the other patient was treated with topical corticosteroid. The two patients showed significant improvement with no evidence of relapse after 3 months of follow-up.

Conclusions

Gliptins, also known as dipeptidyl peptidase-4 (DPP-4) inhibitors are widely used in the treatment of type 2 diabetes mellitus. This treatment have increasingly been implicated in DIBP and its risk doubles. The pathophysiology remains unclear but the inhibition of DPP-4 receptors results in activation of proinflammatory cytokines and an inflammatory response leading to dermoepidermal damage. Males are more likely to develop this condition and the median age is 70, as in our study. Clinically, many reports concluded on the absence of difference between gliptin-induced BP and classical BP. Non inflammatory blisters with a smaller sized and less erythematous bases in limited distribution were found in some series. The age of onset after the initiation of gliptin therapy varied from 1 month to 4 years. In the literature, histological findings showed scant lesional infiltration of eosinophils and direct immunofluoresence is more positive in this group. The treatment consists of the withdrawal of gliptins which together with steroid administration leads to complete remission and morbidity reduction.

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EP1054

Sodium glucose cotransporter 2 inhibitors: place in diabetic nephropathy

Baltagi Myriam, Bchir Najla, Annam Benchhida, Dorra Dorraelguiche, Bel Hadj Sliman Chayma, Zouaoui Chadia & Haroun Ouertani

Introduction

Diabetic nephropathy (DN) stands as the predominant cause of chronic kidney disease globally. Although therapies targeting the renin-angiotensin-aldosterone system inhibitors (RAASi) offer partial benefits, additionnal strategies are needed. This study was conducted to evaluate the impact of sodium glucose cotransporter 2 inhibitors (SGLT2i) on renal biological parameters.

Methods

We conducted a prospective, evaluative and comparative study at a single center, involving 115 patients with DN matched according to age, sex and stage of DN: Groupe 1 comprised 54 patients on both SGLT2i and RAASi while groupe 2 included 61 patients on RAASi only. The study spanned three periods: T0 at the treatment onset, T1 and T2 after three and six months.

Results

The mean age was 60.2 ± 9.2 years. Examining the renal effects of SGLT2i, our results indicated a statistically lower albuminuria difference between the two time points (T1-T0 and T2-T0, respectively) in group 1 compared to group 2($P < 10^{-3}$). The albuminuria difference between T1 and T0 was -16 (-116-8) for group 1 and 35 (-3-230) for group 2. After 24 weeks, the albuminuria difference between T2 and T0 was -29 (-180-16.5) for group 1 and 50 (-2-207) for groupe 2. Regarding the evolution of creatinine clearance, a non-significant negative difference was noted in both groups between T1 and T0 ($P = 0.155$) after 12 weeks of treatment. However, after 24 weeks of treatment, group 1 exhibited a positive creatinine clearence difference between T0 and T2 in group 1 (0.58 (-5-3)), contrasting with group 2, which maintained a negative differential in creatinine clearance (-0.6 (-5-1)) ($P = 0.044$).

Conclusion

Our findings underscored the role of SGLT2i in treating DN in conjuction with RAASi and their nephroprotective efficacy.

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EP1055

Anemia in patients with type 2 diabetes on metformin therapy

Dunja Šojat, Nikolina Tomić & Tatjana Bačun

Faculty of Medicine Osijek, Osijek, Croatia

Aim of the study

The main objectives were to determine incidence and type of anemia in patients with type 2 diabetes and the differences considering gender, age and duration of type 2 diabetes.

Material and methods

The research was structured as a cross-sectional research with historical data. The research used data collected during regular check-ups in primary health care clinics in the Osijek Health Center, Croatia, from April to June 2023. Collected data were: demographic data, duration of type 2 diabetes, the occurence of microvascular and macrovascular complications and type of therapy used for type 2 diabetes. The following parmeters were obtained form laboratory findings: hemoglobin values, MCV, MCH, MCHC, iron values, UIBC, TIBC, fasting glucose and glycated hemoglobin A1c.

Results

The study comprised 59 metformin-treated participants (46 % men and 54 % women), median age of 68. The median duration of type 2 diabetes was 8 years. 29 % of patients had macrovascular and 17 % of them had microvascular complications. 20 % of patients had anemia. 42% had mild anemia, whereas 58% had significant anemia. There was no statistically significant difference in the incidence of anemia based on gender (Fischer's exact test, $P = 0.33$), the presence of microvascular (Fischer's exact test, $P = 0.48$) and macrovascular complications (Fischer's exact test, $P = 0.41$), age (Mann Whitney U test, $P = 0.07$), or type 2 diabetes duration (Mann Whitney U test, $P = 0.62$). According to the morphological division normocytic and normochromic anemia were most often represented while etiologically the most represented were non-specific anemias. Subjects with normocytic anemia were significantly older, with a median age of 81 years (interquartile range from 78 to 82 years) compared to patients with microcytic and macrocytic anemia (Kruskal Wallis test, $P = 0.04$).

Conclusion

Anemia is one of the most prevalent blood diseases among type 2 diabetics, and it can be caused by a variety of factors, including antidiabetic medications. Based on our findings, we can infer that anemia in individuals with type 2 diabetes on metformin medication is caused by iron deficiency and chronic illness. Because of the high incidence of anemia in these patients, constant monitoring and management of the values critical to detecting the presence and type of anemia is very important.

Keywords anemia; diabetes mellitus; haemoglobin; metformin

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EP1060

Incidence of maternal and fetal complications in diabetic pregnancies

Syrine Trabelsi, Olfa Lajili, Yesmine Jallouli, Sana Khamassi, Yosra Htira, Hedfi Imene, Chaima Jemai, Zohra Hadj Ali & Feika Ben Mami

National Institute of Nutrition and Food Technology, C, Tunis

Introduction

Pre-existing diabetes during pregnancy can negatively affect the health of women and their babies. The aim of our study was to describe the incidence of maternal and fetal complications in women with diabetic pregnancies.

Methods
This was a retrospective descriptive study, including 30 patients followed at the 17SPO2 "Diabetes and Pregnancy" research unit in ward "C" over a 6-month period (January-June 2023).
Results
Mean age was 34.8±5.7 years with 66.7% T1DM and 33.3% T2DM. Mean HbA1c and fasting plasma glucose were 7.8±1.3% and 8.2 ±3.1 mmol/l. The mean weight gain at the end of pregnancy was 8.3 ±3.2 kg. More than half of patients (58.6%) were not educated about pregnancy planning. However, 86.2% of patients had regular medical follow-up during pregnancy. The main maternal complications associated with diabetes were lower urinary tract infections (44.8%) and gestational hypertension/pre-eclampsia (24.1%). Fetal complications were dominated by hypoglycemia, macrosomia, hydramnios and threatened preterm delivery in 48.8%, 48.3%, 31% and 24.1% of patients respectively, followed by neonatal jaundice (17.2%), spontaneous miscarriage/late-term abortion (6.8%) and fetal death in utero (6.9%). In addition, 20 patients delivered full-term by Caesarean section.
Conclusion
Our study showed that the main maternal-fetal complications observed during diabetic pregnancies were lower urinary tract infections, gravid hypertension and macrosomia. Education about pregnancy planning and close monitoring of these patients could improve the maternal and fetal prognosis of these high-risk pregnancies.

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EP1062

Importance of the urgent establishment of plasmapheresis in the treatment of pancreatitis induced by extreme hypertriglyceridemia secondary to ketosis-prone type 2 diabetes

María Zurdo López[1], Miguel-Angel Ruiz-Gines[1,1], Juan-Antonio Ruiz-Gines[2] & Mercedes Agudo-Macazaga[1]
[1]Hospital Universitario de Toledo, Análisis Clínicos, Toledo, Spain; [2]Hospital Clinico Universitario Lozano Blesa, Neurocirugía, Zaragoza, Spain

Introduction
Acute hyperlipidemic pancreatitis is a rare clinical entity that usually affects patients with previous lipid alterations (triglyceride concentration >500 mg/dl) associated with triggering secondary factors, such as poorly controlled diabetes mellitus (DM).
Clinical Case
We present the case of a 60-year-old man who came to the Emergency Department with a picture of acute abdominal pain secondary to acute pancreatitis in which a small hypodense area indicative of necrosis at the level of the pancreatic tail secondary to hypertriglyceridemia (triglycerides 5640 mg/dl) was observed (abdominal CT). The 'milky' appearance of the plasma (lipemic index >1000) makes it impossible to study most biochemical parameters. Hyperglycemia (540 mg/dl) associated with a progressive polyuria and polydipsia picture of several days of evolution with elevation of amylase and lipase and the presence of glucosuria and ketone bodies in the urine systematized. In view of the analytical and imaging findings, the Endocrinology Service was contacted, which initiated initial treatment with insulin and oral antidiabetics, however, the patient did not improve, maintaining hypertriglyceridemia (4496 mg/dl). Given the clinical severity, it was agreed with the Nephrology Service to perform two urgent sessions of plasmapheresis. After the first session, triglyceride levels were reduced to 2122 mg/dl and with the second to 830 mg/dl. It should be noted that the glycated hemoglobin level was 14.9% with a normal C-peptide of 3.9ng/ml, which, associated with the previous analytical findings, would suggest a probable and infrequent cause of DM2, called Ketosis-prone type 2 diabetes (KPD). KPD is a clinical entity characterized by a debut with severe hyperglycemia and ketoacidosis similar to the presentation of DM1. However, it appears in subjects with a DM2 phenotype. This situation is caused by an acute and reversible dysfunction of the beta cells in individuals with insulin resistance. Subsequently, with pharmacological (insulin and hypolipidemic treatment) and dietary measures, glycemia was within normal limits with triglyceride concentrations <250 mg/dl.
Discussion and conclusions
Plasmapheresis, although an invasive technique, is the best therapeutic option that achieves a rapid decrease (85%) in triglyceride levels, possible complications (high morbidity and mortality), and a shorter hospital stay (in our case only 6 days). We consider the importance of implementing the use of plasmapheresis as an urgent primary treatment for pancreatitis secondary to moderate-extreme hypertriglyceridemia, which is more beneficial given the severity and risk of mortality associated with lower hospital resource consumption.

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EP1065

Is the occurrence of degenerative complications of type 2 diabetes mellitus influenced by gender?

Takoua Moussa[1], Chaima Jemai[1], Sami Fitouri[1], Dorsaf Ben Salem[1], Zohra Hadj Ali[1], Olfa Lajili[1], Imen Hedfi[1], Yosra Htira[1] & Faika Ben Mami[1]
[1]National Institute of Nutrition of Tunis, C

Introduction
Diabetes is a chronic disease that can lead to macroangiopathies and microangiopathies. The aim of our study was to describe the characteristics of these degenerative complications according to gender.
Methods
We conducted a cross-sectional study from September to December 2023, at Department C of the national institute of nutrition of Tunis. We included 70 patients with type 2 diabetes, evolving from 5 to 20 years, and with ages ranging from 35 to 65 years. Sex ratio was 1. The two groups of men and women were matched for age, diabetes duration, BMI and Hba1c. Clinical and biological data were collected from medical records. Data were analyzed using SPSS 23.
Results
The mean ages of the men and women were 56.23±6.77 and 57.17 ±8.2 years respectively ($P=0.65$). 17 men and one woman were active smokers ($P=0.021$). The mean body mass index (BMI) for women and men was 30.26±6.4 and 26.24±5.68 kg/m^2 respectively ($P=0,06$). Mean HbA1C was 9.2±1.1% with extremes of 8.5 and 12% (8.7±1.3% and 9.2±1.1% for men and women respectively, $P=0,23$). The association between gender and microvascular and macrovascular complications did not reach statistical significance with $P=0.569$ and 0.06 respectively. We found a statistically significant association between male gender and the occurrence of obliterating arteriopathy of the lower limbs ($P=0.042$). No statistically significant association was found with either gender for retinopathy ($P=0.4$), nephropathy ($P=0.33$), autonomic neuropathy ($P=0.16$), peripheral neuropathy ($P=1$), coronary artery disease ($P=1$) nor stroke ($P=0.63$).
Conclusion
According to our study, chronic obliterating arteriopathy of the lower limbs seems to affect men more frequently. Tobacco could be a factor biasing this result.

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EP1066

Gastroparesis at the heart of major complications: a case report

Malak Riznat[1,1], Mohamed Malad[2] & Guerboub Anas[1]
[1]Mohamed V Military Training Hospital, Endocrinology, Rabat; [2]Mohamed V Military Training Hospital, Rabat

Introduction
Gastroparesis is one of the dysautonomic manifestations of diabetic disease, particularly type 1. Often unnoticed or undetected by the clinician, it can be at the heart of a permanent imbalance, giving rise to all the microvascular and macrovascular complications of dysglycemia. We report the case of a diabetic patient who, after diagnosis and treatment of gastroparesis, achieved spectacular glycemic control.
Observation
This is a 20-year-old patient with known type 1 diabetes since the age of 4, treated with insulin analogues in the basal bolus regimen; multicomplicated in all respects with diabetic renal disease classified as stage 3, diabetic neuropathy under treatment and having already undergone amputation of the right foot. The patient was a poorly controlled diabetic with multiple hospitalizations for episodes of decompensation and hypoglycemia. During her hospitalization, the diagnosis of gastroparesis was suspected in view of her postprandial hypoglycemia, nausea and sensation of early satiety, and confirmed by gastric scintigraphy. Appropriate education and treatment with metoclopramide were implemented. The evolution was marked by the appearance of an optimal glycemic balance and the disappearance of glycemic variability.
Discussion and conclusion
Gastroparesis is a disorder of the intestine-brain axis, defined as an objective slowing of gastric emptying in the absence of pyloric stenosis. It is common in diabetics, with an estimated prevalence of 1-5%, and can be responsible for a permanent imbalance with high glycemic variability. Several tests have been proposed for diagnosis, such as the carbon-13 breath test, evaluation of pyloric function or the 4-hour gastric scintigraphy, which remains the reference test; the latter allows diagnosis if the 4-hour retention time exceeds 10%. Treatment is based on dietary measures in the 1st instance, then depending on the stage of gastroparesis, anti-mimetics for a short period of 3 months, prokinetics or even gastric stimulation may be proposed in the severe stages or if the previous methods fail. It is essential to diagnose gastroparesis in diabetic patients, so that

treatment can be introduced early to restore glycemic control and limit the occurrence of complications.

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EP1067

Atypical diabetic neuropathy with poor response to usual pharmacological treatment: a case report

Yosra Ben Hmida, Chaima Jemai, Achwak Mehrez, Yasmine Fakhfekh, Syrine Trabelsi, Sami Fitouri, Imen Hedfi, Olfa Lajili, Zohra Hadj Ali, Yosra Htira & Faika Ben Mami
National Institute of Nutrition of Tunis, C

Introduction
Diabetes is currently a worldwide pandemic. Neuropathy is Among its most disabling complications. We report the case of a patient with diabetic neuropathy with atypical presentation.
Case presentation
This is a 54-year-old patient hospitalized at department C of the National Institute of Nutrition of Tunis for uncontrolled type 2 diabetes (HbA1C = 11.2%). Her diabetes has been evolving since 8 years. She was put on insulintherapy since 2 years. She was an active smoker at a rate of 50 packs a years and had adequately substituted hypothyroidism. She did not consume alcohol. She had no macroangiopathic nor microangiopathic complications. She had been suffering, for the last 3 years, from hyperalgesic neuropathic pain with a DN4 score of 7. The pain was in gloves and socks, bilateral, symmetrical and more severe in the upper limbs. As part of the etiological assessment, hypovitaminosis B12 and vitamin D deficiency were screened and treated. Electromyography showed moderate axonal sensory neuropathy of the lower limbs, probably of diabetic origin. The patient was initially started on Pregbalin 600 mg/d, which was later associated with Gabapentin 300 mg/d given the persistence of symptoms. The evolution was marked by a partial improvement despite good compliance with treatment. The patient was referred to a specialized pain centre for further management.
Conclusion
Hyperalgesic diabetic neuropathy rarely affects the upper limbs. It usually responds well to optimal dose of pregabalin. This complication would probably present poorly elucidated mechanisms attested by the case of our patient.

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EP1068

Hidradenitis suppurativa in an obese diabetic patient

Oumayma Zarrouk, Taieb Ach, Rihab Khochtali, Ghada Saad, Asma Ben Abdelkrim, Molka Chadli Chaieb & Koussay Ach
University Hospital of Farhat Hached, Endocrinology Departement, Sousse

Introduction
Verneuil's disease, also known as Hidradenitis suppurativa, is a chronic inflammatory dermatosis characterized by recurrent episodes. It's manifested by painful deep inflammatory nodules, comedones, and scarring in areas rich in apocrine glands. Its prevalence is estimated at 1% of the population. It is influenced by factors such as obesity, smoking, and genetics. We report the case of a patient admitted for diabetes in whom Hidradenitis suppurativa was diagnosed.
Case report
It is about a 35-year-old patient, a smoker with a 35 pack-year history, and no significant medical history. Type 2 diabetes was diagnosed due to the onset of cardinal signs over the past 5 months. Upon examination, the BMI was 38 kg/m^2;, and the waist circumference was 139 cm. The patient presented with evident acanthosis nigricans. Cardiovascular examination was normal. Dermatological examination revealed multiple cutaneous abscesses in the groin and armpit folds, all at stage III according to Hurley staging. Some nodules in the groin were fistulized with pus secretion. The affected areas were inflammatory and painful, but there was no fever. The patient was treated with an anti-staphylococcal agent following the isolation of Staphylococcus in the pus sample, with improvement observed after 14 days. Diabetes was managed with oral antidiabetic medications, including metformin and sulfonylureas, resulting in a fasting blood glucose level of 1.24 g/l.
Conclusion
Hidradenitis suppurativa develops when sebaceous glands and hair follicle openings are blocked by fluid, as well as by dead skin cells or other materials released around the apocrine sweat glands. It is frequently associated with obesity, as described in our patient. Although the disease is chronic and characterized by recurrent episodes, the prognosis is improved with adherence to hygiene and dietary measures, along with weight loss.

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EP1069

Bone mineral density in women with type 2 diabetes mellitus and postmenopause: a single center spanish experience

Ana Paola Leon Ocando, Oliver Quintero Rodríguez, Selena Rodríguez Fernández, Kevin Diaz Gorrin & Itziar Aznar Ondoño
Hospital Universitario de Canarias, Endocrinology and nutrition, San Cristóbal de La Laguna, Spain

Introduction
T2DM is associated with an increased risk of fractures. This heightened risk is attributed to factors such as prolonged disease duration and chronic glycemic control. Interestingly, despite this increased fracture risk, patients with T2DM often exhibit normal or even elevated BMD compared to non-diabetic individuals. This phenomenon is thought to be a result of reduced bone remodeling, coupled with changes in bone microarchitecture.
Objective
This study aims to assess BMD in postmenopausal women with T2DM who are under observation at our center.
Materials and Methods
We conducted a cross-sectional, descriptive study on an incidental sample of 84 postmenopausal T2DM patients. These patients, monitored for carbohydrate metabolism disturbances at specialized care centers linked to our hospital, had undergone DXA in 2022 or 2023. The inclusion criteria were the absence of clinical evidence of other pathologies that could cause secondary BMD alterations and an age limit of 65 years or younger.
Results
The average age of participants was 63.29 years [95% CI 62.98-63.59]. The mean T-Score for the spine was -0.85 SD [95% CI -1.12— -0.58], and for the femur, it was -0.98 SD [95% CI -1.23— -0.73].
Conclusion
The mean T-Score for both the spine and femur falls within the normal to osteopenia range, not extending into osteoporosis, despite examining a high-risk group (menopausal patients). For future research, it would be beneficial to compare these findings with similar demographic groups without DM2. Such a comparison could clarify the specific impact of carbohydrate metabolism disorders on BMD in our population.

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EP1070

Prevalence and factors associated with anemia in a tunisian population with diabetes mellitus

Yasmine Fakhfakh, Chaima Jemai, Chaima Sdiri, Dorsaf Ben Salem, Siwar Saoudi, Hadhemi Belhassen, Lajili Olfa, Imen Hedfi, Yosra Htira & Faika Ben Mami
National Institute of Nutrition, Department C, Tunisia

Introduction
Anemia is a pathology frequently associated with diabetes mellitus (DM). The aim of this study was to assess the prevalence of anemia among patients with DM and to identify its associated factors.
Methods
We included 95 patients with diabetes mellitus hospitalized during November and December at department C of the national institute of nutrition of Tunis. We did not include pregnant women. Demographic characteristics, anthropometric parameters, past medical history, current treatments, glycemic control, cardiovascular risk factors, diabetes-related complications and biological parameters were collected from medical records.
Results
The mean age was of 53.41 ± 18.8 years. Sex ratio was 0.55. Mean body mass index was 27.2 ± 6 kg/m^2;. Mean HbA1c was 11.17 ± 2.17 %. The prevalence of anemia was 36.8% of our total population, 80% of which were women and 65.7% had type 2 diabetes. The study revealed that anemia was significantly more frequent in female gender ($P = 0.02$) and was associated with complicated diabetes ($P = 0.01$), with diabetic peripheral neuropathy ($P = 0.01$) and with diabetes duration (> 10 years) ($P = 0.001$). Likewise, anemia was significantly more prevalent in non-smokers ($P < 0.001$). No significant association was found with type of diabetes, BMI nor diabetes treatment.

Conclusion
In light of our results, systematic screening for anemia should be considered in routine assessment of patients with diabetes mellitus, especially in female gender, in patients with long diabetes duration and those with degenerative complication.

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EP1071

Prevalence and characteristics of painful diabetic neuropathy in patients with diabetes mellitus and normoalbuminuria

Hadhemi Belhassen, Ramla Mizouri, Siwar Saoudi, faten mahjoub, Rym Ben Othman, Chaima Sdiri, Nadia Ben Amor, Olfa Berriche & Jamoussi Henda
National Institute of Nutrition, A, Tunis, Tunisia

Introduction
Diabetes is known as a risk factor of microangiopathy which generally appear concomitantly. Diabetes is also the most common cause of peripheral polyneuropathy and all these complications are related to chronic hyperglycemia. The main objective of the present study is to determine the prevalence of the diabetic peripheral neuropathy (DPN) and its characteristics in people with normoalbuminuria.
Methods
Descriptive cross-sectional study conducted over 4 months in ward A of The National Institute of Nutrition Tunis which included patients with diabetes mellitus and normoalbuminuria.
Results
Fourty-five patients were included of whom were 32 women and 13 men. The characteristics of the patients were respectively: age: 49 ± 17.34 years, type 2 diabetes: 32 patients, type 1 diabetes: 11 patients, diabetes typing in progress: 2 patients, HbA1C: $10.18 \pm 2.01\%$, duration of diabetes more than 10 years: 25 patients, duration of diabetes less than 10 years: 20 patients. The diagnosis of painful diabetic neuropathy was evaluated by using the questionnaire Douleur Neuropathique (DN4) and diagnosed when DN4 is more than or equal to 4/10. Results have shown that 38 patients which means 84.4% of the population had no painful diabetic neuropathy. The percentage of DPN among non-smokers was 8.3%, while 28.5% of active smokers had DPN, without a statistically significant correlation ($P = 0.18$). DPN was more frequent in these cases: patients with type 2 diabetes (16.66%), diabetes with a duration less than 10 years (8.3%) and non-controlled diabetes. There wasn't a statistically significant correlation in all these cases, ($P = 0.19$), ($P = 0.38$) and ($P = 0.31$), respectively.
Conclusion
It is important to screen the painful diabetic neuropathy in all diabetics regardless of the patient profile or even the glycemic profile especially in the absence of other microangiopathies in order to prevent complications.

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EP1072

Diabetic, neuropathic and arterioapthic foot:assessment and management

Siwar Saoudi, Rym Ben Othman, Hadhemi Belhassen, Ramla Mizouri, Chaima Sdiri, Olfa Berriche & Jamoussi Henda
Institut de Nutrition Tunis, A, tunisia, Tunisia

Introduction
Diabetic foot is a major public health and it's the combination of arteriopathy, neuropathy and infection. Among all possible complications of diabetes mellitus, diabetic foot problems are a leading cause of hospitalisation. The aim of our study was to assess different diabetic foot factors in diabetic patients and to classify them into risk groups according to the guidelines of the International Working Group on Diabetic Foot (IWGDF)
Methods
It was a descriptive cross sectional study conducted over 6 months in department A of the institute of Nutrition of Tunis which included patients with diabetes.
Results
The total number of patients who participated in the study was 77. The characteristics of the patients were respectively: age 54 ± 10.3 years, BMI:29 ± 4.5 kg/m^2, HBA1C:$10.1 \pm 1.57\%$. The mean duration of diabetic patients was 11 ± 3 years. On examination, 58% of subjects reported neuropathic pain, with 47% having a DN4 greater than or equal to 4/10. As for arteriopathy, 21.3% reported intermittent claudication. On examination, 16% had absent pedal and posterior tibial pulses. Thus, 39% of subjects were classified as being at high risk of ulceration (groups 2 and 3), while 47% were at low risk (group 0).
Conclusion
In conclusion, our study revealed a substantial prevalence of diabetic foot complications among the assessed patients, highlighting the significant burden of arteriopathy, neuropathy and infection in diabetes underscoring the urgent need for targeted interventions and preventive measures in diabetic care.

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EP1073

Sociodemographic, clinical and evolutionary profile of elderly diabetics

Maryam Cheikhrouhou, Kamilia Ounaissa, Chaima Sdiri, Emna Bornaz, Nesrine Dhieb, Haifa Abdesslem & Chiraz Amrouche
national nutrition institute, Department of Nutritional Diseases D, Tunisia

Introduction
The number of elderly diabetics is increasing in Tunisia. We aimed to describe, sociodemographic, clinical and evolutionary profile of elderly diabetic patients.
Methods
Retrospective study of elderly diabetic subjects was carried out. Data were collected from patients' medical records and by questioning during a direct interview with patients.
Results
Twohundred patients aged 70 and over, were included. The average duration of diabetes was 16.5 ± 9.2 years. More than half of the patients were illiterate (53.5%) and 43.5% had a low socioeconomic level. Almost14.5% of diabetic elderly livedalone, 32% lived with spouses and 53.5% lived with their families. Smoking was reported by 22.5% of patients. The most frequent comorbidities were dyslipidemia, hypertension and obesity noted in respectively 88%, 76% and 40% of patients. The treatment of diabetes was insulin only or combined with oral antidiabetics in 75% of patients. The average HbA1c was 8,66% and 56,5% of subjectshad not reached their glycemic goals. Regarding the impact of diabetes, One-third of patients had at least one macroangiopathy. Concerning microangiopathy: retinopathy, neuropathy and nephropathy were noted in respectively 52.5%, 47% et 41% of patients.
Conclusion
In elderly people with diabetes, social fragility and precariousness, associated with numerous cardiovascular risk factors, make it challenging for clinicians to help them to achieve individualized therapeutic goals.

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EP1074

Study of the characteristics and factors associated with anemia in a population with diabetes mellitus

Yasmine Fakhfakh, Chaima Jemai, Chaima Sdiri, Dorsaf Ben Salem, Siwar Saoudi, Sami Fitouri, Zohra Hadj Ali, Olfa Lajili, Imen Hedfi, Yosra Htira & Faika Ben Mami
National Institute of Nutrition, Department C, Tunisia

Introduction
Anemia is a pathology frequently associated with diabetes mellitus. The aim of our study was to determine the characteristics of anemia in a population of patients with diabetes mellitus (DM).
Methods
This was a cross-sectional study conducted in Department C of the National Institute of Nutrition of Tunis. Recruitment was spread over 2 months. We enrolled patients hospitalized for diabetes control with anemia, as defined by the World Health Organization. We did not include pregnant women.
Results
Thirty eight patients were enrolled. The mean age was 49.9 ± 15 years and the sex ratio was 0.4. Patients presented type 2 diabetes in 60.5% of cases. The majority (86.8%) had diabetes with degenerative complications. Two-thirds of the population had diabetic nephropathy. More than half (55.3%) had diabetic neuropathy. Diabetic retinopathy was present in 44.7% of cases. Clinically, almost half the population presented with conjunctival pallor (47.4%). Two patients had arterial hypotension and one patient had resting tachycardia. Anemia was mild in 52.6% of cases, with a mean hemoglobin level of 10.82g/dl ± 1.23. It was hypochromic in 42.1%, normochromic in 57.9%, microcytic in 34.2% and normocytic in 65.8%, with a mean Red blood cell distribution width (RDW) of 14.37 ± 2.34. Anemic diabetic women had significantly lower mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and ferritinemia ($P = 0.006$; $P = 0.004$; $P = 0.002$) than men. No statistically significant association was found between metformin intake and anemia characteristics.

Conclusion
Anemia is a fairly widespread pathology in Tunisia. Studies suggest that it is associated with glycemic imbalance and degenerative complications. Larger-scale studies are needed to investigate these associations.

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EP1076

Accuracy of urine dipstick tests for assessment of glucosuria

Omar Gargouri[1], Rim Marrakchi[2], Ines Mezghani[3], Boudaya Mariem[3], Kamel Jammoussi[3] & Mouna Turki[3]
[1]Hedi-Chaker University Hospital of Sfax, Biochemistry Departement, Sfax, Tunisia; [2]Hedi-Chaker University Hospital of Sfax, Biochemistry Departement, Tunisia; [3]Sfax, Biochemistry Departement, Sfax, Tunisia

Introduction
Early diagnosis is therefore important for patients with asymptomatic diabetes mellitus. The aim of this study is to validate the use of Urine Dipstick in the screening of glycosuria (Gu).
Material and methods
Our study involved 30 fresh urine specimens. Urinalysis was performed by dipstick (SPINREAT®). Gu was measured by the hexokinase method (DxC800® Beckman Coulter). The gold standard to diagnose Gu was concentration measured $\geq$ 0.833 mmol/l
Results
To detect Gu the urine dipstick test had 66,6 sensitivity, 100% specificity, 100% positive predictive value (PPV) and 96% negative predictive value (NPV)
Conclusions
Test strips do not appear to be a good alternative to quantitative assay for screening glucosuria.

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EP1077

Association of hypertension and diabetes in the elderly: 100 cases

Yesmine Jallouli, Rym Ben Othman, Syrine Trabelsi, Ramla Mizouri, Olfa Berriche, Faten Mahjoub & Henda Jamoussi
Tunis, dapartment A, Tunis, Tunisia

Introduction
Hypertension is common in elderly diabetic patients, and is responsible for an increased cardiovascular risk and an acceleration of the degenerative effects of diabetes.
Objectives
To determine the characteristics of hypertension in elderly diabetic patients.
Patients and Methods
Descriptive study including 100 hypertensive type 2 diabetic patients aged >65 years followed up in department A of the national institute of nutrition in Tunis. Hypertension was defined as blood pressure $\geq$140/90 mmHg. Variables studied were anthropometric measurements, cardiovascular factors (smoking, hypertension, dyslipidemia), degenerative complications (retinopathy, neuropathy, nephropathy, ischemic heart disease) and treatment administered (Insulin therapy, oral antidiabetics, antihypertensive).
Results
The mean age of our patients was 73 ± 2.4 years, predominantly female (65.1% of cases). The mean duration of diabetes was 10.4 years, with 42% of patients on insulin therapy and 28% on oral antidiabetics. The diagnosis of diabetes preceded that of hypertension in 58.7% of cases. Sixty-three percent of patients had Grade I hypertension. Mean BMI was 27.8 ± 4.6 kg/m^2. Dyslipidemia was found in 85.7% of our patients. Ischemic heart disease was found in 32.5% of cases, and 19% of patients had a history of ischemic stroke. Retinopathy was found in 61.4% of patients, neuropathy in 23.8%.
Discussion
The frequency and severity of hypertension in elderly diabetics are unique, requiring comprehensive management of cardiovascular risk factors in order to improve quality of life in this population.

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EP1080

Fungal necrotizing external otitis complicated by a retropharyngeal abscess in a diabetic patient: a case report

Rachida Bouattay, nawres bouaziz, Jemli S, Mehdi Ferjaoui, elkorbi amel, Naourez Kolsi. harrathi khaled & Jamel Koubaa
مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Background
Fungal necrotizing external otitis (NEO) is a serious and potentially life-threatening infection that is challenging to manage. It affects almost exclusively elderly diabetic patients. The diagnosis is often delayed and it is a rare disease, although its frequency has increased over the last few years. We aim through this study to share our experience in the management of a case of fungal NEO complicated by a retropharyngeal abscess in a diabetic patient and discuss its diagnosis tools, anti-fungal treatment choice, and outcomes.
Methods
We report a rare case of invasive necrotizing external otitis caused by Aspergillus flavus in a diabetic patient without other underlying immunosuppression. A review of Aspergillus spp. malignant external otitis since voriconazole became the first line for invasive aspergillosis was performed.
Case Presentation
We present a case of a 77 year old man with a history of type 2 diabetes, dyslipidemia and an ischemic cerebrovascular accident. He was admitted to our department 8 months ago for the management of bilateral NEO, which was treated with optimal antimicrobial therapy and cured. The reason for his consultation was facial palsy associated with odynophagia for two days. Physical examination revealed a right peripheral facial paralysis grade V and a swelling in the posterior pharyngeal wall. The rest of the examination was normal. Laboratory tests indicated a biological inflammatory syndrome. A computed tomography scan was performed, revealing a retropharyngeal collection measuring 4 cm with osteitis of the skull base. The patient was treated with empiric courses of antibiotics until a fungal infection was diagnosed and he underwent endoscopic endonasal drainage of the abscess under general anesthesia. Proven Apsergillus infection was based on culture and serologic test. The equilibration of diabetes was obtained. Treatment was based on a combination of ceftazidime and fluoroquinolone for several weeks, associated with voriconazole during 3 months. After a follow-up of one year, he had been cured with normalization of the biological, and imaging features, but with persistent facial palsy.
Conclusions
Given our experience and the literature review, fungal NEO is an aggressive and potentially fatal infection. A fungal etiology should be considered early in the course of invasive necrotizing external otitis unresponsive to a conventional broad spectrum antibiotic therapy or in case of complications, with the need for positive culture swabs and/or positive serologic test to a fungal pathogen to confirm the diagnosis.

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EP1084

Is obesity associated with hyperalgesic diabetic peripheral neuropathy?

Chaima Jemai, Achwak Mehrez, Wafa Ben Brahim, Mouna Djobbi, Yosra Ben Hmida, Takwa Moussa, Zohra Hadj Ali, Olfa Lajili, Imen Hedfi, Yosra Htira & Faika Ben Mami
National institute of nutrition of Tunis, C

Introduction
The aim of our study was to evaluate the weight status of a population with type 2 diabetes and with diabetic peripheral neuropathy, and to study its association with hyperalgesic diabetic peripheral neuropathy.
Methods
This was a cross-sectional study about 100 T2DM patients hospitalized in department C of the national institute of nutrition of Tunis, and having diabetic peripheral neuropathy, diagnosed using the monofilament test and the DN4 score. For each patient eligible for the inclusion criteria's, we conducted an interview and physical examination to collect epidemiological characteristics, characteristics of T2DM (duration, glycemic balance, antidiabetic treatment and degenerative complications), and we collected biological parameters from medical records. Data were analyzed using SPSS 23.
Results
The mean age was 60.4 ± 10.6 years with extremes of 32 and 72 years and a median of 49.5 years. The sex ratio in our population was 0.53. The majority of the population (71%) had a secondary or higher level of education. The majority was not smoker (41%). We did not identify any use of illicit substances. The diabetes was type 2 in all cases. The average diabetes duration was 14 ± 5.2 years with extremes of 6 and 21 years. All patients were treated with insulin therapy combined with metformin in 65% of cases. Hyperalgesic diabetic neuropathy (DN4$\geq$4) was

the most frequent degenerative complication (56%) followed by diabetic retinopathy (38%). Mean BMI was 29,1 ± 5,7 kg/m^2 with extremes of 23 and 40.2 kg/m^2. 50% of the population has a BMI of 30,55 kg/m^2. BMI was normal in 21 % of the cases. Almost half of the population was obese (49%). Obesity was class 1,2 and 3 in 32%, 9% and 8% respectively. According to BMI, 66,7% ($n=14$) patients with normal BMI, 63,3% ($n=19$) of those with preobesity, 78,1% ($n=25$) of those with obesity class 1, 100% ($n=9$) of those with obesity class 2 and 87,5% ($n=7$) of those with obesity class 3 had hyperalgesic diabetic neuropathy with a statistically significant difference between these percentages ($P=0.021$).

Conclusion

According to our result, weight reduction seems to be a promising non-pharmacological way to act on neuropathic pain in patients with type 2 diabetes.

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EP1085

MODY type diabetes: diagnostic and therapeutic difficulties in the light of 2 cases

Jaddi Oussama, Zineb Ait Si Ali, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Mohammed VI university hospital of Marrakesh, Department of Endocrinology, Diabetes, Metabolic diseases and Nutrition, Marrakesh, Morocco

Introduction

MODY (maturity-onset diabetes of the young) is a group of heterogeneous diabetic disorders characterized by dysfunction of insulin secretion by the β-cell and genetically transmitted. MODY diabetes is thought to account for 2-5% of all diabetic disorders, but is often under-diagnosed. We report two suspected cases of MODY diabetes.

Observations

Case 1: 40-year-old patient, known diabetic for 3 years, initially on Gliclazide 60 mg and Metformin 2 g, currently on Mixtard 30 (20-00-10), diabetic heredity in mother, brother and 2 maternal uncles, SD: unknown, patient with familial polycystic kidney disease (in mother, brother and 2 maternal uncles) and renal transplant in mother in 2011, MODY 5 was suspected. Case 2: 20-year-old patient, known diabetic for 3 years, put on Mixtard 30 (16-00-20) heredity in father and paternal grandfather, Hearing loss since birth, Admitted for diabetic ketosis (first episode) MODY 2 ans mitochondrial diabetes were suspected.

Discussion

MODY is therefore a highly heterogeneous condition, both at the molecular level, in terms of the genes involved, and in terms of the severity and evolution of the insulin secretion deficit, the level of hyperglycemia and the frequency of complications. The initial definition of MODY was purely clinical: non-ketotic diabetes, early onset, usually before age 25, autosomal dominant, and is frequently misdiagnosed as type 1 or type 2 diabetes. Molecular diagnosis is necessary to better understand the evolution of the disease, propose appropriate treatment and screen relatives. High-throughput sequencing has enabled a major advance in the diagnosis of monogenic diabetes. Mutations in the glucokinase (GCK) (MODY 2) and hepatocyte nuclear factor (HNF) 1A/4A genes (MODY 3 and MODY 1, respectively) are the most common causes of MODY.

Conclusion

These observations illustrate the diagnostic difficulties of MODY diabetes. In the event of clinical suspicion, genetic confirmation enables therapeutic adaptation and early management of other affected family members.

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EP1086

Primary hyperparathyroidism in the elderly: analysis of 12 cases

Mohamed Abderrahmane Ahmed Ebett, Chadli Asma, El Aziz Siham & Haraj N.E
University Hospital Center Ibn Rochd - Casablanca, Casablanca, Morocco

Introduction

Hyperparathyroidism in the elderly is an endocrine pathology characterized by excessive secretion of parathormone by the parathyroid glands, leading to elevated blood calcium levels. This condition has significant implications for bone and renal health in this population.

Objectives

To determine the prevalence of parathyroid adenomas and their association with calcium and PTH levels in elderly patients, to improve diagnostic strategies and management of hyperparathyroidism.

Methods

Retrospective analysis of clinical and imaging data of 12 patients from Ibn Rochd Hospital, Casablanca, from January 2018 to October 2023, to identify epidemiological and therapeutic signs of primary hyperparathyroidism in the elderly.

Results

Among 12 patients with an average age of 70 years, predominantly female (9 women and 3 men), high levels of calcium (average calcemia of 114.18 mg/l) and phosphorus (average of 12.61 mg/l) were observed. PTH was notably increased with an average of 825.84 pg/ml. Ultrasounds revealed that 10 patients had parathyroid adenomas. Scintigraphy indicated hyperfixation in 7 patients. Osteoporosis was diagnosed in half of the patients, while renal lithiasis was identified in 3 patients. Additionally, 2 patients showed pathological factors, and 8 patients were discovered incidentally. Bone pain was present in 8 patients, and 3 suffered from a polyuria-polydipsia syndrome.

Conclusion

Hyperparathyroidism in the elderly manifests with various complications, such as osteoporosis, renal lithiasis, and bone pain. The prevalence of parathyroid adenomas in this study underscores the importance of ultrasound screening. The incidental findings suggest that regular examinations could be beneficial for this population.

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EP1088

Fournier's gangrene in diabetics: a study of 26 patients

Nora Boutatss, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy-University Hassan II, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction

Fournier's gangrene is a rapidly progressive necrotizing fasciitis affecting the perineum and external genital organs, requiring prompt, comprehensive, and multidisciplinary therapeutic intervention due to its severity. Diabetic patients are particularly at risk of developing Fournier's gangrene due to their vulnerability to infections and healing complications.

Objective

To present the clinical, therapeutic, and evolutionary aspects in diabetic patients.

Patients and Methods

A retrospective descriptive study, including 26 diabetic patients with Fournier's gangrene hospitalized at Ibn Rochd University Hospital in Casablanca. Twenty patients had known diabetes, while in 6 cases, gangrene was indicative of diabetes. Statistical analysis was conducted using Excel.

Results

The average age of our patients was 56 years, with a male predominance (24 men and 2 women). Twenty-five patients had type 2 diabetes (96%), and one patient had type 1 diabetes. All patients were uncontrolled at the onset of gangrene (average HbA1c of 9.8%). Uro-genital and ano-rectal causes were noted. Medical management involved parenteral tri-antibiotic therapy, intensive insulin therapy (basal-bolus regimen), and hypercaloric feeding (parenteral nutrition in 4 cases). Surgical treatment (necrotomy) was performed in all cases. Colostomy was carried out in 6 cases. Skin grafting was necessary in 1 case. Two deaths (7.69%) were recorded in cases of septicemia.

Conclusion

Fournier's gangrene remains a severe condition, especially in diabetic patients, and prognosis can only be improved through early diagnosis and appropriate medical and surgical management.

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EP1096

Sexuality in obese and pre-obese women: a cross-sectional analytical study

Kouloud Boujelben, Mohamed Khairi Arous, Fatma Mnif, Mouna Elleuch, Dhouha Ben Salah, Rim Djebbi[2], Faten Haj Kacem, Nadia Charfi, Mouna Mnif, Mohamed Abid & Nabila Rekik Majdoub
Hedi Chaker Hospital, Endocrinology, Sfax, Tunisia; [2]Faculty of medecine of Sfax, Sfax, Tunisia

Introduction

Obesity continues to rise globally, exerting a significant impact on physical, mental, and sexual health. Few studies have addressed sexual dysfunction in

obese women within our Tunisian context. The objective of our study was to investigate the parameters influencing sexuality in obese and pre-obese women through a standardized assessment.
Methods
We conducted a cross-sectional analytical study involving women who engaged in sexual intercourse within the past four weeks and whose body mass index exceeds 25 kg/m^2;. For the assessment of sexual function, we utilized the Arabic version of the Female Sexual Function Index (arFSFI), consisting of six parameters: desire, arousal, lubrication, orgasm, satisfaction, and pain. A score below 23 indicates female sexual dysfunction
Results
The study included 50 overweight and obese women, with a mean age of 38.5 ± 9.45. The average duration of marriage/cohabitation was 11.8 years. The majority of women were educated (88%). More than two-thirds of participants (78%) were obese, and 22% were overweight. Most women (80%) were in the reproductive age group, 6% had primary or secondary amenorrhea, and 14% were menopausal. The mean BMI was 37 ± 8.7 kg/m^2. The average Female Sexual Function Index (FSFI) score was 27.4 ± 6.2. We observed that 12% had sexual dysfunction, 42% had a lack of desire, and 24% experienced pain during sexual intercourse.
Discussion and conclusion
The rate of women experiencing sexual dysfunction is lower than that reported in the literature. This could be explained by the difficulty women in our context face in discussing their sexuality in general and their discomfort in particular. The lack of desire may be associated with a negative perception of body image. Our study emphasizes the need to raise awareness and educate healthcare professionals working with obese women on sexual health, in order to detect dysfunctions and improve the quality of life for patients.

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EP1104

Testosterone and anthropometrics indices in type 2 diabetes: cross-sectional study

Anis Grassa[1], Manel Jemel[1], Salma Salhi[1], Bel Hadj Sliman Chayma[1], Asma Krir[2], Ahlem Benhmid[2], Radhouane Gharbi[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technologies, Zouheir Kallel, Endocrinology, Tunis, Tunisia; [2]Pasteur Institute of Tunis, Tunis, Tunisia

Introduction
In the context of Type 2 Diabetes (T2D), understanding the interplay between testosterone levels and anthropometric data holds crucial implications. This study aims to explore the intricate relationship between testosterone, obesity, and anthropometric measurements, offering insights that contribute to a deeper understanding of the intricate physiological dynamics within this diabetic population.
Methods
This Cross-Sectional Study included 250 men with T2D consulting at the National Institute of Nutrition in Tunisia. Free Testosterone (FT) and Bioavailable Testosterone (BT) using the Vermeulen formula[1]. For all patients we measured weight, height and waist circumference (WC). Body mass index (BMI) was calculated. Obesity was defined by a BMI $>$ 30 kg/m^2;, and android fat distribution was identified by a waist circumference (WC) $\geq$ 94 cm.
Results
The median age of our participants was 58 years, with an interquartile range (IQR) of [52.7–62]. The average weight of the patients was 83.3 ± 12.4 kg [59 - 125 kg]. The mean Body Mass Index (BMI) was 27.9 ± 4 kg/m^2;,[19.8 -40]. Approximately 29.2% of patients were classified as obese, (n = 73 patients). In terms of anthropometric measurements, the mean WC was 97.5 ± 9.2 cm, [77 - 138 cm]. Android distribution of body fat was observed in 67.2% of participants, accounting for 168 individuals. A significant inverse correlation was found between BMI and the levels of Total Testosterone (TT) (r: -0.311; $P < 10^{-3}$), FT (r: -0.150; $P = 0.021$), and BT (r: -0.143; $P = 0.027$). The same relationship exists between WC and levels of TT (r: -0.275; $P < 10^{-3}$), FT (r: -0.146; $P = 0.024$), and BT (r: -0.136; $P = 0.038$).
Conclusion
These findings suggest a significant negative association between BMI, waist circumference, and testosterone levels, emphasizing the potential role of testosterone in the regulation of body composition within this specific population.
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EP1106

Sleeve gastrectomy: a retrospective analysis of its efficacy in obesity treatment and metabolic improvement

Mirjana Kardum Pejić[1,2], Nives Gojo Tomić[1], Irena Martinis[1], Domagoj Vergles[1], Mirna Šporčić[1], Martina Bituh[1], Jelena Pugelnik[1] & Josip Pejić[1]
[1,2]University Hospital Dubrava, Department of Endocrinology and Diabetology, Zagreb, Croatia

Introduction
Obesity is one of the fast growing diseases in the modern world. Over the years, bariatric surgery has proven its effectiveness in treating obesity, improving its associated comorbidities, and even potentially curing them. A body mass index (BMI) greater than 40 kg/m^2 or a BMI greater than 35 kg/m^2 with associated comorbidities is an indication for such surgery. Sleeve gastrectomy (SG) has emerged as a prominent and effective surgical intervention for the management of obesity and its associated comorbidities. The aim of study was to evaluate patients' nutritional status before surgery and their post-operative metabolic improvements.
Results and discussion
Data for the study were gathered retroactively from BIA analysis and laboratory values for 50 patients (44 women and 6 men) who had SG at University Hospital Dubrava between 2019 and 2023. Before surgery type 2 diabetes was diagnosed in 19 patients, arterial hypertensio in 21, dyslipidaemia in 14 patients and thyroid diseases (hypothyreoidisam) in 13 patients. In the two controls after the procedure there was a statistically significant decrese total body mass, body mass indeks and fat mass. In most patients there was a significant reduction in arterial pressure. Regarding the biocemical parameters there was a statistically significant decrese in glycemia, HbA1c, ($P < 0,05$), C-reactive protein while among the parameters of the lipid profile, there was a significant decrese only in HDL cholesterol, which was close to the limit of the reference value even before the operation, which is undesirable factor in the contex of cardiovascular diseases. Other lipid profile values are not statistically significant but show a decreasing trend.
Conclusions
The study confirmed SG to be efficient in treating obesity, controlling glycemia and arterial hypertension and reducing lipid profile. Keywords: Sleeve Gastrectomy, Obesity, Type 2 Diabetes Mellitus, Body Mass Index, Arterial hypertension

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EP1107

Sarcopenia in breast cancer patients undergoing chemotherapy

Berriche Olfa[1], Selma Mohsen[1], Ben Mansour Hajer[2], Rym Ben Othman[1], Dorra Ben salem[1], Mezlini Amel[2] & Jamoussi Henda[1]
[1]national institute of nutrition, service A, Tunis, Tunisia; [2]national institute Salah Azaiez, oncology, Tunis, Tunisia

Introduction
Sarcopenia, defined by a loss of strength and muscle mass, is initially described in elderly subjects but now is increasingly observed in younger patients with cancer. In addition, loss of muscle mass appears to be progressive during neoadjuvant chemotherapy. The aim of this study was to analyse the body composition of breast cancer patients and determine the prevalence of sarcopenia during chemotherapy.
Methodology
This was a cross-sectional comparative study conducted over a 6-month period in breast cancer patients undergoing chemotherapy. An analysis of body composition with calculation of the non-fat mass index was carried out using an impedance meter to assess the reduction in muscle mass. A reduction of muscle strength was assessed by a hand strength $<$16 kg. The diagnosis of sarcopenia was made according to the criteria of the EWGSOP 2019. The population was divided into 2 groups according to the chemotherapy molecule used; G1: group receiving anthracyclines, G2: group receiving taxane.
Results
During this period 107 patients were recorded. The mean age was 52 ± 9.75 years. The age group most affected was between 50 and 60. In the body composition analysis, reduced muscle mass was noted in 55% of patients. It was more marked for group 1. An increase in body fat was noted in the majority of cases (70%) and the percentages were comparable for the two groups. A non-fat mass index of less than 15 was noted in 14 patients. The majority of which belonged to G1. Furthermore, a decrease in grip strength was noted in 34 patients, 61% of whom were receiving anthracyclines. Finally, sarcopenia was diagnosed in 12% of all cases. Both sarcopenia and reduced muscle strength were significantly associated

with G1 receiving anthracyclines with respectively$P$ 0.028, $P < 10^{-3}$. The increase in body fat was not correlated with the chemotherapy molecule.
Conclusion
This reflects the under-diagnosis of sarcopenia and its close relationship with chemotherapy, justifying early detection and management of this entity in order to prevent its potential consequences.

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EP1108

Impact of hibiscus tea consumption on clinical and biological parameters in patients with type 2 diabetes and/or hypertension

Kouloud Boujelben[1,2], Mariem Ayedi[2,3,4], Fatma Mnif[2], Mouna Elleuch[2], Dhoha Ben Salah[2], Mouna Mnif[2], Nadia Charfi[2], Faten Haj Kacem Akid[2], Mohamed Abid[2] & Nabila Rekik Majdoub[2]
[1,2], Tunisia; [3]Hedi Chaker Hospital, Endocrinology Diabetology, Tunisia; [4]Hedi Chaker Hospital, Endocrinology Diabetology, Sfax, Tunisia

Introduction
Medicinal plants and their benefits on human health in the treatment of non-communicable diseases such as hypertension, overweight or obesity, diabetes, and dyslipidemia present a current issue of several research studies. Among these plants is 'Hibiscus sabdariffa', known for its hypotensive, hypoglycemic, hypolipidemic, and anti-obesity actions. Our work aimed to assess the impact of Hibiscus tea consumption on clinical (systolic and diastolic blood pressures, weight) and biological parameters (blood glucose level, cholesterol level, and triglycerides level) in patients with type 2 diabetes and/or hypertension.
Materials and Methods
Our study involved 20 patients, aged between 18 and 60 years old, who were followed at the Endocrinology-Diabetology department at Hedi Chaker Hospital in Sfax. 55% were females and 45% were males, with a predominance in the age group between 35-40 years. 20% of the subjects had a normal BMI between 18.5 and 25 kg/m^2, while the rest of our population had a BMI higher than 25 kg/m^2. 25% of the patients were hypertensive, 30% were dyslipidemic, and 25% had both hypertension and dyslipidemia.
Results
In our type 2 diabetic and/or hypertensive patients, our results demonstrate that Hibiscus tea can remarkably modify metabolic parameters. In fact, we observed a significant decrease in blood glucose and glycated hemoglobin levels (47.49% and 9.53%, respectively) as well as a reduction in cholesterol and triglyceride levels by 39.35% and 59.79%, respectively, after one month of tea consumption. Furthermore, we observed an estimated reduction of 17.20% in systolic blood pressure and 9.83% reduction in diastolic blood pressure over the course of one month of treatment.
Conclusion
We can therefore conclude that Hibiscus tea consumption may improve glycemic and lipid profiles, blood pressure, and obesity in patients with type 2 diabetes and/or hypertension. However, further researches involving a larger number of patients are needed to statistically strengthen our results and extrapolate them to the Tunisian population.

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EP1110

Omega-3 consumption profile among a group of tunisian diabetic coronary patients

Asma Cherni, Haifa Abdesselem, Emna Bornaz & Chiraz Amrouche
Institut De Nutrition, Tunis, Tunisia

Introduction
Omega-3 polyunsaturated fatty acids (PUFAs) have emerged as pivotal factors in mitigating the risk of cardiovascular disease. Extensive research has demonstrated their ability to reduce both fatal and non-fatal events such as myocardial infarction, stroke, and coronary artery disease. This study aims to assess the Omega-3 polyunsaturated fatty acids(PUFAs) intake, encompassing all three types of omega-3, within a cohort of diabetic coronary patients.
Material and method
Thirty patients aged between 18 and 70 years, diagnosed with type 2 diabetes mellitus and having experienced at least one coronary event, were included in the study. An alimentary survey utilizing the 24-hour dietary recall technique and a validated questionnaire of frequency was conducted and analyzed using dietetic software to assess omega-3 polyunsaturated fatty acids intake.
Results
The mean age of the consultants was 55.7 ± 13 years, with extremes ranging from 38 to 82 years. The M/F sex ratio was 0.4 and the mean BMI 30.41 kg/m^2. Among the patients, 89% had an insufficient apport of omega-3 polyunsaturated fatty acids and 61% of them take fish only one time a month. The mean intake of alpha-linolenic acid (ALA) was 45.7 mg ± 18.9, that of Docosahexaenoic acid (DHA) was 60.2 mg ± 22.8 g.
Discussion
Despite the crucial need for an adequate daily intake of omega-3 polyunsaturated fatty acids, especially in a population with a very high cardiovascular risk, such as the subjects in our study, actual intake falls significantly below recommended levels, primarily due to ignorance and limited resources. A comprehensive dietary education, particularly tailored for this patient category, should be considered in the future.

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EP1118

Assessment of nutritional status and dietary protocol in post ischemic stroke patients

Zaynab Hifdi, Saloua Elamari, Soukaina Laidi & Marouan Fatima
Cheikh Khalifa Bin Zayed Al Nahyan Hospital, Casablanca, Morocco

Introduction
Nutritional factors play an important role in reducing the morbidity and mortality of ischemic stroke, as well as in the effectiveness of post-stroke secondary rehabilitation. We were interested in these nutritional factors and conducted this study to assess the nutritional status of post-stroke patients.
Methods
Our study is a prospective study including post-stroke patients, spread over a period of three months within the neurology services of the Cheikh Khalifa Hospital in Casablanca. We collected epidemiological, clinical, anthropometric and biological data, as well as data from a 24-hour dietary survey.
Results
We included 10 patients, mostly male, with a sex ratio of 7/3. Fifty percent of patients had swallowing and motor disorders, and 70% had impaired memory. In terms of nutrition, 60% of patients had dietary intakes below their nutritional requirements, 30% had criteria for undernutrition, 40% had sarcopenia according to clinical criteria, and 60% were vitamin D deficient. Only 10% of patients saw a dietician after their stroke episode.
Conclusion
Nutritional management is an important, but often neglected, pillar in the management of an ischemic stroke. It plays an important role in primary and secondary prevention, but also and above all in reducing the risk of undernutrition and its impact on post-stroke morbidity and mortality. This undernutrition is due to neurological and swallowing disorders, but also to psychological factors linked to the ischemic stroke.

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EP1122

Resistant otorrhea in a diabetic; revealing form of an exceptional carcinoma of the external ear canal

El Omri Malika, Jemli S, Bellakhdher Mouna, Meherzi Abir, Houas Jihene, Ghammem Monia, Ach Taieb[2], Kermani Wassim & Abdelkefi Mohamed
ENT Department Farhat Hached hospital, Sousse, Tunisia; [2]Endocrinology Department Farhat Hached Hospital, Sousse, Tunisia

Introduction
Necrotizing otitis externa (NOE) is a serious pathology frequently observed in diabetics. Its differential diagnosis of carcinoma of the external auditory canal (EAC) is, however, a rare pathology observed only in 0.2% of cases, the most frequent histological type is epidermal carcinoma, adenoid cystic carcinoma (ACK) is exceptionally observed. We report the case of ACK treated in our department initially considered as an NOE and whose diagnosis was made on deep biopsies. The aim of our work is to draw attention of clinicians to a differential diagnosis of necrotizing otitis externa and to describe its therapeutic modalities.
Observation
A 70-year-old patient, type 2 diabetic evolving for 6 years, admitted for left ear pain associated with chronic otorrhea resistant to outpatient treatment. Physical examination revealed an inflammatory EAC. No granulation tissue or protruding polyp was found. Temporal Computed tomography showed the appearance of a

left NOE without endocranial extension. Bacteriological and mycological samples were negative initially then positive for *corynebaceruim*. The patient was then put on antibiotics for 21 days with good control of her diabetes and regular local care, without any improvement. Given the slow progress, it was decided to perform deep bone biopsies which were in favor of a ACK of the CAE. The patient underwent a lateral petrectomy followed by adjuvant radiation. The evolution was favorable.
Conclusion
The place of deep biopsy in NOE is controversial, but it can sometimes support a differential diagnosis in the face of the dragging evolution of a well-monitored NOE.

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EP1132

Metabolic profile of obese tunisian adults

Wissal Ghamgui, Elleuch Mouna, Maalej Souhir, Hadj Kacem Faten, Mnif Mouna, Mnif Fatma, Charfi Nadia, Rekik Nabila & Abid Mohamed
Hedi Chaker Hospital, Endocrinology and Diabetology department, Sfax, Tunisia

Introduction
Obesity is recognized as a risk factor for cardiovascular diseases. She can be associated with cardio-metabolic diseases. The objective of our study was to determine the metabolic profile of our obese adults.
Materials and methods
This is a descriptive cross-sectional study involving obese adults consulting the service of Endocrinology of Sfax, Hedi Chaker University Hospital in 2023.
Results
We recruited 40 obese patients with an average age of 43.47+/-16.56. The sex ratio was 0.21. The average duration of obesity was 20 years +/-13.25. Average weight was 95.17 kg with a minimum of 74 kg and a maximum of 134 kg. The average body mass index was 35.96+/-5.04 kg/m^2. Twenty percent of patients had morbid obesity (BMI=40 kg/m^2). There mean systolic blood pressure was 131+/-2 mmHg with a minimum of 100 mmHg and a maximum of 170mmHg. The mean diastolic was 79.62+/-10 mmHg. The average of fasting blood sugar was 6.68+/-3.33 mmol/l. For the lipid profile, the average cholesterol total and HDL cholesterol were 4.24+/0.87 mmol/l and 1.05+/-0.19 mmol/l respectively. There average triglycerides was 1.36+/-0.46 with a maximum of 2.5 mmol/l.
Conclusions
Obesity puts you at risk of metabolic syndrome with all its harmful effects on health. There insulin sensitivity and fasting insulinemia should be part of the criteria to be assessed for define metabolic normality in obese subjects.

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EP1133

Assessment of environmental factors influencing weight behavior

Veranika Lobashova[1,1], Yuliya Dydyshka & Alla Shepelkevich
Belarusian State Medical University, Endocrinologic, Minsk, Belarus

Introduction
The prevalence of overweight and obesity is risen dramatically especially among children and adolescents. Increased BMI is an independent risk factor for cardiovascular diseases, diabetes mellitus, and some types of cancers (including endometrial, breast, ovarian, prostate, liver, gallbladder, kidney, and colon). Changes in dietary and physical activity patterns are often the result of environmental and social impact. Studies carried out revealed that people globally are currently trying to lose weight.
Methods
We examine 67 patients seeking to lose weight to dietician. The mean age was 46, 5+ 8.5 years, the mean BMI 39.7+5.3 kg/m^2. 12% (8 persons) were men, 88% (59 persons) were women. We examine anamnesis of obesity, family history and comorbidity.
Results
We revealed that among men 2 participants had (25%) had the excess weight from childhood, 2 (25%) of them were stigmatized. 1 patient (12.5%) had diagnosed eating disorder, 1 patient (12.5%) - other mental disorder. 2 (25%) participants made attempts to lose weight; 50% of them used supplements and pills. 3 (37.5%) patients had cardiovascular diseases, 3 smoked, 6 of 8 persons (75 %) had obesity on maternal line, 3 (37.5%) on the paternal line. 2 respondents(25%) had diabetes mellitus in closer relatives. Among women 16 participants(27 %) had had the excess weight from childhood, 7 of them (12%) were stigmatized. 9 patients (15%) had diagnosed eating disorders, 4 patients (7%) - other mental disorders. 33 participants (56%) made attempts to lose weight; 36% of them used diet supplements and pills. 35 persons (59 %) had obesity on maternal line, 25 (42%) on the paternal line. 14 respondents (24%) had diabetes mellitus in closer relatives.
Conclusion
Family factors play a huge into transition normal weight to obesity and affecting eating disorders. ~50 % of participants had attempts to lose weight including use of supplements. Level of mental disorders and stigmatization are high.

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EP1134

Carbohydrate metabolism according to obesity phenotype

Tetiana Sekret
National Pirogov Memorial Medical University, Endocrinology, Vinnytsya

Introduction
Diabetes mellitus is the most common disease of the 21st century. The main challenge for modern doctors is to prevent its development.
Purpose
Study the state of carbohydrate metabolism in individuals with different obesity phenotypes.
Materials and methods
We examined 96 individuals (18-64 y.) according to each obesity phenotype during 2019 - 2021 on the basis of the Vinnitsa Regional Clinical High-Specialized Endocrinological Center. An anamnesis was collected according to the FINDRISK Diabetes risk scale. Biochemical analysis was performed laboratory.
Results
Patients in the first clinical group have normal body weight, some have overweight (BMI - 24.7±4.3 kg/m^2), but the waist volume (102.45±9.63 cm in men, 88.64± 4.27 cm in women) is higher than the normative values, which is tracked in all obesity phenotypes, which may indicate insulinresistance. Violations of carbohydrate and lipid exchanges according to screening surveys in this group were not found. With normal body weight (BMI-23.7±2.44 kg/m^2), metabolic disorders are already observed in the second clinical group. According to carbohydrate metabolism data, all patients were diagnosed with prediabetes combining fasting hyperglycemia and impaired glucose tolerance (fasting glucose - 5.93±0.36 mmol/l, 2 hours after glucose - 8.45±0.27 mmol/l, HbA1c - 6.23±0.18%), and existing dyslipidemia (CL - 5.88± 0.26 mmol/l). It is worth noting that not always as we expect in obesity (BMI - 34.57±3.31 kg/m^2) there will be changes in the lipid and carbohydrate profile, demonstrating the results of the examination of the 3rd clinical group (fasting glucose - 5.23±0.17 mmol/l, glucose 2 hours after glucose - 7.4±0.32 mmol/l, HbA1c - 5.32±0.21%; CL - 4.98±0.46 mmol/l, TG - 1.32±0.14 mmol/l, LDL - 2.75±0.22 mmol/l). In patients of the 4th clinical group, metabolic disorders were detected (fasting glucose - 5.78±0.13 mmol/l, glucose 2 hours after glucose - 8.83±1.67 mmol/l, HbA1c - 5.97±0.32%; CL - 6.73± 0.21 mmol/l, TG - 2.46± 0.57 mmol/l, LDL - 4.13± 1.07 mmol/l, SAP - 145.58±19.34 mm Hg, DAP - 94.8 ±5.61 mm Hg) with obesity (BMI - 35.8 ±4.42) Given a long course without proper treatment, this can provoke diabetes mellitus.
Summary and conclusions
The results of the study will give rise to timely preventive measures aimed at combating diabetes mellitus.

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EP1135

Prevalence of sarcopenia in obese tunisian adults

Berriche Olfa[1], Rim Rachdi[1], Chaima Ammar[2], Rym Ben Othman[1], Nadia Ben Amor[1], Ramla Mizouri[1], Amel Gammoudi[1] & Jamoussi Henda[1]
[1]National Institute of Nutrition, Department A, Tunis, Tunisia; [2]Higher School of Health Sciences and Techniques, Tunis, Tunisia

Introduction
Sarcopenia is a clinical condition defined as low skeletal muscle mass and function. It has been identified and described as a geriatric syndrome, increasing the risk of frailty, comorbidities and mortality. However, sarcopenia may arise in individuals with obesity at any age. Our objective was therefore to screen for sarcopenia in a group of obese adults.
Materials and methods
This was a descriptive cross-sectional study, carried out on 53 obese patients who consulted the Human Obesity Research Unit of the National Institute of Nutrition and Food Technology of Tunis, between November 2022 and February 2023. Screening

for sarcopenia has been established according to pathological thresholds proposed by the European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Association for the Study of Obesity (EASO)[1].
Results
The mean age of patients was 44.34±13.51 years. The majority of our patients were female (79.2%), with a gender ratio (M/F) of 0.26. Mean BMI was 39.78±5.92 kg/m^2;. Average waist circumference was 125±11 cm for men and 120±11 cm for women. Mean visceral fat was 11.35±5.38 l. Mean body fat percentage was 46.2±7.23%. Almost all patients (94.3%) had a high body fat percentage. The mean values for skeletal muscle mass (SMM) and percentage of skeletal muscle mass to weight (SMM/W) were 31.37±7.30 kg and 29.26±5.01% respectively. More than half the patients (54.7%) had low skeletal muscle mass. 17% of patients had poor grip strength. Sarcopenia was present in 7.5% of the population (SO+). The mean age of the obese sarcopenic was 50.25 years, compared with 43.86 years for the non-sarcopenics ($P=0.444$). Half of SO+ patients were men, compared with 18.37% of SO- patients ($P=0.134$). 50% of sarcopenic obese patients (SO+) had a low socioeconomic status, vs 4% of non-sarcopenic obese patients (SO-). The difference was statistically significant ($P=0.004$). All sarcopenic obese people were sedentary, compared with only 77.5% of non-sarcopenic obese people. The difference was statistically significant ($P<0.001$).
Conclusions
Screening for sarcopenia should be carried out in obese patients regardless of age in order to better assess obesity severity beyond body mass index (BMI), which is now recognized as an insufficient criterion for defining this chronic disease with multiple comorbidities.
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EP1136

The impact of obesity on bone and joint:about 502 cases

Imane Hasbi[1], Nassim Essabah Haraj[2], Siham El Aziz[3] & Asma Chadli[4]
[1]Ibn Rochd University Hospital, Endocrinology and Metabolic Diseases, casablanca, Morocco; [2]Ibn Rochd University Hospital, Endocrinology and Metabolic Diseases, Casablanca, Morocco; [3]Ibn Rochd University Hospital, Endocrinology and Metabolic Diseases, Casablanca, Morocco; [4]Ibn Rochd University Hospital, Endocrinology and Metabolic Diseases, Casablanca, Morocco

Introduction
Obesity poses a major challenge to public health, not only due to its cardiovascular and metabolic complications but also because of its impact on the musculoskeletal system.
The aim of this study is to analyze the frequency of various osteoarticular complications in obese individuals.
Patients and Methods
This is a retrospective study conducted on 502 obese patients aged 13 to 80 years, hospitalized in the endocrinology department of CHU Ibn Rochd in Casablanca. Osteoarticular manifestations and their respective locations were examined. Each patient underwent anthropometric measurements, as well as biological and radiological evaluations based on indications. The statistical analysis was performed using the SPSS software, version 25.
Results
The average age of our patients was 51.7 years (13-80 years), with a marked female predominance at 83.5%. The mean body mass index (BMI) was 35.2 kg/m^2, and the average abdominal circumference was 113.8 cm. Among the patients, 38.5.% had osteoarticular complications, Their average BMI was 38.2 kg/m^2, with a prevalence of 43.7% for morbid obesity and 34.6% for severe obesity. Various joint issues reported included knee pain observed in 58.2% of cases, knee pain associated with lower back pain in 28.4% of cases, and isolated lower back pain in 13.4%. Osteoarthritis was present in 21.3% of patients, while bone densitometry revealed osteopenia in 17.8% of cases and osteoporosis in 15.8% of cases. Vitamin D deficiency was identified in 18.2% of patients.
Discussion and conclusion
Several studies have demonstrated an increased association between obesity and the risk of osteoarthritis in the knee, hip, and finger joints, although the impact is less pronounced for the hip. This correlation between obesity and arthritic pathology is frequently observed, especially in the elderly, which aligns with the results of our study. Obesity exacerbates functional limitations, leading to a significant deterioration in the quality of life due to painful symptoms. It becomes imperative to prevent obesity and/or intervene early for optimal management.

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EP1137

Nutritional risk factors associated with the development of sarcopenic obesity

Berriche Olfa[1], Rim Rachdi[1], Chaima Ammar[2], rym ben othman[1], Amel Gammoudi[1] & Jamoussi Henda[1]
[1]National Institute of Nutrition, Department A, Tunis, Tunisia; [2]Higher School of Health Sciences and Techniques, Tunis, Tunisia

Introduction
Sarcopenic obesity (SO), characterized by the coexistence of obesity and sarcopenia, is a condition increasingly recognized for its clinical and functional features, which impairs patients' quality of life and increases the risk of morbidity and mortality. In order to improve the management of obese patients, we aimed to screen for sarcopenia in obese adults and to identify the nutritional risk factors associated with sarcopenic obesity.
Materials and methods
This was a descriptive cross-sectional study, carried out on 53 obese patients who consulted the Human Obesity Research Unit of the National Institute of Nutrition and Food Technology of Tunis, between November 2022 and February 2023.
Results
The mean age of patients was 44.34±13.51 years. Mean BMI was 39.78±5.92 kg/m^2;. Almost all patients (94.3%) had a high fat mass percentage. More than half the patients (54.7%) had low skeletal muscle mass (SMM/W). Prevalence of Sarcopenia was 7.5% (SO+). Mean energy intake was 3100 kcal/d in SO+ and 2800 kcal/d in SO- ($P=0.886$). The average intake of lipids and saturated fatty acids was higher in sarcopenic obese people, but with no significant difference. Average cholesterol intake was significantly higher for SO+ than for SO- (354.93 mg/24 h vs 320.53 mg/24 h respectively; $P<0.001$). Regarding the average vitamin intake, there was no statistically significant difference between SO+ and SO-. Furthermore, a statistically significant relationship was found between low skeletal muscle mass (SMM/W) and the average intake of vitamin PP ($P=0.014$) and vitamin B9 ($P=0.009$). There was no significant difference between the two groups regarding the average intake of mineral salts, except for the average copper intake, which was significantly higher in sarcopenic obese people (2.91 mg/d for SO+ vs 1.84 mg/d for SO-; $P=0.038$).
Conclusions
In the light of our results and those of the literature, a high-calorie diet combined with sedentary lifestyle contributes to the development of sarcopenic obesity. We therefore recommend promoting a balanced, low-energy-density diet in order to reduce the risk of sarcopenia and associated comorbidities.

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EP1138

Clinical risk factors associated with sarcopenic obesity

Berriche Olfa[1], Rim Rachdi[1], Chaima Ammar[2], rym ben othman[1], Ramla Mizouri[1], Nadia Ben Amor[1], Amel Gammoudi[1] & Jamoussi Henda[1]
[1]National Institute of Nutrition, Department A, Tunis, Tunisia; [2]Higher School of Health Sciences and Techniques, Tunis, Tunisia

Introduction
Sarcopenia, defined as the loss of skeletal muscle mass and function, is common for individuals with obesity due to adipose tissue disorders, metabolic changes associated with a sedentary lifestyle and during the ageing process. However, sarcopenia can occur in obese people at any age. Our objectives were therefore to screen for sarcopenia in a group of obese adults, and to identify the clinical risk factors associated with sarcopenic obesity.
Materials and methods
This was a descriptive cross-sectional study, carried out on 53 obese patients who consulted the Human Obesity Research Unit of the National Institute of Nutrition and Food Technology of Tunis, between November 2022 and February 2023.
Results
Average age of patients was 44.34±13.51 years. Mean BMI was 39.78±5.92 kg/m^2;. Almost all patients (94.3%) had a high fat mass percentage. More than half the patients (54.7%) had low skeletal muscle mass (SMM/W). Sarcopenia was present in 7.5% of the population (SO+). Mean Body Mass Index (BMI) (45.86 kg/m^2 for OS+ vs 39.29 kg/m^2 for OS-; $P=0.03$) and mean visceral fat (16.55 l for OS+, vs 10.93 l for OS-; $P=0.043$) were significantly higher in sarcopenic obesity. Similarly, mean BMI (41.57 kg/m^2 for low SMM/W vs 37.62 kg/m^2 for normal SMM/W; $P=0.006$), and mean percentages of severe obesity (58.62% for low SMM/W, vs 25% for normal SMM/W; $P=0.048$) and fat mass (49.25% for low SMM/W, vs 42.52% for normal SMM/W; $P<0.001$) were significantly higher in cases of low skeletal muscle mass. Mean visceral fat was also higher in cases of low skeletal muscle mass than in cases of normal skeletal muscle mass, but with no significant difference (12.21 l for low SMM/W, vs 10.65 l for normal SMM/W; $P=0.3$).

Conclusions
Our results showed that high BMI and altered body composition, including increased fat mass percentage and high viceral fat, were the anthropometric risk factors associated with the development of sarcopenic obesity. We therefore recommend a balanced diet combined with regular physical activity to reduce the risk of sarcopenia and associated comorbidities.

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EP1139

Biological parameters associated with sarcopenic obesity

Berriche Olfa[1], Rim Rachdi[1], rym ben othman[1], Chaima Ammar[2], Amel Gammoudi[1], Emna Talbi[1] & Jamoussi Henda[1]
[1]National Institute of Nutrition, Department A, Tunis, Tunisia; [2]Higher School of Health Sciences and Techniques, Tunis, Tunisia

Introduction
Loss of skeletal muscle mass and function, which defines sarcopenia, generally occurs with ageing, and is commonly associated with relative or absolute fat mass gain; this process contributes to the potential development of sarcopenic obesity. However, sarcopenia can occur in people suffering from obesity at any age. We aimed therefore to screen for sarcopenia in a group of obese adults, and to identify the biological risk factors associated with sarcopenic obesity.
Materials and methods
This was a descriptive cross-sectional study, carried out on 53 obese patients who consulted the Human Obesity Research Unit of the National Institute of Nutrition and Food Technology of Tunis, between November 2022 and February 2023.
Results
The mean age of patients was 44.34 ± 13.51 years. Mean BMI was 39.78 ± 5.92 kg/m^2;. Almost all patients (94.3%) had a high fat mass percentage. More than half the patients (54.7%) had low skeletal muscle mass (SMM/W). Sarcopenia was present in 7.5% of the population (SO+). The study of biological parameters revealed a statistically significant relationship between insulin resistance and low skeletal muscle mass, as attested by mean insulinemia (28.81 µIU/ml for low SMM/W, vs 14.48 µIU/ml for normal SMM/W; $P=0.004$) and HOMA index (7.94 for low SMM/W, vs 3.49 for normal SMM/W; $P=0.002$), which were higher in cases of low skeletal muscle mass. However, there was no statistically significant difference in biological parameters or Homa index between sarcopenic (SO+) and non-sarcopenic (SO-) obese subjects.
Conclusions
In the light of our results and those of the literature, we recommend promoting a balanced, low-energy-density diet in order to improve insulin sensibility and thus reduce the risk of sarcopenia and associated comorbidities. Regular physical activity and limiting sedentary activities are also strongly recommended.

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EP1140

Prevalence of undernutrition in adult patients consulting for underweight

Dorra Ben salem, Emna Bornaz, Sana Khamassi, Haifa Abbassi, Selma Mohsen[2], Fatma Boukhayatia, Asma Ben Brahim, Rim Yahyeoui, Kamilia Ounaissa & Chiraz Amrouche
National Institute of Nutrition, Outpatient Department and Functional Exploration, Tunis; [2]Tahar Sfar Hospital, Mahdia

Introduction
Undernutrition is a pernicious and frequent situation that often remains undetected and insufficiently treated. The aim of our study was to determine the prevalence of malnutrition in adult patients seen in specialized nutrition consultation.
Materials and methods
It was a cross-sectional study, including adult patients consulting our specialized nutrition unit in the outpatient department and functional exploration of the National Institute of Nutrition of Tunis. Demographics, clinical characteristics, biochemistry and outcome data were collected. Among the phenotypic criteria, we find the muscular strength, evaluated by the Hand Grip test (HG), the body mass index (BMI) and weight loss (WL). Their limits were those defined by the high health authority (HAS) 2021. One of these criteria associated with an etiological criterion establishes the diagnosis of malnutrition. We also measured the upper arm circumference (AC) and calf circumference (CC).
Results
Thirty five patients with the mean age of 35.14 ± 15.95 years [20; 68] were included in the study. The sex ratio was 0.2. The main reported symptoms were anorexia (54.3%) and asthenia (34.3%). The average BMI, WL, HG, AC and CC were 17.51 ± 4.3 kg/m^2; 15.83 ± 9.63%; 23.27 ± 10.1 kg; 22.89 ± 3.18 cm and 30.82 ± 4.11 cm respectively. The prevalence of undernutrition with BMI, WL and HG as isolated criteria were 74.28%, 65.71% and 31.42%, respectively. It was 65.71% associating at least a phenotypic and an etiological criterion as the HAS recommends. The undernutrition was moderate in 43.47% of cases and severe in 56.52% of them. Severity was related to a BMI under 17 kg/m^2; in 84.61% of cases, to WL greater than 15% in 61.53 % of cases and to an albumin level under 30g/l in 15.38 % of them. BMI was significantly correlated with age ($P=0.05$), upper arm circumference ($P<0.0001$) and calf circumference ($P=0,006$) but no correlation was found with HG and WL. Undernutrition was correlated with WL ($P=0,001$).
Conclusion
The presentation of undernutrition is often subtle and there is a need to pay additional attention to nutrition status by the use of reliable screening toolsand increasing physician awareness. HAS recommendations constitute an appropriate tool to establish a malnutrition situation and should be applied whenever this diagnosis is suspected.

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EP1141

A simple blood screening tests for predicting non-alcoholic fatty liver disease in obese patients

Meriam Dalhoum[1], Olfa Berriche[1], Rim Ben Othmen[1], Emna Talbi[2], Raja Tlili[3], Sahar Hamza[3], Amel Gammoudi[1], Awatef Kacem[1], Lamia Kallel[3] & Henda Jamoussi[1]
[1]National Institute of Nutrition in Tunis, Human Obesity Research Unit, Tunis, Tunisia; [2]National Institute of Nutrition in Tunis, Biochemistry Laboratory, Tunis, Tunisia; [3]Mahmoud El Matri Hospital, Ariana, Tunis, Gastroenterology Department, Tunis, Tunisia

Introduction
Obesity is becoming increasingly common in the world's population. Its pandemic nature has made it the leading cause of chronic liver disease especially non-alcoholic fatty liver disease (NAFLD).
Objective
To develop a simple blood screening tests to predict the risk of NAFLD in the obese patient.
Methods and Materials
This is a cross-sectional study including 208 patients who consulted at the Human Obesity Research Unit of the National Institute of Nutrition in Tunis. Patients were interviewed, anthropometric measurements (weight, height, body mass index (BMI) and waist circumference) were taken, biological hepatic assessment (aspartate transaminase (AST), alanine transaminase (ALT), Gamma-glutamyl Transferase (GGT) and Alkaline phosphatases (ALPs)) and abdominal ultrasound were conducted to look for hepatic steatosis. We subdivided our patients into two groups: G1 (patients with hepatic steatosis) and G2 (patients without hepatic steatosis).
Results
The mean age of our patients was 49 ± 12 years with a female predominance (98.9%). The mean BMI was 40,43 ± 6,38 kg/m^2. The mean waist circumference was 117,60 ± 14,58 cm. The frequency of hepatic steatosis was 76 %. Mean AST, ALT and GGT levels (IU/l) were significantly higher in the presence of steatosis, respectively G1: 25.30 ± 14; 21 ± 16 and 24 ± 18 vs G2: 20.72 ± 6; 17.23 ± 13 and 18 ± 15 ($P=0.036$; $P<0.001$ and $P=0.006$ respectively). Similarly, PAL levels (IU/l) were higher in G1, but with no statically significant difference (G1: 83.67 ± 21 vs G2: 79.26 ± 26; $P=0.246$). The AST/ALT ratio was significantly lower in G1 (G1: 1.07 ± 0.31 vs G2: 1.27 ± 0.35; $P<0.001$). In multivariate analysis, only ALT (OR = 1.109; $P=0.001$) predicted NAFLD.
Conclusion
Hepatic steatosis is common in obese subjects and the hepatic screening tests represents a simple and reliable way for early early detection.

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EP1142

A simple score for predicting obstructive sleep apnea syndrome (OSAS) among obese patients

Meriam Dalhoum, Olfa Berriche, Rim Ben Othmen, Ramla Mizouri, Nadia Ben Amor & Henda Jamoussi
National Institute of Nutrition in Tunis, Human Obesity Research Unit, Tunis, Tunisia

Introduction
Obesity is undeniably a major factor in obstructive sleep apnea syndrome (OSAS). Diagnosis of the latter relies on polysomnography, but this test is not widely available. Screening of subjects at risk could be relevant, using tools such as the Berlin Questionnaire.
Objective
To determine the prevalence of symptoms and risk factors for OSAS in a group of obese subjects.
Methods
This was a cross-sectional study of 100 patients being monitored for obesity, who volunteered to complete the Berlin Questionnaire. All subjects benefited from the collection of clinical, anthropometric (weight, height, body mass index (BMI)) and biological data.
Results
Mean age was 48 ± 11 years. Women represented 84% of the sample and men 16%, for a sex ratio of 0,2. Mean BMI was 38.20 ± 6 kg/m^2. In terms of OSA symptoms, snoring was present in 74 obese subjects, and daytime sleepiness was reported in 31 subjects. The prevalence of hypertension was 44%, and all our patients had a BMI > 30 kg/m^2. The prevalence of subjects at high risk of OSA was 31% in the overall study population. In univariate analysis, the factors significantly associated with a high risk of OSAS in this population were age ($P = 0.01$), male sex ($P < 0.001$) and diabetes ($P = 0.02$).
Conclusions
In view of our study, the Berlin Questionnaire could be considered as a first step in screening subjects at risk of OSAS.

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EP1143

Metabolic regulation of adipose stem cell fate and function: from bench to clinic

Alice Pollard[1] & Sophia Bustraan[2]
[1]Imperial College London, Institute of Clinical Sciences, London, United Kingdom; [2]Mestag Therapeutics Limited, United Kingdom

White adipose tissue is a vital endocrine organ required for the storage of energy in the form of triglycerides, which is released in response to nutrient deprivation, and for the production of hormones such as leptin and adiponectin. In this way, adipose tissue is at the forefront of whole organism energy homeostasis. Adipose tissue dysfunction is associated with many metabolic diseases including T2D, cardiovascular disease and non-alcoholic fatty liver disease (NAFLD). Adipose tissue is rich in mesenchymal stem cells, known as adipocyte precursors, or adipose-derived stem cells. These multipotent cells are responsible for the production of new adipocytes, signaling to existing adipocytes, for the production of chemokines and for response to tissue stress and inflammation. The maintenance of adipose stem cell function is therefore imperative for healthy adipose tissue expansion and homeostasis. Loss of ADSC potency, function and ability to respond correctly to stimuli are emerging hallmarks of metabolic disease. Our work focuses on understanding the mechanisms leading to ADSC dysregulation, using a combination of mouse and human ADSC cell models, paired with primary adipose stem cell cultures obtained from healthy volunteers. In clinic, we derive ADSC cultures from patients undergoing bariatric surgery to better understand these processes in diseased states, and to identify potential targets for pharmaceutical intervention. Our previous work identified AMPK as a regulator of adipocyte cell fate, with exciting consequences including promotion of mitochondrial content and improved insulin sensitivity. We are currently exploring the potential of small molecule AMPK activators in ADSC metabolic regulation, particularly in the suppression of leptin, which will form the basis of this talk.

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EP1144

Impact of undernutrition in breast cancer patients during chemotherapy

Selma Mohsen[1], Berriche Olfa[1], Ben Mansour Hajer[2], Rym Ben Othman[1], Msolly Skander[1], Mezlini Amel[2] & Jamoussi Henda[1]
[1]National Institute of Nutrition, Service A, Tunis, Tunisia; [2]National Institute Salah Azaiez, Oncology, Tunis

Introduction
Malnutrition is a common issue observed in patients undergoing treatment for cancer. It stems from various factors and poses a significant challenge in the effective care of these individuals, adding complexity to their overall management. The aim of our study was to determine the prevalence of undernutrition and risk of undernutrition in women with breast cancer and its effect on chemotherapy digestive tolerance.
Methodology
This was a cross-sectional, descriptive study conducted over a 6-month period in patients with cancer patients undergoing chemotherapy. The risk of malnutrition was assessed using the Malnutrition Universal Screening Tool (MUST score). The diagnosis of undernutrition was made according to the criteria of the French National Authority for Health. A BMI < 18.5 kg/m^2;, weight loss > 10% in 6 months, grip strength < 16 kg and/or fat-free mass index < 15 kg/m^2; were the phenotypic criteria on which the study was based. The digestive effects studied were vomiting, diarrhoea and constipation. The tolerance was assessed according to WHO grades ranging from 0 to 5. High grades 3 and 4 signified toxic grades.
Results
During this period 107 patients were recorded. The mean age was 52.56 ± 9.75 years. The mean BMI was 29.85 ± 5.72 kg/m^2;. According to the MUST score, 10% was classified as being at high risk of malnutrition and 31% were at moderate risk. A BMI < 18.5 kg/m^2 was noted for only 2 patients. On the other hand, weight loss, reduced grip strength and reduced muscle mass were more frequent, with percentages of 12%, 31% and 13.1% respectively. Forty-one percent of patients were finally diagnosed as undernourished. The most marked digestive effects were transit disorders found in 80% of cases followed by nausea (70%) and vomiting (63%). They were of high grade in a third of cases. In multivariate analysis, BMI was not associated with digestive signs. However, significant weight loss and undernutrition were identified as risk factors associated with the severity of digestive effects. Undernutrition was significantly associated with the severity of vomiting (OR = 17.5) and diarrhoea (OR = 1.06). In addition, the MUST score was linearly associated with high grades of all digestive toxicities.
Conclusion
There is a close relationship between undernutrition and digestive toxicity, justifying early nutritional management in order to improve the tolerance and efficacy of chemotherapy.

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EP1145

Management of patients with obesity in the time of pandemia COVID-19

Olena Antonyuk[1,2,3]
[1]Kyiv, Nephrological Clinic with wards for Endocrinological Patients, Kyiv, Ukraine; [2]Main Military Clinical Hospital, Kyiv; [3]Bogomolets National Medical University, Kyiv

Introduction
Health promotion of decreasing weight, giving up smoking, and regular physical activity could be helpful in the improvement of individual health.
Materials and methods
We analysed the attitude of obesity and high risks for severe COVID-19 for doctors involved in diagnosing and treating such patients in 2020-2022.
Results
We asked to admit what type of facility the correspondents represented. We found that 48,4% worked in the state clinics of Ministry of Health, 32.2% chose private clinics, and 16.1% worked in the facility of other ministries (Ministry of Defence, Internal Affairs etc.). 66.7% and 73.3% of doctors answered correctly, defining the criteria of obesity and 3rd degree of obesityabout 90,3% of responders admitted the significance of body weight modification in obese patients. Most of doctors assessed medical care during pandemic as 'satisfactory' (77.4%), while 'enough good' only 16.1% and 'unsatisfactory' 6.5% with average score 3.1 from 5 possible.
Discussion
Almost 97% confirmed that recommend patients to improve their phisical activity (very likely and likely in 77.4% & 19.4% correspondingly). We found significant correlation test results between the following parameters: strong positive direct correlation between age and experience (Rxy = 0,954) and presence of doctoral category (Rxy = 0,839), moderate negative correlation between age and positive attitude to vaccine effectiveness (Rxy = –0,337), mild negative correlation of age with correct answers on the definition of obesity (Rxy = – 0,326) and the grade 3rd obesity (Rxy = –0,239), mild positive correlation of age with attitude to the preventive hospitalisation (Rxy = 0,150) and improving of phisical activity (Rxy = 0,103). Young collegues more likely thought positively on the quality of health care during COVID-19 pandemics (Rxy = – 0,285) than their older collegues. Doctors who practiced in hospital or combined both varients of clinical practice more likely assessed positive influence of preventive hospitalisation (Rxy = 0,212) and more often answered correctly defining criteria of obesity and it's degree (Rxy 0,206 and Rxy 0,118 correspondingly). It could be explained as more likely being concerned with body mass index and hospitalisation outcomes.

Practical recommendations
We propose to use a personalised lethality risk index for the assessment of risk groups of severe COVID-19, including obesity, that should be analysed (Gruzieva, T., & Antonyuk, O. (2023). Analysis of Risk factors for severe COVID-19. KIDNEYS, 12[1], 39–45. https://doi.org/10.22141/2307-1257.12.1.2023.393). In our pilot study we received positive answers on modifying obesity as a core risk factor.

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EP1146

Body satisfaction and determinants of eating behaviour in pregnant women

Yosra Hasni[1], Aya Mlayah[2], Hamza Elfekih[1], Oumayma Zarrouk[1] & Meriem Ghardallou[2]
[1]University Hospital of Farhat Hached, Endocrinology departement, Sousse; [2]University Hospital of Farhat Hached, Higher School of Health Sciences and Technologies, Sousse

Introduction
Nutrition is considered to be one of the main environmental factors influencing the outcome of pregnancy, the child's development and the mother's health (2). Given that this period is characterised by profound physiological changes (15), motherhood is a stage of psychic reorganisation due to the major bodily transformations that reactivate their bodily preoccupations (16), evoking a difficulty in adapting to their new bodies, which may expose pregnant women to anxiety, bodily dissatisfaction and problems with their eating habits (17). Objective: By referring to the multidimensional model of the development of eating disorders, our objective would be to study the eating behaviour of pregnant women and to determine the factors that influence it, and to screen pregnant women who are at risk of developing an eating disorder.
Material and methods
In order to meet this objective, a correlational cross-sectional study was conducted among pregnant women consulting MIPs in theSousse region and in two private practices over a two-month period from 01 February to 31 March 2021. We used three measuring instruments: the FIGO checklist to assess the nutritional status of pregnant women, the BAQ to assess their body image and the SCOFF which is a screening tool for OCD.
Results
Our results showed that almost all (95.5%) of our sample had an unhealthy diet that needs to be reviewed with a nutritionist in more detail. Pregnant women consumed fruit and vegetables moderately (66.5%), wholefoods were the least consumed by the women in our study, while more than half (58.8%) consumed pastries five times a week. The mean global score of the Body Attitude Questionnaire (BAQ) was 140.7 ± 17 with extremes ranging from 87 to 200. Finally, one third (32%) of the women were considered at risk of developing an OCD according to the results of the SCOFF. No significant association was found between the SCOFF and the BAQ, whereas the SCOFF was positively correlated with some subscales of the questionnaire (BAQ).
Conclusion
In terms of conclusion, our results suggest a qualitative evaluation of the nutritional status of pregnant women and action on the determining factors, as well as monitoring by perinatal care providers of their psychological status, including body satisfaction, given its impact in determining the development of CAT in the context of their daily practice.

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EP1151

Therapeutic education in type 2 diabetes, what is the relationship?

Mouna Elleuch, Insaf Nasri, Wissal Ghamgui, Khouloud Boujelbene, Charfi Nadia, Dhouha Ben Salah, Mouna Mnif, Fatma Mnif, Feten Hadj Kacem, Mohammed Abid & Nabila Rekike
Hedi Chaker Hospital, Endocrinology and Diabetology Department, Sfax, Tunisia

Background
Therapeutic Patient Education (TPE) is an educational process designed to guid people with chronic diseases, such as type 2 diabetes, to improve health care self management.
Aim
Our study seeks to determine the relationship of diabetic patients with therapeutic education programmes.
Methods
Our study involved 61 type 2 diabetic patients followed at the endocrinology department of the university hospital or followed at the city basic health centre.
Results
The mean age was 61 ± 10 years. Females predominated (60.7%), with a sex ratio (M/F) of 0.65.. We found that only one patient participated in a diabetes association. The most common explanation was "I didn't think there was such an association" and the second reason was "I'm not interested". Only 24.6% of patients were aware of therapeutic education programs. The medical and paramedical framework, as part of complementary care, was the main source of education (93.4%) required by patients. The majority (75%) of our population preferred an individual education programmes, the remainder (25%) preferred TVE in a group setting. Brochures and documents related to prescriptions were the most frequently requested by our patients (46%).
Conclusion
Despite the clinical and personal benefits offered by diabetes education, programmes of TPE are under-estimated by patients, with a lack of interest in the educational process.

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EP1163

Diabetes and autism: what correlation exists?

Malak Riznat & Guerboub Ahmed Anas
Mohamed V Military Training Hospital, Endocrinology, Rabat

Introduction
Autism is a neurodevelopmental disorder (NDD). It manifests itself in early childhood, with varying degrees of impact on the child's developmental spheres. Although the underlying mechanisms have yet to be elucidated, ASD is considered to be multifactorial, with both genetic and non-genetic risk factors. Is there an established link between diabetes and autism?
Observation
This is a 16-year-old child with no maternal history of hyperglycemia during pregnancy. No personal history of autoimmune disease, followed since the age of 4 for autistic spectrum disease, and who presented to the emergency department with a ketoacidotic decompensation.Biological signs of autoimmunity came back negative, as did the anti-GAD AC assay.
Discussion
The correlation between diabetes and the risk of developing autistic disease has been well established. A meta-analysis identified pregnancy-related factors such as diabetes as a risk factor for developing the disease [1]. The results of a retrospective cohort study show that in utero exposure to type 1 diabetes, type 2 diabetes or gestational diabetes diagnosed at 26 weeks would increase a child's risk of developing autism spectrum disorder compared with children not exposed to diabetes in utero. Meta-regression analyses revealed that children with autism had a higher associated risk of developing diabetes and hypertension than adults (3).
Conclusions
Children with autism are at high risk of developing cardiometabolic diseases such as diabetes and hypertension. Hence the need for vigilant monitoring.

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EP1170

MODY 5 associated with pancreatic intraepithelial neoplasia

Oumeyma Trimeche, Ekram Hajji, Bilel Ben Amor, Ines Bayar, Sana Abid, Héla Marmouch & Inès Khochteli
Fattouma Bourguiba University Hospital, Monastir, Tunisia

Introduction
Monogenic diabetes is a rare type of diabetes that should be evoked in the presence of associated features. Here we report a female patient with complete phenotype of MODY5 while discussing its possible complications.
Case report
A.B was 35-year-old patient with a rich family history of diabetes and renal cysts. Sha had a personal medical history of Diabetes since the age of 23 years, on basal bolus insulin regimen, recurrent episodes of urinary infections, recurrent episodes of bilateral renal lithiasis. She also had a primary amenorrhea until the age of 23 years. Gynecologic evaluation concluded to a pseudounicornuate uterus requiring hemi hysterectomy at the age of 23 years. She was admitted in our Endocrinology

department for a poorly-controlled diabetes. Upon her admission, she weighed 50 kg and had a BMI of 20.3 g/m^2. She had no signs of insulin resistance (no acanthosis nigricans nor abdominal obesity), neither autoimmune features (no vitiligo or melanoderma, nor goiter). Her HbA1c level was elevated 12 % attributable to poor adherence to her treatment s well as to diabetic diet and the recurrent urine infections. Her diabetes was complicated with severe proliferative diabetic retinopathy and sensitive diabetic neuropathy. Otherwise, she had hypomagnesemia and slightly elevated uric acid level. Her creatinine level was within the normal range. She also had elevated level of gamma-glutamyl transferase and aminotransferase. Given the family history and the association of renal cysts, renal lithiasis, young age of onset of diabetes with negative antibodies and uterine malformation, the diagnosis of MODY5 was highly suspected. Genetic testing is still ongoing. Abdominal MRI revealed the presence of an atrophic pancreas and intriguingly, pancreatic intraepithelial neoplasia (PIEN) in addition to signs suggesting chronic pancreatitis.
Discussion
This case highlights the broad clinical spectrum of MODY5 while suggesting a possible occurrence of precancerous pancreatic lesions requiring long-term follow-up. Pancreatic dysplasia often present in MODY 5 can be complicated with chronic pancreatitis and thus PIEN.

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EP1171

Glycemic balance and oral disorders

Yesmine Jallouli, Zohra Hadj Ali, Syrine Trabelsi, Olfa Lajili, Imen Hedfi, Chaima Jemai, Yosra Htira & Faika Ben Mami
National Institue of Nutrition and Food Technology, Department C, Tunis

Introduction
Diabetes is a chronic pathology. Hyperglycemia, which modifies the oral ecosystem, weakens tooth enamel and gums, thus paving the way for periodontal disease.
Aim of the study
The aim of our study was to determine the relationship between glycemic control and oral pathologies.
Materials Methods
This is a descriptive cross-sectional study that took place during the period between November 17 and December 15, 2022 in 36 diabetic patients hospitalized in department C at INNTA. Data were collected based on a stomatological examination and a biological tests.
Results
We enrolled 36 diabetic patients, 63.9% of whom were women. The mean age of our population was 45.94 ± 14.52 years. Type 2 diabetes predominated (67%) and was poorly controlled in 97% of patients. The average age of diabetes was 11.37 ± 9 years. 50% of patients were treated with insulin. Complications were frequent, the most common being retinopathy for microangiopathies (30.6% of patients) and obliterative arteriopathy of the lower limbs for macroangiopathies (16.7%). In our study, 61.1% had poor oral hygiene. The two most frequent manifestations were dental caries and mucosal inflammation in 91.7% and 75% of patients respectively. In addition, 75% of patients complained of tooth loss, 40% of whom had between 5 and 19 teeth lost. Patient knowledge and education about the oral complications of diabetes was inadequate.
Conclusion
Glycemic control plays a vital role in preventing oral complications, which must be taken into consideration.

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EP1172

Topographic diagnosis of primary hyperparathyroidism

Mohamed Abderrahmane Ahmed Ebett, Chadli Asma, El Aziz Siham & Haraj N.E
University Hospital Center Ibn Rochd - Casablanca, Casablanca, Morocco

Introduction
Primary hyperparathyroidism (PHPT) is primarily diagnosed through biological analyses. Modern imaging, particularly ultrasound and scintigraphy, plays a crucial role in localizing parathyroid adenomas.
Methods
A retrospective analysis of 132 patients with PHPT from the endocrinology-diabetology department at Ibn Rochd Hospital Casablanca, including cervical ultrasounds and parathyroid scintigraphy. Computed tomography (CT) and MRI are used as secondary resources. To have the below statistics we used SPSS software.
Results
In this studied population, the average age is 53.4 years, with a clear female predominance (85.93%). Biological examinations showed elevated levels of calcium and phosphorus, averaging 114.93 mg/l and 22.20 mg/l respectively. The average PTH level was also high, reaching 830.56 pg/ml. The majority of patients (71.87%) reported bone pain, and 23.43% were diagnosed with kidney stones. In terms of imaging, ultrasound detected parathyroid adenomas in 64.06% of patients, while scintigraphy revealed hyperfixation in 85.93% of them. CT confirmed the presence of parathyroid adenomas in 64% of cases, with hyperplasia in 6.25% and parathyroid carcinomas in 1% of cases. Additionally, vitamin D deficiency was observed in 67% of patients.
Conclusion
Cervical ultrasound appears to be more effective than parathyroid scintigraphy in the topographic diagnosis of PHPT. CT and MRI are recommended in cases of discordant results or for atypical localizations.

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EP1174

The influence of pre-existing diabetes type on the progression of pregnancy

Meryem Chakir, Salma Bensbaa, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy-University Hassan II-Casablanca-Morocco, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
The prevalence of pre-existing diabetes in pregnant women has increased over the last decade. Studies conducted on women with pre-existing diabetes type 1 (DT1) and type 2 (DT2) show higher rates of complications compared to those observed in the general population.
Objective
Comparing the two types of diabetes during pregnancy to identify whether they should be managed similarly or if a different approach is necessary.
Materials and methods
Case-control study conducted at the Endocrinology-Diabetology Department of Ibn Rochd University Hospital in Casablanca, focusing on patients with type 1 diabetes (DT1) with over 10 years of diabetes history and those with type 2 diabetes (DT2) experiencing an ongoing pregnancy.
Results
Eighty-three women with type 1 diabetes (DT1) and 94 patients with type 2 diabetes (DT2) were included in the study. The average age was 34.7 years for DT2 vs 31.7 years for DT1. History of miscarriages was 34% for DT2 vs 20.7% for DT1, and macrosomia occurred in 32% of DT2 vs 17%. The average body mass index (BMI) was 32.7 kg/m^2 for DT2, higher than 27.6 kg/m^2 for DT1. Weight gain during pregnancy was 7.2 kg for DT2 vs 5.19 kg for DT1. HbA1c during the organogenesis period was 9.2% for DT2 and 7.7% for DT1. Glycemic control was achieved in 56% of DT2 vs 45.7% of DT1. Obstetric complications were reported in 11.2% for DT2 vs 9.6% for DT1 (p: 0.4).
Conclusion
Our study indicates that the type of diabetes has no impact on the progression of pregnancy and the occurrence of obstetric complications. The early initiation of care and proper planning are crucial factors for the success of these pregnancies.

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EP1176

Study of the effect of obesity on degenerative complications of diabetes mellitus

Yasmine Fakhfakh, Chaima Jemai, Chaima Sdiri, Dorsaf Ben Salem, Hadhemi Belhassen, Sami Fitouri, Zohra Hadj Ali, Imen Hedfi, Olfa Lajili, Yosra Htira & Faika Ben Mami
National Institute of Nutrition, Department C, Tunisia

Introduction
Obesity is often associated with type 2 diabetes mellitus (T2DM). We aimed to investigate associations between obesity and degenerative complications of diabetes mellitus.
Methods
This was a cross-sectional study conducted at department C of the national institute of nutrition of Tunis including patients hospitalized for uncontrolled diabetes, in November and December 2023. Demographic characteristics, anthropometric parameters, past medical history, current treatments, glycemic control, cardiovascular risk factors, diabetes-related complications and laboratory data were collected from medical records.

Results
Ninety five patients were enrolled in our study. Sex ratio was 0.34. The mean age was 53.4±18.8 years. Mean BMI was 27.2±6 kg/m^2;. One quarter of the population (25.3%) had obesity. Hypertension and dyslipidemia frequencies were 48.4% and 48.4% respectively. The majority of our patients (70.5%) had type 2 diabetes. Mean duration of diabetes was 13.63±10 years. 67.4% were on insulintherpay and 87.4% had at least one degenerative complication, with a medical history of obliterating arteriopathy of the lower limbs, coronary artery disease and stroke in respectively 7.4%, 14.7% and 4.2% of cases. Mean HbA1c was 11.17±2.17%. Obesity was significantly associated to hypertension ($P=0.004$), dyslipidemia ($P=0.03$) pathologic albuminuria ($P<0.001$), diabetic neuropathy ($P=0.01$), coronary artery disease ($P=0.04$) and stroke ($P=0.04$).
Conclusion
According to our study, obesity seems to be associated with degenerative complications of diabetes mellitus. Thus, management of diabetic patients should be holistic. Reducing weight contribute to reach glycemic control and to reduce frequency and severity of chronic complications.

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EP1177

Diabetes and medication: knowledge and error

Yesmine Jallouli, Zohra Hadj Ali, Syrine Trabelsi, Sami Fitouri, Olfa Lajili, Imen Hedfi, Chaima Jemai, Yosra Htira & Faika Ben Mami
National Institue of Nutrition and Food Technology, Department C, Tunis

Introduction
Diabetics represent a major public health issue, which subsequently favors the regular intake of several long-term medications with drug prescriptions that can lead to the risk of iatrogenesis and iterative hospitalization.
Objectives
The aim of our study was to find out patients' knowledge in relation to the proper use of medication.
Materials and methods
This is a prospective descriptive study carried out in Service C at INNTA during the year 2022 on a sample of 50 diabetic patients. Data were collected from medical records and a questionnaire in Tunisian dialect studying the particularities of medication use by our patients.
Results
The mean age of our population was 51.54 with extremes ranging from 14 to 75 years. The sex ratio M/F was 0.6. Hypertension and dyslipidemia were the 2 most frequent comorbidities in 68% and 72% of cases respectively. Diabetes was poorly controlled in 90% of cases. A third of our patients were polymedicated, but only 56% knew their treatment by name. Most of them stored their insulin in the refrigerator (84%), but 50% did not know the shelf life of the insulin vial after opening. When it came to storing insulin on the move, 60% used a plastic bag and 36% an isothermal bag. Proper use of insulin was significantly correlated with female gender.
Conclusion
The association of several co-morbidities has a negative impact on the attitude of our patients towards taking their medication carefully, so good education is essential to limit the risk of errors, which are a source of morbidity and mortality.

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EP1190

Cognitive disorders in T2DM patients: case reports of 152 patients

Benzineb Sara[1], Saloua Elamari[2], Soukaina Laidi[2] & Marouan Fatima[2]
[1]Cheikh Khalifa Bin Zayd Al Nahyan Hospital-University Mohamed VI of Health Sciences, Endocrinology, Casablanca; [2]Cheikh Khalifa Bin Zayd Al Nahyan Hospital-University Mohamed VI of Health Sciences, Endocrinology, Casablanca, Morocco

Introduction
Cognitive decline is recognized as an important comorbidity of diabetes. The aim of this study was to determine the prevalence and predictive factors of cognitive decline in patients with type 2 diabetic patients.
Materials and methods
This was a prospective study including all elderly patients with type 2 diabetes aged between 45 and 75 years with a diabetes duration of more than five years, admitted to the endocrinology department Sheikh Khalifa University Hospital in Casablanca, between February and December 2022, we collected the clinical and metabolic characteristics. Cognitive decline was assessed by the Mini mental state examination and was retained if the score was less than 27.
Results
We included 152 patients. The median age was 64 years, median duration of diabetes was 15 years, 48.68% of patients had cognitive decline. In multivariate analysis, cognitive decline was significantly associated with the presence of diabetic retinopathy OR 0.00 (CI 4.85-0.09), elevated creatinine OR1.29 (CI 1.01-1.64) and the presence of dyslipidemia OR10.87 (CI 69-70.00).
Discussion
It is necessary to consider cognitive decline in diabetic patients because of its impact on disease progression and treatment compliance.

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EP1202

Charcot neuroarthropathy-still an unsolvable issue?

Snezana Vujosevic & Sanja Borozan
Clinical Centre of Montenegro, Department of Endocrinology, Montenegro

Charcot's neuroarthropathy (CN) is a destructive disease of the bone and joints in patients with neuropathy, often found in people with diabetes. Despite being recognized for over 150 years, the early detection and therapeutic approach remain a challenge for physicians. We present a 40-years old women, non-smoker, who was referred to endocrinologist for poorly-controlled type 2 diabetes mellitus (T2DM) and swollen left ankle and foot with sharp, stabbing pain when standing or walking. She denied any local injury. Swelling and redness developed suddenly, with increased local warmth, pain and reduced sensation; she was treated with antibiotics, local antiseptic and anticoagulant therapy for 2 weeks but without any improvement. In past medical history, she had diabetic polyneuropathy for 6 years, proliferative retinopathy, hypertension and dyslipidemia. On hospital admission, the collapse of the midfoot arch (rocker bottom foot) was noted, together with intact skin surface and slightly more diminished pulse in left dorsalis pedis artery. Plain radiograph, CT scan and NMR of the left foot were performed and joint destruction and defragmentation with multiple bone fragments (debris-loose bodies), calcifications in soft tissue around navicular bone and calcaneus, dislocation and altered structure of navicular bone and old calcaneal fracture with irregularly formed callus pointed out to CN. The condition was further managed together with orthopedic doctor using conservative, non-surgical treatment (non-weightbearing) and protective orthosis. Since the first description of CN, the pursuit for the appropriate treatment continues. Anti-resorptive treatment with bisphosphonates (mostly zolendronic acid), calcitonin, recombinant parathyroid hormone (rhPTH) showed some improvement but there is no definitive evidence of better clinical outcomes. Although the sample sizes in studies were small, the published data regarding the use of denosumab are encouraging.

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EP1203

Chronic complications of type 2 diabetes: time from diagnosis to the appearance of complications and the influence of glucoregulation on complications

Tatjana Bačun[1,2], Dunja Šojat[3], Domagoj Šimić[1], Marko Pirić[3] & Ivan Lekić[1,4]
[1]Medicinski fakultet, Department of Internal medicine, Osijek, Croatia; [2]Clinical Medical Center Osijek, Department of Internal Medicine - Endocrinology, Osijek, Croatia; [3]Osijek Health Center, Osijek, Croatia; [4]Dom zdravlja Zagreb - Centar, Zagreb, Croatia

Research objective
To examine the frequency of chronic complications of type 2 diabetes with regard to age, sex, duration of diabetes and glucoregulation.
Subjects and methods
The research included 78 subjects of both sexes with a diagnosis of type 2 diabetes treated in the Health Center of the Osijek-Baranja County. The following data were collected: gender, age, duration of diabetes, type of diabetes therapy and HbA1c, and complications of diabetes.
Results
The research was conducted on 78 patients with type 2 diabetes (T2DM), of which 34 (43.6%) were men and 44 (56.4%) were women. The median age of the subjects is 71 years, and the median duration of T2DM is 8 years. 39.7% had microvascular complications, and 26.9% had macrovascular complications. The most common microvascular complication is diabetic retinopathy (26.9%), followed by diabetic neuropathy (16.7%) and diabetic nephropathy (9%). Cerebrovascular disease (10.3%) is the most common macrovascular complication, followed by cardiovascular disease (5.1%) and peripheral vascular disease (5.1%). No complications were diagnosed in 33.3% of patients. Nephropathy was diagnosed 3 years after T2DM diagnosis,

neuropathy, retinopathy, and coronary artery disease after 5 years, cerebrovascular insult after 6 years, and peripheral vascular disease after 8 years. Patients whose HbA1c values are higher than 7.5% have retinopathy ($P=0.002$), neuropathy ($P=0.03$) and ischemic heart disease ($P=0.02$) more often. In women, the incidence of neuropathy is statistically significantly more frequent than in men ($P=0.004$). Subjects with microvascular complications were significantly older ($P=0.04$), median age 74 years, compared to those without microvascular complications.
Conclusion
Chronic complications in patients with T2DM occur most often in older patients with a longer duration of the disease and poorer regulation of diabetes. A third of the patients had microvascular complications, a quarter of the subjects had macrovascular complications. The most common microvascular complication is diabetic retinopathy, followed by diabetic neuropathy and diabetic nephropathy. Of the macrovascular complications, cerebrovascular disease is the most common, followed by cardiovascular and peripheral vascular disease. Diabetic nephropathy, diabetic retinopathy, diabetic neuropathy and coronary disease were diagnosed in the first 5 years after the diagnosis of diabetes, and cerebrovascular disease and peripheral vascular disease in the second 5 years. Patients with elevated HbA1c more often have retinopathy, neuropathy and ischemic heart disease.
Key words: Type 2 diabetes, Chronic complications, Diabetic retinopathy, Diabetic neuropathy, Diabetic nephropathy
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EP1204

Anemia and diabetic retinopathy in type 2 diabetes mellitus

Hadhemi Belhassen[1,1], Ramla Mizouri, Siwar Saoudi, Rym Ben Othman, Chaima Sdiri, Nadia Ben Amor, Olfa Berriche & Jamoussi Henda
National Institute of Nutrition, A, Tunis, Tunisia

Introduction
Anemia, known as a common complication in diabetic type 2 population, was observed to be an independent risk factor for the development of high-risk proliferative diabetic retinopathy. The aim of our study is to estimate the prevalence of anemia in persons with type 2 diabetes mellitus and its role as a risk factor in the presence and the severity of diabetic retinopathy, in a population based study.
Methods
Descriptive cross-sectional study conducted over 3 months in ward A of The National Institute of Nutrition Tunis which included patients with type 2 diabetes mellitus.
Results
Fourty-four patients were included of whom 27 were women and 17 men. The characteristics of the patients were respectively: age: 57 ± 11.2 years, Body Mass Index: 28 ± 6.5 kg/m^2, HbA1C: 10.39 ± 1.66%. The prevalence of anemia (Hb <12 g/dl in women, and <13 g/dl in men) was 18.2%. The prevalence of diabetic retinopathy which diagnosis is based on the modified Klein classification was 36.4%. In patients with a diabetic retinopathy, 33.33% were diagnosed with an anemia and 66.67% had a normal rate of Hemoglobin. In patients without diabetic retinopathy, 7.69% were diagnosed with anemia. There was no statistically significant correlation between anemia and the risk of development of diabetic retinopathy ($P=0.117$) neither the severity of diabetic retinopathy ($P=0.632$) if diagnosed.
Conclusion
Anemia is important to diagnose in patients with type 2 diabetes mellitus. However, its presence doesn't predispose neither to a high risk of diabetic retinopathy nor to a severe diabetic retinopathy if established.

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EP1208

Using hot water for heating in neuropathic diabetics: beware of disasters

Ahmed Boukhalfa, hanane boualam, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Mohamed VI University Hospital Center, Marrakech, Morocco, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Introduction
Diabetic 'neuropathies are a heterogeneous group of disorders with diverse clinical manifestations. Up to 50% of diabetic peripheral neuropathy may be asymptomatic. Glycemic control can effectively prevent diabetic peripheral neuropathy (DPN) in type 1 diabetes (T1D) (1,2) and may modestly slow their progression in type 2 diabetes (3). We report the case of a patient who presented leg burns with no healing making treatment extremely difficult.
Clinical Case
Eighty one years-old patient, diabetic since 34 years treated with insulin, admitted for complicated thermal (contact) burns to the right leg following the use of hot water contained in an unsuitable plastic bottle. Clinically, patient was hemodynamically and respiratorily stable. Examination of the right leg: deep ulceration of the anterior face of the lower third, approx. $10\times6\times1$ cm, with exposed tendons and fibrin deposits with warm red swelling of the homolateral forefoot. Biological tests: capillary glycemia: 5;29 g/l without ketosis, WBC: 11600, CRP: 290 mg/l. A dressing protocol provided by the plastic surgeons was instituted with antibiotic therapy, with no clear improvement and no scarring after 2 months of follow-up. The patient was hospitalized for skin grafting.
Discussion
Symptoms of DPN vary according to the class of sensory fibers involved. The most common early symptoms are induced by the involvement of small fibers and include pain and dysesthesia. The involvement of large fibers may cause numbness and loss of protective sensation (LOPS) and it is a risk factor for diabetic foot ulceration. Near-normal glycemic control, implemented early in the course of diabetes, has been shown to effectively delay or prevent the development of DPN mainly in T1D. Dyslipidemia is a key factor in the development of neuropathy in people with type 2 (4,5). Positive effects of physical activity, weight loss, and bariatric surgery have been reported in individuals with DPN, but use of conventional lipid-lowering pharmacotherapy (such as statins or fenofibrates) does not appear to be effective in treating or preventing DPN development (6). Our patient's long-standing diabetes and inability to feel the high temperature when using hot water, testify to the absence of the sensation of protection and confirm the advanced damage to the essentially large sensory fibers. The absence of healing is evidence of associated vascular damage.
Conclusion
Foot ulcerations and amputations are common complications associated with diabetes especially when there is a triggering mechanism such as burns.
Keywords: DPN, burn, glycemic balance, healing.
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EP1210

Carob powder-enhanced bread: a promoting alternative for the gluten-free diet

Kouloud Boujelben[1], Mohamed Khairi Arous[1], Fatma Mnif[1], Dhoha Ben Salah[1], mouna elleuch[1], Faten Haj Kacem Akid[1], Nadia Charfi[1], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker Hospital, Endocrinology, Sfax, Tunisia

Introduction
The gluten-free diet is a challenge not only for the patient and their treating physician but also for specialists in the agro-food industry. Gluten-free breads, especially those made from corn, are reputed to be of lower quality than wheat bread. In this context, we conducted a study to test gluten-free cornbread enriched with carob (GFCEC) in terms of flavor, acceptability, and glycemic index
Methods
This is a prospective study involving a group of healthy Tunisians. Our study included 7 healthy volunteers to investigate the glycemic response. We tested 3 foods: white bread, gluten-free cornbread (GFC) and GFCEC. Each tested food contains 50 g of carbohydrates, which are present in 100 g of white bread, 87 g of GFC, and 60 g of GFCEC. A rating test was employed to assess the tasted products based on a 5-point increasing hedonic scale (1 = extremely unpleasant, 5 = very pleasant) and involved 30 participants. All participants filled out an evaluation form focusing on taste, smell, aftertaste, and overall appreciation. At the end, participants selected their preferred product among the three options.
Results
The average age was 25 ± 10.18 years, and the average Body Mass Index (BMI) was 23.63 ± 5.17 kg/m^2. All 7 volunteers for the glycemic response study were females (100%). The glycemic index of GFC was 61.04%, while that of GFCEC was 40.13%, compared to the reference white bread. GFCEC had the highest percentage of taste preference (85%). The smell of GFCEC was significantly more appreciated ($P<0.001$). The aftertaste of GFCEC was the favorite among the majority of tasters (85%). Overall appreciation of GFCEC was the highest among tasters (85%). GFCEC was preferred by 90% of the participants.
Conclusion
Carob, thanks to its polyphenol-rich fiber content, possesses beneficial metabolic effects, particularly acting as a hypocholesterolemic, anti-hyperglycemic, and antioxidant agent. Its incorporation into GFC could provide both health and hedonic benefits. GFCEC could be a preferred alternative, especially for diabetic patients with celiac disease, for whom dietary management remains a perpetual challenge.

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EP1211

Psychological effects of gpp-1 agonists in the treatment of young overweight patients with type 2 diabetes mellitus (clinical case)

Liana Jashi[1], Tamar Peshkova[2], Tamar Sharashenidze[3], Ketevan Dundua[4], tamar shervashidze[4] & Sophio Beridze[1]
[1]Avicena-Batumi Medical University, Georgia, Medicine, Batumi, Georgia; [2]Batumi Shota Rustaveli state University, Medicine, Batumi, Georgia; [3]Sulkhan-Saba Orbeliani University, Medicine, T'bilisi, Georgia; [4]David Aghmashenebeli University Of Georgia, Medicine, T'bilisi, Georgia

Background
Patient: male, 34 years old, height 32.4 cm (height 182 cm, weight 118 kg), heredity not severe, history of cholecystectomy, depressive background, takes Solian and Lemonex. Bad habits - smokes tobacco, does not drink alcohol. Covid 19 in 2021, vaccinated with 2 doses of Pfizer-BioNTech vaccine. 2023 In May, he was hospitalized with hyperglycemia, where insulin therapy was started: Apidra - 9^{00} - 16IU 14^{00} – 14IU 19^{00} - 12 IU, Lantus 22^{00} - 28 IU, but the glycemic profile ranged from 160 mg% to 270 mg%.
Method
He went to our clinic in September 2023. The main complaints were glycemic variability, weight gain, burning and pain in the extremities, and numbness. Based on the conducted examinations: HbA1c - 8.2% Vitamin D3 - 13.2 ng/ml (> 30ng/ml) Complete blood and urine count Cardioechoscopy with abdominal ultrasound: liver enlarged, thyroid v = 20 ml, echogenicity normal, no nodes present—astigmatism of the eye. Hepatitis is negative, and liver function and lipid metabolism are normal. Free testosterone 7.76 ng/dl (3.03-14.8 ng/dl), GSPG-18,94 mmol/l (17.30-65.80 mmol/l, Cortisol 10.95 μg/dl (4.3-22.4 μg/dl), Creatinine 77.18 μmol/l (62.0) -115.00 μmol/l), SCF-116 ml/min (75-128.00 ml/min), Anti-GAD-antibodies 0.61 U/ml (< 5.0 U/ml), Urea 31.12 mg/dl (15.00-38.50 mg/dl), C-peptide 0.32 nmol/l (0.2-0.8 nmol/l);
Results
Diagnosis: uncontrolled T2DM (A1C >8.2%), obesity (BMI 32.4 kg/m^2), D3 vitamin deficiency. The treatment regimen/lifestyle was changed. Previously, the patient received no dietary recommendations; he was currently obese. The patient realized that excessive carbohydrate intake influenced his glucose control and agreed to improve his eating habits and walk 15–20 minutes twice daily. The treatment regimen changed and was prescribed: Ozempic 0.25 1 time a week (1 month), 0.5 1 time a week (1 month) at 1 mg... titration of the dose by months, simultaneously began to reduce the insulin dose with strict glucose control. In the evening, the patient was added metformin XR 1000 mg. Also, vitamin D3 used 5000 IU per day. A month later, the patient was completely canceled from insulin, he lost 8 kg. Motivation increased, and antidepressants decreased. After 3 months, weight decreased by 32 kg, HbA1c - 6.2%, glycemic profile adjusted, antidepressants discontinued, and the last dose of Ozempic - 1.5 mg. Treatment is ongoing.
Conclusion
Therefore, the proper management of a young patient with diabetes is of great importance; the use of GLP 1 inhibitors in relation to this patient not only reduced weight but also significantly changed his psycho-emotional state.

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EP1212

A rapid action plan to improve diagnosis and management of lipodystrophy

Lindsay Fourman[1], Josivan Lima[2], Vinaya Simha[3], Marco Cappa[4], Saif Alyaarubi[5], Renan Montenegro Jr[6], Baris Akinci[7] & Ferruccio Santini[8]
[1]Massachusetts General Hospital and Harvard Medical School, Metabolism Unit, Boston, MA, United States; [2]Hospital Universitário Onofre Lopes, Universidade Federal do Rio Grande do Norte, Departamento de Clinica Medica, Natal-RN, Brazil; [3]Mayo Clinic, Division of Endocrinology, Rochester, MN, United States; [4]Bambino Gesù Children's Hospital, IRCCS, Research Area for Innovative Therapies in Endocrinology, Rome, Italy; [5]Oman Medical Specialty Board, Pediatric Endocrinology, Muscat, Oman; [6]Federal University of Ceará, Department of Clinical Medicine, Fortaleza, Brazil; [7]DEPARK & Izmir Biomedicine and Genome Center, Izmir, Turkey; [8]University Hospital of Pisa, Obesity and Lipodystrophy Center, Endocrinology Unit, Pisa, Italy

Introduction
Lipodystrophy is a rare disease that can present with a broad range of symptoms. Delays in diagnosis are common, which in turn, may predispose to the development of severe metabolic complications and end-organ damage. Many patients with lipodystrophy are only diagnosed after significant metabolic abnormalities arise.
Aim
Prompt action by clinical teams may improve disease outcomes in lipodystrophy. The aim of the Rapid Action Plan is to serve as a set of recommendations from experts that can support clinicians with limited experience in lipodystrophy.
Methods
The Rapid Action Plan was developed using insights gathered through a series of advisory meetings with clinical experts in lipodystrophy. A skeleton template was used to facilitate interviews. A consensus document was developed, reviewed, and approved by all experts.
Results
Lipodystrophy is a clinical diagnosis. The Rapid Action Plan discusses tools that can help diagnose lipodystrophy. The roles of clinical and family history, physical exam, patient and family member photos, routine blood tests, leptin levels, skinfold measurements, imaging studies, and genetic testing are explored. Additional topics such as communicating the diagnosis to the patients/families and patient referrals are covered. A set of recommendations regarding screening and monitoring for metabolic diseases and end-organ abnormalities is presented. Finally, the treatment of lipodystrophy is reviewed.
Discussion
The Rapid Action Plan may assist clinical teams with the prompt diagnosis and holistic work-up and management of patients with lipodystrophy, which may improve outcomes for patients with this rare disease.

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EP1213

Cardiac insufficiency in morbid obesity

Ifigenia Kostoglou-Athanassiou[1], Lambros Athanassiou[2], Sofia Nikolakopoulou[3], Alexandra Konstantinou[3], Charilaos Samaras[3] & Panagiotis Athanassiou[4]
[1]Asclepeion Hospital, Voula, Department of Endocrinology; [2]Asclepeion Hospital, Voula, Department of Rheumatology; [3]Asclepeion Hospital, Voula, 1st Department of Medicine; [4]St. Paul's Hospital, Department of Rheumatology, Thessaloniki, Greece

Morbid obesity is accompanied by multiple comorbidities and may be associated with a high mortality risk. Cardiac manifestations accompany morbid obesity and may account for the increased morbidity and mortality risk which accompanies the disorder. However, cardiac insufficiency as the first cardiovascular manifestation in morbid obesity is a less recognized comorbidity. The aim was to describe cardiac insufficiency as the first cardiovascular disease manifestation in morbid obesity. A cohort of 10 morbidly obese patients (3 female and 7 male) aged 43.8 ± 6.9 years (mean ± SD) is described. Patients had a MBI of 51.3 ± 3.8 kg/m^2. None of the patients had a history of cardiac disease. Patients presented for evaluation with multiple symptoms, mainly inability to exercise and peripheral edema. They were metabolically evaluated. Mild diabetes mellitus was diagnosed. Cardiological evaluation revealed the presence of cardiac insufficiency. Morbid obesity severely affects quality of life. The disease is difficult to treat and persists. Patients although they may try to lose weight, either they cannot attain their goal, or they may gain weight again. Cardiac insufficiency as the first symptom of cardiovascular involvement in morbid obesity severely affects quality of life and may lead to early mortality. In other studies obesity accompanied by malnutrition has been associated with adverse cardiac remodeling. Patients with morbid obesity should be counseled appropriately on the possible adverse effects of morbid obesity on cardiovascular health and the possibility of early and severe cardiovascular involvement.

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EP1216

Comparison of changes in body anthropometric measurements with medical nutrition treatment of turkish and arab individuals with obesity

Ferhan Mantar[1,1], Rabia Oner Kiliç[1] & Nurseli Gürsoy[1]
[1]Bahçeşehir University, Health Science Faculty, Nutrition and Dietetics, Istanbul, Turkey

Differences in individuals' eating habits affect adherence to diets and the weight management process. Identifying factors that influence the prevalence of obesity is crucial for addressing obesity-related health issues and implementing necessary preventive measures. This study aims to compare the changes in body composition resulting from medical nutrition therapy applied to individuals of Arab and Turkish origin seeking weight loss at a specialized clinic. Additionally, it explores the impact of demographic and sociocultural characteristics, as well as dietary habits, on these changes. In this context, adults aged 20-64 with a BMI > 30 who sought weight loss at a specialized clinic were individually consulted with medical nutrition therapy. The consultations occurred at the initial meeting, followed by sessions with a one-month interval, totaling three months. Weight losses and anthropometric measurements were repeated. The Mann-Whitney U test was used to determine the source of differences in anthropometric measurements at the end of the third month. According to the test results, the differences in measurements between the first and third months were statistically significant for Turkish participants compared to Arab participants, based on mean rank values ($P<0.05$). In conclusion, personalized medical nutrition therapy within the same timeframe yielded better results for Turkish participants compared to Arab participants. The dietary habits and cultural norms of the Arab community had a more adverse impact on the diet process.

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Endocrine-Related Cancer

EP14

Machine Learning-based Online Survival Prediction Tool for Adrenocortical Carcinoma

Emre Sedar Saygili[1], Yasir S Elhassan[2], Alessandro Prete[2], Juliane Lippert[3], Barbara Altieri[4] & Cristina L Ronchi[2]
[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Faculty of Medicine, Canakkale Onsekiz Mart University, Çanakkale, Turkey; [2]Institute of Metabolism and Systems Research, University of Birmingham, United Kingdom; [3]Institute of Human Genetics, University of Wuerzburg, Germany; [4]Division of Endocrinology and Diabetes, University Hospital of Wuerzburg, Germany

Background
Adrenocortical carcinoma (ACC) is a rare endocrine cancer. We aimed to develop machine learning (ML) models for predicting clinical outcomes of patients with ACC and deploy them as a web-based decision support tool.
Methods
The S-GRAS dataset[1] was used as a training cohort ($n=942$), while the COMBI dataset[2] and new patients were used as a validation cohort ($n=220$). We used S-GRAS parameters previously described[1] for ML models. The PyCaret 3.1.0 ML library in Python was used to create models. The F1 score is calculated as the harmonic mean of sensitivity and precision. We compared sixteen ML models and chose the best by F1 score. Clinical outcomes were defined as 5-year overall mortality (OM), 1-year disease progression (DP), and 3-year DP, respectively.
Results
The study has 579, 968, and 858 patients' data for clinical outcomes, respectively. The study's 5-year OM, 1-year DP, and 3-year DP rates were 55.1%, 39.7%, and 67.6%, respectively (training + validation cohorts). Quadratic Discriminant Analysis (QDA), Light Gradient Boosting Machine (LGBM), and AdaBoost Classifier (ABC) were the best models for predicting clinical outcomes. The F1 scores of the best ML models for the training cohort were 0.79 for OM, 0.63 for 1-year DP, and 0.83 for 3-year DP; while for the validation cohort were 0.72, 0.60, and 0.83, respectively. Sensitivity and specificity for 5-year OM were 77% and 77% in the training cohort and 65%, and 81% in the validation cohort, respectively. Streamlit in Python is used for deploying the models as a website (https://acc-survival.streamlit.app).
Conclusion
We could demonstrate that S-GRAS parameters can predict OM and disease progression with an AUC range of 0.74-0.87. To the best of our knowledge, this is the first ML-based online survival tool for ACC. This app instantly gives the probability of outcomes for patients with ACC based on S-GRAS parameters after resection. Medical professionals could use it in clinical practice to drive personalised management decisions.

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EP27

Analysis of DNA methylation profiles and single nuclei RNA-seq of pediatric adrenocortical tumors reveal subgroups of clinical relevance and distinct tumor biology

Victoria Fincke[1], Maurice Lossner[1], Irmengard Sax[2], Marlena Mucha[1], Felix Dorn[1], Stefan Wudy[3], Christian Vokuhl[4], Rainer Claus[5], Marina Kunstreich[1], Christoph Slavetinsky[6], Jörg Fuchs[6], Matthias Schlesner[2], Michael Frühwald[1], Antje Redlich[7], Michaela Kuhlen[1] & Pascal Johann[1]
[1]University Hospital Augsburg, Pediatrics and Adolescent Medicine, Swabian Children's Cancer Center, Augsburg, Germany; [2]University of Augsburg, Faculty of Applied Computer Sciences, Biomedical Informatics, Data Mining and Data Analytics, Augsburg, Germany; [3]University Hospital Giessen, Pediatric Endocrinology and Diabetology, Giessen, Germany; [4]University Hospital Bonn, Department of Pathology, Section of Pediatric Pathology, Bonn, Germany; [5]University Hospital Augsburg, Augsburg, Germany; [6]University Childreńs Hospital Tuebingen, Department of Pediatric Surgery and Urology, Tuebingen, Germany; [7]University Hospital Magdeburg, Pediatric Hematology and Oncology, Magdeburg, Germany

Pediatric adrenocortical tumors (pACTs) represent a group of rare entities arising from the cortex of the adrenal gland. The mean patient age at diagnosis is 4,8 years. pACTs are divided into highly malignant pediatric adrenocortical carcinomas (pACCs) and the more benign pediatric adrenocortical adenomas (pACAs), although the exact identification of patients at high risk and the accurate pathological differentiation between pACCs and pACAs remain difficult. Most patients show signs of virilization, Cushing syndrome, or both, and germline variants of *TP53* are common. Complete tumor resection is required to achieve cure, which is particularly difficult in children with advanced disease. In our study, we analyzed DNA methylation data of pACTs from 149 patients and identified four distinct methylation subgroups of clinical relevance: One of which confered a significantly poorer prognosis than the other subgroups, with a 5-year overall survival (OS) of only 27%, while OS in the other subgroups ranged between 81%-95%. Importantly, the high-risk subgroup also contained tumors previously considered as pACA. In addition, we performed single nuclei RNA sequencing (snRNA-Seq) to reveal the biological heterogeneity underlying this disease. The methylation-derived subgroups differed in the composition of regulatory modules (so called meta-signatures), with the high-risk subgroup being enriched for proliferation-related programs (with an upregulation of e.g. *PLK1*, a pharmacologically targetable protein kinase, and *CCNE2*). Other regulatory modules which were enriched in the standard risk ACC groups displayed genes involved in steroidogenesis (such as *SULT2A1*), but also in the detoxification of xenobiotics (such as *CYP2E1*), which may contribute to chemotherapy resistance in these tumors. Performing trajectory analyses, we found that the single cell distribution of pediatric ACC recapitulates the centripetal differentiation of the adrenocortex from Zona glomerulosa to Zona reticularis - with the high-risk tumors displaying more glomerulosa-like transcriptional profiles. In accordance with this, we detected strongly upregulated WNT signaling (mainly through *WNT4*) in these high-risk tumors when performing receptor-ligand analyses. Overall, our study not only sheds light on the intertumoral and intratumoral heterogeneity of pACTs but provides means for improved risk stratification by establishing four distinct subgroups. Moreover, the single cell dissection of these tumors highlights novel drug targets, thus potentially opening new avenues for targeted therapy.

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(Abstract EP14) Table 1. Performance of the best ML models

Outcomes	Best model	Cohort	Accuracy	AUC	Sensitivity	Precision	F1	Specificity
OM	QDA	Training	0.77	0.85	0.77	0.80	0.79	0.77
		Validation	0.73	0.79	0.65	0.80	0.72	0.81
1-year DP	LGBM	Training	0.74	0.78	0.57	0.70	0.63	0.84
		Validation	0.68	0.74	0.53	0.71	0.60	0.81
3-year DP	ABC	Training	0.76	0.79	0.88	0.83	0.83	0.50
		Validation	0.77	0.87	0.79	0.83	0.83	0.71

EP36

Germline mutation in the CHEK2 gene in papillary thyroid cancer and the coexistence of other cancers

Danuta Gąsior-Perczak[1,2], Artur Kowalik[3,4], Paweł Macek[1,5], Janusz Kopczyński[6], Krzysztof Gruszczyński[3], Iwona Palyga[1,2], Agnieszka Walczyk[1,2], Piotr Przybycień[2], Monika Siołek[7], Stanislaw Gozdz[1,8] & Aldona Kowalska[1,9]
[1]Jan Kochanowski University, Collegium Medicum, Kielce, Poland; [2]Holycross Cancer Center, Endocrinology Clinic, Kielce, Poland; [3]Holycross Cancer Center, Department of Molecular Diagnostics, Kielce, Poland; [4]Jan Kochanowski University, Division of Medical Biology, Institute of Biology, Kielce, Poland; [5]Holycross Cancer Center, Department of Epidemiology and Cancer Control, Kielce, Poland; [6]Holycross Cancer Center, Surgical Pathology, Kielce, Poland; [7]Holycross Cancer Center, Genetic Clinic, Kielce, Poland; [8]Holycross Cancer Center, Clinical Oncology, Kielce, Poland; [9]Kielce, Endocrinology Clinic, Kielce, Poland

Introduction
The *CHEK2* gene is involved in DNA repair. Germline mutations in the *CHEK2* gene impair this mechanism, increasing the risk of various cancers, including papillary thyroid cancer (PTC). There are four different mutation variants in the *CHEK2* gene in the Polish population: three truncating mutations (1100delC, IVS2+1G>A and del53950) and one missense mutation (I157T).
Material
The study included 1,547 PTC patients (1,358 women and 189 men) treated in single center, median age 50 years (range 15-85).
Method
DNA samples from peripheral blood and *CHEK2* mutation genotyping was performed using TaqMan PCR (I157T) or allele-specific PCR and chip electrophoresis (IVS2 + 1G > A del5395, and 1100delC). Detected mutations (I157T, IVS2 + 1G > A, and 1100delC) were confirmed by Sanger sequencing. The patient's age, *CHEK2* mutation type and co-occurrence of other cancers were assessed.
Results
A mutation in the *CHEK2* gene was found in 240 (15.5%). The dominant mutation in the *CHEK2* gene was the missense mutation I157T, found in 189 (12.3%), while the truncating mutation (IVS2+1G>A, del5395, 1100delC) was found in 44 (2.8%). The co-occurrence of two mutations was found in 7 (0.4%) patients. No mutations in the *CHEK2* gene were detected in 1,307 (84.5%) patients. The age of patients with a *CHEK2* mutation at the time of diagnosis ranged from 18 to 76 (mean age 51 years), compared to the age of patients without the mutation - 15 to 85 (mean age 50 years). Other cancers were found in 33/240 (13.8%) patients with *CHEK2* mutations compared to 158/1307 (12.1%) patients without *CHEK2* mutations. The difference was not statistically significant ($P=0.4721$) The most common malignant tumor in women was breast cancer ($n=49$, 30.8%), including 36 (27.9%) without the *CHEK2* mutation, 10 (40.0%) with the I157T missense mutation and 3 (60.0%) with truncating mutation. There was a significant difference ($P=0.0416$) in the incidence of breast cancer in patients with and without the *CHEK2* (any) mutation. The proportion of women with breast cancer with a *CHEK2* mutation (any) was almost twice as high 13 (6.0%) compared to women with breast cancer without a *CHEK2* mutation 36 (3.2%).
Conclusions
1. Mutations in the *CHEK2* gene occur in 15.5% of PTC patients. 2. The occurrence of mutations in the *CHEK2* gene in PTC patients is associated with a higher risk of breast cancer in women, especially in the case of truncating mutation (60%), the most common in the case of del5395.

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EP45

"Deciphering the genomic complexity of thyroid cancers: an in-depth exploration through pan-exomic analysis using whole exome next-generation sequencing"

Ramesh Bangaraiahgari[1], Rajesh Bangaraiahgari[1], Ramakanth Bhargav Panchangam[2], Udaya Kumar[3], Banala Rajkiran Reddy Banala[4] & Chakrapani Bangaraiahgari[5]
[1]TRR Institute of Medical Sciences, Hyderabad, India; [2]Bhargav Endocare Hospital, Endocrine and Metabolic Surgery, Andhra pradesh, India; [3]Arundathi Institute of Medical Sciences, Pediatrics, Hyderabad, India; [4]Sunshine Hospital, CRL, Hyderabad, India; [5]Chakri Neuro Hospital, Neurology, Nizamabad, India

Background
Thyroid cancers represent a diverse group of malignancies characterized by intricate genomic landscapes, necessitating advanced molecular investigations for a comprehensive understanding of their underlying genetic alterations. This study harnesses the power of Whole Exome Next-Generation Sequencing (WES) to unravel pan-exomic mutations in thyroid cancer samples. The primary objectives include correlating genomic changes with clinicopathologic features and unravelling the intricate mechanisms steering disease onset and progression.
Methods
Raw sequencing data derived from both normal and cancerous thyroid tissues underwent a meticulous analytical pipeline. Leveraging tools such as the NGS QC Toolkit, Burrows-Wheeler Aligner, and GATK, the study commenced with a thorough assessment of read quality. Subsequent steps involved alignment of sequences to the human reference genome (hg19), recalibration of base quality, and calculation of coverage metrics. Somatic variations were identified using MuTect for single nucleotide variations (SNVs) and VarScan for small insertions and deletions (indels). ANNOVAR facilitated comprehensive annotation of the identified variants. Stringent filtering criteria excluded common single nucleotide polymorphisms (SNPs), noncoding variants, and those residing within repetitive genomic regions. Manual validation using the Integrated Genomics Viewer ensured the accuracy of the identified mutations.
Results
The study unveiled significant mutations predominantly in BRAF, CDKN2A, HRAS, NRAS, PI3KCA, RET, RAS, and TP53 genes. Noteworthy common mutations included RET (M918T), NRAS (Q61R), BRAF (V600E), HRAS (Q61R), and a missense mutation in TP53 (c.217 – c.1178). Additionally, a mutation in the KMT2D gene was identified in one patient sample, introducing an intriguing aspect to the genomic landscape.
Conclusion
This research significantly contributes to the evolving field of thyroid cancer genomics. By identifying prevalent mutations and indicating the need for ongoing efforts to detect rare mutations, our findings underscore the complexity of these cancers. The discerned genomic landscape not only advances scientific understanding but also lays the groundwork for the potential integration of precision medicine into thyroid cancer diagnosis and treatment strategies. The structured approach offers a comprehensive overview of the research methodology, key findings, and their broader implications.

Keywords: Thyroid cancers, Whole Exome Sequencing, Pan-exomic mutations, Somatic variations, Precision medicine.
Disclosure of interest: None declared
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EP83

Paraneoplastic hypoglycemia

Mouna Elleuch[1], Yassmine Abdelkafi[1,1], Khouloud Boujelben[1], Faten Hadjkacem[1], Rihab Khochtali[1], Souhir Maalej[1], Nadia Charfi[1], Fatma Mnif[1], Mouna Mnif[1], Dhoha Ben Salah[1], Mohamed Abid[1] & Nabila Rekik[1]
[1]CHU Hedi Chaker, Endocrinology, Tunisia

Introduction
Non-Islet Cell Tumor Hypoglycemia (NICTH) is a rare but serious condition. We report a case of NICTH in a patient with a gastrointestinal stromal tumor.
Observation
The patient was a 56-year-old with a history of metastatic gastrointestinal stromal tumor (GIST), diagnosed and operated on in 2016. He received tyrosine kinase inhibitors: Imatinib for 5 years, followed by sunitinib with two courses, and was later declared in palliative care due to tumor progression. He was admitted to the endocrinology department for exploration of recent severe hypoglycemic episodes occurring unexpectedly at any time of the day, with a capillary blood glucose level of 0.15 g/l at admission. Iatrogenic causes were ruled out through questioning, and general pathologies were eliminated based on normal test results. Hormone counter-regulation deficiencies were also excluded. Endogenous hyperinsulinism was refuted with insulin levels at 1 mIU/l, a collapsed C-peptide level at 0.04 ug/l, and a concurrent venous blood glucose level of 2 mmol/l. IGFII level was normal at 444 ng/ml, while IGFI level was suppressed at 30.5 ng/ml. NICTH was confirmed with an IGFII/IGFI ratio > 10. The patient was treated with corticosteroids at a dose of 80 mg/day in four divided doses (20 mg× 4/day). The course of the disease showed a decrease in the frequency and severity of hypoglycemic episodes. However, the patient succumbed to the progression of his illness one month later.
Discussion
NICTH is attributed to the secretion of an abnormal IGFII molecule, mainly by malignant tumors such as mesenchymal tumors. This molecule, called BIG IGFII immature, has a threefold stronger effect than mature IGFII. It binds to the insulin receptor, leading to its hypoglycemic effect. Diagnosis is established with an IGFII/IGFI ratio greater than 10. Treatment involves tumor excision, dietary measures to increase caloric intake and the number of snacks, along with

corticosteroid therapy at the minimum effective dose. Combining with rhGH (recombinant human growth hormone) may assist in minimizing the doses and side effects of each treatment.

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EP84

Insulin autoimmune syndrome due to alpha lipoic acid: a case report

Safiye Kızışar Yılmaz[1], Bilge Dibeklioğlu[1], Kübra Durmuş Demirel[1], Neslihan Çuhacı Seyrek[2], Oya Topaloğlu[2], Reyhan Ersoy[2] & Bekir Çakır[2]
[1]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Turkey; [2]Ankara Yıldırım Beyazıt University, Endocrinology and Metabolism

Insulin autoimmune syndrome is a condition characterized by production of autoantibodies against insulin. Drugs are one of the ethiological factors, especially when they contain the sulfydryl group such as methimazole and alpha lipoic acid. Herein we present a case report of insulin autoimmune syndrome due to alpha lipoic acid. A 77 year-old female patient presented to emergency department with syncope because of hypoglycemia. She was diagnosed with type 2 diabetes mellitus a year ago. Metformin and gliclazide was prescribed. During her follow-up, she had complaints of neuropathy, so alpha lipoic acid was added to her treatment. She also had autoimmune thyroid disease but didnot need for levothyroxine replacement. When she was questioned it was learned that she hadnot been taking metformin and gliclazide aproximately for 2 weeks, but she continued to take alpha lipoic acid. During a hypoglycemic episode insulin and c-peptide levels were examined and was compatible with hyperinsulinemic hypoglycemia. Anti-insulin antibody titer was high. She was considered to have insulin autoimmune syndrome due to alpha lipoic acid. Alpha lipoic acid was stopped, afterwards hypoglycemia was ceased, anti-insulin antibody titer decreased accordingly. There are several case reports of insulin autoimmune syndrome presented in literature due to intake of alpha lipoic acid. All of the cases had autoantibodies against insulin at presentation, cessation of hypoglycemia and deacrease of anti-insulin antibody titer after discontinuation of alpha lipoic acid. There are certain HLA allels which causes predisposition to this syndrome. Also these patients have higher incidance of other autoimmune diseases. If a patient who takes a drug containing sulfydryl group and has any of the autoimmune diseases presents with hyperinsulinemic hypoglycemia, insulin autoimmune syndrome must be considered.

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EP106

"Quantitative RT-PCR profiling reveals the regulatory landscape of miRNAs (miRNA-149-5p, miRNA-548c-3p, miRNA-3619-3p) in anaplastic thyroid cancer: implications for progression and metastasis"

Ramesh Bangaraiahgari[1], Rajesh Bangaraiahgari[1], Ramakanth Bhargav Panchangam[2], Udaya Kumar[3], Rajkiran Reddy Banala[4] & Chakrapani Bangaraiahgari[5]
[1]TRR Institute of Medical Sciences, Hyderabad, India; [2]Bhargav Endocare Hospital, Endocrine and Metabolic Surgery, Andhra pradesh; [3]Arundathi Institute of Medical Sciences, Pediatrics, Hyderabad; [4]Sunshine Hospital, CRL, Hyderabad, India; [5]Chakri Neuro Hospital, Neurology, Nizamabad, India

Objective
Anaplastic Thyroid Cancer (ATC) represents a formidable challenge in oncology due to its aggressive nature and high metastatic potential. This study delves into the quantitative assessment of microRNAs (miRNAs), specifically miRNA-149-5p, miRNA-548c-3p, and miRNA-3619-3p, to elucidate their roles in ATC progression and metastasis. Employing the robust technique of quantitative Reverse Transcription Polymerase Chain Reaction (RT-PCR), we meticulously examine the expression profiles of these miRNAs in ATC tissues, juxtaposed against adjacent normal thyroid tissues. Our findings reveal distinct and quantifiable alterations in the expression levels of miRNA-149-5p, miRNA-548c-3p, and miRNA-3619-3p in ATC, providing valuable insights into their potential as diagnostic and prognostic markers. Furthermore, the study employs RT-PCR to quantitatively assess the impact of these miRNAs on key cellular processes integral to cancer progression, such as proliferation, invasion, and metastasis.
Material and Methods
miRNA-149-5p, miRNA-548c-3p, miRNA-3619-3p expression was analyzed in ATC tissue and whole blood by Real-Time Quantitative Polymerase Chain Reaction.
Results
The investigation extends to delineating the regulatory influence of the selected miRNAs on target genes associated with ATC pathogenesis. Through quantitative analyses, we unravel the intricate molecular mechanisms underlying the suppressive effects of miRNA-149-5p on cell proliferation, as well as the regulatory roles of miRNA-548c-3p and miRNA-3619-3p in modulating cellular migration and invasion. The quantitative RT-PCR data presented herein not only contribute to a comprehensive understanding of miRNA involvement in ATC but also lay the foundation for potential therapeutic interventions. The precise quantification of miRNA expression provides a basis for developing targeted therapeutic strategies aimed at modulating these molecular regulators, thereby offering new avenues for personalized treatment approaches in the pursuit of mitigating ATC aggressiveness.
Conclusion
This study, leveraging the quantitative power of RT-PCR, advances our understanding of miRNA-mediated mechanisms in ATC, presenting a promising framework for future research and therapeutic exploration in the field of precision medicine.

Keywords: Anaplastic Thyroid Cancer (ATC), miRNAs (149-5p, 548c-3p, 3619-3p), Cancer biomarkers (early diagnostic), Therapeutic targets, Prognostic factors, Epithelial-mesenchymal transition (EMT).
Disclosure of interest: None declared
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EP132

Papillary thyroid microcarcinoma: to treat or not to treat - that is the question

Nataliya Druzhkova[1], Zinaida Afanasieva[1,2], Sofia Vasilevskaya[2], Vladimir Chernyshev[3], Vyacheslav Saveliev[4], Farida Khamzina[5], Farida Muzafarova[6], Rail Gazizov[7] & Alexei Sabirov[8]
[1]Republican Clinical Oncological Dispensary of the Ministry of Health of the Republic of Tatarstan, Department of endocrine tumors, Kazan; [2]Kazan State Medical Academy —Branch Campus of the FSBEI FPE RMACPE MOH, Department of Oncology, Radiology and Palliative Medicine, Kazan, Russian Federation; [3]Republican Clinical Oncological Dispensary of the Ministry of Health of the Republic of Tatarstan, Head and neck tumors department (#5), Kazan, Russian Federation; [4]Republican Clinical Oncological Dispensary of the Ministry of Health of the Republic of Tatarstan, Otolaryngological Department (#12), Kazan, Russian Federation; [5]Kazan State Medical Academy —Branch Campus of the FSBEI FPE RMACPE MOH, Department of Ultrasound Diagnostics, Kazan, Russian Federation; [6]Republican Clinical Oncological Dispensary of the Ministry of Health of the Republic of Tatarstan, Department of Ultrasound Diagnostics, Kazan, Russian Federation; [7]Republican Clinical Oncological Dispensary of the Ministry of Health of the Republic of Tatarstan, Department of Cytology, Kazan, Russian Federation; [8]Republican Clinical Oncological Dispensary of the Ministry of Health of the Republic of Tatarstan, Department of Pathology, Kazan

Introduction
Recently, the incidence of thyroid carcinoma (TC) has been increasing rapidly worldwide and caused with significant increase in detection of papillary thyroid microcarcinomas (PTMC), especially among young women. Most authors associate the high incidence of microcarcinomas with improved quality of diagnosis and medical supervision of population. The clinical course of microcarcinomas can be different, which gives rise to many controversies regarding their diagnosis and treatment.
Objective
The aim of the study was to assess the experience of diagnosis and management of patients with PTMC in Republican Clinical Oncological Dispensary (RCOD) of the Ministry of Health of the Republic of Tatarstan (Kazan, Russia) in the period from 2020 to 2022.
Materials and Methods
42 patients with PTMC, treated in RCOD between 2020 and 2022, were included in this study. This accounted for 4.35% of total number of patients, operated for TC over these years (966 people).
Results
There were 36 women (85.7%), aged from 21 to 83 years and 6 men (14.3%), aged from 28 to 67 years. Patients aged 45 and older accounted for 57.1% (24), fertile-age female patients - for 41.7% (15). PTMC was an accidental finding during thyroid ultrasound in most cases with EU-TI-RADS 4 and 5 in 78.6% of patients. Thyroid cytopathology reported Bethesda V and VI in 75.5% of patients. 15 patients (33.3%) underwent hemithyroidectomy with isthmusectomy, including one with central lymph node dissection (LND). Thyroidectomy was performed in 27 patients (66.7%), including 15 patients with LND (55.5%): 13 -

with central, 2 - with central and lateral. Papillary thyroid cancer was verified histologically in 100% of cases, including follicular variant in 3 patients (7.4%). Capsular invasion was found in 15 patients (35.7%), regional metastases – in 8 (19%). Combination of capsular invasion with regional lymph node metastases was diagnosed in 5 of 8 patients (62.5%). No distant metastases were detected. Tumor size up to 0.5 cm was detected in 4.7% (2), from 0.6 cm to 1 cm – in 95.3% (40) of cases. Multifocal tumor growth occurred in 6 patients (14.3%). In two of them (33.3%), multifocal microcarcinoma growth was combined with regional lymph node metastases. 12 patients (28.6%) underwent radioiodine therapy. All patients are alive without disease recurrence.
Conclusion
PTMC often affects fertile-age women (41.7%). 19% of patients had regional lymph node metastases, 35.7% - capsular invasion, 14.3% - multifocal tumor growth. Papillary microcarcinoma requires timely diagnosis and radical treatment.

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EP142

Magnetic resonance imaging in patients with immune check point inhibitors induced hypophysitis

Athina Karampela[1], Anna Angelousi[1], Akrivi Savelli[1], Petros Papalexis[1], Vasiliki Siampanopoulou[1], Alexandros-Aristeidis Lafioniatis[1], Ekaterini Leontari[2], Panagiotis Diamantopoulos[3] & Helen Gogas[4]
[1]Medical School of Athens, National and Kapodistrian University of Athens, Unit of Endocrinology, First Department of Internal Medicine, Laikon General Hospital, Athens, Greece, Athens, Greece; [2]National and Kapodistrian University of Athens, Department of Economic Studies, Athens, Greece, Athens, Greece; [3]Medical School of Athens, National and Kapodistrian University of Athens, First Department of Internal Medicine, Laikon General Hospital, Athens, Greece, Athens, Greece; [4]Medical School of Athens, National and Kapodistrian University of Athens, Unit of Medical Oncology, First Department of Internal Medicine, Laikon General Hospital, Athens, Greece, Athens, Greece

Introduction
Immune checkpoint inhibitors (ICIs), are widely used as therapeutic option in oncological patients. However, ICIs treatment is often complicated by endocrinological adverse events, such as hypophysitis. Although diagnostical approach of hypophysitis is standardized, imaging features have not been characterized yet.
Methods
Pituitary gland magnetic resonance imaging (MRI) findings were retrospectively recorded in 59 oncological patients with ICI-induced hypophysitis. Patients with cerebral or pituitary metastases were excluded. 59% of patients were treated with PD-1/PDL-1, 8% with CTLA-4, and 33% with combined PDL-1/PD-1 and CTLA-4 therapy.
Results
First MRI assessment was performed at a median time of 12 months from ICI initiation. Pituitary MRI abnormalities were described in 29 (49%) patients. Abnormal MRI findings included microadenoma ($n=8/59$, 14%), increased dimensions with heterogeneous enhancement of the pituitary gland ($n=7/59$, 12%), partially empty sellar ($n=8/59$, 14%), cyst at the adeno-neuropituitary border ($n=2/59$, 3%), reduced size of the pituitary gland ($n=1/29$, 2%), slight deviation of the pituitary peduncle with submergence in the sellar ($n=1/59$, 2%), thickening of the lower peduncle of the pituitary gland ($n=1/59$, 2%) and pathological tissue in sellar (possibly inflammation) ($n=1/59$,2%). Seven patients had a second MRI performed at a 17 months median time from the first MRI. Four patients presented with stable MRI findings. From the remaining patients, one with a microadenoma showed a partially empty sellar turcica, another one with a normal initial MRI also had a partially empty sellar turcica, and the last one with thickening of the pedicle, showed increased dimensions of the gland. Twenty patients out of 29 with an abnormal MRI presented an affected corticotrophin axis. 69% ($n=6/19$) of them represented mostly pituitary microadenomas. Five patients out of 29 presented with corticotropin and thyrotrophic axis deficiency and the last 4 patients had 3 axis insufficiency (corticotrophin, thyrotropin and gonadotrope). Although hypophysitis was biochemically reversible in 6 out of 59 patients, MRI pathological findings persisted in 5 of them even after pituitary-axes restoration after a median follow-up 37 months.
Conclusion
An abnormal MRI was found in 49 % (29/59) of patients with ICI-induced hypophysitis. Microadenoma and empty sella were the commonest findings (28% of the cases). In some cases, MRI abnormalities persisted even after restoration of the pituitary axes.

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EP152

Tumor behaviour in neuroendocrine tumors (NETs) of unknown primary versus known primary site location

Calin Cristiana[1,2], Ramona Dobre[1,2], Iulia Florentina Burcea[1,2], teodor constantin[1] & Catalina Poiana[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Pituitary and Neuroendocrine Disorders Department, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Endocrinology Department, Bucureşti, Romania

Introduction
While most of neuroendocrine tumors (NETs) primary sites are discovered, NETs of unknown primary are not entirely uncommon in the clinical setting. The primary site is a significant factor in terms of overall prognosis. The aim is to determine whether NETs of unknown primary site location (NET-USs) have more aggressive behavior than those with a known primary location.
Matherials and Methods
We retrospectively studied 50 consecutive patients with NETs, who presented in our clinic between 2018 and 2023: 9 patients with NET-USs and 41 patients with well-differentiated, gastroenteropancreatic neuroendocrine tumors (GEP-NETs, 16 patients with pancreatic NETs).
Results
The incidence of NET-USs was 18% ($n=9$). The median age at diagnosis and duration of disease in the NET-USs patients were 55 $\pm$15.9 years, respectively 4.5$\pm$3.8 years, compared to 62$\pm$11.2 years, respectively 5$\pm$5.6 years in GEP-NETs patients. At the time of diagnosis, 66.7% of NET-USs patients presented with distant metastases (mainly hepatic - 88%), versus 31.7% of patients with known primary. Majority of NET-USs patients underwent 68Ga-DOTATATE PET/CT or 99mTc-Octreotide SPECT/CT, with no origin discovered, only high uptake in hepatic metastases. Incidence of multiple organ metastases was 11.1% in NET-USs patients, respectively 31.7% in the known primary group. All patients with NET-USs received treatment with somatostatin analogues (SSAs), and one underwent hepatic metastases removal, while patients with known primary received, in addition to SSAs, more aggressive regimens, systemic therapy (chemotherapy, Everolimus, Sunitinib) and liver metastases-targeted therapies (PRRT, chemoembolization). Median progression free survival was 38 months in NET-USs patients compared to 30 months in GEP-NETs patients. At the last evaluation, 33.3% of NET-USs patients and 36.6% of patients with known primary presented progressive disease, according to RECIST criteria. No death was registered in NET-USs subgroup, while 5 deaths occurred in the GEP-NETs patients, with an overall survival of 60 months.
Conclusions
Althought the majority of studies in the literature postulated that patients with unknown primary site exhibit markedly poor prognosis, we showed similar outcomes in both subgroups. In fact, in our serie, NETs with known primary site showed a greater tendancy for multiple organ involvement, respectively more agressive regimens were needed to acquire disease control, nevertheless expressed a poorer progression free survival compared with NET-USs, most likely due to a higher tumor burden.

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EP157

A rare case of functioning adrenocortical carcinoma: attaining the balance between deep vein thrombosis, pulmonary embolism and post-operative hemorrhage

Ada Teo[1], Pei Chia Eng[1], Rajeev Parameswaran[2], Michelle Poon[3], Run Ting Chin[1], Chin Meng Khoo[1] & Doddabele Deepak[1]
[1]Division of Endocrinology, Department of Medicine, National University Hospital, National University Health Systems, Singapore; [2]Division of Endocrine Surgery, Department of Surgery, National University Hospital, National University Health Systems, Singapore; [3]Department of Hematology-Oncology, National University Hospital, National University Health Systems, Singapore

Background
Adrenocortical carcinomas (ACC) are rare aggressive tumors occurring at a rate of less than two per million per year. Uncommonly, there can be intravascular extension into renal veins and inferior vena cava (IVC), with resultant poorer prognosis.
Clinical Case
A 26-year-old woman was referred for investigation of a two-month history of persistent left-sided abdominal pain - Computed tomography (CT) revealed a heterogeneous 12 cm left adrenal mass with thrombosis of left renal vein and IVC. On suspicion of ACC, biochemical tests showed combined hypercortisolism and

hyperandrogenism (unsuppressed 1 mg dexamethasone overnight test 546 nmol/l [$n<50$], midnight salivary cortisol 364 ng/dl [$n<100$], DHEA 50.59 µmol/l [$n<13.9$], testosterone 12.4 nmol/l [$n<1.9$], ACTH <0.7 pmol/l [1.6-13.9]). Further imaging by ^{18}F-FDG-PET-CT showed no distant metastasis. As the imaged thrombus was heterogeneous with high FDG avidity (Standard uptake volume SUV_{max} 19.6, compared to tumor SUV_{max} 23.1), it was determined as tumor thrombus instead of bland thrombus. Therefore, only prophylactic dose subcutaneous enoxaparin 40 mg daily was administered. Whilst awaiting curative resection, she developed lower limb deep vein thrombosis over the left common, internal and external iliac veins. Doppler ultrasound features suggested bland thrombus this time, with repeat CT revealing new pulmonary embolism. Anticoagulation was then escalated to therapeutic dose enoxaparin 1 mg/kg twice-daily until the day before surgery. The patient underwent enbloc left adrenalectomy, left nephrectomy, caval thrombus resection with mechanical thrombectomy of IVC and iliac thrombus. Intra-operatively, embolic protection discs were also deployed into the suprahepatic segment of IVC. Histopathology was consistent with ACC, with Ki67 index of 25%. The post-operative process was complicated by anterior abdominal wall hematoma. In view of ongoing need for anticoagulation, prophylactic embolisation of inferior epigastric and iliac arteries was carried out. 48h post-embolisation, therapeutic dose enoxaparin was restarted. However, 2 months later, she experienced hemorrhagic shock with hemoglobin level of 5.4 g/dl ($n>11.5$g/dl). Abdominopelvic CT then showed a large 14.5 cm hematoma, but with concomitant thrombosis of right renal vein, adjacent IVC, splenic infarct and spinal cord infarct.

Conclusion

This interesting case highlights the importance of recognising ACC as a hypercoagulable state-due to direct tumor invasion, tumor thrombi or secondary to hypercortisolism. Clinicians should be aware of this unique sequence of progression and associated complications. Recognition of venous invasion has clinical significance and management implications, highlighting the value of radiological modalities in differentiating tumor thrombus from bland thrombus. Timely implementation of anticoagulation is crucial and should be a tailored regimen considering individual risk factors and surgical plans.

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EP158

A new kind of hypophysitis: adverse effect of ICPIs

Belvis Torres Arroyo[1], Ana Martinez[1], Carolina Suarez[1], Gonzalo Maldonado[1], Jose Gomez[2], Miguel Angel Valero[1], Ivan Quiroga[1] & Benito Blanco[1]

[1]Hospital General Universitario Nuestra Señora del Prado, Endocrinology, Talavera de la Reina, Spain; [2]Hospital General Universitario Nuestra Señora del Prado, Oncology, Talavera de la Reina, Spain

Introduction

Hypophysitis is a rare disease. Lately, it is more frequent due to the use of Inmune Check Point Inhibitor (ICPIs). Ipilimumab or combo Ipilimumab + Nivolumab are the main cause. Agree with literature, 17-18% of the patients with these drugs suffer from. By contrast, with Idiopatic Autoimmune Hypophysitis and Lymphocytic Hypophysitis, this type of hypophysitis occurs in sixties men. Autoinmunity mechanism is known, but precise pathophysiology is unclear

Case

A seventy-four years old man diagnosed renal carcinoma (T3NxMx) seven years ago. In 2023, a progression lymphatic nodal mediastinal and lung micrometastasis were confirmed. Consequently, he received first line treatment with Ipilumab-Nivolumab. Twelve weeks later, previous to filth cycle, he had a syncopal crisis with hypotension and bradycardia. Moreover, the patient referred to feel cold, mental slowing, constipation and visual disturbances one month ago. Also, sickness and weakness two weeks ago. Urgently stress dose of Hydrocortisone was started. Finally, analytics confirmed the diagnosis: 0,1 mg/dl cortisol, Na 133,4 mmol/l, K 3,51 mmol/l. TSH 0,06 mcUI/ml, T4L 0,93 ng/dl, T3L 4,54 ng/dl. Rest of pituitary hormones are regular. So, Levotiroxina was started too. Magnetic Resonance showed pituitary enlargement. One month later, the patient refers visual deficit had corrected. Overall status of the patient is better and blood pressure is normal. In the analytics, hypocortisolism and hypothyroidism are with replacement treatment correctly. Three months later, Magnetic Resonance showed pituitary smaller and partial empty sella. On the other hand, lung micrometastasis disappeared and lymphatic nodal mediastinal were stabled. So, the patient received fifth cycle of Ipilimumab-Nivolumab

Conclusion

- Nowadays, hypophysitis is more frequent in Oncology Patients.
- The main immune-related adverse effects (IrAE) produced by CTLA-4 inhibitor (Ipilumumab) is hypophysitis
- According to literature, Hypophysitis secondary to Ipilimumab-associated is a clinical entity distinct from anti-PD-1 hypophysitis (Nivolumab, Pembrolizumab)
- In our case the diagnosis did when four treatment cycles were received, according to literature.
- Hormonal deficiency more frequent is ACTH, followed to TSH and FSH/lH
- IrAE due to Ipilimumab-Nivolumab need hormonal treatment by long term, permanently in most cases.
- Recognition and timely diagnosis of these patients avoid unnecessary potential effects on morbidity and mortality from untreated adrenal insufficiency and stopping ICPIs

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EP183

Clinical and pathological predictors of death for adrenocortical carcinoma

Eduardo Pato[1], Victor Srougi[1], Claudia Zerbini[2], Felipe Ledesma[3], Fabio Tanno[1], Madson Almeida[4], William Nahas[1], Ana Claudia Latronico[4], Berenice Mendonca[4], Jose Chambô[1] & Maria Candida Fragoso[4]

[1]Hospital das Clínicas, University of São Paulo School of Medicine, Division of Urology, São Paulo, Brazil; [2]Hospital das Clínicas, University of São Paulo School of Medicine, Division of Pathology, São Paulo, Brazil; [3]Hospital das Clínicas, University of São Paulo School of Medicine, Division of Pathology, São Paulo, Brazil; [4]Hospital das Clínicas, University of São Paulo School of Medicine, Division of Endocrinology, São Paulo, Brazil

Adrenocortical Carcinoma (ACC) is a rare and lethal disease with a poor prognosis. This study aims to share our 41-year experience as a referral center, focusing on identifying risk factors associated with ACC mortality. Our retrospective analysis included a cohort of 150 adult patients with ACC in all stage categories, treated between 1981 and 2022. Tumor hormonal hypersecretion was observed in 78.6% of the patients, and the median age of diagnosis was 40 years. The majority presented as ENSAT III or IV (22.9% and 31.2%, respectively), and the overall mortality rate was 54.6%. Independent predictors of death were elevated secretion of cortisol (HR = 2.0), androstenedione (HR = 2.2), estradiol (HR = 2.8), 17-OH progesterone (HR = 2.0), and 11-deoxycortisol (HR = 5.1), higher Weiss (HR = 4.3), modified Weiss (HR = 4.4), and Helsinki scores (HR = 12.0), advanced ENSAT stage (HR = 27.1), larger tumor size (HR = 2.7), higher Ki-67% (HR = 2.3), and incomplete surgical resection (HR = 2.5). Mitosis >5/50HPF (HR = 5.6), atypical mitosis (HR = 2.3), confluent necrosis (HR = 15.4), venous invasion (HR = 2.8), and capsular invasion (HR = 2.4), were also identified as independent predictors of death. Knowing the risk factors for ACC's mortality may help determine the best treatment option.

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EP185

Translaryngeal ultrasound (TLUS) as a novel method of vocal folds evaluation in patients undergoing neck surgery

Sylwia Wolff[1], Adam Gałązka[1] & Marek Dedecjus[2]

[1]National Oncology Institute of Maria Sklodowska-Curie – National Research Institute, Department of Endocrine Oncology and Nuclear Medicine, Warsaw, Poland; [2]National Oncology Institute of Maria Sklodowska-Curie – National Research Institute, Department of Head and Neck Cancers, Warsaw, Poland

Introduction

One of the most serious complications after thyroid surgery is dysfunction of the recurrent laryngeal nerve (RLN). RLN damage leads to disorders of the vocal folds (VFs). The "gold standard" method in VFs assessment is laryngoscopy, which causes significant discomfort to patients, requires consultation with an ENT specialist and additional equipment.

Purpose

The aim of the study was to prospectively evaluate translaryngeal ultrasound (TLUS) in the assessment of VFs function in patients after thyroid, parathyroid and neck lymph node surgeries. An additional goal was to identify preoperative and intraoperative factors that increase the risk of RLN damage.

Methods

The prospective study included a total of 219 patients who underwent 230 surgical operations. Patients' vocal folds were analyzed independently by both TLUS and laryngoscopy before and after surgery. Additional variables obtained during TLUS were assessed, such as vocal fold displacement velocity (VFDV), arytenoids symmetry and more. In addition, a questionnaire was conducted to assess the discomfort experienced by patients during the examination with both

methods. A multivariate analysis of prognostic factors for the occurrence of RLN dysfunction was performed.
Results
Thyroid cancer surgeries constituted 85% of all procedures. The incidence of RLN injury was 10.4% in all patients and 11.7% in the oncological subgroup. There were 1.7% transient and 8.7% permanent RLN injuries. The accuracy of TLUS compared to laryngoscopy was 98.3%, sensitivity 98.1%, specificity 100%. Laryngoscopy caused significantly more discomfort than TLUS. Detection of VFs in the whole group using TLUS was 94%. VFs were visualized in more women (99.0%) than men (76%). VFs visibility was lower among males, smokers, patients with higher BMI, multifocal cancer, higher left thyroid lobe volume. VFDV was lower for the vowels "a" and "e" on the right and "e" on the left side after RLN injury. Among patients with RLN damage TLUS more often showed VFs and arytenoids asymmetry and crescendo-decrescendo Doppler wave pattern. Factors contributing to RLN dysfunction included: lateral nodes metastases and theirs dissection, lymph nodes involvement and RLN entrapment to the tumour.
Conclusions
TLUS in a majority of cases can adequately assess whether the function of the VFs is intact or paresis/paralysis has occurred. It is non-invasive and rapid. It adds no extra cost and can be a part of the preoperative examination of the thyroid gland. TLUS in VFs assessment before and after thyroid surgery is a highly accurate tool and in most patients was not inferior to laryngoscopy.

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EP191

Proteins and peptides from granin family in patients with adrenal incidentalomas and PPGLs

Alicja Szatko[1,2], Dorota Leszczynska[1], Nadia Sawicka-Gutaj[3], Barbara Bromińska[3], Urszula Ambroziak[4], Lucyna Papierska[1], Marta Araujo Castro[5,6], Henrik Falhammar[7,8], Wojciech Zgliczyński[1] & Piotr Glinicki[1,2]
[1]Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland; [2]EndoLab Laboratory, Centre of Postgraduate Medical Education, Warsaw, Poland; [3]Department of Endocrinology, Metabolism and Internal Medicine, Poznań University of Medical Sciences, Poznań, Poland; [4]Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland; [5]Endocrinology & Nutrition Department, Hospital Universitario Ramón y Cajal & Instituto de Investigación Biomédica Ramón y Cajal (IRYCIS), Madrid, Spain; [6]University of Alcalá, Madrid, Spain; [7]Department of Endocrinology, Karolinska University Hospital, Stockholm, Sweden; [8]Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden

Introduction
Adrenal incidentalomas are tumors incidentally discovered on imaging tests. Regarding functionality, although 75% of adrenal incidentalomas are non-functioning cortical adenomas (NFAA), there is a subset of adrenal incidentalomas associated with important clinical consequences: adrenocortical cancer (ACC), pheochromocytoma (PHEO, together with paraganglioma (PGL) referred as PPGL), primary aldosteronism (PA), mild-autonomous cortisol secretion (MACS) and Cushing syndrome (CS). The granin family consists of numerous proteins and derived peptides. The aim of this project was to evaluate the clinical usefulness of various proteins/peptides from the granin family in the diagnostics of patients with adrenal incidentalomas and PGLs.
Materials and methods
80 patients with various adrenal tumors (PHEO, PA, ACC, MACS, CS, NFAA) and PGL were enrolled in the study. Plasma/serum concentrations of selected proteins/peptides were determined in all patients: Chromogranin A and derived peptides: Pancreastatin, Serpinin, WE-14, Catestatin, Vasostatin-2, and Chromogranin B, Secretogranin II and Secretoneurin. The concentration of the tested proteins and peptides in serum/plasma were determined by the ELISA/EIA method.
Results
The following results of tested biomarkers differentiating individual syndromes (PHEO, PGL, PA, ACC, MACS, CS) against patients with NFAA were obtained: PHEO vs NFAA: CgA ($P=0.005$), Vasostatin-2 ($P=0.019$), Secretoneurin ($P=0.002$), and SgII ($P=0.001$). PA vs NFAA: Pancreastatin ($P=0.039$). PGL vs NFAA: Secretoneurin ($P=0.021$), and SgII ($P=0.002$). ACC vs NFAA: Serpinin ($P=0.044$). CS vs NFAA: Serpinin ($P=0.011$), Pancreastatin ($P=0.045$), Secretoneurin ($P=0.039$), and SgII ($P<0.001$). MACS vs NFAA: SgII ($P=0.011$). Usefulness of the biomarkers tested in differentiating between the two groups of patients with hypercortisolemia, was not demonstrated.
Conclusions
The obtained results showed different usefulness of the tested proteins and peptides from granin family: CgA (PPGLs), Secretoneurin (PPGLs, CS, PA), SgII (PPGLs, CS), Pancreastatin (PA, CS), Vasostatin-2 (PPGLs) and Serpinin (ACC).

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EP199

A rare case of encapsulated medullary thyroid cancer

Emin Mammadov[1], Ionut Bogdan Sandu[1], Dana Terzea[2] & Mihai Ciprian Stoicea[1]
[1]Regina Maria Private Healthcare Network, Bucureşti, Romania; [2]Onco Team Diagnostic, Bucureşti, Romania

Background
Medullary thyroid carcinoma (MTC) is a rare thyroid tumor (around 2% of thyroid cancers). Its prognosis is generally worse than for differentiated thyroid cancers. A very rare subset of MTC is described as encapsulated MTCs. To date, a limited number of case reports and case series have been published, and this type of tumor presents with no evidence of metastases even in case of very high levels of serum calcitonin.
Case
A 33-year old pregnant woman, diagnosed incidentally with a suspicious nodule in the right thyroid lobe (taller-than-wide, hypoechoic, well-defined, regular border). She also had slightly elevated serum calcitonin 20 pg/ml, which increased to 27 pg/ml in 4 weeks, along with slightly increased CEA 5.08 ng/ml, and FNAB was performed. The cytological result was benign (Bethesda II). She returned to our clinic at 3 months post-partum with a calcitonin level of 36 pg/ml and increased anxiety, her thyroid nodule had less suspicious appearance (wider-than-tall, more anechoic zones). She underwent a core-needle biopsy with a result suggesting a Hürthle-cell neoplasm (KTA-CNB IVc). The next step was a diagnostic right hemithyroidectomy with a pathology report suggesting a benign follicular lesion with some atypia. Hence, the IHC (immunohistochemistry) was performed and revealed a low-grade encapsulated MTC, follicular variant with Ki-67 1%, CK-19 and CD-56 positive, Thyroglobulin and Galectin-3 negative, Calcitonin, CEA, Chromogranin-A positive. Postoperatively, the patient had undetectable calcitonin, normal CEA (1.26 ng/ml), no pathological findings on neck ultrasound (no nodular lesions in her left thyroid lobe, no suspicious lymph nodes in central or lateral neck) . The endocrinologist's advice was to test for hereditary RET mutations, as well as somatic mutations and to follow up with neck ultrasound and calcitonin measurements. The surgeon advised her to opt for total thyroidectomy and the patient's decision was to avoid any risk and undertake surgery. A contralateral lobectomy with ipsilateral lymph node dissection were performed to minimize any risk and better stage the disease. Postoperative pathology did not reveal any foci of thyroid cancer in the left lobe and no lymph node metastases.
Conclusion
This case reflects the importance of the multidisciplinary team discussion. Logistic and financial difficulties in genetic testing also contributed to patient's decision to choose the second surgery. We probably need more data on these tumors to be able to classify them as benign (adenoma?) or very low-risk tumors which could reduce anxiety of the patients and doctors.

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EP213

Chromogranin A (CgA) in patients with pheochromocytomas and paragangliomas (PPGLs)

Piotr Glinicki[1,2], Alicja Szatko[1,2], Jan Calissendorff[3,4] & Henrik Falhammar[3,4]
[1]Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland; [2]EndoLab Laboratory, Centre of Postgraduate Medical Education, Warsaw, Poland; [3]Department of Endocrinology, Karolinska University Hospital, Stockholm, Sweden; [4]Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden

Introduction
Pheochromocytomas (PHEO) and paragangliomas (PGL) - (PPGLs) are neuroendocrine tumors derived from chromaffin cells of the adrenal medulla or extraadrenal nonchromaffinic tissue, respectively. PPGLs occur in 0.05% to 0.1% of patients with secondary hypertension. Chromogranin A (CgA) is the main non-specific biomarker of neuroendocrine tumors. It is produced and secreted into the blood by endo- and neuroendocrine cells of various organs (e.g., adrenal glands). The sensitivity of the determination of this biomarker in the diagnosis of pheochromocytoma exceeds 80%-90%. Current immunoassays for the determination of CgA concentrations in the blood differ from each other, e.g. they recognize different fragments of CgA, are calibrated differently, and use different antibodies (monoclonal/polyclonal).
Aim of the study
The aim of this study was to compare the determination of CgA concentrations and the CgA/URL (Chromogranin A concentration/Upper Reference Limit) ratio by different immunochemical methods in patients with PPGLs diagnosed in two European centers (Poland and Sweden).

Materials and Methods
The analysis included 161 patients with PPGLs from 2 centers: Poland (PHEO 63, PGL 7) and Sweden (PHEO 74, PGL 17). Serum or plasma CgA concentrations were determined by various immunochemical methods (RIA, IRMA and ELISA), and plasma metanephrine and normetanephrine concentrations were determined by chromatographic methods (LC-MS/MS or HPLC-ECD) in all subjects. Reference range for the tests: CgA < 98 ng/ml (Poland), CgA < 3 nmol/l (Sweden). Results are presented as concentration ranges (median) and CgA/URL ratio (multiplicity URL).
Results
In the patient population (Poland), CgA concentrations in patients with PHEO were in the range of 16-1234 ng/ml (median 176.8 ng/ml), while the CgA/URL_{PHEO} ratio was 0-12. In PGL patients, the range of CgA concentration was 46-772.5 ng/ml (median 98 ng/ml), and the CgA/URL_{PGL} ratio was 0-8. In the patient population (Sweden), CgA concentrations in patients with PHEO were in the range of 1.0 - 367.0 nmol/l (median 8.85 nmol/l), while the CgA/URL_{PHEO} ratio was 0 - 122. In PGL patients, the range of CgA concentration was 1.1-23.0 nmol/l (median 6.9 nmol/l), while the CgA/URL_{PGL} ratio was 0-6.7.
Conclusions
The CgA/URL ratio in PPGLs is more useful than the determination of blood CgA concentration in the comparative diagnosis of patients diagnosed at different centers and allows clinical comparison of different immunoassays used in routine clinical diagnosis.

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EP214

Malignancy subtype and clinical evolution of thyroid nodules with indeterminate cytology

Diana-Simina Luca[1], Laura Zaifu[2], Bogdan Radu Ditescu[1], Andrei Stan[1], Dana Terzea[3], Carmen Cristea[3], Dumitru Ioachim[3], Dan Alexandru Niculescu[1,2] & Catalina Poiana[1,2]
[1]"C.I. Parhon" National Institute of Endocrinology, First Endocrinology Department, Bucharest, Romania; [2]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [3]"C.I. Parhon" National Institute of Endocrinology, Department of Pathology, Bucharest, Romania

Introduction
The Bethesda System for Reporting Thyroid Cytopathology (TBSRT) allows the correlation between six individual diagnostic categories with the risk of malignancy, and offers a standardized management algorithm for each category. Atypia of undetermined significance (AUS) and follicular neoplasm categories are considered indeterminate categories, with varying malignancy rates and subtypes.
Aim
To establish the malignancy rate and subtype of cancer in thyroid nodules with indeterminate cytology results and to observe their clinical evolution.
Materials and Methods
We retrieved from our endocrinology center database all fine-needle aspiration (FNA) procedures performed by a single endocrinologist between February 2018 and April 2023. We excluded the first 500 procedures, which represented the learning curve, and all parathyroid and lymph node FNA procedures.
Results
There were 2465 nodules. Of the 51 (2.06%) patients with AUS, 15 (29.41%) patients had an available pathology report: 11 (73.33%) patients with follicular adenoma and 4 (26.66%) patients with thyroid carcinoma - 1 classic papillary thyroid carcinoma (PTC), 2 diffuse sclerosing PTC, 1 medullary thyroid carcinoma (MTC). Of the 100 (4.05%) patients with follicular neoplasm, 57 (57%) had an available pathology report: 31 (54.38%) patients with follicular adenoma and 26 (45.61%) patients with thyroid carcinoma - 21 patients with PTC (9 classic, 5 follicular, 2 tall cell, 2 diffuse sclerosing, 1 solid/trabecular, 1 NIFTP, 1 oncocytic), 4 with follicular neoplasm and 1 with poorly differentiated thyroid carcinoma. Twenty (66.66%) patients with carcinoma underwent radioiodine therapy, 11 (36.66%) had a suppressed thyroglobulin at the last follow-up, 4 (13.33%) had a persistent/recurrent local disease, 4 (13.33%) had metastatic disease and 10 (34.48%) were lost to follow up. The patient with MTC had a negative MEN2A screeing, a negative RET mutation and an increasing serum calcitonin value at the last follow up. None of the patients have had a thyroid carcinoma related death.
Conclusions
Although the majority of operated nodules with indeterminate cytology results are benign (58.33%), these results reported in our centre are lower than literature data. The most common type of carcinoma in these patients was classic PTC (33.33%). The clinical evolution of these patients varies widely according to malignancy subtype.

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EP223

Opposing effects of cannabidiol (CBD) on pheochromocytoma/paraganglioma and neuroendocrine tumor cell lines and individual patient-derived primary cultures

Katharina Wang[1], Laura Schober[1], Alessa Fischer[2], Nicole Bechmann[3], Julian Maurer[4], Lea Peischer[1], Astrid Reul[2], Constanze Hantel[2,4], Martin Reincke[1], Felix Beuschlein[1,2,5], Mercedes Robledo[6,7], Hermine Mohr[8], Natalia Pellegata[8,9], Katharina Schilbach[1], Thomas Knösel[10,11], Matthias Ilmer[11,12], Martin Angele[11,12], Matthias Kroiss[1,13], Umberto Maccio[14], Martina Broglie-Däppen[15], Diana Vetter[16], Kuno Lehmann[16], Karel Pacak[17], Ashley Grossman[18,19], Christoph Auernhammer[1,11], Kathrin Zitzmann[1] & Svenja Nölting[1,2]
[1]LMU University Hospital, Department of Internal Medicine IV, Munich, Germany; [2]University Hospital Zurich (USZ) and University of Zurich (UZH), Department of Endocrinology, Diabetology and Clinical Nutrition, Zurich, Switzerland; [3]University Hospital Carl Gustav Carus, Institute of Clinical Chemistry and Laboratory Medicine, Dresden, Germany; [4]University Hospital Carl Gustav Carus Dresden, Department of Internal Medicine III, Dresden, Germany; [5]The LOOP Zurich - Medical Research Center, Zurich, Switzerland; [6]Spanish National Cancer Research Center (CNIO), Hereditary Endocrine Cancer Group, Madrid, Spain; [7]Centro de Investigación Biomédica en Red de Enfermedades Raras, Madrid, Spain; [8]Helmholtz Center Munich, Institute for Diabetes and Cancer (IDC), Munich, Germany; [9]University of Pavia, Department of Biology and Biotechnology, Pavia, Italy; [10]Faculty of Medicine, LMU Munich, Institue of Pathology, Munich, Germany; [11]LMU University Hospital, Interdisciplinary Center of Neuroendocrine Tumors of the GastroEnteroPancreatic System (GEPNET-KUM, ENETS certified Center of Excellence), Munich, Germany; [12]LMU University Hospital, Department of General, Visceral, and Transplantation Surgery, Munich, Germany; [13]University Hospital Würzburg, Department of Medicine I, Division of Endocrinology and Diabetes, Würzburg, Germany; [14]University Hospital Zurich, Department of Pathology and Molecular Pathology, Zurich, Switzerland; [15]University Hospital Zurich, Department of Otorhinolaryngology, Head and Neck Surgery, Zurich, Switzerland; [16]University Hospital Zurich, Department of Visceral and Transplantation Surgery, Zurich, Switzerland; [17]Eunice Kennedy Shriver NICHD, Bethesda, United States; [18]University of Oxford, Green Templeton College, Oxford, United Kingdom; [19]Royal Free Hospital, NET Unit, ENETS Centre of Excellence, London, United Kingdom

The recreational use of cannabis is becoming more widespread since many countries, including parts of Europe, are currently discussing legalisation. Moreover, the medical use of cannabinoids is already established and has many indications such as multiple sclerosis-induced spasticity or supportive therapy in the case of tumour-associated pain or loss of weight or appetite. However, the effects of cannabinoids on tumour growth still remain largely unexplored in many tumour entities, including phaeochromocytomas and paragangliomas (PPGLs), and neuroendocrine tumours (NETs). Therefore, we have now evaluated the effects of cannabidiol (CBD) in PPGL/NET cell lines, a PPGL 3D spheroid model and, most importantly, in patient-derived PPGL/NET primary cultures. In the PPGL cell lines (MPC, MTT) and in some NET cell lines (BON1, NCI-H727), CBD showed significant anti-tumour effects. Similarly, CBD also showed efficacy in PPGL (MPC) 3D spheroids, leading to a significant reduction in spheroid diameter. However, in a human pancreatic NET cell line (QGP1) we found significant tumour-*promoting* effects – thus demonstrating overall opposing effects of CBD on cell viability in different cell lines. Due to these results, we also validated these data in individual human primary cultures derived from patients with PPGLs ($n = 35$) and NETs ($n = 11$) and confirmed the opposing effects induced by CBD. In clinically relevant doses, we found significant anti-tumour effects in 14% and significant tumour-promoting effects in 17% of PPGLs. These effects were more pronounced using slightly higher doses of CBD, leading to significant anti-tumour effects in 27% and significant tumour-promoting effects in 18% of both PPGLs and NETs. Moreover, we performed genetic testing of individual PPGLs, which allowed us to evaluate cluster-dependent drug responsivity: In the cluster 2-associated PPGLs we found a significantly stronger CBD-induced cell viability reduction compared to the cluster 1-associated PPGLs. In conclusion, we offer clinically relevant data on a potential novel treatment option for PPGLs and NETs, particularly regarding personalised therapy in cluster 2-associated PPGLs, but also evidence for potential tumour-promoting effects of CBD in some PPGLs and NETs. Therefore, caution may be needed when treating PPGL or NET patients with cannabinoids as supportive therapies or even possibly as health supplements

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EP247

Endocrine sequelae of adult recipients of hematopoietic stem cell transplantation

Georgia Ntali[1], Efstratios Kardalas[1], Aikaterini Beka[1], Evrydiki Theodorou[2], Maria Zotou[1], Anastasia Lambraki[1], Elisavet Tiaka[1], Vasiliki Antonopoulou[1], Frini Karaolidou[2], Zoi Arapidou[2], Barvara Vlassopoulou[1], Dimitrios Karakasis[2], Tatiana Tzenou[2], Ifigenia Tzannou[2], Ioannis Tsonis[2], Marinella Tzanela[1], Stavros Gigantes[2] & Ioannis Baltadakis[2]
[1]Evangelismos General Hospital, Department of Endocrinology "Dionysios Ikkos"-Diabetes Center, Athens, Greece; [2]Evangelismos General Hospital, Department of Hematology and Bone Marrow Transplantation Unit, Athens, Greece

Introduction
Hematopoietic stem cell transplantation (HSCT) is the standard of care treatment for high-risk hematological malignancies. HSCT recipients are exposed to chemotherapy and/or radiation prior to HSCT, as part of the conditioning, or following HSCT for management of disease relapse. They may receive steroids for chronic graft-versus-host disease (cGvHD) and they are at high risk for endocrine complications.
Aim
To evaluate endocrine complications in HSCT survivors.
Patients/Methods
Retrospective analysis of HSCT recipients, who were referred to the Outpatient Endocrine Clinic of Evangelismos Hospital (Athens).
Results
109 patients (45 males) were enrolled. Their median age at diagnosis of hematological malignancy and HSCT was 31 (range 13-64) and 33 years (13-65) respectively. Patients had received a single allogeneic ($n=81$) or autologous ($n=9$) HSCT, or a 2nd allotransplant ($n=1$). Data for transplant type missed for 18 patients. Median follow-up duration from HSCT was 71 months (3-300). Data for thyroid function before HSCT were available for 86 patients. 81/86 (94%) were euthyroid, 5/86 (6%) were hypothyroid. At last assessment, thyroid data were available for 83. 58/83 (70%) were euthyroid, 25/83 (30%) were hypothyroid. Amongst hypothyroid patients 4 (16%) had been treated with total body irradiation (TBI), including 3 (12%) with a dose of $\geq$12Gy. At last assessment, data for metabolic syndrome (MS) were available for 106. Fifty-two (48.5%) fulfilled (MS) criteria. Of those, 9 (17%) had received TBI and 30 (61%) glucocorticoids. At last assessment, data for osteoporosis were available for 45 patients. Osteoporosis was noted in 12 (26.6%), and 8/12 (66.6%) had received glucocorticoids. Eleven had developed avascular necrosis, all following steroids. Data for cGvHD were available for 80 patients. Fifty-seven (71%) had a cGvHD diagnosis and 51 (89.4%) had received glucocorticoids. Age at transplant was a predictor of the development of metabolic syndrome, hypothyroidism and osteoporosis, with older patients being more vulnerable. Odds Ratio (OR) for (MS) was 2.51 (95%CI:1.07-5.93, $P=0.02$) for patients aged $\geq$35 vs $<$35 years. OR for hypothyroidism was 2.89 (95%CI: 0.8-10.04, $P=0.056$) for patients aged $\geq$50 vs $<$50 years. OR for osteoporosis was 4.38 (95%CI: 0.87-22.35, $P=0.03$) for patients aged $\geq$40 vs $<$40 years. TBI and glucocorticoids did not emerge as significant predictive factors.
Conclusions
The population of HSCT survivors steadily increases over time. Endocrine complications may ensue during follow-up, with older age at transplantation as a significant predisposing factor. The long latency interval from HSCT necessitates their life-long monitoring for endocrine sequelae.

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EP249

Multiple endocrine neoplasia type 1 in children and adolescents, the importance of clinical monitoring

Simone Della Valentina[1], Laura Pierotti[1], Elena Pardi[1], Chiara Sardella[2], Anna Dal Lago[1] & Filomena Cetani[2]
[1]University of Pisa, Department of Translational Researche and Innovative Technology in Medicine and Surgery, Pisa, Italy; [2]Unit of Endocrinology, University Hospital of Pisa, Department of Surgery and Endocrine Metabolic and Transplantation Medicine, Pisa, Italy

Multiple endocrine neoplasia type 1 (MEN1) is a rare autosomal dominant disorder, characterized by the predisposition to the development of multiple endocrine tumors mainly affecting parathyroids, gastroenteropancreatic neuroendocrine tissues (GEP-NET) and pituitary (PT). Mutations of the *MEN1* gene are responsible for the disease and may be inherited from one of the parents or more rarely can occur *de novo*. In children and adolescence there is a paucity of clinical studies. The aim of this study was to describe our experience in MEN1 children and adolescents aged $\leq$21 years collected and followed-up at our outpatient clinic from 1993 to 2023. A total of 20 patients (10 females and 10 males), affected by familial MEN1 were collected. Mean age at first MEN1 diagnosis was 17 ± 3 years (range 8-21). All patients carried *MEN1* mutation. Sixteen patients (80%) developed an endocrine tumor $\leq$21 years (mean 16 ± 3 years, range: 8–21) and 5 were healthy carriers. Seventy percent of patients had primary hyperparathyroidism (PHPT), (mean 17 ± 2.7 years, range 12-21), 35% a GEP-NET tumor (mean 19.0 ± 1.5 years, range 17-21) and 35% a PT tumor (mean 17 ± 4.5 years, range 8-21). Patients with PHPT at diagnosis had a mean albumin-corrected serum calcium of 11.1 ± 0.74 mg/dl and PTH (evaluated as fold increase of the upper limit of reference range) of 1.37. At diagnosis, 9/15 subjects had at least one target organ involvement of PHPT (hypercalciuria in 6; nephrolithiasis in 3, reduced bone mineral density in 6: mean lumbar *Z*-score -2.4; femoral neck -2.4; total femur -2.3; 1/3 distal radius -2.9 DS). During the follow up (mean 10 years), one-third (27 %) of patients underwent parathyroid surgery, with a mean age of 20 years (range 16–25); four had the removal of GEP-NET tumor between 21 and 32 years, with histological diagnosis of insulinoma in one, gastrinoma in one and non-functioning in two. No patient had metastases. All except one patient with PT tumors underwent pituitary surgery. The only symptomatic patient had a PRL-microadenoma, treated with cabergoline. Our study suggests that morbidity from MEN1-related manifestations occurred during childhood and adolescence in 80% of patients, being PHPT the most frequent. These findings have implications for the counseling of young MEN1 patients and their families and underscore the importance of initiating surveillance screening early in childhood. Furthermore, it is important to carry out periodic monitoring of all MEN-related endocrine pathologies in order to define the most appropriate therapeutic procedure.

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EP256

Association between insulinoma and adrenal insufficiency in a patient with type 2 diabetes: a case report

Samir Mkaouer[1], Khessairi Nadia[1], Merhbene Yasmine[1], Kamoun Elyes[1], Yazidi Meriem[1], Oueslati Ibtissem[1], Chaker Fatma[1] & Chihaoui Melika[1]
[1]La Rabta University Hospital, Endocrinology Department, Tunis, Tunisia

Introduction
Insulinomas are rare pancreatic endocrine tumors causing severe hypoglycemia in non-diabetic patients. We report a case of a rare association between insulinoma and type 2 diabetes.
Presentation of the case
A 65-year-old diabetic patient presented with a one year history of recurrent hypoglycemia even after the withdrawal of antidiabetic drugs. First, a functional hypoglycemia was suspected and an oral glucose tolerance test showed hypoglycemia after 4 hours confirming the diagnosis. We recommended split diet with acarbose. Due to the appearance of signs of neuroglycopenia, the patient was started on a 72-hour fast, and within 10 hours, he had a hypoglycemic episode. The subsequent laboratories drawn revealed venous hypoglycaemia (23 mg/dl), elevated insulin (15.75 UI/l), elevated C peptide (4.81 ng/ml) and negative sulfonylureas screening. The diagnosis of insulinoma was confirmed and an abdomen CT scan revealed a 17 mm pancreatic nodule. In addition to that, the cortisol level drawn during his hypoglycemia revealed that the patient had an inadequate adrenal response to stress. The serum cortisol peak was 14.7 µg/dl and ACTH level was 14.09 ng/l confirming the secondary adrenal insufficiency (SAI). He underwent a left pancreatectomy. One month after surgery, serum glucose levels had increased and the SAI had disappeared with basal cortisol level at 34 µg/dl.
Conclusion
The coexistence of insulinoma and type 2 diabetes is rare and the diagnostic process is often challenging. The association of SAI and insulinoma has been described yet the pathophysiological mechanism remains poorly elucidated. Therefore, precaution is needed in diagnosis even if there is an obvious cause of hypoglycemia.

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EP257

The value of cumulative serum 5-HIAA exposure in diagnostics of carcinoid heart disease: A prospective follow up in patients with small intestinal neuroendocrine tumors

Iiro Kostiainen[1], Piia Simonen[2], Katri Aaltonen[2], Riikka Lindén[3], Noora Karppinen[1], Daniel Gordin[4], Janne Rapola[2], Camilla Schalin-Jäntti[1] & Niina Matikainen[1]

[1]Helsinki University Hospital and University of Helsinki, Endocrinology, Helsinki, Finland; [2]Helsinki University Hospital and University of Helsinki, Cardiology, Helsinki, Finland; [3]Helsinki University Hospital and University of Helsinki, Radiology, Helsinki, Finland; [4]Helsinki University Hospital and University of Helsinki, Nephrology, Helsinki, Finland

Introduction
In small intestinal neuroendocrine tumors (SI-NET), unphysiological exposure to serotonin is considered as a major pathogenic factor predisposing to the development carcinoid heart disease (CHD), a complication of carcinoid syndrome associated with poor prognosis. The ability of biomarkers to predict the development of CHD is limited. The aim of our prospective study was to assess risk factors of CHD development and mortality in SI-NET.
Methods
We performed baseline transthoracic echocardiography (TTE), biochemical and radiological evaluation, and vascular function measurements for 65 patients with SI-NET. 42 (65%) of patients had liver metastases. 54 patients had follow-up TTE at median of 61 months. Vital status of patients was assessed at median follow-up of 72 months. Clinical data, including demographics, treatments, radiological and laboratory data was collected from electronic patient records. Hepatic tumor load was assessed at the time of TTE. Cumulative upper limit of normal (ULN) exceeding serum-5-HIAA exposure at the time of TTE was calculated. Westberg score of $\geq$3 in TTE was considered diagnostic for CHD.
Results
At the end of the follow-up, 22 (34%) patients had died. In 89%, death was due to SI-NET. Three patients had CHD at initial assessment, two patients (4%) were diagnosed with CHD during the 61-month median follow-up. At the follow-up TTE, 54% of the patients had received peptide receptor radionuclide therapy (PRRT) and 46% non-systemic treatments for metastases. Cumulative ULN exceeding serum-5-HIAA and proBNP had correlation with Westberg score (Spearman's ρ 0.32, 0.31, respectively). Cumulative ULN exceeding serum-5-HIAA had good diagnostic capability in ROC analysis with AUC at 0.98 (95% CI 0.94-1.00), surpassing performance of proBNP and individual serum-5-HIAA measurements (AUC 0.75, 0.91, respectively). In TTE, minor alterations in regurgitation were frequent, with increase or decrease noted in 29% of tricuspid and 30% of pulmonic valves. CHD, hepatic tumor load, serum-5-HIAA, and elevated aortic pulse wave velocity were found to be associated with increased mortality in patients with SI-NET.
Conclusions
Exposure to serotonin measured as cumulative ULN exceeding serum-5-HIAA improves case detection and appears as a promising biomarker for assessing the risk of CHD. Aortic pulse wave velocity was found to be a novel prognostic marker in SI-NET. The incidence of CHD was small when compared to previous literature, possibly reflecting the frequent use of PRRT and other tumor burden reducing treatments.

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EP260

Carcinoid heart disease - a single centre experience

Anna Kurzyńska[1], Agnieszka Stefańska[2], Magdalena Kolasa[2], Anna Sowa Staszczak[1] & Alicja Hubalewska-Dydejczyk[1]
[1]Jagiellonian University Medical College, Chair and Department of Endocrinology, Kraków, Poland; [2]University Hospital in Krakow, Department of Endocrinology, Oncological Endocrinology and Nuclear Medicine

Carcinoid heart disease (CHD) affects about 20-50% of patients with carcinoid syndrome (CS) and is the main cause of mortality in this group of patients. The 3-year survival rate in patients with CHD is 31% compared to 68% in those without cardiac involvement. The cause of the development of CHD is the flow of serotonin-rich blood, and the lesions affect the right heart (localizing mainly in the endocardium and inner membrane of large vessels). The study aim was to present a single centre experience with CHD. Ten patients with CHD selected from the group of 162 patients with disseminated and/or inoperable neuroendocrine tumours treated with long-acting somatostatin analogues were included in a retrospective analysis. The study group consisted of 2 females (median age 72 years) and 8 males (median age 61,5 years). There were 2 patients with NET G1 and 6 patients with NET G2. In 8/10 patients the primary site was small intestinal NET (in 100% of these patients the primary site was resected), in 2 cases the primary site was unknown. Elevated serum chromogranin A (CgA) concentration with a median value 105,5 nmol/l (range 42,5-255) [reference value 0,0 - 6,0] was observed in all patients, and 5-hydroxy indoleacetic acid (5-HIAA) excretion in 24-hour urine collection was also elevated in all patients - median value 71,4 mg/24h (range 21,3-766) [reference value 0 - 8,2]. N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentrations were above the upper limit of normal in 9/10 patients: median value 390 pg/ml (range 245-11162) [reference value $<$ 125]. Two patients presented symptoms of heart failure in NYHA I class, 3-NYHA II, 3-NYHA III and 2-NYHA IV. In all patients tricuspid regurgitation was confirmed in a transthoracic two-dimensional echocardiography (in 6 cases moderate, and in 4 severe). Two patients underwent a cardiac surgery for tricuspid valve replacement (under the cover of a short-acting somatostatin analogue). Two patients were treated with Peptide Receptor Radionuclide Therapy (PRRT) receiving 4 cycles of [177Lu]Lu-DOTATATE. Six patients from the study group are alive, of whom five have CS symptoms well controlled with a long-acting somatostatin analogue. CHD is a life-threatening complication of CS. CgA, 5-HIAA and NT-proBNP are screening tools to diagnose this state and transthoracic two-dimensional echocardiography is essentialfor imaging CHD. Multidisciplinary approach is mandatory to offer a patient a proper treatment.

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EP271

Parathyroid carcinoma: clinical manifestations and long-term post-operative follow-up of seven patients

Ewa Zalewska[1], Sonia Kaniuka-Jakubowska[1], Łukasz Obołończyk[2], Anna Lewczuk-Myślicka[1], Jarosław Jendrzejewski[1], Maria Gnacińska[1], Dominika Okroj[1], Krzysztof Sworczak[1] & Renata Świątkowska-Stodulska[1]
[1]Medical University of Gdansk, Department of Endocrinology and Internal Medicine, Faculty of Medicine, Gdańsk, Poland; [2]Institute of Maritime and Tropical Medicine, Department of Occupational, Metabolic and Internal Diseases, Faculty of Medicine, Gdynia, Poland

Background
Parathyroid carcinoma causes less than 1% of primary hyperparathyroidism and is one of the rarest human malignancies. Clinical symptoms are ambiguous, and the diagnosis is usually made postoperatively based on histopathological examination.
Methods
We present clinical manifestations, pathological features, and follow-up of seven patients from our department after parathyroidectomy performed between 2008 and 2024.
Results
There were two male and five female patients with parathyroid carcinoma whose average age at the time of diagnosis was 54 $\pm$ 13.4 years. Osteoporosis was diagnosed in three patients (42.9 %), one of whom had a brown tumour and another had nephrolithiasis. Moreover, one patient (14 %) had osteopenia. Before treatment for primary hyperparathyroidism, the mean calcium concentration was 13.3 $\pm$ 1.27 mg/dl, parathyroid hormone 461 $\pm$ 283 pg/ml, and phosphorus 2.03 $\pm$ 0.57 mg/dl. One patient had a tumour encountered in the left lower parathyroid gland, and six patients had a mass located on the right side of the thyroid gland, five of them near the lower pole and one next to the upper. All patients were diagnosed based on postoperative histopathological examination: the vascular invasions were confirmed in all cases, and the average tumour size was approximately 18 mm (IQR 17–23). None of our patients had regional lymph nodes or distant metastases. Two patients, initially identified as having parathyroid adenomas, were verified to have parathyroid carcinoma after the second surgery (three and seven years after the first operation). Postoperative laboratory examinations revealed a significant decrease in calcium levels (9.57 $\pm$ 0.79 mg/dl) and parathyroid hormone concentration (62.1 $\pm$ 47 pg/ml), with an increase in phosphorus level (2.97 $\pm$ 0.65 mg/dl). The average follow-up time of our patients is 54 months (IQR 30 – 138), and all of them are currently in remission. The patient, who has been followed for the longest time, since 2008, initially required two reoperations due to disease recurrence but has now been in remission for 15 years.
Conclusion
Even though some clinical and biochemical clues may raise the suspicion of parathyroid cancer, the histopathological examination seems to be mandatory to distinguish it from parathyroid adenoma and set the final diagnosis. Because this cancer is so ultra-rare, there is insufficient research in this field, and clinicians must base their treatment decisions mainly on case series. However, the surgery, which may lead to a long-lasting tumour recurrence even when performed at the time of disease recurrence, is undoubtedly the mainstay of treatment.

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EP303

Penetrance and clinical phenotype of SDHA related phaeochromocytomas and paragangliomas: A single centre experience

Mark Quinn[1], Paul Carroll[1], Anand Velusamy[1], Rebecca Oakey[2], Rupert Obholzer[1] & Louise Izatt[1]

[1]Guy's and St Thomas' NHS Foundation Trust, United Kingdom; [2]King's College London, United Kingdom

Background
Phaeochromocytomas and paragangliomas (PPGLs) are histologically identical tumours that exhibit significant clinical heterogeneity. At least 40% of PPGLs arise due to the presence of a pathogenic germline variant (PGV) in a known susceptibility gene. PGVs affecting the mitochondrial enzyme succinate dehydrogenase (*SDHA, SDHB, SDHC* and *SDHD*) are the most common. Phenotypic features of PPGLs secondary to *SDHB* and *SDHD* PGVs are well documented and demonstrate a variability (tumour location, rates of catecholamine secretion, metastatic risk etc.) that is not currently understood. Due to their rarity the behaviour of *SDHA* related PPGLs are less well documented. Cascade screening is now offered to all patients with an *SDHA* PGV and so we can expect to encounter unaffected carriers more frequently in our clinical practice. Here we will discuss our experience of 18 index cases of *SDHA* related PPGLs and 10 relatives diagnosed as carriers via cascade screening.
Methods
Patients presenting with a PPGL with either a PGV or a VUS of *SDHA* were identified via our neuroendocrine tumour multidisciplinary team database. A retrospective chart review was carried out. An additional 14 *SDHA* PGV carriers were also identified via cascade screening ($n=12$) or via the 100,000 genome project ($n=2$).
Discussion
We report 18 cases (8F, 10M) of a PPGL related to an *SDHA* PGV ($n=12$) or VUS ($n=6$). Patients were aged 16-64 (median age of 40). 38.9% of PPGLs were found in the head and neck, 27.8% were abdominal PGLs, 11.1% were in the bladder, 11.1% presented as pheochromocytomas, 5.6% were found in the mediastinum and 5.6% had widespread metastatic disease at initial presentation. Catecholamine excess was diagnosed in at least 44.4% of cases. The most common presenting complaint was of swelling or symptoms related to tumour compression (44.4% of cases). Symptoms related to catecholamine excess were present in 33.3% of cases. 33.3% of this cohort went on to develop metastatic disease. Of the 14 patients identified as an *SDHA* PGV carrier, one patient was diagnosed with renal cell carcinoma (identified via the 100,000 genome project) but no patient identified via cascade screening went on to develop a PPGL.
Conclusion
The penetrance of disease in non-index cases of an *SDHA* PGV is low in this cohort. We also show a variability in tumour location and catecholamine production that is distinct from other *SDHx* related disease. In this small cohort there was a high rate of metastatic disease.

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EP313

Safety and outcomes of laparoscopic adrenalectomy for metastatic tumors – experience in a high-volume urological center

Emilia Niedziela[1,2], Łukasz Niedziela[2,3], Jarosław Jaskulski[2,3], Mateusz Obarzanowski[2,3] & Aldona Kowalska[1,2]
[1]Holy Cross Cancer Center, Department of Endocrinology, Kielce, Poland; [2]Collegium Medicum, Jan Kochanowski University, Kielce, Poland; [3]Holy Cross Cancer Center, Department of Urology, Kielce, Poland

Introduction
In case of isolated adrenal metastases, complete surgical resection of the disease is a potentially curative treatment. Minimally invasive adrenalectomy is recommended in most patients with focal adrenal lesions without evidence of local invasion. However, data on surgical outcomes and survival after laparoscopic adrenalectomy (LA) for adrenal metastases are still lacking to clearly define the role of this procedure in the management of metastatic disease.
Aim
The aim of the study is to assess the safety and outcomes of LA for metastatic adrenal tumors.
Methods
We retrospectively analyzed the data of patients undergoing LA between 2015 and 2021 in tertiary medical center. Perioperative and postoperative complications, as well as long-term outcomes were recorded.
Results
A total of 141 patients were enrolled in the study. 22 LAs were performed for adrenal metastases of different origin, including 18 for renal cell carcinoma (RCC; 81.8%), 3 for lung cancer (LC; 13.6%) and 1 for colorectal cancer (CC; 4.5%). One patient underwent a single-stage bilateral adrenalectomy, while the others had unilateral surgery. 4 patients had second LA due to metachronous adrenal metastases. Intraoperative complications occurred during 2 LAs (9.1%) including injury of the inferior vena cava and pancreatic tail. Open conversion was performed during 2 LAs (9.1%). 30-day postoperative complications were reported in 4 cases (18.2%). No life-threatening complications were observed in the postoperative period. 90,9% resection margins were tumor-free (R0). At the follow-up, systemic treatment was administrated to all patients with metastatic LC and CC, and to 27.8 % of patients with RCC. After a median follow-up of 4 years (range 0.2–8.8), 10 patients (45%) died of cancer or other causes. The 1-, and 5-year overall survival (OS) rate after LA were 85% and 40%, respectively. Tumor size on imaging tended to be associated with shorter OS.
Conclusions
LA for adrenal metastases is a safe method with good surgical and oncologic outcomes. It requires a proper qualification of patients for the procedure by a multidisciplinary team and surgeon's experience.

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EP316

Retroperitoneal ganglioneuroma: a case report in a 16-year-old girl presenting as lower back pain

Anastasios Stofas[1] & Amalia Patereli[2]
[1]1st Department of Pathology, School of Medicine, National and Kapodistrian University of Athens, Greece; [2]Pathology Department, Agia Sofia Children's Hospital, Athens, Greece, Greece

Introduction
Retroperitoneal ganglioneuromas (RGN's) are rare benign tumors originating from the retroperitoneal sympathetic ganglia. They are usually sporadic; though an association with neurofibromatosis type II and multiple endocrine neoplasia (MEN) IIB has been reported. RGN's are usually asymptomatic. Occasionally they may show symptoms due to local pressure effect or rarely are hormonally active, releasing peptides such as vasoactive intestinal peptide, somatostatins or androgen hormone and present with adrenergic symptoms, such as diarrhea, sweating and hypertension, virilism and hypokalemia.
Case report
A 16-year-old female patient, with no significant past medical history, who presented with lower back pain. MRI revealed a well circumscribed solid mass in the left retroperitoneal site adjacent to the left adrenal gland, the psoas muscle and the head of the pancreas, measuring 6×5.4x3 cm. The tumor was resected, and the histopathological examination confirmed the diagnosis of ganglioneuroma characterized by the presence of fascicles of spindle cells of Schwannian origin (S100+ and NF+) mixed with scattered and small clusters of ganglion cells (Synaptophysin+, S-100+, NF+). Desmin, smooth-muscle actin and MelanA were negative. Ki-67 labeling index was low (~1-2%).
Conclusion
Due to lack of specific characteristics RGNs are quite difficult to differentiate from other tumors of the area. The prognosis for a RGN following complete surgical resection is good. Their close relationship with surrounding vital organs makes surgical excision of these tumors challenging and may act as a limiting factor in complete surgical resection. Also, since they may release catecholaminergic peptides, surgeons should be aware of the possibility of hypertensive crisis during the surgery. Regular and periodic long-term follow-up is recommended.

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EP339

The association between early/precocious puberty and the risk of breast cancer

Ashraf Soliman[1], Nada Alaaraj[1], Fawzia Alyafei[1], Noor Hamed[1] & Shayma Mohamed[1]
[1]Hamad General Hospital, Pediatric Endocrinology, Doha, Qatar

Introduction
The contribution of reproductive factors to breast cancer (BC) susceptibility requires further investigation. This study aims to explore the potential link between early puberty (menarche) and the risk of breast cancer in women.
Aim
This study systematically reviews research conducted between 2000 and March 2023, aiming to evaluate the association between early/precocious puberty and the incidence of BC.
Methods
A comprehensive search was performed across databases including Medline, PubMed, Google Scholar, and Web of Science to identify relevant studies. The review encompassed a variety of study designs, including metanalyses, prospective studies, and case-control studies.

Results
A total of 12 studies were analyzed: A comprehensive analysis of 117 epidemiological studies, involving 118,964 women with invasive breast cancer and 306,091 controls, demonstrated that younger age at menarche correlated with an increased BC risk. Each year younger at menarche was associated with a 5% increase in relative breast cancer risk, particularly for luminal A tumors. The risk rose by a factor of 1.050for each year younger at menarche. Endogenous ovarian hormones appeared more influential for estrogen receptor-positive disease and lobular tumors. A case-control study of 237 BC cases and 237 age-matched controls found that early menarche (OR = 1.60, 95% CI: 1.08–2.38) significantly heightened breast cancer risk. A prospective US cohort study on women aged 35–74 without BC history but with a diagnosed sister revealed that early ages at thelarche and menarche were positively associated with BC risk. Women with both early thelarche and menarche exhibited a 30% higher risk of breast cancer compared to those without these risk factors. Multiple investigations consistently indicate that commencing menstruation before the age of 11 increases BC risk, while later menarche (14 years) reduces the risk. Sister-matched case-control research involving 1,406 women diagnosed with BC before age 50 and 1,648 controls reaffirmed the relationship between older age at menarche and reduced young-onset breast cancer risk. A study involving 1811 pairs of female twins with BC demonstrated that the twin with earlier puberty was more likely to receive the diagnosis of BC first. The Collaborative group on hormonal factors reported up to an 18% risk reduction in girls with late menarche ($\geq$13) compared to those starting menstruation at 11.
Conclusion
The collective evidence supports the notion that earlier ages at thelarche, and menarche may heighten susceptibility to BC and add an advantage to hormonal suppressive therapy.

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EP342

Heterogeneity of responses of dynamic tests in patients with ectopic cushing's syndrome (ECS). the half of patients with ECS have an increase in ACTH in the CRH/desmopressin test, nearly 1/3 have complete or some inhibition of cortisol in HDDST

Aleksandra Gamrat[1,2], Mari Minasyan[1], Maria Aleksandra Komisarz-Calik[1], Alicja Hubalewska-Dydejczyk[1] & Aleksandra Gilis-Januszewska[1]
[1]Jagiellonian University Medical College, Chair and Department of Endocrinology, Kraków, Poland; [2]Jagiellonian University Medical College, Doctoral School of Medical and Health Science

Introduction
According to the literature, the CRH test has the highest specificity in excluding ECS (ACTH 93.9%, cortisol 89.4%). A combination of the high dose dexamethasone test (HDDST) and CRH/desmopressin test (CRH/desmopressinT) is used to increase the discriminatory capacity in ACTH-dependent CS.
Objectives
This study aims to investigate the response to dynamic tests in ECS patients.
Methods
35 consecutive ECS patients were analyzed (3 SCLC patients were excluded from further analysis). Neuroendocrine tumor (NET) constituted 47% of all EAS (60% gastroenteropancreatic, 40% thoracic (1 thymic and 5 pulmonary carcinoids (PC)), 4 cases were occult. The cut-off points for CRH/desmopressinT was >20% increase in cortisol concentration (Δcortisol%), >35% increase in ACTH (ΔACTH%) and for HDDST >50% decrease of cortisol (-Δcortisol%). The CRH/desmopressinT was performed in 18/32 (16 CRH/2desmopressin), HDDST in 25/32 patients.
Results
All patients responded to CRH/desmopressin (ACTH surge range: 12-197%), with average increase of cortisol and ACTH by 25.5% and 63%. The CRH/desmopressinT ΔACTH% and Δcortisol% were observed in 50% patients, in all PC and in 35.7% of other ECSs ($P=0.02$). The average percentage increase of ACTH in the CRH/desmopressinT was higher in the PC compared to other ECSs (98% vs 32% $P=0.08$). In HDDST -Δcortisol% was observed in 3 patients/12% (uterus clear cell carcinoma, PC and occult origin), 28% of the patients responded with a >30% decrease in cortisol. Positive results in both tests, indicative of Cushing's disease was observed in two ECSs (PC, occult). Patients with ΔACTH%, compared to the remaining ECSs, were characterized by a significantly higher potassium concentration (3.69 vs 2.51 mmol $P=0.02$) and a higher baseline ACTH concentration (281 vs 214 pg/ml). Patients with -Δcortisol% in HDDST also had higher potassium concentration compared to the non-inhibition group (4.3 mmol/l vs 2.91 mmol/l, $P=0.04$). There were no significant differences in response to dynamic tests between men and women. There was a strong correlation between the increase in cortisol in the CRH/desmopressinT and the decrease in cortisol in the HDDST (Spearman's correlation coefficient -0.89 $P<0.05$).
Conclusion
Half of ECS patients have Δcortisol% and ΔACTH% in CRH/desmopressinT and nearly one third in HDDST have cortisol decrease >30%. Our results also suggest that an increase in cortisol in the CRH/desmopressinT is associated with a decrease in cortisol in the HDDST. Further, multicenter studies are needed to understand the response of ECS patients to dynamic tests and to establish/improve diagnostic differential criteria.

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EP343

In silico and ex vivo identification of gonadotropin-related genes involved in ovarian cancer

Clara Lazzaretti[1], Beatrice Melli[2,3,4], Samantha Sperduti[1], Carmela Perri[1,3], Lara Baschieri[1,3], Vincenza Ylenia Cusenza[2], Sandra Martinelli[2], Davide Nicoli[2], Andrea Palicelli[5], Dario Vincenzo Mandato[4], Lorenzo Aguzzoli[4], Manuela Simoni[1,6] & Livio Casarini[1]
[1]Unit of Endocrinology - University of Modena and Reggio Emilia, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy; [2]Unit of Molecular Pathology - Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy; [3]International PhD School in Clinical and Experimental Medicine (CEM) - University of Modena and Reggio Emilia, Modena, Italy; [4]Unit of Obstetrics and Oncological Gynecology - Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy; [5]Unit of Pathology, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy; [6]Azienda Ospedaliero-Universitaria di Modena, Department of Medical Specialties, Modena, Italy

Serous ovarian cancer is one of the leading causes of death among all gynaecological malignancies. Even though a hereditary component has been suggested, most ovarian carcinomas are sporadic and markers for a diagnosis at an early stage of the disease are still to be identified. Since gonadotropins may stimulate the growth of certain cancer cells, we aim to identify tumour markers linked to gonadotropin receptor-mediated pathways. Through an *in silico* and *ex vivo* approach, we characterized high-grade serous ovarian cancer features. A network of genes associated with gonadotropin-dependent regulatory pathways of ovarian follicle development was identified. Gene expression data of 60 genes from two groups of high-grade serous ovarian cancer patients, as well as two control groups, were obtained from the GEO-NCBI database. Principal component analysis (PCA) performed on the datasets revealed that the 60 genes have a differential expression pattern in cases vs controls. PCA was repeated considering 7 genes better discriminating healthy individuals vs patients. These genes described 50-70% of the total variance in each dataset, resulting in a clear clusterization of cases vs controls. PCA was also performed on a group of housekeeping genes serving as a negative control, which did not discriminate between cases vs controls. To further confirm the differential expression pattern of the genes identified through *in silico* analysis, RNA samples were extracted from high-grade serous ovarian cancer and healthy tissue of 30 women to perform a gene expression analysis by digital droplet PCR. In pathological tissues, results revealed upregulation of proliferative genes together with those associated with gonadotropin-dependent signalling pathways. In conclusion, we found a set of genes linked to gonadotropin functions which may be involved in ovarian cancer progression, as potential targets for specific pharmacological approaches.

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EP344

Paediatric differentiated thyroid cancer: a single-centre retrospective study

Raquel Calheiros[1], Sara Gil-Santos[1], Pedro Souteiro[1], Joana Oliveira[1], Isabel Inácio[1], Ana Paula Santos[1] & Isabel Torres[2]
[1]Instituto Português de Oncologia do Porto FG, EPE (IPO-Porto), Endocrinology Department, Porto, Portugal; [2]Instituto Português de Oncologia do Porto FG, EPE (IPO-Porto), Paediatrics Department, Porto, Portugal

Introduction
Differentiated thyroid cancer (DTC) is rare in the paediatric population when compared to adults. Paediatric patients often present with advanced disease at diagnosis, characterized by multifocal disease, heightened lymph node involvement, and distant metastasis. Additionally, they face a higher risk of post-operative complications in comparison to adults. Despite that, paediatric DTC exhibits an excellent prognosis.

Methods
A retrospective study was conducted, analyzing medical data of 25 individuals under 18 years diagnosed with differentiated thyroid cancer in an oncology center in Portugal from January 2013 to December 2023.
Results
Twenty-four patients were diagnosed with papillary thyroid carcinoma, and one with oncocytic thyroid carcinoma. The mean age at diagnosis was 15.28 years, and 68% of the patients were females. Histology reports indicated that at least one aggressive feature was present in 20 cases (80%). Lymph node involvement was observed in 9 patients (36%), and 2 of them had distant metastasis, both pulmonary (8%). Sixteen patients underwent total thyroidectomy and 9 had hemithyroidectomy, 5 of which later underwent surgery totalization based on the histopathological results. Lymph node dissection was initially performed in 8 individuals (33%). Post-operative complications were reported in 9 patients, including transient primary hypoparathyroidism ($n=3$), persistent primary hypoparathyroidism ($n=6$), and transient dysphonia ($n=4$). Sixteen patients (64%) were submitted to radioiodine therapy after surgery. Regarding follow-up, 14 patients were classified as having an excellent response (56%), 5 had an indeterminate response (20%) and the remaining ones presented either a biochemical ($n=3$; 12%) or structural ($n=2$; 8%) incomplete response. Due to persistent/recurrent disease, 2 patients had to be submitted to lymph node dissection and 4 individuals were retreated with radioiodine.
Discussion
These findings underscore the unique clinical characteristics of paediatric DTC. The relatively high prevalence of patients needing thyroidectomy totalization and lymph node dissection emphasises the need for a careful assessment when deciding the extent of thyroid surgery. In addition, the significant rates of early postoperative complications and therapy incomplete responses underline that close surveillance is crucial after surgery.

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EP345

Cellular localization of clock gene PER2 plays an essential role in tumour aggressiveness and drug resistance in in vitro models of hepatocellular carcinoma

Mariarosaria Negri[1], Feliciana Amatrudo[1], Donatella Paola Provvisiero[2], Roberta Patalano[2], Tatiana Monto[2], Cristina De Angelis[2], Chiara Simeoli[2], Renata Simona Auriemma[2], Annamaria Colao[2,3], Rosario Pivonello[2,3] & Claudia Pivonello[4]
[1]Università Telematica Pegaso, Dipartimento di Scienze Umanistiche, Naples, Italy; [2]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia, Andrologia e Nutrizione, Naples, Italy; [3]Federico II University, UNESCO Chair for Health Education and Sustainable Development, Naples, Italy; [4]Università Federico II di Napoli, Dipartimento di Sanità Pubblica, Naples, Italy

Acquired resistance has limited the use of systemic molecular therapy in the management of hepatocellular carcinoma (HCC). Immunotherapy, alone and in combination with systemic molecular therapy, is now the first-line standard of care for HCC. The current in vitro study aims at investigating PER2 role in the HCC aggressiveness and drug resistance acquisition. Parental PLC/PRF/5, PLC/PRF/5 resistant to Everolimus (EveR) and to Sorafenib (SorR) cell lines were used. To evaluate PER2 involvement in aggressiveness and drug resistance, PER2 expression was genetically manipulated by using small interfering RNA (siRNA) to knockdown (KD) and CRISPR/Cas9 Plasmid to knockout (KO) PER2 gene in parental PLC/PRF/5. PER2 mRNA and protein expression were investigated by RT-qPCR and immunofluorescence (IF), respectively. The epithelial and mesenchymal transition (EMT) markers and TP53 expression was evaluated by IF and western blot, respectively. The role of PER2 on the onset of aggressiveness was evaluated through cell proliferation and cell migration assays. PLC/PRF/5 EveR, SorR, PER2KD and PER2KO significantly expressed lower mRNA *PER2* levels, with a reduction of 72.7%, ($P<0.01$) in EveR, 59.6.% ($P<0.05$) in SorR, 91.5% ($P<0.001$) in PER2KD and 97.2% ($P<0.001$) in PER2KO compared to parental PLC/PRF/5. Remarkably, PER2 protein expression in PLC/PRF/5 EveR and SorR completely localized in cytoplasm contrary to parental ones. In PLC/PRF/5 EveR, PER2KD and PER2KO but not SorR, E-Cadherin was significantly decreased (24.9%, $P=0.05$; 33.8%, $P=0.04$; 55.5%, $P=0.0002$; +37.2%, $P=0.05$ respectively) while Vimentin protein expression was significantly increased in all cell models (+148.1%,+202.9%, +110.3%,+552.0%, $p<0.0001$ respectively). Interestingly, TP53 expression was reduced in PER2KO and completely absent in PLC/PRF/5 EveR and SorR. Significant cell proliferation inhibition of EVE10^{-9}M and SOR5$\times$10^{-6}M in the parental PLC/PRF/5 (19.6%, $P<0.0001$ and 34.7%, $P<0.05$, respectively) was partially but not significantly reverted when *PER2* was KD while it was completely reverted when *PER2* was KO ($P<0.01$ vs EVE10^{-9}M and $P<0.001$ vs SOR5$\times$10^{-6}M, respectively). Similarly, the significant inhibition of cell migration of EVE10^{-9}M and SOR5$\times$10^{-6}M in the parental PLC/PRF/5 (20.7%, $P<0.0001$ and 8.6%, $P<0.01$, respectively) was reverted when PER2 was KD ($P<0.0001$ vs EVE10^{-9}M and vs SOR5$\times$10^{-6}M, respectively), and when PER2 was KO ($P<0.0001$ vs EVE10^{-9}M and vs SOR5$\times$10^{-6}M, respectively). These results suggest that the acquisition of aggressive phenotype is characterized by PER2 reduced expression and loss of nuclear translocation that in turn induces resistance to HCC systemic therapy. Further studies are mandatory to evaluate the impact of PER2 expression on immunotherapy efficacy in HCC improving patient's management.

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EP374

Refractory hypokalaemia secondary to an aggressive adrenal cortical carcinoma – a case report

Charlotte Choo[1]
[1]Singapore General Hospital, Endocrinology, Singapore

Adrenal cortical carcinoma (ACC) is notorious for its aggressiveness and poor prognosis. A 71-year-old woman was found to be hypokalaemic with a serum potassium of 2.6 mmol/l [reference 3.6-5.0 mmol/l] on routine blood screening. Previous serum potassium readings were normal. She was asymptomatic and reported no gastro-intestinal losses. Her medical history was significant for hypertension, hyperlipidemia and hypothyroidism following total thyroidectomy for Graves' Disease. She had been on stable doses of amlodipine, simvastatin and levothyroxine. There was no use of traditional medications or diuretics. Two weeks later, despite being on potassium replacements, she re-presented with persistent hypokalaemia 2.5-3.2 mmol/l associated with increased bicarbonate 36.7 mmolL [reference 19.0-29.0 mmol/l] and proximal myopathy. She was normotensive and her weight was stable. Besides facial acne and proximal myopathy, no discriminatory features of Cushing's syndrome were present. 24-hour urinary potassium of 88 nmol indicated urinary potassium loss. Further investigations revealed a markedly elevated 0800 hours cortisol at 1080 nmol/l, with an undetectable adrenocorticotropic hormone (ACTH). Further investigations revealed hyperandrogenism with total testosterone 6.9 nmol/l [reference 0.30-2.8 nmol/l], 17alpha hydroxyprogesterone 11.1 nmol/l and dehydroepiandrosterone-sulfate (DHEA-S) 25.3 umol/l [1.1-11.8 umol/l]. This raised concerns for ACC with non-ACTH dependent hypercortisolism. Cross sectional imaging showed a 7.4 $\times$ 6.5 cm^2 enhancing mass in the left adrenal with tumour thrombus extending to the left adrenal vein, with no distant metastases. Within a month of diagnosis, the tumor had enlarged to 10 $\times$ 8 $\times$ 7.2 cm^3 when she underwent open left adrenalectomy. Histology revealed a high-grade tumour invading through the adrenal capsule into periadrenal adipose tissue. Post-operative day three 0800 hours cortisol of 383 nmol/l was worrying for incomplete resection. Nevertheless, ACTH and adrenal androgens normalized shortly postoperatively. She was started on adjuvant mitotane but shortly developed rapidly worsening transaminitis with alkaline phosphatase 105 U/l [reference 12-42 U/l] and gamma-glutamyl transferase 1138 umol/l [reference 7-32 umol/l] which contraindicated further use of mitotane. Repeat imaging revealed extensive loco-regional and distant metastases in her liver and lungs. 0800 hours cortisol had risen to 1261 nmol/l (while on mitotane) as did adrenal androgens. Her prognosis was guarded and metyrapone was initiated for symptom control of hypercortisolism particularly that of muscle weakness, with some initial relief. She passed away three weeks later, within three months from diagnosis. This case highlights the aggressive nature of ACC and the importance of having a high index of suspicion to allow early diagnosis and intervention, and the need for research and new therapeutics.

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EP377

Acromegaly associated with papillary thyroid carcinoma: report of a case

Amira Bouchenna[1], Lachkhem Aicha[1] & Bensaleh Meriem[1]
[1]central hospital of army, endocrinology, algiers, Algeria

Introduction
The association between acromegaly and neoplasia is rare but described, particularly colorectal and thyroid cancers, especially since the disease is not controlled.
Observation
We report the case of a 44-year-old patient, hypertensive, diabetic, followed for acromegaly clinically retained in the face of dysmorphic syndrome, an IGF1 at 3.5

times normal on a pituitary macroadenoma of 9.9x13x9.3. The assessment of the impact of this acromegaly was without abnormalities. For the neoplastic risk, a colonoscopy returned without abnormalities and a cervical ultrasound revealed a right mid-lobar nodular formation of 10x9 mm classified Eu-Tirads 5, with a fine puncture in favor of a papillary carcinoma of the thyroid. He underwent a total thyroidectomy and the anatomo-pathological examination confirmed the diagnosis: papillary carcinoma of the thyroid of 9 mm right infiltrating the thyroid capsule without crossing it with vascular emboli and perineural sheathing classified pT1a NxMx is classified at high risk of recurrence according to ATA2015 supplemented by 100mci iratherapy.

Discussion

The occurrence of differentiated thyroid cancers is reported in acromegaly. It is related to active secretion of GH-IGF1. Acromegaly is associated in 25% of cases with papillary thyroid carcinoma independently of the BRAF mutation according to one study. In our patient, the number of years of progression of his disease as well as the failure to obtain biological control would be incriminated.

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EP380

Hypophysitis secondary to treatment with pembrolizumab: uncommon endocrinology effects of immunotherapy

Miguel-Angel Ruiz-Gines[1], Juan-Antonio Ruiz-Gines[2], María Zurdo López[1], Mercedes Agudo-Macazaga[1], Macarena Dubert-Perez[1], Vanessa Portillo-Maestre[1], Maria-Carmen Gutierrez-Melendez[1], Susana Vicente-Pantoja[1], Dolores Benitez-Segura[3] & Sandra Ballesteros-Moron[4]
[1]Hospital Universitario de Toledo, Análisis Clínicos, Toledo, Spain; [2]Hospital Clínico Universitario Lozano Blesa, Neurocirugía, Zaragoza, Spain; [3]Centro Regional de Transfusión de Toledo, Hematología y Hemoterapia, Toledo, Spain; [4]Hospital General Universitario Nuestra Señora del Prado, Análisis Clínicos, Talavera de la Reina, Spain

Introduction

Immunotherapy is the oncological treatment whose objective seeks, through the use of immunomodulatory monoclonal antibodies, to block the regulation of the activation and response of T cells, increasing their antitumor response. Pembrolizumab is a new monoclonal antibody directed against the surface protein PD 1, (Programmed Cell Death-1), responsible for the inhibition of the immune response, mediated by T cells, against cancer cells; indicated in the treatment of different malignant neoplasms (non-small cell lung carcinoma). Despite being well tolerated, they have a different adverse effect profile than conventional chemotherapy, with an immune-mediated profile. Among them, endocrinological ones stand out, which can be the cause, among others, of severe hormonal deficits. Our objective is to describe the case of a patient diagnosed with lung adenocarcinoma (stage IV), under treatment with Pembrolizumab, who suffered, as a rare adverse effect, lymphocytic hypophysitis, causing hypopituitarism in the form of central adrenal insufficiency (alteration of the hypothalamic-pituitary-adrenal-axis) and GH deficiency.

Clinical Case

A 39-year-old male, with the oncological history already described, being treated with Pembrolizumab and Pemetrexed (antifolate), referred to the Emergency-Department due to clinical symptoms of diarrhea, abdominal pain, nausea, involuntary vomiting and intense asthenia. He is admitted with a suspected diagnosis of immune-mediated colitis. Complementary-studies: The analysis highlights the involvement of the corticotropic axis and IGF-1 deficiency: TSH 0.175 uU/ml, fT4 1.420 ng/dl, fT3 1.630 pg/ml, FSH 11.6U/l, LH 10.30 U/l, Testosterone 6.51 ng/ml, Prolactin 4.77 ng/ml, ACTH < 1.50 pg/ml, Cortisol 0.8 mg/dl, HGH 0.32 ng/ml, IGF-1 46.2 ng/ml. b. Pituitary-MRI with contrast: Loss of the normal hyperintensity of the neurohypophysis in T1 and moderate thickening of the pituitary stalk, findings that may be compatible with lymphocyti hypophysitis. Given suspicion of adrenal insufficiency, 50mg-IV hydrocortisone was prescribed along with fluid therapy with clear clinical improvement. At discharge, hydroaltesone 20 mg/8h, with progressive decrease to replacement dose. The outpatient study showed ACTH 12.0pg/ml and Cortisol 15.2 mg/dl. After clinical stability, Pembrolizumab cycles are reintroduced.

Discussion and conclusions

The side effects of immunotherapy can occur at different levels in the same patient. Hypophysitis, jointly associating corticotropic and somatotropic deficiency, is an adverse reaction not described to date after studying the available literature, with serious consequences and the need for urgent treatment. Given its potential severity, it is essential, in patients undergoing treatment based on immunotherapy, to maintain a high level of suspicion, so that, in the event of nonspecific symptoms such as nausea, vomiting and/or fatigue (very common), an urgent evaluation should be prompted, including exhaustive hormonal study.

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EP409

Glutaminase 2 expression is associated with adrenocortical carcinoma patients' survival

Sofia B. Oliveira[1,2,3], Clara Pinto[4], Madalena M. Costa[1], Diana Sousa[2,5], Sofia S. Pereira[1] & Duarte Pignatelli[2,3,6]
[1]UMIB - Unit for for Multidisciplinary Research in Biomedicine; ICBAS - School of Medicine and Biomedical Sciences; ITR - Laboratory for Integrative and Translational Research in Population Health, Portugal; [2]i3S – Institute for Research and Innovation in Health, Portugal; [3]CHUSJ – Department of Endocrinology, Hospital São João, Portugal; [4]FCUP - Faculty of Sciences, University of Porto, Portugal; [5]UCP – Universidade Católica Portuguesa, Faculdade de Medicina Dentária, Viseu, Portugal; [6]FMUP – Faculty of Medicine, University of Porto, Portugal

Adrenocortical carcinomas (ACC) are rare and usually very aggressive tumors with heterogeneous outcomes. The individual variability in tumor progression and patients' survival is linked to ACC biology and molecular heterogeneity, reinforcing the need to identify markers with prognosis value, to allow an accurate clinical strategy. Currently, in the absence of specific molecular markers, ACC prognosis is mainly predicted by the European Network for the Study of Adrenal Tumors (ENSAT) tumor stage and tumor proliferation index, assessed by Ki-67 immunohistochemistry. Glutaminolysis is one of the most studied metabolic processes in cancer metabolism context, since it plays a role in cell signaling transduction, proteins, and nucleotides biosynthesis, contributing to cell survival. Therefore, this study aimed to evaluate the role of glutaminolysis in ACC pathophysiology, and to estimate the potential usefulness of its molecular players for ACC prognosis. For that, the expression of proteins involved in glutaminolysis, namely glutaminase 2 (GLS2) and glutamate dehydrogenase 1 (GLUD1), was assessed by immunohistochemistry (IHC) in ACC ($n = 13$) with different clinicopathological behaviors. The percentage of stained area for both molecular markers was quantified using the morphometric analysis tool, ImageJ. Positive staining for GLS2 and GLUD1 was observed in all ACC. Among these molecular markers, only GLS2 expression was positively correlated with ENSAT and Weiss scores. ACC with sinusoidal invasion presented higher GLS2 levels when compared to ACC without sinusoidal invasion. Additionally, GLS2 expression was associated with lower survival rates, whereas Ki-67 expression was not correlated with the survival of these patients. As conclusion, this study demonstrated that glutaminolysis seems to play a role in ACC tumor progression. Remarkably, GLS2 expression was linked with more aggressive malignant features, in particular advanced tumor stage and lower patients' survival. Furthermore, in these cases, GLS2 showed to have a greater prognosis value when compared to the molecular marker currently used in clinical practice, Ki-67. To validate these data, a larger ACC cohort and mechanistic studies are needed.

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EP411

IGF2 and Ki-67 as immunohistochemistry markers for adrenocortical tumors differential diagnosis: a systematic-review and meta-analysis

Sofia B. Oliveira[1,2,3], Mariana Machado[4], Diana Sousa[2,5], Sofia S. Pereira[4] & Duarte Pignatelli[2,3,6]
[1]UMIB - Unit for for Multidisciplinary Research in Biomedicine; ICBAS - School of Medicine and Biomedical Sciences; ITRLaboratory for Integrative and Translational Research in Population Health, Portugal; [2]i3S – Institute for Research and Innovation in Health, Portugal; [3]CHUSJ – Department of Endocrinology, Hospital São João, Portugal; [4]UMIB – Unit for Multidisciplinary Research in Biomedicine; ICBAS - School of Medicine and Biomedical Sciences; ITR- Laboratory for Integrative and Translational Research in Population Health, Portugal; [5]UCP – Universidade Católica Portuguesa, Faculdade de Medicina Dentária, Viseu, Portugal; [6]FMUP - Faculty of Medicine, University of Porto, Portugal

Most of adrenocortical tumors (ACT) are benign and non-functioning tumors, in contrast to adrenocortical carcinomas (ACC), which are rare and usually very

aggressive tumors with a poor prognosis. The pathological discrimination between adrenocortical adenomas (ACA) and ACC is mainly based on unspecific and subjective histological features, resulting in inaccurate diagnosis in several cases. Numerous studies have previously described the potential value of immunohistochemistry (IHC) markers, such as Insulin like-growth factor 2 (IGF2) and the proliferation marker, Ki-67, to detect malignancy in ACT. However, these data were not compiled before. This review aimed to collect the evidence on the potential diagnosis value of IGF2 and Ki-67 immunostaining for ACT. In addition, a meta-analysis was conducted to assess the accuracy of Ki-67 as diagnostic marker for ACC. The systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines. The literature search was carried out in three electronic databases, including PubMed, Scopus, and Web of Science. A total of 25 studies met the pre-defined eligibility criteria being enrolled in the systematic review. Among these, 10 reports assessing Ki-67 IHC expression were identified as eligible for the meta-analysis. All the studies assessing IGF2 expression reported higher levels of this protein in ACC when compared to ACA, despite the differential immunostaining evaluation among the studies. The diagnostic performance of Ki-67 was assessed at the most widely used threshold (5% of stained cells) among the included studies. Ki-67 showed a pooled sensitivity, specificity, and log diagnosis odds ratio of 0.82 (95%CI: 0.65 to 0.92), 0.98 (95%CI: 0.95 to 0.99), and 4.26 (95%CI: 3.40 to 5.12), respectively. At the 5% cut-off value, the area under the summary receiver operating characteristic curve (sROC) was 0.949. As conclusion, Ki-67 marker for a 5% cut-off value showed an excellent specificity but only moderate sensitivity, which translates the failure to diagnosis all ACC. Hence, different Ki-67 thresholds should be considered in the future. Additionally, more studies using similar immunohistochemistry analysis methodologies are needed to assess the accuracy of IGF2 for ACT differential diagnosis.

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EP481

Renal metastasis from papillary thyroid carcinoma: about a case

Amira Bouchenna[1] & Bansaleh Meriem[1]
[1]Central Hospital of Army, Endocrinology, Algiers, Algeria

Introduction
Papillary thyroid cancer is a cancer with a good prognosis and slow progression. Only 2 to 10% of distant metastases, the most frequent at the pulmonary level, cranial metastases represent 2.5 to 5.8% of cases. Renal metastases are extremely rare. We report a case.
Observation
74-year-old patient, without suggesting, presents papillary thyroid carcinoma in its trabecular variant classified pT2NxM1, discovered following a left iliac metastasis. On extension assessment, CT-TAP: found a large left iliac lytic lesion measuring 68×57×71mm, A pulmonary hamartochondroma, bilateral cortical renal cysts including one suspected of malignancy, A harmonious thickening of the outer arm of the right adrenal 9mm and a left renal mass. A biopsy confirmed the secondary origin of the left iliac and renal masses. The patient received 200mci iratherapy, with post-therapeutic scanning of areas of hyperuptake in the left hemi-pelvis and the left renal compartment. Given the risk of bleeding from her left iliac mass, she underwent embolization before orthopedic surgery. Currently she has accumulated 800 mci of iodine with a good response.
Discussion
Renal metastases from differentiated thyroid carcinomas represent 2.5 to 2.7% of cases. Diffusion occurs mainly by the hematogenous route, more rarely by the lymphatic route.

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EP494

Dazzeling evolution with unusual metastases of a medullary thyroid carcinoma: about a case

Amira Bouchenna[1], Benabdelatif Katia[1] & Bensaleh meriem[1]
[1]Central Hospital of Army, Endocrinology, Algiers, Algeria

Introduction
At the time of diagnosis of medullary thyroid carcinoma (MTC) 10 to 15% of patients have distant metastases, 25% of them develop them over a longer or shorter period of time. The usual metastases concern cervical lymphadenopathy, bone, lung and liver. There are also unusual secondary localisations. We report a case.
Observation
A 56-year-old patient who consulted a year after apparition of cervical lymphadenopathy, whose fine needle aspiration returned in favor of a MTC with serum thyrocalcitonin (TCT) level at 2000 pg/l. The extension assessment was negative, the patient was operated on and the anatomopathological study confirmed the diagnosis of MTC classified as PT3N1bM0. The genetic study of the RET mutation could not be carried out. 6 weeks after surgery the TCT level returns to 1500 pg/l. At 3 months after surgery, the patient presented with inguinal lymphadenopathy, the fine needle aspiration of which revealed a carcinomatous process with a TCT level in the liquid washing was 2342 pg/l. the serum TCT level returned to 3789 pg/l, and the extension assessment found a right adrenal metastasis of 14mm (the diagnosis of pheochromocytoma was ruled out), multiple right femoral and vertebral bone metastases with spinal cord compression of L1, the latter's surgery is rejected, so he benefits from decompression radiotherapy. The patient is put on vandetanib
Discussion
The rapid evolution in our patient with the appearance of multiple metastases, two of which are unusual in 2 months, raises fears of a codon 918 mutation of the RET proto-oncogene. Few studies specify the proportion of rare localizations of MTC; one study of 19 patients reported 10% adrenal and digestive metastases, while another of 35 patients found no cases. In our reading we found only two described cases of metastatic inguinal lymphadenopathy.
Conclusion
Metastases from unusual locations do not seem so rare, they must be sought in the event of a doubling of TST values and be treated in patients whose survival is sometimes very prolonged.

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EP546

Grade 2 gastric neuroendocrine tumours type 1: not always an indolent disease

Marina Tsoli[1], Maria Panagaki[1], Katerina Ioannidou[1], Aggeliki Karapanagioti[1], Kosmas Daskalakis[2] & Gregory Kaltsas[1]
[1]EKPA-LAIKO ENETS CoE, Laiko Hospital, National and Kapodistrian University of Athens, Greece; [2]2nd Surgical Department, Korgialenio-Benakio, Hellenic Red Cross General Hospital, Athens, Greece

Background
Gastric neuroendocrine tumors (g-NETs) type I are increasingly recognized and are usually well-differentiated grade 1 neoplasms. However, rare cases of metastatic spread and adverse prognosis have been described in the literature.
Aims
The aim of this study was to evaluate the characteristics and the natural history of grade 2 g-NETs type I.
Materials and Methods
We collected retrospectively the data of patients with g-NETs type I and analyzed the epidemiological, histological and imaging features as well as the clinical outcome of grade 2 tumors.
Results
We analyzed the data of 60 patients (39 female) with mean age (±SD) at diagnosis 55±14 years and a median follow-up time 41 (range: 11-207) months. The median size of the neoplasms was 4.5 mm (range: 1-35 mm) while the median Ki-67 was 5% (range: 3-15%). In nine cases the GC1 were resected using endoscopic techniques while 11 patients were treated surgically (wedge resection or subtotal/total gastrectomy). Eight patients received treatment with long-acting somatostatin analogs (SSA). Two patients displayed regional lymph node infiltration while two others had liver metastases that were resected during primary tumor surgery. The Ki-67 of tumours with liver metastases was 8% and 15% whereas the tumor with the Ki-67:15% was Ga-DOTATATE PET/CT and FDG-PET/CT positive. No recurrence has been observed after surgical resection in patients with locally advanced or metastatic tumors after a median follow-up time of 95 (range: 54-158) months.
Conclusions
Despite the overall favorable prognosis of g-NETs type I, grade 2 neoplasms may in some cases display a more aggressive behavior being associated with distant metastases albeit with no apparent impact on patient's prognosis.

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EP552

Prevalence of adrenal incidentalomas in patients with neuroendocrine tumours

Adam Maciejewski[1], Paweł Komarnicki[1], Kamila Łachut[1], Jan Musiałkiewicz[1], Kosma Woliński[1], Paweł Gut[1] & Marek Ruchała[1]
[1]Poznan University of Medical Sciences, Department of Endocrinology, Metabolism and Internal Medicine, Poznań, Poland

An increasing prevalence of incidental adrenal lesions (adrenal incidentalomas) has been reported in recent years. It is now estimated that adrenal incidentalomas can be found in about 4% of the general population by CT and in up to 10-15% at autopsy. Patients with neuroendocrine tumours (NETs) (including mainly GEP-NETs and pulmonary carcinoids) are expected to have an even higher prevalence of adrenal incidentalomas because of the known genetic preponderance in a subgroup of them (e.g. MEN1 syndrome) and the generally increased risk of second neoplasms postulated in this group. Therefore, the aim of this study was to estimate the prevalence of adrenal incidentalomas in patients diagnosed with NETs and to evaluate their clinical and radiological pattern. A group of 181 NET patients treated in one centre were retrospectively analysed (patients on somatostatin analogue therapy in the course of locally advanced or metastatic NETs). All patients underwent repeated abdominal CT (with initial assessment in an adrenal protocol) and clinical and laboratory evaluation (including serum cortisol and DHEA-S and urine methoxycatecholamine measurement). Of these, 26 (14.4%) had adrenal lesions (35 different lesions). The incidence was similar in women and men (13.6% and 15.4%, respectively). Among the 35 lesions, there were 27 adenomas (77.1%), 3 NET metastases (8.6%), 2 metastases of other origin (renal cell carcinoma; 5.7%), 2 pheochromocytomas (5.7%) and 1 myelolipoma (2.9%). The highest frequency of adrenal incidentalomas was observed in pulmonary NETS (7/20 patients, 35%). Adrenal incidentalomas were found in 15.1% of pancreatic (8/53 patients) and 11.7% of small bowel (7/60 patients) NETs. The prevalence of adrenal incidentalomas in patients with unknown primary NETs was also high - 25% (3/12). As expected, the frequency of adrenal incidentalomas was higher among MEN1 patients (6/9, 66.7%) compared to sporadic cases (20/171, 11.7%). Of the adrenal lesions, 92% were hormonally inactive. Progression in size over time was observed in 11.4% (4/35) of lesions, but only in 3.7% (1/27) of adenomas. The mean diameter of the lesions was 17.0 +- 10.6 mm, with 24 out of 35 (68.6%) located in the left adrenal gland. The prevalence of adrenal incidentaloma is relatively high in NET patients. However, after excluding MEN1 and other genetic syndromes such as VHL, the prevalence drops closer to the values observed in the general population. The majority of incidentally found adrenal lesions are hormonally inactive adenomas that do not exhibit significant growth over time.

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EP553

Idiopathic SIADH can precede cancer diagnosis by a few years: Two case reports and literature review

Tahir Omer[1,2], Shahriar Shafiq[3] & Malgorzata M. Lubczynska[4]
[1]University Hospitals of Northamptonshire, Endocrinology and Diabetes, Northampton, United Kingdom; [2]University of South Wales, United Kingdom; [3]University Hospitals of Northamptonshire, Northampton, United Kingdom; [4]University Hospitals of Northamptonshire, United Kingdom

Introduction
Syndrome of inappropriate antidiuretic hormone secretion(SIADH) is frequently encountered in clinical settings. Hyponatraemia is often seen in cancer and correlates with poor prognosis. It can rarely precede cancer diagnosis. We present a case series of two patients with idiopathic SIADH, who developed terminal malignancy later in life.
Case 1
A 59-year-old female presented in 2016 with seizure due to severe euvolemic hyponatraemia Na103 moml/l (135-145 mmol/l). She received hypertonic solution followed by fluid restriction. Biochemistry showed plasma osmolality 267 mOsmol/kg, urine osmolality 304 mOsmol/kg, urine sodium 55 mmol/l, 9am cortisol 414 nmol/l, TSH 2.1 mU/l. CXR showed small left pleural effusion. MRI brain/CT Chest/abdomen/pelvis were unremarkable. Citalopram was ceased. A diagnosis of idiopathic SIADH was made with advice on long term fluid restriction. Mild hyponatraemia (Na 126-135) persisted until presentation in 2023 with severe hyponatraemia 113 mmol/l requiring hospital admission. CT chest/abdomen/pelvis showed a pulmonary nodule 23×15 mm in the left upper lobe confirming small-cell lung cancer.
Case 2
A 51-year-old female presented in 2014 with severe euvolemic hyponatraemia Na110 mmol/l. She had a history of anorexia nervosa. Biochemistry showed plasma osmolality 260 mOsmol/kg, urine osmolality 342 mOsmol/kg, urine sodium 62 mmol/l, 9 am Cortisol 280 nmol/l, TSH 3.0 mU/l and unremarkable CT head/chest/abdomen and pelvis. No regular medications that could lead to hyponatraemia were identified. Following a diagnosis of idiopathic SIADH, patient was commenced on tolvaptan due to difficulty maintaining stable sodium by fluid restriction. In 2018, she developed dysphagia and was diagnosed with metastatic squamous cell carcinoma of the oesophagus.
Discussion
Although hyponatraemia was observed in several types of cancer, the aetiology of cancer-associated hyponatremia (CAHN) remains poorly understood. About 14% of inpatients hyponatraemia is due to underlying cancer-related-condition. The most common cause of hyponatremia in cancer is thought to be SIADH. There is, however, an increasing evidence for functional involvement of Na^+-transporting-proteins in malignancy. It is hypothesised that various sodium transporting proteins are expressed during early cancer development which gradually deplete sodium. Therefore, hyponatremia can predate cancer diagnosis; however, the evidence overall is not completely clear. As most studies of cancer-related hyponatraemia are carried out in oncology, these patients have multiple confounding variables making it difficult to discern whether hyponatraemia predates or follows malignancy. In the cases presented, hyponatraemia preceded the diagnosis of cancer by a few years further strengthening the role of sodium-transporting proteins in CAHN.
Conclusion
Meticulous follow up in patients with previously diagnosed idiopathic SIADH appear to be the key to early cancer diagnosis and better patients' outcomes.

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EP554

Second neoplasms in patients with sporadic neuroendocrine neoplasms (NENs)

Konstantinos Iliakopoulos[1], Ariadni Spyroglou[1], Panagiota Konstantakou[1], Nikolaos Memos[1], Pantelis Antonakis[1], Vasiliki Michalaki[1], Konstantinos Bramis[1], Eleni Memi[1], George Mastorakos[1], Antonios Vezakis[1], Christos Papadimitriou[1], Ioannis Papaconstantinou[1], Manousos Konstadoulakis[1] & Krystallenia Alexandraki[1]
[1]National & Kapodistrian University of Athens, 2nd Surgical Department, Aretaieion Hospital

Background
Neuroendocrine neoplasms (NENs) are rather uncommon while they have an incidence of no more than 0,5 per 100.000 people. The aim of this study is to investigate the prevalence of second neoplasms among patients diagnosed with sporadic NENs.
Methods
Clinical and histological data from patients followed to our NENs clinic between 2020-2023 were retrospectively evaluated. Patients with a known genetic syndrome were excluded from the analysis.
Results
A total of 40 patients were evaluated, 60% of whom were women, with an age range at diagnosis of 18-78 years. In our cohort, 17 patients were diagnosed with pancreatic NEN (42,5%), 7 patients (17,5%) with small bowel NEN, 7 patients (17,5%) with gastric NEN, 3 patients (7,5%) with appendix NEN, 3 patients (7,5%) with rectal NEN, 2 patients (5%) with lung NEN and one (2,5%) with duodenal NEN. Among these tumors 7 (17,5%) were functioning (three with carcinoid syndrome, two with insulinoma, one with VIPoma, one with gastrinoma). Regarding their differentiation, 29% of the gastroenteropancreatic NENs had a Ki-67 index below 3%, being grade 1, 66% had a Ki-index between 3-20%, being grade 2, one patient had neuroendocrine carcinoma and in one patient no Ki-67 was available. Twenty-eight seconds neoplasms were documented in 22 (55%) of the patients; 5 patients had more than one second neoplasms. The most common diagnoses were adrenal incidentalomas (9, 32%), followed by meningiomas (3, 11%) and 2 (7%) for each of papillary thyroid carcinoma, pancreatic adenocarcinoma, and prostate cancer. From the rest of second neoplasms 3 were malignant and 7 benign neoplasms. Regarding the time of presentation, 10 (36%) had a synchronous diagnosis together with the NEN, 6 of them had a metachronous diagnosis of the secondary neoplasm, while in 12 (43%) patients the NEN diagnosis followed the other neoplasm. Overall, one fourth of the second neoplasms were malignant.
Conclusions
In our study, more than half of the patients diagnosed with NEN displayed in parallel a second neoplasm. This observation is suggestive of a possible genetic association triggering these neoplasms. Further prospective clinical and genetic studies will be needed to elucidate these mechanisms.

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EP555

Genotype-phenotype correlation in serbian patients with multiple endocrine neoplasia type 2 and a mutation in codon 634 of the RET proto-oncogene

Dusan Ilic[1], Sanja Ognjanovic[1], Bojana Popovic[1], Valentina Elezovic Kovacevic[1], Milica Opalic Palibrk[1], Lena Radic[1], Katarina Krstic[1] & Djuro Macut[1]
[1]University Clinical Centre of Serbia, Clinic of Endocrinology, Diabetes and Metabolic Diseases, Belgrade, Serbia

Introduction
Multiple endocrine neoplasia type 2 is an autosomal dominant polyglandular cancer syndrome. It arises as a result of a germline mutation of the *RET* proto-oncogene. The aim of this study was to evaluate the aggressiveness of medullary thyroid carcinoma (MTC) in patients with a proven germline mutation in codon 634 *RET* proto-oncogene, the occurrence of other associated diseases and survival analysis.
Methods
The retrospective study included 66 patients, 26 probands and 40 family members, with a confirmed germline mutation in codon 634 *RET* proto-oncogene. The stage of the disease was determined on the basis of pathohistological findings after surgery for MTC, imaging studies before and after surgery, as well as determination of levels of serum tumor markers.
Results
In the total population of subjects (probands and family members), median age at diagnosis of MTC was 34.18 ± 16.02 years. In the group of probands, carriers of Cys634Arg mutation were diagnosed in younger age compared to carriers of Cys634Phe (31.87 ± 5.01 vs 46.5 ± 4.12 years, p 0.035). Metastatic disease was verified in 28.6% of probands and 21.6% of family members. In both groups, the disease was most often diagnosed in stage 2. No statistically significant difference was found between the preoperative levels of calcitonin and CEA between the groups (p 0.762, P 0.937). The occurrence of disease recurrence was statistically significantly more frequent in probands (p 0.034). In family members who underwent prophylactic thyroidectomy, no MTC was found in two patients at the age 4 and 14, but both had C-cell hyperplasia. The presence of pheochromocytoma was verified in 71% of subjects during follow-up, more often in probands (p 0.004). Median age at diagnosis was 40.90 ± 14.10 years. In 64% of patients with pheochromocytoma tumor was bilateral. The type of mutation in codon 634 did not significantly affect the occurrence of pheochromocytoma (p 0.732). There was no statistically significant difference in the prevalence of primary hyperparathyroidism between the groups (p 0.165). Survival was significantly shorter in patients with stage 4 disease at the time of diagnosis compared to other stages of the disease (p 0.005).
Conclusion
The results obtained in this study indicate the need for early testing of family members of patients in order to enable timely prophylactic thyroidectomy, or to diagnose medullary thyroid cancer or pheochromocytoma at the earliest stage when the possibility of cure is greatest, or to avoid catastrophic consequences of catecholamine excess.

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EP556

Testosterone replacement therapy and prostatic specific antigen monitoring in men with hypogonadism

Kavitha Ganapathy[1] & Brian Lee[1]
[1]Sandwell and West Birmingham Hospitals NHS Trust, Department of Diabetes, Endocrinology and Lipid Metabolism, Birmingham, United Kingdom

Introduction
Testosterone Replacement Therapy (TRT) is used for aged-related or other forms of hypogonadism and prostatic specific antigen (PSA) is primary screening tool for prostatic cancer in men. The European Academy of Andrology guidelines on investigation, treatment and monitoring of functional hypogonadism in males (EAA-TRT) endorsed by European Society of Endocrinology (ESE) states *Recommendation #31. We suggest performing digital rectal examination and checking PSA at 3 to 12 months for men >40 years of age after initiating T treatment. After the first 12 months, local guidelines for prostate cancer screening for the general population should be followed. Recommendation #32. We suggest further evaluation and/or urological consultation if there is: (a) an increase in serum PSA concentration > 1.4 ng/ml within 12 months of initiating T treatment, (b) a confirmed PSA > 4 ng/ml at any time and (c) detection of a prostatic abnormality on DRE or a substantial worsening of LUTS*. Currently we have a local follow up arrangement, namely PSA at TRT initiation with annual check and further urological assessment if PSA increase if beyond age-adjusted limit. We would like to apply retrospectively the above-mentioned (EAA-TRT) PSA monitoring schedule and determine the outcome in patients who have received intramuscular TRT for first 5 years period of therapy.
Description of Methods/Design
We retrospectively analysed PSA and reviewed outcome in patients receiving intramuscular TRT every 10-14 weeks with 5 years follow up.
Results
$n = 22$. Age 52 (41-73) years and PSA at TRT initiation 0.89 (0.09-5.06) μg/l (median and range). 21/22 (95%) patients had no PSA increase >1.4 μg/l after one year of therapy. Among these, one patient (aged 61) identified as having raised PSA at TRT initiation and subsequently confirmed benign prostatic hypertrophy with stable PSA. Only one (aged 73) with PSA rise >1.4 μg/l after one year and found to have prostatic carcinoma and treated. There is no correlation between PSA and age at TRT initiation, Spearman coefficient $\rho = 0.13$.
Conclusion
Using the EAA-TRT PSA monitoring schedule, we would have identified same individuals at risk of prostatic pathology who warrant urological investigations and some individuals would not need further PSA monitoring beyond one year. However, the majority would still need PSA testing anyway because of increased risk of prostatic cancer based on their age (>50) and ethnicity (up to 15% of Black and Afro-Caribbean origins) and who would normally be included in the PSA testing programme.

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EP557

Oligo- and polymetastatic paediatric adrenocortical carcinoma – distinct conditions necessitating different treatment approaches?

Michaela Kuhlen[1], Christoph Slavetinsky[2], Jörg Fuchs[2], Marina Kunstreich[1], Pascal Johann[1], Rainer Claus[3], Michael Frühwald[1], Peter Vorwerk[4] & Antje Redlich[4]
[1]University of Augsburg, Pediatrics and Adolescent Medicine, Augsburg, Germany; [2]University Childreńs Hospital Tuebingen, Department of Paediatric Surgery and Paediatric Urology, Tuebingen, Germany; [3]University of Augsburg, Pathology, Augsburg, Germany; [4]Otto-von-Guericke-University, Department of Paediatrics, Paediatric Haematology/Oncology, Magdeburg, Germany

Background
Metastatic adrenocortical carcinoma (ACC) is a highly aggressive endocrine malignancy with event-free survival rates <10% in most paediatric reports. About 15-25% of patients present with metastases at diagnosis. Complete surgical resection is the mainstay of therapy while chemotherapy and mitotane proved to be ineffective in children with metastatic disease highlighting the need for new approaches. Details on children with metastatic ACC are scarce but desperately needed.
Methods
Data from children and adolescents with metastatic ACC registered with the German Malignant Endocrine Tumour (MET) studies of the German Society for Paediatric Oncology and Haematology (GPOH) were included. We investigated the number, size, and sites of metastases, resectability, and speed of disease spread in patients with primary metastatic disease and metastatic relapse for guiding treatment concepts in future clinical trials.
Results
By December 2022, 20 patients with M+-disease at diagnosis and 22 patients with metastatic relapse had been reported. Median age at diagnosis was 12.8 years and 8.3 years. 2-year event-free survival (EFS) was 15.8% and 22.7%, respectively. Metastases were present in the lungs ($n = 30$), liver ($n = 15$), distant lymph nodes ($n = 14$), bones ($n = 6$), and central nervous system (CNS; $n = 4$). Concurrent metastases in two or more organs were evident in 21 patients. Oligometastatic cancer (herein defined as ≤3 metastases limited to one organ) was reported in 9 patients while it was polymetastatic in 33 patients. R_0 resection of all metastatic sites was achieved in 7 patients including 2 patients with two affected organs. In one patient with a single CNS metastasis, radiotherapy was applied. R_0 resection was not reported in any patient with polymetastatic disease. Sixteen (of 20) and 15 (of 22) patients, respectively, demonstrated progressive disease. In oligometastatic ACC, disease progression was evident after a median of 9.2 months (range, 1.2-37.9), in polymetastatic ACC after a median of 5.5 months (range, 0-34.1). In 4 patients with metastases at diagnosis and 7 patients with metastatic relapse first/second complete remission was achieved. All of these 11 patients presented with oligometastatic disease including one patient with metastases in two organs (liver and lung).
Conclusion
Number, site, and resectability of metastases define prognosis in children and adolescents with metastatic ACC. We observed distinct clinical courses (with

different prognosis) in children and adolescents with oligo- and polymetastatic ACC. New treatment approaches are urgently needed in children and adolescents with metastatic ACC.

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EP558

99mTechnetium-labeled GRPR antagonist for the imaging of prostate cancer – first clinical images

Barbara Bromińska[1], Berthold A. Nock[2], Theodosia Maina[2], Aikaterini Kaloudi[2], Panagiotis Kanellopoulos[2], Barbara Janota[3], Renata Mikołajczak[3], Marek Ruchała[1] & Rafał Czepczyński[1]
[1]Poznan University of Medical Sciences, Department of Endocrinology, Metabolism and Internal Diseases, Poznań, Poland; [2]Molecular Radiopharmacy, INRaSTES, NCSR 'Demokritos', Athens, Greece; [3]National Centre for Nuclear Research, Radioisotope Centre Polatom, Otwock-Świerk, Poland

Introduction
Nuclear medicine procedures offer a possibility of tracing tumor cells based on their physiology. Gastrin-Releasing Peptide receptor (GRPr) is aberrantly expressed in numerous cancers, among them prostate cancer. Demobesin-15 ([^{99m}Tc]DB15) is a novel GRPR-antagonist designed for the evaluation of GRPr expression in different tumors. It has been shown to accumulate in animal prostate cancer models. Hereby, we present our experiences with the first in-human use of [^{99m}Tc]Tc-DB15 SPECT/CT in PCa patients.
Materials and Methods
We qualified three male patients with a newly diagnosed PCa for the study. Diagnosis was based on the prostate biopsy. There were no metastases or extra prostatic extension in any of the patients. All of the patients agreed to participate in the research and gave their informed consent. Firstly, [^{99m}Tc]Tc-DB15 SPECT/CT was performed followed by [^{18}F]-choline PET/CT that served as a reference method. Patients were observed for adverse events directly after injection of the tracer and laboratory measurements were recorded over 28 days.
Results
In all three patients, moderate focal [^{99m}Tc]Tc-DB15 focal uptake in the prostate was visible at planar and pelvic SPECT/CT images. No foci of increased [^{99m}Tc]Tc-DB15 uptake outside the gland was observed. In the PET/CT images of the prostate showed increased ^{18}F-choline accumulation in the same areas of the gland as depicted in [^{99m}Tc]Tc-DB15 SPECT/CT scans. PET/CT did not show any sign of extra prostatic extension of the cancer, nor metastases. We did not record any adverse events post injection of [^{99m}Tc]Tc-DB15.
Conclusions
Accumulation of [^{99m}Tc]Tc-DB15 in the PCa tissue provides preliminary evidence for the utility of this modality in the in vivo detection of GRPr expression in the tumor. What is important, we did not notice any side effects, thus confirming biosafety of [^{99m}Tc]Tc-DB15. For confirmation of clinical utility of [^{99m}Tc]Tc-DB15 SPECT/CT in PCs further research should be conducted.

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EP559

Diagnostic approach and clinical outcome. experience of one clinical centre in managing ectopic ACTH secreting syndrome

Anca Matei[1,2], Viviana Popa[1,2], Diana Martiniuc[1], Maria Lazarescu[1], Simina Plesca[1], Letitia Leustean[1,2], Stefana Bilha[1,2], Maria Christina Ungureanu[1,2] & Cristina Preda[1,2]
[1]Saint Spiridon County Hospital, Iaşi, Romania; [2]Universitatea de Medicină şi Farmacie "Grigore T. Popa' din Iaşi, Iaşi, Romania

Ectopic ACTH secreting syndrome is a rare cause of endogenous ACTH dependent Cushing syndrome. We aim to analyze clinical, biochemical, imaging profile, as well as management and outcomes of 7 EAS patients diagnosed in our clinic within the last 10 years, based on clinical presentation, hypercortisolism, high ACTH levels, specifically over 100pg/ml, with failed high dose dexamethasone suppression test. Clinical presentation was characteristic in 5 of the patients, but 2 showed no signs of Cushing syndrome. The common biochemical feature in 5 of 7 cases was severe, treatment-resistant hypokalemia. All patients also presented with or quickly developed classic complications like diabetes, hypertension, osteoporosis and fractures, recurrent bacterial infections and poor wound healing. A CT scan helped in identifying the causative lesions - 3 neuroendocrine tumors and 3 bronchopulmonary tumors. In one case, the primary tumor couldn't be identified. In almost all cases, coincidental CT findings such as ovarian cystadenoma, adrenal lesions, or benign hepatic and pulmonary lesions, made identifying the primary lesion more difficult. Tektrotide scintigraphy was also necessary in two cases to identify the lesion and assess somatostatin receptor expression. While the therapeutic approach varies, resection of the primary tumor and metastases is the therapeutic goal. When impossible, therapeutic approach can range from steroidogenesis inhibitors such as ketoconazole, which were initiated in all cases, but were therapeutically inefficient or caused side effects (primarily alteration of liver function tests), which led to discontinuation of medication; but also somatostatin analogues, which we initiated both before and after scintigraphic confirmation of receptor expression. Palliative mytotane and osilodrostat therapy was also used to attempt disease control until surgical intervention. Ultimately, bilateral adrenalectomy was the only solution in 3 of the 7 cases. Of 7 cases, only one patient was cured following primary tumor resection one went through primary tumor resection and metastasectomy last week and is currently stable; while the others died within 1 month to 4 years since diagnosis because of sepsis, ischemic stroke or respiratory failure caused by primary bronchopulmonary tumor. In conclusion, ectopic ACTH secreting syndrome is a life-threatening condition, and management and outcome depend both on early diagnosis and prompt therapeutic intervention. The main challenges are identifying the primary lesion and managing the many associated comorbidities, such as hypertension, diabetes, electrolyte imbalances and recurrent infections. A multidisciplinary team comprising of endocrinologists, internal medicine specialists, infectious disease specialists and surgeons is mandatory for the best outcome of these patients.

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EP611

The co-existence of endocrine diseases in patients with neurofibromatosis 1: a case series

Shahini Winson Gnanathayalan[1], Beminahennadige Fernando[1], Manilka Sumanatilleke[1] & Uditha Bulugahapitiya[1]
[1]National Hospital Sri Lanka, Diabetes and Endocrinology, Colombo, Sri Lanka

Background
Neurofibromatosis 1 (NF-1) is an autosomal-dominant multisystemic neurocutaneous disorder. It has long been appreciated that NF-1 is associated with endocrine conditions. The well reported endocrine conditions in NF-1 are growth hormone deficiency, central precocious puberty, pheochromocytoma and gastrointestinal neuroendocrine tumors including insulinoma. Furthermore, individuals with NF-1 are at increased risk of some malignancies including soft tissue sarcomas, peripheral nerve sheath tumors and gastrointestinal stromal tumors (GISTs). These tumors are known to cause non-islet cell tumor cell hypoglycemia (NICTH) due to excessive secretion of insulin like growth factor 2. Here, we describe 2 cases of different endocrine disorders in patients with NF 1.
Case description
Case 1: A 33-year-old lady presented with ischemic stroke. She had elevated blood pressure. But she did not have classic triad of symptoms or spells suggestive of pheochromocytoma. Further assessment revealed the presence of multiple café-au-lait patches, neurofibromas, axillary freckling and bilateral lisch nodules concluding the diagnosis of NF-1. Investigations into the possibility of pheochromocytoma confirmed it with elevated urinary metanephrines more than 5 times the normal upper reference range and large left adrenal tumor. She underwent adrenalectomy and histology further supported the diagnosis of pheochromocytoma. Case 2: A 57-year-old male with NF-1 was evaluated for recurrent major hypoglycemic events and concurrent symptoms of melena, loss of appetite, loss of weight and lethargy for 3-month duration. He was diagnosed to have metastatic GIST. Parallel assessment for frequent spontaneous hypoglycemia made the diagnosis of NICTH with suppressed levels of insulin, c-peptide and beta-hydroxy butyrate with low IGF-1 and positive glucagon challenge test. As the tumor was surgically non-curable, imatinib was started. Due to recurrent level-3 hypoglycemia with hospital admissions, he was initiated on high dose prednisolone. There was initial improvement in hypoglycemia with steroids but after 6 months he gradually deteriorated with gastrointestinal symptoms as well as hypoglycemia and succumbed to death after one year of diagnosis.
Conclusion
Though there are no specific recommendations for surveillance of patients with NF-1, physicians should have a high-index of suspicion in those with symptoms suggestive of endocrine conditions and appropriate screening tests should be performed.

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EP710

Car accident leading to an incidental finding of multiple endocrine neoplasia type 1 (MEN-1)

Iva Jakubíková[1], Barbora Hagerf[1] & Václav Hána[2]
[1]Institute for Clinical and Experimental Medicine, Diabetes Centre, Prague, Czech Republic; [2]First Faculty of Medicine, Charles University and General University Hospital, Third Department of Internal Medicine, Prague, Czech Republic

Introduction
MEN-1 syndrome is an autosomal dominant disorder caused by mutations in tumor suppressor gene MEN1 and is characterized by the occurrence of parathyroid, pancreatic islet and pituitary tumors. Finding such patient means very pro-active approach to be followed as shows our clinical case.
Case-report
A 30-year-old male was sent for an endocrinological investigation due to an incidental finding of a pituitary lesion on a CT scan after a car accident. He had a history of renal colic 3 years before and his mother underwent a parathyroid gland surgery. During an endocrinological examination a neck ultrasound was performed revealing an enlarged parathyroid gland (8×10×13 mm) under the left thyroid lobe. The localization study was then confirmed by scintigraphy scan and primary hyperparathyroidism was biochemically confirmed: total calcium 3.17 mmol/l (2-2.75), phosphate 0.73 mmol/l (0.65-1.61), PTH 8.6 pmol/l (1.58-6.03). Regarding the brain finding the MRI scan revealed an expansion 10×9×9 mm in the infundibular part of the pituitary gland in close attachment to chiasma opticum, the eye perimeter was normal. Prolactin level was slightly elevated 55.59 µg/l (2.1-17.7), other endocrine axes were normal. Because of a strong clinical suspicion, a genetical testing was performed confirming the diagnosis of MEN1. Following current guidelines a subtotal parathyroidectomy was performed with a prophylactic thymectomy decreasing the risk of future malignant neuroendocrine tumors (NET) in this area. Further active surveillance of NET tumors was done, laboratory testing for chromogranin A and gastrin was negative, but the gadolinium PET/CT scan revealed 5 lesions with high expression of somatostatin receptors in the pancreas. According to the MRI pancreatic scan the biggest lesion in the tail had 23 mm and 13 mm the one in the head. Based on multidisciplinary decision the patient underwent surgery: resection of pancreatic tail and enucleation of the NET tumor in the pancreatic head. Lifelong active follow-up is scheduled, including the brain lesion, which was so far managed in a conservative approach.
Conclusion
Patients with MEN1 have a decreased life expectancy, their prognosis might be improved by presymptomatic tumor detection and undertaking treatment specific for MEN1 tumors. MEN1 patients and their families should be cared for by multidisciplinary teams.

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EP753

Rare but real: case report of sertoli-leydig cell ovarian tumor

Nada Aitkassi[1,1], Riad Amal[1], El Mazouni Zainab[1], Rifai Kaoutar[1], Iraqi Hinde[1] & Gharbi Mohamed El Hassan[1]
[1]Hopital IBN Sina Mohamed V University, Endocrinology, Rabat

Introduction and importance
Ovarian Sertoli-Leydig cell tumors (SLCT) are rare sex cord-stromal tumors, representing less than 0.5% of all ovarian malignancies. Typically diagnosed at a young age, with 75% of patients having an average onset age of less than 30, these tumors often present a management challenge due to their early detection in young women. The primary dilemma lies in striking the right balance between implementing an effective treatment to prevent recurrences and preserving fertility. Notably, the majority of these tumors produce hormones, with up to 80% of ovarian Sertoli-Leydig cell tumors manifesting signs of virilization.
Case presentation
We report the case of a 28-year-old patient, followed for secondary amenorrhea evolving for 4 years, with a moderate hirsutism scored at 23 according to the Ferriman and Hallway scale, without signs of virilization. The biological assessment revealed elevated testosterone levels at 6.91 ng/ml, confirmed in three subsequent tests. Other hormonal markers, including Delta 4 androstenedione, DHEA sulfate, 17-OH hydroxyprogesterone, and tumor markers (CA 125, ACE, AFP) returned negative results. In terms of morphological assessment: Abdominopelvic CT scan: A pelvic tissue mass measuring 64 mm, probably of ovarian origin. Pelvic MRI: A tissue mass above and lateral to the left uterus of ovarian origin, with a suspicious appearance of malignancy. The case was discussed in a multidisciplinary consultation meeting, and the patient initially underwent a left annexectomy; the histopathological examination revealed a moderately differentiated Sertoli-Leydig tumor.
Conclusion
In conclusion, ovarian Sertoli-Leydig cell tumors remain rare entities, often posing diagnostic challenges due to their low incidence. Early recognition of these tumors, especially in the context of virilization, is crucial for optimal management. Their secretory nature, the need for histological confirmation post-surgery, and the prognosis linked to the degree of cellular differentiation underscore the importance of a multidisciplinary approach. Treatment, primarily surgical, may be supplemented with adjuvant chemotherapy, and postoperative follow-up is essential due to the risk of recurrence.

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EP754

Hidden culprit: case report of pancreatic insulinoma

Nada Aitkassi[1], Khamel Ghita[1], El Mazouni Zainab[1], Rifai Kaoutar[1], Iraqi Hinde[1] & Gharbi Mohamed El Hassan[1]
[1]Hopital Ibn Sina Mohamed V University, Endocrinology, Rabat

Introduction and importance
Insulinoma is a rare pancreatic neuroendocrine tumor characterized by hypersecretion of insulin, leading to neuroglycopenia symptoms and heightened sympathoadrenal activity. Incidence ranges from 1 to 4 cases per million inhabitants annually, with a predilection for females in their fourth or fifth decade. Despite its rarity, underdiagnosis is suggested by autopsy studies, revealing higher prevalence. Clinical manifestations often mimic other conditions, causing diagnostic delays. Insulinomas can be sporadic or linked to genetic predispositions like type 1 multiple endocrine neoplasia (MEN1). Diagnosis involves clinical and biochemical assessments, with confirmation through tumor localization using non-invasive imaging techniques and for difficult cases invasive modalities could be needed.
Case presentation
We present a case involving a 61-year-old patient who experienced recurring episodes of malaise for over four years, initially misdiagnosed and treated as Parkinson's disease. Upon admission for the investigation of hypoglycemic episodes, the patient underwent a fasting test that indicated endogenous hyperinsulinism based on elevated insulin and C-peptide levels: 18.43 µUi/ml and 4.84 ng/ml. While a CT scan showed no abnormalities, a pancreatic MRI also revealed no lesions; however, an endoscopic ultrasound identified a 5mm lesion in the upper part of the pancreatic body. Subsequent enucleation of the lesion confirmed its neuroendocrine nature through histopathology.
Conclusion
In summary, insulinomas, while usually benign and treatable, pose a risk of misdiagnosis, particularly as their symptoms overlap with epilepsy and psychiatric conditions. Despite their rarity, these tumors can be life-threatening due to severe hypoglycemia, emphasizing the need for continued clinical follow-up post-surgery. The diagnostic challenge, often requiring invasive measures for accurate localization, highlights the importance of a vigilant and multidisciplinary medical approach for effective management.

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EP756

Clinical case: MEN2A and pregnancy

Dovilė Dėnaitė[1] & Diana Šimonienė[2]
[1]Lithuanian University of Health Sciences, Medical Academy, Kaunas, Lithuania; [2]Hospital of Lithuanian University of Health Sciences, Kauno Klinikos, Department of Endocrinology, Kaunas, Lithuania

Introduction
Multiple endocrine neoplasia type 2A (MEN2A) is a rare autosomal-dominant hereditary cancer syndrome characterized by medullary thyroid carcinoma (MTC), pheochromocytoma, and primary hyperparathyroidism. Pregnancy complicating MEN2A is exceedingly rare, with only 29 reported cases. This case discusses an unusual instance where an enlarged thyroid, displaying sonographic features indicative of cancer, led to the diagnosis and management of RET proto-oncogene-positive MEN type 2A during pregnancy.
Clinical case
A 34-year-old woman, initially seen for hyperglycemia, received a diagnosis of type 1 diabetes mellitus and insulin therapy was initiated. Subsequent thyroid sonography revealed suspicious hypoechoic nodule (~0.8×0.7 cm, EU-TIRADS

4). Fine-needle aspiration confirmed MTC, with markedly elevated calcitonin levels (9.9 pmol/l, normal range <2.6 pmol/l). Parathyroid hormone, serum total calcium, metanephrine, and normetanephrine levels were within normal ranges. The patient underwent genetic testing confirming a positive nucleotide sequence analysis of the RET proto-oncogene, establishing the MEN2A syndrome diagnosis. The confirmation of MTC coincided with the patient's pregnancy at gestational week 5. Subsequently, a decision was made to perform thyroidectomy immediately after the termination of pregnancy, with the expectation that MTC would manifest in a non-aggressive manner. During the second trimester at gestational week 20, repeated assessments showed a twofold increase in calcitonin levels (23.9 pmol/l) and an enlarged right lobe with a hypoechoic nodule (0.7 × 0.6 cm, EU-TIRADS 5) containing microcalcifications. The left lobe displayed a similar nodule (0.5 × 0.4 cm, EU-TIRADS 5), confirming disease progression. The clinical case was discussed by a multidisciplinary team, resulting in a consensus that determined the necessity of total thyroidectomy with lymphadenectomy during pregnancy. The operation proceeded without complications. After the baby was delivered, a suprarenal glands MRI was arranged, revealing no pathological findings. Calcitonin and metanephrines were in the normal range, and a follow-up checkup for recurrence is scheduled for a year later. The patient was also advised to undergo RET genetic screening for the baby and family members to rule out the same mutation in the RET proto-oncogene. A mutation has been

Conclusion

Managing rare conditions like MEN2A during pregnancy necessitates heightened awareness and comprehensive clinical assessment. Early detection and intervention are crucial, emphasizing the significance of the RET proto-oncogene mutation in MTC. This case underscores the delicate balance required in managing such cases, emphasizing the importance of a multidisciplinary approach.

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EP757

SDHB gene mutation in a young patient with paraganglioma presented with abdominal pain

Christina Lymniati[1,1], Amalia Sertedaki[2], Georgios Kyriakopoulos[3], Christina Kanaka-Gantenbein[2] & Charalampos Tsentidis[1]
[1]General Hospital of Nikaia Piraeus 'Agios Panteleimon', Endocrinology, Diabetes and Metabolism, Nikaia, Greece; [2]Medical School, National and Kapodistrian University of Athens, Greece, Division of Endocrinology, Diabetes and Metabolism, Aghia Sophia Children's Hospital ENDO-ERN Center for Rare Paediatric Endocrine Diseases, First Department of Pediatrics, Athens, Greece; [3]Evaggelismos General Hospital of Athens, Department of Pathology, Athens, Greece

Introduction

Paragangliomas are rare neuroendocrine neoplasms originating from the chromaffin cells of the neural crest and projecting from the extra-adrenal paraganglia. For more than 30% of patients with paragangliomas there is a genetic predisposition. According to W.H.O. paragangliomas should be treated as potentially metastatic diseases. We describe the case of a patient with a paraganglioma and a pathogenic variant in the SDHB gene.

Case Presentation

A 17-year-old female patient, presented with sudden, abdominal pain, localized around the umbilicus and reflected in the right iliac fossa. Magnetic resonance imaging (MRI) revealed a 2 cm para-aortic mass with characters of probably lymph node. During surgical excision of the mass, the patient had a hypertensive spike that was treated with an increase in anesthesia. The postoperative course was completely satisfactory. However the biopsy revealed a paraganglioma with GAPP score 7. The patient came to our department for further evaluation and follow-up. Clinical examination revealed no symptoms of catecholamine hypersecretion, nor she reported anything remarkable in the past, except for occasional headaches attributed to an intensive study program. Laboratory testing for catecholamines was within normal range, but due to her young age, additional histological immunohistochemistry testing was requested, where a complete absence of staining for the SDHB subunit was found. Whole Exome Sequencing revealed the presence of the maternally inherited heterozygous variant, c.201-2A>G, in the SDHB gene (NM_003000.3). This variant affects intron 2 acceptor splice site and was classified as Pathogenic according to the ACMG criteria and SDHB variant classification recomendations. To date, 6 family members have been found to be carriers of this variant, presenting no symptoms or pathological imaging, indicating low variant penetrance. The patient is currently free of disease, both according to laboratory and imaging tests (DOTADOC, MIBG), and is being monitored based on the relevant guidelines.

Conclusions

A common location of sympathetic paragangliomas is the abdomen (para-ortically, Zuckerkandl body), and, with few exceptions, they secrete catecholamines. For this reason, it should be included in the differential diagnosis of an intra-abdominal mass, even without obvious symptoms of catecholamine hypersecretion, especially when it comes to young people, in order to carry out the appropriate laboratory test preoperatively. Pathogenic variants in the succinate dehydrogenase (SDH) gene and specifically the SDHB, SDHC and SDHD genes, accounts for approximately 50% of hereditary paragangliomas. The combination of paraganglioma with increased GAPP score and SDHB gene mutation is an important predictor of the possibility of metastases.

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EP758

A case study of multiple endocrine neoplasia type 2a

Ines Mezghani[1], Omaima Hammami[1], Rim Marrakchi[1], Faten Hajkacem[2], Mariem Boudaya[1], Kamel Jammoussi[1], Nabila Rekik[2], Mohamed Abid[2] & Mouna Turki[1]
[1]Hedi Chaker University Hospital, Biochemistry Departement, sfax, Tunisia; [2]Hedi Chaker University Hospital, Endocrinolgy Departement, sfax, Tunisia

Introduction

Multiple endocrine neoplasia type 2A (MEN2A) is a rare genetic tumor syndrome due to germline mutations of the RET proto-oncogene, which is characterized by medullary thyroid cancer (MTC), pheochromocytoma, and primary hyperparathyroidism. Our aim was to report a case of a patient with MEN2.

Observation

A 45-year-old patient, with a history of diabetes and corticotropic insufficiency, consulted for paresthesias. The biology showed hypercalcemia at 2.7 mmol/l. The etiological investigation concluded to primary hyperparathyroidism (PTH = 280 ng/l). Cervical ultrasound showed a right thyroid nodule TIRADS 5 and scintigraphy MIBI showed a right parathroid adenoma. The patient underwent surgery. The pathological examination concluded that there was a right parathyroid adenoma with medullary thyroid cancer (MTC) (T1N0M0). The assessment of the postoperative evolution was: PTH: 8.28 ng/l and hypocalcemia: 1.93 mmol/l. After surgery, the patient was addressed for paroxysmal hypertensive crises. The dosage of plasma methoxylated derivatives were elevated to 11× the normal. The topographical assessment revealed two large adrenal masses fixing the MIBG confirming the diagnosis of a bilateral pheochromocytoma. The patient was operated by a bilateral adrenalectomy in 2 stages. The diagnosis of MEN2a neoplasia was made and the genetic study is in progress.

Conclusions

MEN2 is a rare disease. This case study illustrates the importance of recognizing the clinical manifestations of MEN2. Early diagnosis and optimal workup allow for prompt interventions and to decrease the morbidity and mortality associated with MEN2.

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EP763

Erythrocytosis as the initial presentation of an adrenocortical carcinoma: a case report and literature review

Zydrune Visockiene[1,2], Rasa Juskiene[2], Domas Grigoravicius[1,2] & Joana Semigrejevienė[1,2]
[1]Vilnius University Faculty of Medicine, Clinic of Internal Diseases, Family Medicine and Oncology, Vilnius, Lithuania; [2]Vilnius University Hospital Santaros Klinikos, Center of Endocrinology, Vilnius, Lithuania

Background

Adrenocortical carcinoma (AC) is a rare malignancy (0.7–2 cases per million in Western countries) of the adrenal gland. AC can be associated with various syndromes and conditions, one of the rarest being polycythemia. Erythrocytosis refers to an increase in the number of circulating red blood cells. Secondary erythrocytosis, which is characterised by increased levels of Erythropoietin (EPO), can occur due to several causes, among which - hyperandrogenism and EPO-secreting tumors – both have been previously linked to AC. Although the association of AC and polycythemia is known, literature data concerning this comorbidity is lacking.

Case presentation

We present a 41-year-old male, assessed for new-onset hypertension, mild weight gain and abdominal fullness. On physical examination, he was hypertensive with central obesity. Initial laboratory tests revealed erythrocytosis (HgB 206 g/l, RBC $6{,}90\times10^{12}$). Imagining of the adrenals showed a large 11.5×10.5 cm left adrenal mass, consistent with adrenocortical carcinoma. Further investigation revealed elevated late night serum cortisol, non-suppressible early morning cortisol after 1

mg dexamethasone, low adrenocorticotropic hormone (ACTH) and increased dehydroepiandrosterone (DHEA). Patient underwent erythropheresis, followed by adrenalectomy. A histopathological diagnosis of left adrenocortical carcinoma with vascular invasion was made. After surgery RBC and HgB returned to normal and hypercortisolism disappeared. The patient was later referred for subsequent management by oncologist.
Conclusions
This clinical case illustrates a rare presentation of AC. Awareness of this presentation may aid early assessment and timely management.
Keywords: Adrenal carcinoma; Erythrocytosis; Cushing disease.
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EP767

Epidemiology and treatment of adrenal cancer. a case series
Marcin Lewicki[1], Agnieszka Zwolak[1], Joanna Świrska[1], Anna Gołda[1] & Ewa Tywanek[1]
[1]Center of Oncology of the Lublin Region St. Jana z Dukli, Endocrinology, Lublin, Poland

Introduction
Adrenal cancer is a rare, highly invasive malignant tumour with the incidence estimated for approximately 0,5-2,0 cases per milion people annually. Considering the fact that adrenal cancer is very sporadic not much data on its epidemiology is available.
Aim of the study
The aim of the study was to present the single-center data on the epidemiology of the adrenal cancer.
Material and methods
Patients with the diagnosis of adrenal cancer who were treated in Center of Oncology of the Lublin Region St. Jana z Dukli in the years 2021-2023 were enrolled into the study. The following data were analyzed: patients' age at moment of diagnosis, primary disease staging according to ENSAT staging classification, histopathologic examination according to Weiss system, clinical presentation (presence or absence of adrenal hormones excess) and treatment applied to the patients.
Results
The study included 14 patients (8 men and 6 women). The youngest patient was 31 years old (a woman), the eldest was 77 years old (a man). The mean age at the moment of establishing diagnosis was 57 years. In 7 patients the cancer was hormonally active - one female patient presented hyperandrogenemia and hypercortisolemia, two female patients and four male patients had overt Cushing syndrome. In ENSAT staging classification for adrenocortical carcinoma, four patients had ENSAT II stage; seven patients had stage III; three patients had stage IV. In the examined group, 11 patients underwent adrenalectomy. In histopathological examination Weiss system was performed in 12 patients. with the maxuimum score of nine points in one of the patients. All 14 patients received adjuvant mitotane therapy. Five patients received additional adjuvant chemotherapy with etoposide, doxorubicin and cisplatin.
Conclusion
Adrenal cancer is a neoplasm with varied clinical presentation. It demands specific diagnostic tools and treatment protocols. Therefore, treatment sgould be conducted in the high-reference centers.
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EP871

Immunotherapy induced endocrinopathies
Furhana Hussein[1], Gideon Mlawa[2], Swetha Kotha[2], Nancy Mangemba[2], Mahamud Bashir[2] & Aneliya Sirkova[2]
[1]Queen's Hospital, Endocrinology and Diabetes/Acute Medicine, London, United Kingdom; [2]Queen's Hospital, London, United Kingdom

Introduction
Ongoing advancements in the treatment of malignancy has witnessed an increasing use in new immunotherapies, including immune checkpoint inhibitors. Immune-related endocrinopathies affect around 10% of patients treated with checkpoint inhibitors. Common endocrinopathies include thyroid disease and hypophysitis.
Aim
Baseline monitoring test for endocrine disorder in patients started on immunotherapy for cancer treatment and implementation of new trust guidelines to help aid this.
Method
Retrospective single-centre study looking at baseline test for monitoring of endocrine disorders in patients started on immunotherapy for cancer treatment. 22 patients were identified at Queen's Hospital, London, UK (BHRUT–Barking, Havering and Redbridge University Hospitals NHS Trust) in 2023. Measuring baseline cortisol levels, Thyroid Function Tests (TFTs) and HbA1c monitoring before starting immunotherapy.
Results
22 patients identified on immunotherapies including Anti-PD-1 Pembrolizumab (11 patients) and anti-PD-L-1 such as Atezolizumab (7patients) and Durvalumab (4 patients). Patients on Pembrolizumab had 55% baseline cortisol, 73% baseline TFTs and 18% baseline HbA1c. Patients on Atezolizumab had 71% baseline cortisol, 29% baseline TFTs and 14% baseline HbA1c. Patients on Durvalumab had 50% baseline cortisol, TFTs and HbA1c checked. Our team presented findings in a departmental teaching and developed local trust guidelines to help aid recommended endocrine test monitoring and recommended advice/action.
Discussion
Immune checkpoint inhibitors use in cancer treatment has increased. Some studies have shown incidence of severe events is reported as 26% for monotherapy and 55% with combination therapy. PD-1 inhibitors are commonly associated with thyroid abnormalities (5-10%) and can occur 4-10 weeks after initiation of treatment. Diabetes Mellitus (DM) incidence of 1% including new-onset type 1 DM or worsening type 2 DM. CTLA-4 inhibitors are commonly associated with hypophysitis (3-6%) and usually present in 8-10weeks of initiation of treatment. Some studies have reported pituitary hormone deficiencies such as secondary adrenal deficiency (83%), secondary hypothyroidism (77%) and hypogonadotrophic hypogonadism (53%). Primary adrenal insufficiency incidence of 1% as monotherapy and 7% in combination therapy. If undiagnosed early these endocrinopathies can be life threatening.
Conclusion
Our study showed more patient and clinician information on awareness of endocrinopathy complications induced by immunotherapy treatment is important. If undiagnosed early these endocrinopathies can be life threatening. It is important to send baseline endocrine testing and monitoring to aid early diagnosis and treatment of complications. There are no national guidelines; our team have developed local trust guidelines for baseline endocrine test monitoring for patients on immunotherapy treatment. We plan to repeat our study in 6months time with a larger sample size.
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EP962

Non-islet cell tumor hypoglycemia
Eugénie Van Mieghem[1], Hadi Mazlom[2], Isabel Clinck[1] & Christophe De Block[1]
[1]Antwerp University Hospital, Department of Endocrinology-Diabetology-Metabolism, Edegem, Belgium; [2]AZ Klina, Department of Endocirnology-Diabetology, Brasschaat, Belgium

Introduction
A rare cause of hypoglycemia is non-islet cell tumor hypoglycemia (NICTH), a paraneoplastic syndrome caused by tumoral overexpression of insulin-like growth factor 2 (IGF-2) and pro-IGF-2.
Case presentation:
A 57-year old woman presented with odd behavior each morning that improved after breakfast and extensive weight loss (13 kg in 3 years). The patient was hypoglycemic (2.6 mmol/l) with low insulin levels ($<$ 1.39 pmol/l) and C-peptide (0.089 nmol/l). Blood ketones were negative. She was eating normally and did not report alcohol consumption. Sulfonylurea screening was negative. Liver- and kidney function were normal. Further work-up revealed an enlarged liver with several focal lesions and multiple pulmonary nodules, suspicious for metastases. IGF-1 levels were immeasurably low. A liver biopsy revealed primary hepatocellular carcinoma. Due to the hypo-insulinemic non-ketotic hypoglycemia with immeasurably low IGF-1 levels, NICTH was suspected. IGF-2 was not tested due to the limited availability and the high cost at the patient's expense. Therapy with octreotide and diazoxide was attempted but not successful. Therapy with dexamethasone elevated the glycaemia enough to be able to reduce the IV glucose infusions, but had to be tapered as quickly as possible due to initiation of immune therapy. Therefore, continuous glucose monitoring and pasireotide in compassionate use were initiated. Afterwards, she reported a subjectively better quality of life with fewer nightly hypoglycemic arousals. The dose of dexamethasone was reduced, the IV glucose was stopped and the patient was able to go home. Unfortunately, the patient was re-hospitalized after a few weeks due to progression of the malignancy under immune therapy.
Discussion
NICTH is a rare paraneoplastic syndrome caused by oversecretion of (immature) IGF-2 by benign or malignant tumors. IGF-2 can cause hypoglycemia due to insulin-like effects. In patients who fulfill the Whipple triad, other causes of hypoglycemia should be ruled out. NICTH should be suspected in a known or new diagnosis of malignancy with hypo-insulinemic non-ketotic hypoglycemia. If surgical resection,

the mainstay of treatment for NICTH, is not feasible and an increase in frequency or volume of caloric intake isn't enough, further drug therapy can be initiated. Different treatment strategies (glucagon infusions, glucocorticoids or recombinant human GH) are only feasible in the short-term and can have potential detrimental effects. Therapy with diazoxide or octreotide is not successful. Pasireotide has been attempted before in NICTH due to HCC with improved glycemic control. In our case, therapy with glucocorticoids was suboptimal considering her immune therapy. Pasireotide improved her quality of life.

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EP971

Secondary amenorrhea – an inconspicuous presentation of sporadic MEN1 syndrome

Preda-Ivascu Monalisa[1], Radu Iorgulescu[2], Sorina Schipor[3], Andrei Muresan[3], Elena Braha[3], Serban Radian[1,4] & Catalina Poiana[1,4]
[1]C.I. Parhon National Institute of Endocrinology, Endocrinology 1, Bucharest, Romania; [2]Sf Ioan Emergency Clinical Hospital, Surgery, Bucharest, Romania; [3]C.I. Parhon National Institute of Endocrinology, Molecular Biology and Genetics, Bucharest, Romania; [4]C. Davila University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania

Introduction
The MEN1 syndrome is caused by inactivating mutations of MEN1, a tumor suppressor gene encoding menin. A sporadic presentation is relatively rare (8-14%) and could be due to *de novo* mutations.
Aim
To present an MEN1 case diagnosed following a routine consultation for amenorrhea
Case presentation
A 44-year-old female presented with secondary amenorrhea and a history of complicated renal lithiasis requiring repeated urological intervention. Biochemical workup showed moderate hyperprolactinemia (78 ng/ml) and pituitary MRI demonstrated a microprolactinoma, as well as primary hyperparathyroidism with mild hypercalcemia. Bilateral inferior parathyroid adenomas were identified on neck ultrasound examination and confirmed through PTH measurement in FNAB aspirate. Family history was negative for MEN1 manifestations, but the father had died suddenly at 41 yrs of age. There were no clinical manifestations suggestive of neuroendocrine pancreatic tumours.
Management
Prolactinemia was normalized with cabergoline treatment (1 mg/week) and the menses resumed. The patient underwent parathyroid surgical exploration; a right inferior parathyroid adenoma was removed and the left adenoma was not identified, leading to a central compartment dissection and block removal of central lymph nodes; superior parathyroids were macroscopically normal and were preserved. Postoperatively, calcium and PTH were normalized. Postoperatively, results of MEN1 Sanger sequencing of coding exons 2-10 and adjacent intronic sequences identified a likely pathogenic small insertion heterozygous mutation NM_001370259.2:c1700_1701insTTGGTGGC, leading to a frameshift (p.Thr568Trpfs*23). Further workup for MEN1-associated neuroendocrine tumors, as well as genetic screening of family members is pending.
Conclusions
Our patient illustrates an atypical presentation of MEN1, as well as management challenges of hyperparathyroidism in this setting. Genetic testing is recommended in sporadic cases and cases with high suspicion (e.g. multigland hyperparathyroidism). A *de novo* MEN1 mutation remains a possibility in our patient, but its demonstration will be difficult, due to a deceased parent.

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EP998

Pancreatic neuroendocrine tumor in the context of neurofibromatosis type 1

Virginia Soria Utrilla[1], Viyey Kishore Doulatram Gamgaram[1], Marta Iturregui Guevara[1], María Jose Vallejo Herrrera[1] & Stella González Romero[1]
[1]Hospital Regional de Málaga, Endocrinology and Nutrition

We present the case of a 68-year-old man from Ireland with a history of neurofibromatosis type 1, diagnosed in 2000, who underwent surgery for a right pheochromocytoma in 2005. He was recently admitted to hospital for acute cholecystitis, which was treated conservatively with antibiotics. During his hospitalisation, an abdominal CT scan revealed a 1.8 cm lesion in the uncinate process of the pancreas compatible with a neuroendocrine tumor (NET). In addition, multiple lesions were detected in several liver segments, consistent with microabscesses. 18F-FDG PET/CT was performed and confirmed the presence of a hypermetabolic lesion in the uncinate process. Blood tests were performed to assess the functionality of the NET, which showed that it was a non-functioning tumour. A somatostatin receptor scintigraphy was negative for pathological findings. Based on these results, an endoscopy was performed to obtain a tissue sample from the pancreatic lesion. Histological examination confirmed the diagnosis of a well-differentiated NET (G1) with Ki67 $<1\%$ and 0 mitoses/10 HPF. The case was presented to a multidisciplinary committee and it was decided to request an abdominal MRI to assess the evolution of the microabscesses and to complement the study with 18F-DOPA PET/TC. The MRI showed multiple liver lesions compatible with metastasis in addition to the known pancreatic lesion. The 18F-DOPA PET/CT showed no pathological uptake. A Ga-68-DOTATOC PET/CT was also requested and showed no pathological uptake. The patient was referred to medical oncology and started on everolimus 10 mg daily. However, he developed a generalised skin reaction, which necessitated discontinuation of the drug. The case was reassessed by the committee and a two-stage surgical procedure was deemed the most appropriate course of action. Initially, a cephalic pancreaticoduodenectomy with pyloric preservation was performed. Histopathological analysis of the resected tissue revealed a well-differentiated NET, G1, measuring 2.2 cm, with extensive vascular-lymphatic invasion and lymph node involvement (18 lymph nodes involved). Liver lesions were subsequently resected: two in segment II, two in segment III, one in segment IVa, two in segment V, one in inferior segment VI and two in segment VIII. Histopathological evaluation confirmed that these lesions were metastases from a well-differentiated NET. This case highlights the importance of multidisciplinary management in the diagnosis, treatment and follow-up of NETs. A comprehensive approach involving oncologists, endocrinologists, surgeons and radiologists is essential for optimal patient care.

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EP1001

The Inflammasome molecular machinery as a novel source of diagnostic, prognostic, and therapeutic targets in endocrine-related cancers

Ignacio Gil-Duque[1,2,3,4], Miguel E. G-García[1,2,3,4], Ana S. De la Rosa-Herencia[1,2,3,4], Alvaro Flores-Martínez[1,2,3,4], José H-Hernández[1,2,3,4], María Ortega Bellido[1,2,3,4], Manuel D. Gahete[1,2,3,4], Antonio C. Fuentes-Fayos[1,2,3,4] & Raúl M. Luque[1,2,3,4]
[1]Instituto Maimónides de Investigación Biomédica de Córdoba, Córdoba, Spain; [2]Universidad de Córdoba, Departamento de Biología Celular, Fisiología e Inmunología, Córdoba, Spain; [3]Hospital Universitario Reina Sofia, Córdoba, Spain; [4]CIBER - Center for Biomedical Research Network, Physiopathology of Obesity and Nutrition (CIBERobn), Madrid, Spain

Glioblastoma (GBM) is the most prevalent and most lethal primary brain endocrine-related cancer (ERC) in adults which, in addition to the late-stage diagnosis and the lack of effective novel therapies, results in the low quality of life of patients and the poor prognosis, with a median survival from 10 to 14 months after diagnosis. Accordingly, the identification of novel molecular biomarkers of diagnosis and/or prognosis, as well as therapeutic targets becomes crucial to combat this devastating ERC. In this context, the inflammasome molecular machinery, the master regulator of cell inflammation, could be critical in the modulation of the tumor microenvironment (TME), which is essential in the initiation, progression, aggressiveness, and endocrine alterations of different ERC types. In this work, with the objective of determining the putative pathophysiological role of this molecular machinery in GBM, we characterized the components of the inflammasome in GBM samples ($n=63$) from a genomic, transcriptomic, and proteomic point of view, demonstrating a profound dysregulation in comparison to non-tumor brain samples ($n=19$). The main results were confirmed through bioinformatic analyses using several external cohorts of patients. Interestingly, the presence of mutations in the inflammasome machinery, as well as the alteration in the transcriptional expression of key Inflammasome components such as *MYD88*, *NLRP2*, and *RBP4*, was found to be associated with relevant clinical parameters of prognosis such as survival rate, recurrence, and *MGMT* methylation status. Of note, an overall upregulation of the effectors of the inflammasome was observed, suggesting a putative activation of this machinery in GBMs that could induce the establishment of a proinflammatory TME. Moreover, we demonstrated that the inhibition of the activity of the inflammasome (using the inhibitor anakinra) failed to alter the proliferation of GBM cells but was able to successfully reverse the dysregulation in the expression pattern of the inflammasome components previously observed in GBMs in response to metformin. Taken together, our results demonstrate a

profound dysregulation of the Inflammasome machinery in GBM, which could serve as a source of new diagnostic/prognostic biomarkers and therapeutic targets to combat this devastating types of ERC.

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EP1004

Chronic headache revealing multiple insulinomas: a case report

Soumia Laib[1]
[1]University Hospital Center Touhami Benflis. University of Batna 2, Metabolism, Endocrinology & Diabetes, Batna, Algeria

Introduction
Insulinoma is a rare small-size pancreatic endocrine tumor with an annual incidence of 0. 4 cases per 100.000 persons. Approximately 10% are multiple tumors, and its diagnosis and detection remain a challenge. Its symptoms are related to neuroglycopenia and increased catecholamine secretion. It may mimic cardiac, psychiatric, or neurological conditions, thus often leading to a delay in diagnosis.
Observation
A 51-year-old female was referred to us for a history of recurrent episodes of severe headaches regardless of food intake, for the last 5 years, without associated signs or symptoms, there were no precipitating factors. She noted that it was relieved by eating. Her appetite has significantly increased over the past years. There was no history of any drug intake. She was obese. On examination, she weighed 80 Kg, and her body mass index was 32, 92 kg/m^2 The neurological exam was normal and visual disturbances were denied. Endocrine analysis, showed a decrease in serum glucose level 24 mg/dl, an increased level of insulinemia 14.9 µUI/ml (normal range: 2.60-24.9 µIU/l) and c-peptide 2.97 ng/ml (normal range: 1.1-4.4 ng/ml). She had no organ failure or endocrine deficiencies. Magnetic resonance imaging (MRI) of the brain showed no intracranial lesions. Abdominal and Pelvic magnetic resonance imaging (MRI) with contrast showed well-defined two pancreatic hypervascular lesions involving the body and tail of the pancreas measuring 13 mm and 17mm respectively. The diagnosis of multiple insulinomas was made because of hyperinsulinemic hypoglycemia with Whipple's triad and magnetic resonance imaging.
Discussion
Chronic and repeated hypoglycemia lowers the patient's glucose threshold triggers the counterregulatory hormones release and adrenergic symptoms can be suppressed, which delays diagnosis. Typically symptoms associated with insulinoma develop while fasting; only 21% of patients develop symptoms in both the fasting and postprandial states.
Conclusion
This case is interesting because it highlights the importance of a history and a complete physical examination to address the underlying causes of headache related to endocrine disorders. A chronic headache may be the symptoms of insulinoma that first bring the patient to the attention of a physician.

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EP1005

Pulmonary and retroperitoneal paragangliomas in a young woman: about a case report and literature review

Mohammed M'Hammedi Bouzina[1], Benabdelatif Katia[1], Aicha Lachkhem[1], Abdelkader Yahi[1], Amira Bouchenna[1], Ould Kablia Samia[1] & Bensalah Meriem[1]
[1]Algiers Province, Department of Endocrinology, Central Army Hospital, Algiers, Algeria., Algeria

Introduction
Paragangliomas are chromaffin cell tumors that arise from neuroectodermal cells. Multiple paragangliomas in the same patient are highly uncommon. These tumors have a variable clinical picture, and a very heterogeneous evolution. The pulmonary localization is one of the most frequent, representing 20 to 30% of all neuroendocrine tumors. The silent or aggressive character causes problems in diagnosis, management and prognosis.
Case report
We report a case of 46-year-old women, with no significant past medical, family and psychosocial history, admitted for management of two left mediastinal and retroperitoneal lesions, revealed by deep asthenia, anorexia, weight loss and recurrent abdominal pain. The clinical examination reveals an anorexic patient presenting profuse sweating, palpitations, nausea, vomiting and flush syndrome without clinical signs of carcinoid syndrome or catecholamine's tumor hypersecretion. Screening test for hypertension revealed correct blood pressure (100/56 mmHg). Biological exploration confirmed the non-secreting nature of these masses, with a negative level of plasma catecholamines and 5 HIAA. Contrast-enhanced CT of the abdomen revealed a left mediastino-pulmonary lesion measuring 105*94 mm in contact with the thoracic aorta, the left subclavian artery, and the left common carotid artery which are permeable, invading the left upper pulmonary lobe. Another similar avidly enhancing necrotic solid lesion was seen in the infrarenal latero-aortic retroperitoneal measuring 53*29 mm. CT-guided transthoracic needle biopsy was done. The anatomopathological and immunohistochemical study concluded to a moderately differentiated neuroendocrine paraganglioma tumor, positive for chromogranin A, synaptophysin andSOX10; with a Ki67% at 5%. The MIBG scintigraphy confirmed the neuroendocrine nature of the tumors and does not reveal any secondary distant location. Surgical approach is rejected by our RCP due to the intime vascular relationships, and a therapeutic MIBG scintigraphy is proposed for the patient.
Conclusion
An associated non-functional thoracic and retroperitoneal paraganglioma is a very rare clinical situation. Often asymptomatic, their prognosis is dependent to local evolution and the presence of distant metastases. Management must be multidisciplinary, and surgical excision remains the standard treatment.

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EP1006

Successful control of hypoglycemia with Lanreotide in a patient with nesidioblastosis

Mennani fatima ezzahra[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Centre Hospitalo-Universitaire Mohammed VI Marrakech, Endocrinolgy, marrakech

Introduction
Nesidioblastosis is a rare disease caused by hyperplasia of the pancreatic islets, resulting in hypoglycaemia due to increased insulin production. It is the main cause of hyperinsulin hypoglycaemia in children, although it accounts for only 0.5 to 5% of cases in adults. We report here the case of a patient with neidioblastosis successfully treated with lanreotide 120 mg LP, after persistent hypoglycaemia post-surgery.
Clinical case
A 62-year-old patient, not known to be diabetic, hypertensive on triple therapy, had been reporting deep hypoglycemia of 0.24 g/l for 2 years, with 3 to 4 episodes per week, mainly in the mornings. Abdominal MRI revealed a nodular formation at the corporo-caudal junction distorting the anterior contour of the pancreas with T2 hypersignal, T1 isosignal hypersignal measuring 21 × 18 mm. Biological tests revealed a C-peptide level of 2980 pmol/l (300-1400 pmol/l), and an insulin level of 676 pmol/l (18-173 pmol/l). The patient underwent two operations. Anatomopathological examination concluded to a nesidioblastosis. Immunohistochemistry was positive, with expression of anti-CK7 antibodies, anti-chromogranin antibodies and anti-synaptophysin antibodies. Given persistent hypoglycemia postoperatively, the patient was put on diazoxide 300 mg/d and hydrocortisone 60 mg/d without improvement, then Lanreotide 120 mg was added every 4 weeks. Daily monitoring did not reveal any hypoglycemia.
Discussion
The antisecretory effects of somatostatin on various hormones in endocrine organs can be regulated primarily by SSTR2 and SSTR5. They inhibit the counter-regulatory hormones glucagon and growth hormone (GH), which antagonize the effects of insulin. Lanreotide 120 mg LP is a long-acting somatostatin analogue. It is commonly used in the management of NETs. In the literature, cases of insulinoma successfully treated with lanreotide have been reported. However, no cases of nesidioblastosis have been reported.
Conclusions
Thus, in patients with neidioblastosis with hypoglycemia resistant to diazoxide treatment or in cases of poor tolerance of this treatment, the use of Lanreotide seems to be a therapeutic option to be considered.

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EP1007

Co-occurrence of papillary thyroid carcinoma and multiple endocrine neoplasia type 1: a case report

Rihab Khochtali[1], Fatma Mnif[1], Abdel Mouhaymen Missaoui[1], Samir Mkaour[1], Meriem Naifar[1], Mouna Mnif[1], Dhoha Ben Salah[1], Mohamed Abid[1] & Nabila Rekik[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Sfax, Tunisia

Introduction
Multiple Endocrine Neoplasia Type 1 (MEN1) represents a rare genetic disorder characterized by a predisposition to various endocrine neoplasms, primarily affecting the parathyroid, endocrine pancreas, and pituitary gland. So far, Papillary Thyroid Carcinoma (PTC) has been detected in more than 25% of individuals bearing the MEN mutation, even though this particular cancer type does not usually belong to the clinical spectrum associated with this condition.
Case report
We report the case of a 48-year-old woman who presented with hypercalcemia (3.17 mmol/l), hypophosphoremia (0.7 mmol/l), and elevated PTH (400 ng/ml). These biological findings were consistent with the diagnosis of Primary Hyperparathyroidism. A familial MEN1 history was confirmed through genetic testing in siblings with a missense mutation in MEN1 gene exon 4. Neck ultrasound was performed, uncovering a suspected malignant left-sided thyroid nodule (EUTIRADS 4) measuring 17 mm in diameter, with an ectopic parathyroid mass situated at the cervicothoracic junction with a diameter of 26 mm. MIBI scintigraphy featured a characteristic uptake in the ectopic parathyroid mass. Considering the presence of severe osteoporosis (T-score in the radius side $<$ -5.9 SD), persistent hypercalcemia, and the young age of the patient, surgical treatment was decided. The patient underwent left hemithyroidectomy, left upper and lower parathyroidectomy. Intraoperative pathology examination revealed incidental PTC. A completion thyroidectomy and lymph node dissection were subsequently performed. The definitive pathological examination revealed adenomas in two parathyroid glands (ectopic and eutopic) and bifocal PTC (15 mm in the left lobe, 10 mm in the right), with lymph node metastasis. Whole-body scan showed iodine uptake in the thyroid bed with no distant metastases. This PTC was staged pT1b(m)N1a M0 with intermediate ATA risk. The patient received 100 mCi radioactive iodine therapy for isotopic ablation with favorable outcomes.
Discussion
Our case underscores a rare occurrence of the association between PTC and MEN1. While PTC is often linked to BRAF V600E mutation other pro-oncogenic mutations, including MEN1 mutation, are also possible. However, this association is not well established. Further cases are required to validate this potential correlation.
Reference
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EP1010

Ectopic adrenocorticotropic hormone secretion secondary to recurrent olfactory neuroblastoma – a case report

Nikhel Sachdev[1] & Charlotte Choo[1]
[1]Singapore General Hospital, Endocrinology

Background
Severe hypercortisolism from ectopic adrenocorticotropic (ACTH) secretion may be life-threatening. The lung is the most common site of ACTH secreting tumours, ranging from bronchial carcinoids to small cell lung carcinoma. Olfactory neuroblastomas (ONB) are rare malignant neuroectodermal tumours. They show neuroendocrine differentiation and may exhibit a wide variety of paraneoplastic syndromes including ectopic ACTH secretion (EAS). We report a case of EAS from a recurrent olfactory neuroblastoma.
Clinical Case
A 64-year-old male presented with an incidental laboratory finding of severe hypokalemia. He had a background of recurrent olfactory neuroblastoma with neck and dural metastases. He had undergone a resection of the tumour ten years ago, but subsequently experienced intracranial recurrence and slow progression of disease despite three lines of chemotherapy. He had been started on oral dexamethasone one week prior, to reduce the mass effect from the tumour edema. His potassium on admission was 2.2 mmol/l (reference range 3.6 – 5.0 mmol/l). It remained persistently low despite aggressive oral and intravenous replacements. Of note, his potassium level one month ago was normal. His main complaint was increasing lethargy and generalized weakness for the past one month. He had not been taking any new medications, supplements or licorice. Physical examination revealed marked cachexia with proximal myopathy, but no other discriminatory features of Cushing's syndrome. Subsequent investigations revealed inappropriate urinary wasting of potassium. His 0800 hours cortisol (sample taken while on dexamethasone 8 mg twice daily) was 2996 nmol/l, with a markedly elevated ACTH at 429 pg/ml. 24 h urine cortisol collection returned at $>$18205 nmol/l (above the detection limit). Computed tomography imaging revealed unremarkable pulmonary parenchyma but noted interval development of diffuse bilateral adrenal thickening. Magnetic resonance imaging of the brain revealed progressive disease with enlarging dural metastases, and no sellar lesion. He was diagnosed with ectopic ACTH secretion secondary to recurrent olfactory neuroblastoma, resulting in rapid onset of hypokalemia and proximal myopathy, as well as ACTH-dependent bilateral adrenal hyperplasia. Dexamethasone was stopped promptly and he was commenced on oral ketoconazole. The dose was gradually escalated to 600 mg twice a day which achieved good control of his hypercortisolism, allowing for the oncologist to initiate systemic chemotherapy to control his disease.
Conclusion
Olfactory neuroblastoma is associated with a wide range of paraneoplastic syndromes including EAS. Aggressive tumours with EAS often present with rapid onset of clinical signs and symptoms including weight loss, hypokalemia and proximal myopathy. Ketoconazole is a useful therapeutic option in the management of EAS.

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EP1011

Atypical thymic carcinoid tumour with ectopic ACTH syndrome: a rare case with a good prognosis

Mohamed Samir Merad[1] & Fatiha Mohammedi[1]
[1]Oran 1 Ahmed Ben Bella Medical University, Endocrinology and Diabetology departement -Larribere Clinic – university Hospital Dr Benzerdjeb, Oran, Algeria

Introduction
Paraneoplastic Cushing's syndrome is a rare manifestation caused by the ectopic secretion of ACTH. The tumors involved are almost always malignant, with bronchopulmonary being the most frequent, followed by pancreatic and, more rarely, thymic. Thymic carcinoid tumors are very rare neuroendocrine tumors that often complicate endocrine disorders; they are generally more aggressive and difficult to treat, and typical carcinoid tumors in the thymus normally have no endocrine symptoms. Only some specific cases occur with carcinoid syndrome or Cushing's syndrome, and it is widely accepted that surgical resection is the only curative treatment for localized lesions.
Observation
This is a 33-year-old male admitted for possible ACTH-dependent Cushing's disease. He appeared to be quickly developing severe hypercorticism, deteriorated by diabetes, hypertension, and osteoporosis. A 2-day high-dose dexamethasone suppression test suggests ectopic ACTH production. Cervical and thoracoabdominal CT scans indicated oval tissue development in the thymus measuring 11/08 mm with significant heterogeneous enhancement. The patient received a synthetic anticortisolic medication, which restored eucorticism. The thymus was totally resected, and the tumor was removed. The histopathological appearance was that of an atypical carcinoid tumor categorized as T1aNxMx (AJCC 2017). The immunohistochemistry profile was positive for Chromogranin A and Synaptophysin with a high ki67 (40%). The postoperative prognosis was excellent, with remission of Cushing's syndrome and good glycemic and blood pressure management without therapy.
Conclusion
As secretory thymic tumors are very rare, their discovery at an early stage and their resection remain the only solutions for treating paraneoplastic Cushing's syndrome.

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EP1012

Hypoglycemia in pancreatic tumor complicated by bilithorax

Jaddi Oussama[1], Zineb Ait Si Ali[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Mohammed VI university hospital of Marrakesh, Department of Endocrinology, Diabetes, Metabolic diseases and Nutrition, Marrakesh, Morocco

Introduction
Hypoglycemia is a common medical emergency, occurring more frequently in diabetic patients. Rarely induced by a tumor cause, but it is important to recognize the syndrome when it occurs. We report the case of a 64-year-old female patient presenting with hypoglycemia on pancreatic tumor complicated by bilithorax.
Observation
64-year-old female patient, known diabetic for 1 year on Glimeperide 3 mg and Metformin 1 g, hypertension for 1 year on Valsartan, presented to the emergency department with abdominal pain and vomiting for 1 month, associated with mucocutaneous jaundice. Clinical examination: patient conscious, hemodynamically and respiratorily stable; hypoglycemia 0.40 g/l, abdominal examination: ascites with collateral venous circulation and epigastric tenderness. On workup; ASAT: 58 (1.7 N) ALAT 180 (5 N) PT: 43% CRP: 48; tumor markers CA 19-9 and CEA elevated Abdominal MRI: heterogeneous swollen appearance of the body and tail of the pancreas measuring 36 mm in maximum thickness and extending over 7 cm, with infiltration of the peripancreatic fat and moderate peritoneal effusion. Chest X-ray: opaque right pulmonary hemichamber; bilious drainage fluid Cytochemical and bacteriological studies of ascites puncture fluids and pleural effusion were requested.
Discussion
Hypoglycemia is defined as a lower-than-normal blood glucose concentration, traditionally defined biochemically as plasma glucose <3.5 mmol/l. Occasionally, hypoglycemia can be induced by tumors, including insulin-secreting pancreatic tumors and IGF2-secreting non-islet cell tumors. The mechanisms that can cause hypoglycemia in pancreatic tumors are: (1) insulin or insulin-like activity produced by the tumor, (2) decreased gluconeogenesis, (3) disturbed glucagon metabolism and (4) increased glucose utilization by the tumor. Local effects of the tumor on the liver parenchyma may also play an important role.
Conclusion
Hypoglycemia of pancreatic tumor origin remains rare, and treatment is based on tumor control.

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EP1013

Adrenocortical carcinoma with refractory cushing's syndrome: could we have done better?

Raquel Calheiros[1], Sara Gil-Santos[1], Pedro Souteiro[1], Joana Oliveira[1], Isabel Inácio[1], Ana Paula Santos[1] & Isabel Torres[1]
[1]Instituto Português de Oncologia do Porto FG, EPE (IPO-Porto), Endocrinology Department, Porto, Portugal

Introduction
Adrenocortical carcinoma is a rare type of cancer that usually has a dismal prognosis. The concurrent hormonal excess of some of these tumours can have an additional negative impact on patientś morbidity and mortality.
Clinical Case
We present the case of a 57-year-old woman diagnosed with stage IV adrenocortical carcinoma, with liver and bone metastasis, and associated ACTH-independent Cushing syndrome and hyperandrogenism. The patient was started on cytotoxic chemotherapy (etoposide, doxorubicin and platinium), mitotane and metyrapone to control both tumour burden and hormonal secretion. Due to hypercortisolism persistence (salivary midnight cortisol 3.01 ug/dl; morning cortisol 50.8 mg/dl; ACTH <10 pg/ml), mitotane was uptitrated to 6 g/day, metyrapone to 750 mg 3id and ketoconazole was initiated. Uncontrolled Cushing's led to recurrent infections with the need for hospital admission including to the intensive care unit. Recurrent severe hypokalaemia ($K+$ 2.7 mEq/l) episodes also prompted prolonged hospital stays with the need for both oral intravenous potassium chloride (100 mEq/l) and spironolactone addition. Medical therapy was further uptitrated exploring their maximum dosages (mitotane 8 gr/day; metyrapone 2.250 mg/day; ketoconazole 1.600 mg/day; spironolactone 400 mg/day). Despite all these efforts, neither mitotane levels reached therapeutic levels nor did Cushing tests attain normal values. Serial imaging studies revealed structural neoplastic progression. The patient's persistent nausea and vomiting limited her compliance with the therapeutic plan. To reduce the daily pill intake and improve medication tolerability, osilodrostat was requested and approved but the patient died due to disease progression and uncontrolled Cushing before starting this new adrenolytic agent.
Discussion
Pharmacologic management of these patients is challenging considering that metyrapone is useful for Cushing's control but promotes hypokalaemia. Low potassium levels can be mitigated by adding spironolactone, but this agent can cause a decrease in the adrenolytic effects of mitotane. In these cases, uncontrolled hypercortisolism may have a higher impact on patients' prognosis than the tumour burden itself.

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EP1015

Rare primary sites of neuroendocrine tumors:two case reports

Andreea Manole[1], Anca Andrei[1], Alicia Ungureanu[1], Andreea Anne-Marie Ștefan[1], Ramona Dobre[1,2], Iulia-Florentina Burcea[1,2] & Catalina Poiana[1,2]
[1]National Institute of Endocrinology "C.I. Parhon", Bucharest, Romania; [2]University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania

Introduction
Neuroendocrine neoplasms are rare heterogeneous malignancies originating from neuroendocrine cells throughout the body. The most common primary sites are the gastrointestinal and respiratory tracts, but can originate from almost any organ, some in unusual locations. The diagnosis is based on the confirmation of the endocrine nature of the tumor and secondly the confirmation of its primary nature. We describe two cases with a very rare primary localization of neuroendocrine tumor: one in the breast and one hepatic.
Discussion
Case 1 A 43-year-old woman presents after self-diagnosing a left breast lump. Breast ultrasound showed a hypoechoic formation of 1.1/0.6 cm, left breast sectorectomy is performed. Histopathological result: G2 mammary neuroendocrine tumor, positive for hormone receptors (estrogen Alfred 7, progesterone Alfred 6), ki67% 30%, synaptophysin, and HER2 negative. SSTR-2 and SSTR-5 receptors, were positive but no other lesions with somatostatin receptor expression on Tektrotyd scintigraphy. Imagistics was negative, preoperative and at 4 months postoperatively. No carcinoid syndrome with normal serotonin. Chromogranin A was 7.7 times than normal but normalized 6 months postoperatively. Polychemotherapy with Epirubicin and Cyclophosphamide was initiated. It is desired to initiate adjuvant therapy with somatostatin analogue, as evidence supports benefits to survival when endocrine therapies are used in the adjuvant setting. Case 2 A 55-year-old woman known to have extensive right hepatectomy with resection of the main bile duct, lympho-dissection of hepatic and retrocephalopancreatic pedicle. Histopathological result shows: G1/G2 hepatic neuroendocrine tumor, with multiple secondary lymph node determinations, positive for synaptophysin, chromogranin A, CD-56, ki67 4%. Postoperatively, CT TAP, abdominal MRI, cholangio-MRI were performed periodically without evidence of other determinations. Biochemically, within normal limits: neuronal specific enolase, chromogranin A, 5-hydroxyindoleacetic acid/urinary 24 h, with a single slightly elevated serum serotonin 271.10 ng/ml (20-206). Treatment with somatostatin analogue was initiated. Octreoscan scintigraphy is awaited.
Conclusion
Neuroendocrine tumors are a very rare entity, breast and hepatic primary location are unusual. The diagnosis can be challenging and is based on pathological examination and immunohistochemistry, as well as the result of the Octreoscan. The gold-standard treatment is represented by surgical resection and long-term prognosis remains favorable.

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EP1016

Benign insulinoma treated with endoscopic ultrasound guided radiofrequency ablation: a case report

Alina Ghitau[1] & Cristina Spiroiu[1]
[1]Bucharest, Central Military University Emergency Hospital 'Carol Davila', Bucharest, Romania

Background
Insulinoma is a rare pancreatic neuroendocrine tumor, occuring in 1-4 people per million in the general population. It may appear at any age, slightly more common in female than male. Most are benign and solitary. Endogenous hyperinsulinism determines symptomatic hypoglycemia. However, the nonspecific symptoms and small size of these tumors lead to challenges in diagnosis and localization. The treatment of choice is surgical resection, but mini-invasive ablative therapies can be used in selected pacients.
Aim
We present the case of a benign insulinoma treated with endoscopic ultrasound guided radiofrequency ablation.
Case report
A 52-year-old woman presented with a 6 months history of repeated episodes of weakness, fatigue and irritability in a fasting state. Symptoms improved with meals. Over that period of time she gained 10 kilograms. She denied having diabetes or any visual field issues, headaches, behavior change, loss of consciousness or seizures. It is decided that the pacient should undergo a prolonged supervised fasting test and within 30 hours the pacient had symptomatic low plasma glucose level of 38 mg/dl (normal range 74-106) and inappropriately high plasma insulin level of 10.1 μU/ml (normal range 6-35).

Following confirmation of an insulinoma, an abdominal computed tomography scan was done for the preoperative localization, but the result was inconclusive. Endoscopic ultrasonography with fine needle aspiration was performed, confirming a well-differentiated pancreatic neuroendocrine tumor G1, with a diameter of 12/10 mm, located at the junction between the pancreatic isthmus and the body. Endoscopic ultrasound guided radiofrequency ablation (EUS-RFA) using a 19G needle represented the treatment option, as an alternative to surgery and insulinoma was successfully removed. The postoperative evolution was favorable, with minimal abdominal pain treated with analgesic drugs. One week following EUS-RFA, the pacient was asymptomatic, the laboratory tests normalised and during the 3 months follow-up visit, the plasma glucose remained within normal range and the pacient had no active complaints.
Conclusion
This case highlights that an accurate preoperative localization of an insulinoma dictates the management and that EUS-RFA may be a potential alternative to surgery in selected cases. However, more studies are needed to establish the long-term efficacy.

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EP1017

Malignant adrenal tumors: a study of 16 cases

Prince Ismael Mbossa Lembopo[1], Nassim Essabah Haraj[1], Siham El aziz[1] & Asma Chadli[1,1]
[1]Ibn Rochd University Hospital, Endocrinology, Diabetology, Metabolic Diseases, and Nutrition, Casablanca

Introduction
Malignant adrenal tumors are primarily represented by adrenocortical carcinoma and malignant pheochromocytomas. These tumors are rare but potentially aggressive, carrying a bleak prognosis. The aim of this study is to report the clinical, laboratory, and evolutionary characteristics of malignant adrenal tumors.
Patients and Methods
A retrospective descriptive study was conducted at the Endocrinology Department over a 12-year period from 2010 to 2022, including all patients presenting with a malignant adrenal tumor at Ibn Rochd University Hospital in Casablanca. Data analysis was performed using Microsoft Excel 2017.
Results
The study comprised 16 patients, including 9 men and 7 women, with an average age of 42 years. None of the patients had a family history of malignant tumors. There were 12 cases of malignant pheochromocytomas, 3 cases of adrenocortical carcinoma, and 1 case of ganglioneuroblastoma. Discovery circumstances included hypertension in 7 cases, Menard's triad in 3 cases, Cushing's syndrome in 2 cases, abdominal pain in 3 cases, general malaise in 2 cases, and follow-up post-adrenalectomy in 2 cases. The average tumor size was 6.8 cm, with bilateral involvement in 2 patients. Adrenalectomy was performed in 13 patients, while 3 others had a contraindication to surgery. Metastases were identified in the liver, lungs, bones, lymph nodes, and stomach. There were 2 cases of recurrence and 1 case of death. Eleven patients were referred to oncology.
Conclusions
The diagnosis of malignancy can be challenging in the absence of metastases. Regional evaluation of the tumor and the presence or absence of metastasis are necessary to establish prognosis and guide treatment decisions. Therapeutic decisions are made in multidisciplinary consultation.

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EP1063

An uncommon case of thyroid metastasis

Tânia Carvalho[1], Gustavo Rodrigues[1], Alice Monsanto[1], Mafalda Ferreira[1], Mariana Lavrador[1], Mara Ventura[1], Joana Saraiva[1], Cristina Ribeiro[1], Teresa Lindo[2], Belmiro Parada[3], Arnaldo Figueiredo[3] & Isabel Paiva[1]
[1]Centro Hospitalar e Universitário de Coimbra, Serviço de Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal; [2]Centro Hospitalar e Universitário de Coimbra, Serviço de Cirurgia Geral, Coimbra, Portugal; [3]Centro Hospitalar e Universitário de Coimbra, Serviço de Urologia, Coimbra, Portugal

Introduction
Metastasis to the thyroid gland is a rare phenomenon and is associated with primary tumors of the kidney, lung, breast, colorectal, and sarcoma. Thyroid metastases account for only 0.4-3.0% of all malignant neoplasms of the thyroid and occur more frequently in patients with goiter, thyroiditis, or nodules than in patients without previous thyroid pathology.
Case report
A 57-year-old woman with a history of clear cell renal cell carcinoma (CCRCC) underwent right radical nephrectomy in 08/2020. During follow-up, on 11/2020, a heterogeneous nodule was detected in the thyroid isthmus measuring 32 mm and extending to the anterior mediastinum (CT scan). Thyroid ultrasound described an 11 mm nodule in the isthmus, and fine-needle aspiration cytology yielded a benign colloid result. In 07/2022, an abdominal CT scan revealed a heterogeneous mass in the right adrenal gland measuring 58mm, prompting referral to Endocrinology. Hormonal studies were negative. Preoperative staging CT scan described the adrenal and retrosternal mediastinal mass of thyroid origin measuring 38mm. Thyroid ultrasound reported a "nodule at the lower pole of the left lobe-isthmus transition, partially submerged, hypoechoic, heterogeneous, solid, with regular borders, doubtful microcalcifications, and measuring 24×20×39mm." Fine-needle aspiration cytology indicated a suspicious result for papillary thyroid carcinoma (Bethesda V). A two-stage surgery was scheduled: first, she underwent right adrenalectomy, whose histopathological examination identified a CCRCC metastasis in the adrenal gland; subsequently, total thyroidectomy was performed, revealing not a primary thyroid neoplasm but a thyroid metastasis from CCRCC and a small follicular adenoma in the isthmus. The patient continued follow-up in Urology and is currently on sunitinib after the emergence of a neoplastic lesion in the left kidney and suspicious subcentimeter lung nodules.
Conclusion
Although thyroid metastases are uncommon, it is important to consider this possibility in patients with thyroid nodules and a history of malignancy. Fine-needle aspiration cytology has a sensitivity of approximately 70-80% in diagnosing metastatic nodules, but the differential diagnosis can still be challenging and established only after histopathological examination. The relevance of this case is also justified by the rarity of metastasis from CCRCC to two endocrine glands - thyroid and adrenal.

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EP1075

Prognostic factors of differentiated papillary carcinomas: a retrospective analysis on 115patients

Hamza Fatma[1], Boujelben Khouloud[2], Hamdi Frikha[2], Ben Salah[2], Maalej Souhir[2], Elleuch Mouna[2], jardak Issam[1], Maaloul Mohamed[1], Mnif Mouna[2], Mnif Fatma[2], Charfi Nadia[2], Hadjkacem Faten[2], Guermazi Fadhel[1], Chtourou Khalil[1], Abid Mohamed[2] & Rekik Nabila[2]
[1]Habib Bourguiba University Hospital, Department of Nuclear Medicine; [2]Hedi Chaker University Hospital, Department of Endocrinology

Introduction
Differentiated papillary carcinomas (DPC) account for 0.5 to 1% of all neoplasms, and their prognosis is usually favorable. However, a local and distant recurrence is found in up to 35 % of patients. The objective of this study was to determine prognostic factors of this entity among Tunisian population.
Patients and methods
We retrospectively retrieved records of 115 patients diagnosed with DTC and who were then followed at the nuclear medicine department of Habib Bourguiba hospital-Sfax –Tunisia. All patients underwent total thyroidectomy. Radioactive iodine was regularly administrated for intermediate and high risk patients. For each patient, we analyzed age at diagnosis, histological features tumor size nodal status and metastasis. The Cox proportional hazards model was applied to estimate the unadjusted and adjusted hazard ratio (HR) of survival.
Results
On average, 9.5 patients per year was diagnosed with DPC. The mean age was 40 years old (13-83). The mean follow-up was of 13.5 years. Our population was divided into two age groups ($\leq$45 years and $>$45 years). The Ten year survival was significantly different between the two groups ($P=0.03$). The 10-year survival rate was 57.1% and 82.1% respectively for men and women ($P=0.01$). In an adjusted analysis, the risk of death from DPC was significantly correlated with tumor size ($P=0.006$). Tumor necrosis and multifocality were demonstrated as poor prognostic factors ($P=0.013$ and 0.038 respectively). The 10-year survival rate was 93.2% for patients with pN0 versus 58,1 % for those with pN1. Then, lymph node metastasis was also identified as a strong prognostic factor in patients with DPC ($p < 0.001$). Nevertheless, the presence of metastasis at the time of diagnosis showed no significant impact on survival ($P=0.431$).
Conclusion
Although DPC is commonly considered as a low-risk tumor, our study identified several factors influencing the prognosis of DPC. Early aggressive should be instituted for patients presenting those factors in order to improve survival and life quality.

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EP1090

Adrenocortical carcinoma mimicking hyperaldosteronism: a case report

Hemmat El Haddad[1], Rokaya Abdel Aziz[1], Abir Zakaria[1], Moataz Fathy[2], Randa Salam[1], Kerolis Youssef[3], Mohamed Hamdy[3], Asmaa Ezzat[3], Yasser Mahmoud[3], Andro Osama[3] & Abanoub Edwar[3]
[1]Cairo University, Internal medicine, endocrinology, Cairo, Egypt; [2]Cairo University, Internal medicine, nephrology, Cairo, Egypt; [3]Cairo University, Internal medicine, Cairo, Egypt

Background
Adrenocortical carcinomas (ACC) are rare malignancy with an incidence of 0.7-2 per million population per year. While ~60% of ACC are functional, clinical manifestations of hyper-secretion are seen in only ~40% of the cases. Here, we report a case of ACC with initial presentations of hypokalemia and hypertension mimicking hyperaldosteronism
Case report
A 37 year old male complaining of generalized weakness of 2 years duration and fatigue with limitation of daily physical activities, the condition wasn't not associated trauma, convulsions, fever or disturbed consciousness level 8 months ago the patient developed another attack of severe weakness and fatigue, he sought medical advice, investigations were done and showed severe hypokalemia for which he was admitted to ICU and was discovered to be hypertensive. His blood pressure was 180/100 mmHg, pulse:100 / minute regular, respiratory rate:18/min, oxygen saturation: 96%. Examinations were unremarkable. Hematological, renal, liver function&thyroid function test were in the normal range serum sodium was 146 mmol/l (N:136-145) mmol/l potassium (1.5 mmol), His antihypertensive medications were optimized and started on Losartan, amlodipine, Beta-blocker, alpha-blocker, and diuretics (spironolactone). An extensive evaluation was done to find the cause of hypokalemia. Serum Cortisol AM 4.6 (6.2 – 19.4 mg/dl) ACTH AM 10 (7.2 – 63.3 pg/ml) Plasma renin activity 14.81 (3–33 pg/ml) Plasma aldosterone 270 (10–310 pg/ml) Urinary VMA 3.9 (1.0–7.0 mg/day) The contrast-enhanced CT abdomen showed well defined, smooth, heterogeneously enhancing mass lesion in the left adrenal gland measuring 11.4 cm × 10.3 cm × 11 cm with central necrosis. Color Doppler of bilateral renal arteries showed normal flow. ABG showed metabolic alkalosis. Potassium was supplemented from the IV route as well as the oral route After confirming our diagnosis, He underwent laparoscopic unilateral adrenalectomy (left) and intraoperative and postoperative periods were uneventful. The Operated left adrenal mass. Histopathological examination showed atypical cells showing marked pleomorphic exhibiting small cells to giant bizarre-shaped cells indicating adrenocortical carcinoma. The capsular invasion was seen (Weiss score 8) He was discharged with antihypertensive medications (calcium channel blocker and alpha-blocker), planned to taper off, Blood Pressure and potassium reached normal range after 3 month
Conclusion
Management for ACC requires a multidisciplinary approach. The principal considerations are surgical, which is the only curative option for ACC Secondary hypertension from aldosterone secreting ACC is not only uncommon but may also be unfamiliar to the practicing clinicians

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EP1121

Endocrine syndromes and challenges in resource limited healthcare settings from clinical management point of view

Shahroz Azhar[1], Sidra Safdar[2] & Ali Naqvi[1]
[1]Pakistan Kidney & Liver Institute and Research Centre, Internal Medicine & Endocrinology, Lahore, Pakistan; [2]INMOL Cancer Hospital, Radiation Oncology, Lahore, Pakistan

A 32 years old female, presented with bilateral moderate flank pain resolved with analgesics. She visited physician and advised CT Abdomen & Pelvis. It showed bilateral adrenal nodules. She referred to PKLI Urology & Endocrinology Department.
Workup advised. Investigations: Normal TFT's Ultrasound neck: normal thyroid gland with TI-RAD IV nodule in right lobe. AM cortisol 7.6 ng/dl Urine VMA 6.79 24 hour urinary metanephrines > 600 and normetanephrines > 800 Calcium 11 mg/dl PTH 218.3 pg/ml Calcitonin 30.5 pg/ml Prolactin 3.4 ng/ml Parathyroid planner imaging with SPECT showed scintigraphic evidence of hyperfunctioning parathyroid tissue at inferior pole of left lobe of thyroid gland. CT with adrenal protocol showed right adrenal gland enlarged and enhancing lesion measuring 5.2 cm with precontrast attenuation of 50 HU, attenuation arterial phase enhancement of 114 HU and absolute washout of 23%, similarly another enhancing lesion measuring 4.6 cm is noted arising from left adrenal gland with non-contrast attenuation of 45HU, arterial phase attentuation of 108HU and absolute washout of 23% with no locoregional lymph nodes. PET-CT-DOTATE scan showed bilateral, avid, heterogenous nodular adrenal masses. Since patient was symptomatic with biochemical and radiological evidence of Phaeochromocytoma, she was started on Alpha and Beta blockers before surgery. Her case was discussed in MDT, recommended bilateral adrenalectomies, genetic testing, total thyroidectomy and parathyroidectomy. She underwent Bilateral Robotic adrenalectomy and started replacement corticosteroids (10 mg +5 mg +5mg) and Fludrocortisone (100 mg/day). On followup, it was discussed about hemithyroidectomy and selective parathyroidectomy. Her clinical and biochemical profile were consistent with MEN-2A, unfortunately we could not be able to perform genetic studies due to financial constraints. Histopathologically, macroscopic cut section revealed yellow lobulated tumour in both adrenal glands. Microscopic findings suggested encapsulated neoplasm in the adrenal gland, composed of cells with basophilic cytoplasm and variable salt and pepper nuclei, polygonal with numerous areas of spindled-shaped appearance have markedly pleomorphic nuclei arranged in Zellbellen pattern with some diffuse areas of capsular invasion seen however, no extension into extraadrenal tissues or vessels, no areas of necrosis seen. Immunohistochemistry: Synaptophysin: Positive Chromogranin: Positive Ki 67: 1-2%, S100:Highlights supraterticular cells Reticulin: Highlights Zellbellen pattern After recovering from previous surgery, she underwent right hemithyroidectomy and parathyroidectomy Histopathology A) LEFT LOWER INFERIOR PARATHYROID:Parathyroid Adenoma B) Right Hemithyroidectomy:Medullary Thyroid Carcinoma Unifocal, size 0.5x0.5x0.2 cm, Angiolymphatic invasion: Identified, Perineural invasion & Extrathyroidal extension: Not identified, Margins:Closest inked margin 0.3 cm Pathologic staging: pT1 pNx pMx Now planning for completion thyroidectomy and neck dissection.

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EP1123

Abdominal paraganglioma: diagnostic and therapeutic challenge! about 2 cases

Ahmed Boukhalfa[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Mohamed VI University Hospital Center, Marrakech, Morocco, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Introduction
Paragangliomas (PGL) are rare neuroendocrine tumors of the chromaffin cells of the sympathic and parasympathic ganglia. They are responsible for catecholaminergic hypersecretion syndrome. Clinical presentation and malignant potential are variable and closely linked to the genetic profile.
Clinical Case 1
Fifty three year old patient, diagnosed with diabetes and high blood pression for 4 years, she reported a Menard's Triad evolving for 5 years. Abdominal CT scan noted a mass in the right adrenal lodge, spontaneous density (40 HU), measuring approximately 51×31×35 mm, completed by Urinary Methoxyled Derivatives (UMD) of 24 h, elevated to 30 times normal for metanephrine (MN). A right adrenalectomy performed but with no clear clinicobiological improvement. UMD controle were positive to 9 times normal for MN. MIBG scintigraphy revealed a retroperitoneal mass over the right kidney measuring 30*29 mm, associated with an 8.7 mm hepatorenal lymph node, suggesting local invasion. Surgical revision was performed, with histological evidence of a paraganglioma. An octreoscan performed after the 2nd surgery revealed the persistence of a 21×17 mm right retroperitoneal mass. After a multidisciplinary staff meeting, the diagnosis was a locally advanced abdominal paraganglioma; the decision was a 3rd surgery.
Clinical Case 2
Forty eight year old patient, followed for multiple breast, ovarian and S2-S3 radicular cysts, abdominal imaging performed in the face of chronic right lumbar pain, revealed a heterogeneous right retrocavous mass measuring 39×28×25.6 mm. She reported a chronic Menard's Triad. Urinary Methoxyled Derivatives (UMD) of 24 h, elevated to 6 times normal for normetanephrine (NMN). A surgical removal of the mass was done with histological evidence of paraganglioma PASS score 2.
Discussion
The frequency of advanced PGLs in certain genetic diseases varies from 1% to 90%. SDH mutations account for 30% of patients with mtastatic PGL. [1]. Retroperitoneal localization is rare. Certain PGL can be hereditary, particularly in the case of VHL syndrome. Surgery is potentially curative, but tumor dissemination limits the chances of curative resection (2). Other treatment modalities include radiopharmaceutical techniques, chemotherapy, radiotherapy and experimental therapies. Targeted radiotherapy with 131 I MIBG is an option for systemic treatment (3,4).

Conclusion
Surgery remains the cornerstone in locally advanced forms, supplemented by chemotherapy depending on progression, with a response rate of around 40-50%, despite the limitation represented by the scarcity of retrospective studies, the lack of impact on overall survival and the associated toxicity profile (5).
Key words: paraganglioma, genetic profil, surgery.
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EP1127

A case study of managing a patient with bilateral pheochromocytoma in the 21st week of pregnancy

Piotr Przybycień[1], Danuta Gąsior-Perczak[1,2], Jarosław Jaskulski[2,3] & Aldona Kowalska[1,2]
[1]Holycross Cancer Center, Endocrinology Clinic, Kielce, Poland; [2]Jan Kochanowski University, Collegium Medicum, Kielce, Poland; [3]Holycross Cancer Center, Department of Urology, Kielce, Poland

Introduction
Pheochromocytomas are rarely diagnosed in pregnancy. The consequences of pheochromocytoma during pregnancy can be devastating for both mother and fetus. Effective treatment requires an accurate and early diagnosis, but sometimes the tumor is diagnosed relatively late, so it is absolutely necessary to respond quickly and effectively.
Purpose
The aim of our study is to describe a patient with a history of medullary thyroid cancer who underwent surgery for bilateral pheochromocytoma in the 21st week of pregnancy.
Material and method
A 33-year-old woman with a germline mutation of the RET 634 proto-oncogene and who had undergone surgery for medullary thyroid cancer (MEN2A syndrome) several years earlier was hospitalized for examination of bilateral adrenal tumors, detected during a routine ultrasound examination due to pregnancy, confirmed by MRI. In the past, the patient gave up endocrine follow-up several years after thyroid surgery. On the day of admission, the patient was 18 weeks pregnant and did not report any symptoms. Blood pressure was 127/85 mm Hg with a regular heart rate of 120 bpm. MRI scans and double checking for urinary catecholamine metabolites, which were well above the reference range, revealed bilateral pheochromocytoma. Perioperatively, alpha-blocker was used to prevent blood pressure spikes. After the patient consented to bilateral adrenalectomy, laparoscopic surgery was successfully performed in the 21st week of pregnancy. Histopathological examination of both adrenal tumors confirmed the diagnosis of bilateral pheochromocytoma. The tumors were 20x55mm in the right adrenal and 12×33mm in the left adrenal. The rest of the pregnancy and the delivery were uneventful. The natural birth took place at 37 weeks of pregnancy.
Conclusions
1. Women with MEN2A syndrome should receive follow-up to prevent delays in pheochromocytoma detection, which can pose serious problems, especially if they become pregnant. 2. Surgery for bilateral pheochromocytoma in the second trimester of pregnancy can be performed with appropriate cooperation of an endocrinologist, gynecologist and surgeon. 3. Our patient and her child had a positive effect as a result of careful pharmacological and surgical treatment.
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EP1128

A case report of a 69-year-old patient with a paraganglioma metastasis to the thyroid gland

Karolina Piechota[1], Danuta Gąsior-Perczak[1,2], Piotr Przybycień[1], Janusz Kopczyński[3], Artur Kowalik[4,5], Stanislaw Gozdz[2,6] & Aldona Kowalska[1,2]
[1]Holycross Cancer Center, Endocrinology Clinic, Kielce, Poland; [2]Jan Kochanowski University, Collegium Medicum, Kielce, Poland; [3]Holycross Cancer Center, Surgical Pathology, Kielce, Poland; [4]Holycross Cancer Center, Department of Molecular Diagnostics, Kielce, Poland; [5]Jan Kochanowski University, Division of Medical Biology, Institute of Biology, Kielce, Poland; [6]Holycross Cancer Center, Clinical Oncology, Kielce, Poland

Introduction
Paragangliomas are rare neuroendocrine neoplasms arising from chromaffin cells in the sympathetic or parasympathetic neural paraganglia that may appear in many places throughout the body. These might be benign or malignant tumors. We report an interesting case of disseminated paraganglioma, the diagnosis of which began with the metastasis to the thyroid gland.
Case presentation
A 69-year-old patient with a history of toxic multinodular goiter, treated with antithyroid drugs for approximately two years. Cytological features of papillary thyroid cancer were found in a fine needle aspiration biopsy. The patient underwent total thyroidectomy with central neck dissection. Primary histopathological diagnosis was a multifocal thyroid paraganglioma. Post-operative evaluation revealed solid liver lesion on abdominal ultrasound. Cell-block of liver biopsy indicated well-differentiated neuroendocrine tumor cells. Laboratory tests showed Increased levels of chromogranin A, calcitonin, CEA, CA19-9, AFP, HE4. Moreover, we observed elevated concentrations of 3-metoksythyramine in 24-hour urine collection, with normal concentrations of metanephrines and normetanephrines. Ga-68 DOTATATE PET/CT revealed lesions with an increased expression of somatostatin receptors: intervertebral foramen infiltration at level C7/Th1, metastases to the brain, bones, liver, thyroid and adrenal gland. Next Generation Sequencing of blood did not detect pathogenic mutations SDHA, SDHB, SDHC, SDHD, VHL, RET, MAX, SDHAF1, SDHAF2. The patient was treated with palliative radiotherapy to the spine.
Conclusions
Diagnosing paraganglioma with fine needle aspiration biopsy in the thyroid gland might be difficult. It can be misdiagnosed as other thyroid tumors, like papillary neoplasms, follicular neoplasms or medullary thyroid cancer. Histopathological diagnosis of thyroid paraganglioma requires differentiation between an extremely rare primary thyroid paraganglioma and metastatic neuroendocrine tumor. Good cooperation between the clinician and pathomorphologist is crucial for the appropriate diagnosing and subsequent treatment.
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EP1147

Bilateral adrenal hyperplasia as a paraneoplastic phenomenon – a cadaveric case report

Ganesh Velayudham[1], Mohammed Siddiqui[1], Isabel Phillips[1], Juliette Saloway[1], Andre Coetzee[1] & Karuna Katti[1]
[1]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom

Background
Ectopic Cushing's syndrome is a paraneoplastic syndrome characterised by adrenocorticotropic hormone (ACTH) secretion from malignant cells. This can in turn result in overstimulation of the adrenal cortex and adrenal cortical hyperplasia. Resulting hypercortisolism can lead to a host of complications for the patient, including hypertension and hypokalaemia. The aim of this cadaver report is to discuss an unusual case of metastatic lung cancer, presenting with bilateral adrenal hyperplasia and two abdominal aortic aneurysms (AAA). Reports containing documented evidence of bilateral adrenal hyperplasia in the context of paraneoplastic syndromes are rare and serve as the motivation behind this report.
Case presentation
An 84-year-old white, male cadaver was dissected. Sectioning of the right lung revealed a pale-yellow mass measuring 10.0 × 7.4 × 7.0 cm. An irregularly defined, necrotic, ulcerated lesion measuring 5.5 × 4.5 × 3.3 cm was present on the lateral surface of the left shoulder and was assumed to be consistent with a history of metastatic lung carcinoma. Upon abdominal dissection, large adrenal glands were noted bilaterally. Given the finding of what macroscopically appeared to be an infiltrative tumour, along with what would be consistent with metastatic tumour to the skin, a conclusion of bilateral adrenal hyperplasia was considered with the right and left adrenal glands measuring 10.0 × 6.5 × 4.5 cm and 7.3 × 4.7 × 3.5 cm, respectively. There were also two AAAs, measuring 6.0 cm and 11.0 cm at their respective widest transverse diameters.
Conclusion
We propose that bilateral adrenal hyperplasia occurred secondary to lung cancer-related paraneoplastic Cushing syndrome. Resulting hypercortisolism may have propagated the growth of the abdominal aortic aneurysms.
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EP1157

Multiple endocrine neoplasia type 1: diverse clinical presentations and diagnostic challenges

Hind Ouakrim[1], Neima Hassan[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Chu Mohamed Vi Marrakesh - Drh, Marrakech, Morocco

Introduction
Multiple endocrine neoplasia type1(MEN1) is a rare autosomal dominant disorder without a good genotype–phenotype correlation, defined as a tumor developing in at least two endocrine glands including the anterior pituitary gland, the parathyroid glands and the duodenopancreatic endocrine tissue. We present a case report of three patients with a strong suspicion of MEN1.
Cases reports
A 39-year-old with a pituitary surgery history presents a recurrent macro-adenoma, experiencing tumoral symptoms, thyrotrope, and gonadotrope deficiencies, along with kidney issues. Clinical signs include acromegalic features, galactorrhea, nevus-like skin lesions, and grade 1 obesity. Hyperprolactinemia, elevated IGF1, and multiple pituitary deficiencies are identified. Surgery reveals a parathyroid adenoma, dystrophic pancreatic parenchyma, and a grade 2 pancreatic neuroendocrine tumor. A27-year-old urgently admitted for renal failure and anemia is diagnosed with hypercalcemia. The patient reports asthenia, diffuse pain, and a tumoral syndrome featuring headaches, decreased visual acuity, and more. Clinical findings include bone pain, hyperpigmented patches, and subcutaneous nodules. Hypophysogram shows corticotrope, gonadotrope, and thyrotrope deficiency. Cervical ultrasound reveals a right lower parathyroid nodule. Resonance imaging reveals a 6 mm microadenoma. The patient undergoes hemodialysis, transfusions, and surgery for parathyroid adenoma. A61-year-old undergoes surgery for a pituitary macroadenoma causing tumoral symptoms, with corticotrope, gonadotrope, and thyrotrope deficiencies. The histological study confirms a non-secreting pituitary adenoma. Screening reveals primary hyperparathyroidism. Scintigraphy indicates a parathyroid origin for a tissue nodule. The patient receives medical treatment for hypercalcemia and undergoes parathyroidectomy, confirming diffuse parathyroid hyperplasia. In all three cases, MEN1was suspected, unfortunately, genetic testing was not available.
Discussion
The prevalence ofMEN1 in the general population is estimated to range from 1/20,000 to 1/40,000. Mutations inthe MEN1 gene are identified as responsible for the development of this syndrome. At the time of diagnosis, the initial endocrine lesion is solitary in 75% of cases, with each of the primary parathyroid, pituitary, and pancreatic lesions potentially being inaugural. However, parathyroid involvement remains the predominant initial manifestation in the majority of patients, followed by pancreatic neuroendocrine tumors and pituitary adenomas The most common type of pituitary adenoma in MEN1is a prolactinoma, whereas non-functioning adenomas are rare. MEN1 should be considered when various conditions, particularly pituitary, parathyroid, and duodenopancreaticendocrine tissue involvement, are observed in an individual or family. Patients withMEN1 face a reduced life expectancy, with a mortality rate of 50% before the age of50. The prognosis for these patients could be enhanced through presymptomatic detection and specific tumor treatment.

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EP1158

Corticosurrenaloma metastasized: when the challenge becomes twofold

Fatma Mnif[1], Mohamed Khairi Arous[1], Dhoha Ben Salah[1], Rim Khlif[1], Kouloud Boujelben[1], Mouna Elleuch[1], Faten Haj Kacem Akid[1], Nadia Charfi[1], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker Hospital, Endocrinology, Sfax, Tunisia

Introduction
The corticosurrenaloma is a rare malignant adrenal tumor with an unfavorable prognosis. The 5-year survival rate at stage IV, defined by the presence of distant secondary locations, does not exceed 28%. We report the case of a patient followed in our department for stage IV corticosurrenaloma and the challenges encountered during her management
Case report
Ms. H, a 42-year-old patient, is under our care for corticosurrenaloma. Her cancer was discovered 7 years ago due to a general deterioration in health with signs of hyperandrogenism. She underwent total left adrenalectomy with an initial pTNM stage of T2N0M0, complicated by adrenal insufficiency requiring hydrocortisone supplementation. A locoregional recurrence after 3 years necessitated surgical reintervention. Currently, a locoregional recurrence, 4 years after the first recurrence, has been diagnosed, involving the head of the pancreas, compressing the splenic vein, and presenting with giant mesenteric nodules of 20 cm. Imaging also revealed a pulmonary metastasis, while bone scintigraphy was normal. Surgical intervention was deemed impossible, leading us to opt for a systemic treatment with mitotane combined with Doxorubicin and Cisplatin chemotherapy. The initial mitotane dose was 1.5 g/day, with a progressive escalation of 1 g every 3 days to reach 6 g/day. The patient developed acute adrenal insufficiency despite parallel increases in hydrocortisone dose, necessitating a reduction in mitotane to 5 g. Thirty days after initiating mitotane and five days after chemotherapy, the patient presented with progressively worsening ataxia. Initially ruling out cerebral metastasis through imaging, we attributed this complication to mitotane's neurological toxicity, leading to a dose reduction to 4 g/day with a favorable outcome.
Discussion and conclusion
The management of corticosurrenaloma is complex, primarily due to the rapidly deteriorating potential of this tumor and, secondarily, the limited therapeutic means available to date. Mitotane stands as the principal alternative in the face of stage IV corticosurrenaloma when surgery becomes unfeasible. Its proven efficacy in controlling disease progression and improving survival is well-established, yet it is accompanied by various undesirable effects, particularly of a neurological nature. The ataxia exhibited by our patient is indeed attributed to mitotane, with its onset five days after chemotherapy possibly suggesting an additive effect, implicating the neurotoxicity of doxorubicin and cisplatin, as reported in the literature.

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EP1159

Elusive insulinoma

Baseer Khan[1] & Samar Jaffri[1]
[1]Liaquat National Hospital, Internal Medicine, Karachi, Pakistan

Introduction
Insulinoma is a pancreatic tumor that induces hypoglycemia due to over secretion of Insulin. Common symptoms include headache, diplopia, palpitations, blurred vision and unconsciousness. Approximately 90% of insulinomas are benign. Insulinoma is characterized by the Whipple triad, which includes symptoms of hypoglycemia, concomitant plasma glucose of less than 50 mg/dl, and reversal of symptoms after correction of hypoglycemia.
Case presentation
We report a case of a 40-year-old female, married, who presented to us with fit-like activity for 8 years and low blood sugars for 3 years. The patient first experienced fit-like activity in 2015. It was characterized by tremors, and up rolling of eyes, followed by decreased responsiveness. She would remain drowsy for a few hours and then regain full consciousness after intravenous treatment, the record of which was unavailable. Anti-epileptic medications were started. Her symptoms resolved after a few weeks. She then experienced the same symptoms in 2017 that resolved simultaneously. Symptoms recurred in 2020; her random blood sugar level at that time was 35 mg/dl. Her symptoms resolved after intravenous treatment. She was hospitalized in 2023 and her lumbar puncture was done which showed predominant lymphocytic leukocytosis, anti-tuberculosis treatment (ATT) was started. Commencement of ATT also did not resolve her symptoms. After admission to our hospital, supervised hypoglycemia was induced with fasting; her fasting Insulin, C-peptide and cortisol levels were sent once the patient got symptomatic. Hypoglycemia was corrected with intravenous dextrose bolus after drawing a blood sample which led to the resolution of her symptoms. Her laboratory investigations ordered at the time of fasting were; Blood sugar: 28 mg/dl, Insulin: 42.8 mIU/l, C-peptide: 4.05 ng/ml, serum cortisol: 17.7 mg/dl. She fulfilled the Whipple triad and was diagnosed with insulinoma. CT scan abdomen with contrast was unremarkable. Insulinoma was localized in the pancreatic tail via endoscopic ultrasound and was ablated via ethanol. Post ablation, the patient's blood sugars were normal. Her MRI brain and EEG were done to rule out any central pathology, and both were unremarkable. Her repeat CSF-DR was in the reference range with nil White-cell count. ATT was continued. She was then discharged and anti-epileptic medications were tapered off. She has had no fit-like activity post-discharge.
Conclusion
Our patient with Insulinoma was misdiagnosed with epilepsy. It led to inappropriate prescription of anticonvulsants. Therefore, we conclude that Insulinoma should be suspected in patients exhibiting fit-like activity associated with hypoglycemia. Appropriate clinical judgment is essential for timely management.

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EP1160

MEN2A – unexplored, remains undiscovered

Otilia-Andreea Tarcau[1], Robu Larisa[1], ilona-beatrice blesneac[1], Ingrid-Ioana Stafie[1,2], Maria Manaila[1], Nada Akad[1,2], Anca Matei[1,2], Maria Christina Ungureanu[1,2], Grigorovici Alexandru[2,3], Liliana Gheorghe[2,4], Gabriela Delia Ciobanu[2,5], Alexandru Florescu[1,2] & Cristina Preda[1,2]
[1]Saint Spiridon, Endocrinology, Iasi, Romania; [2]Grigore T. Popa University of Medicine and Pharmacy, Medicine, Iasi, Romania; [3]Saint Spiridon Emergency County Hospital, Surgery, Iasi, Romania; [4]Saint Spiridon Emergency County Hospital, Radiology, Iasi, Romania; [5]Saint Spiridon Emergency County Hospital, Pathology, Iasi, Romania

Introduction
Multiple endocrine neoplasia type 2A is an autosomal dominant disorder, caused by mutations in the RET proto-oncogene. The genetic testing may help us in the early identification of carriers, and it can guide us on the follow-up and on the treatment. Thus, we can significantly reduce the morbidity and mortality of this syndrome. We will illustrate a case and highlight the importance of follow-up in a MEN2A patient.
Case report
A 41-year-old woman, presented to our clinic for the first time 23 years ago, when she was only 17 years old, to investigate a secondary cause of hypertension. At that moment, her mother was already diagnosed with pheochromocytoma. After explorations, she was also diagnosed with pheochromocytoma, but due to her young age she was fully investigated and she also received the diagnosis of medullary thyroid cancer (MTC). The patient underwent left adrenalectomy, followed by total thyroidectomy. In the following year, MTC receded. The patient underwent another surgical intervention, this time with good results, but in 2005 she was lost from the records. During that time the hypertension reoccured slowly. She got pregnant 5 times. One pregnancy ended with premature birth at 32 weeks. Three pregnancies were lost in the evolution and the last one ended with the intrauterine death of the fetus at 37 weeks – at that point the patient returned to the clinic. Following the fetal extraction intervention, systolic blood pressure increased to 220 mmHg. She was directed to the cardiology service. The increased values of urinary metanephrines - revealed a recurrence of pheochromocytoma. The computed tomography scans showed an inter-hepato-renal tumour mass and two cystic formations on each of the ovaries. After receiving the perioperative management, a surgical intervention was performed, consisting of extraction of all the tumour masses. Histopathological examination confirmed the presence of pheochromocytoma, a mucinous adenoma cyst on the left ovary and a simple cyst on the right ovary. Genetic testing was recommended for the patient and her son and we are waiting for the results.
Discussion
Maybe if the patient had been reevaluated regularly, the outcome of the last pregnancy would have been different.
Conclusion
It is mandatory to fully explore a patient with MTC or pheochromocytoma, due to the possibility of hiding a MEN2A. This requires rigorous follow-up for the patient and in some cases also for the relatives.

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EP1161

Type 1 multiple endocrine neoplasia syndrome - saved by the somatostatin receptors

Anca Matei[1,2], Viviana Popa[1], Florin Braniste[1,2], Diana Martiniuc[1], Robu Larisa[1], Maria Lazarescu[1], Simina Plesca[1], Andreea Rosu[1], Stefana Bilha[1,2] & Cristina Preda[1,2]
[1]Saint Spiridon County Hospital, Iaşi, Romania; [2]Universitatea de Medicină şi Farmacie "Grigore T. Popa" din Iaşi, Iaşi, Romania

Background
Multiple endocrine neoplasia type 1 (MEN1) is a rare autosomal-dominant tumor syndrome associated with a wide tumor spectrum, in endocrine and nonendocrine tissues, key association being pituitary, parathyroid and enteropancreatic neuroendocrine tumors. Management of MEN1 is challenging because of its polymorphic, variable phenotypic expression.
Case report
Here, we present the case of a 68 year old patient diagnosed in 2004 with an 18 mm istmic pancreatic gastrinoma (gastrin $= 14239$ pg/ml), on account of symptomatic, multiple duodenal ulcers. The diagnosis of MEN 1 is supported by the association with a prolactin secreting pituitary macroadenoma, well controled through time with low dose cabergoline; and hyperparathyroidism, which became apparent 10 years later through biological, ultrasound and osteodensitometric expression, but without TcMIBI scintigraphic confirmation so far. Upon surgical resection, the pathology report confirmed a chromogranin positive, moderately differentiated neuroendocrine carcinoma with a Ki67 $< 1\%$. Within a year, the patient developed an infracentimetric within a year. A whole body scan with 111Indium-Octreoscan revealed uptake of the pancreatic lesion, so octreotide treatment was started in 2011, and serum chromogranin and gastrin levels normalized. Treatment was discontinued after a 99m Tc Tektrotide scan revelead a new pancreatic lesion and bilateral pulmonary secondary lesions. A follow-up CT scan reveals two infracentimetric pancreatic lesions; and a possible infracentimetric hepatic lesion. This, together with increasing gastrin, serotonin and cromogranin levels (650 ng/ml, 401 ug/dl and 509 mg/l, respectively), determined reinitiation of Octreotide treatment, which controlled tumor growth and neuroendocrine marker levels until 2023. In April 2023, the patient presents with altered condition and jaundice, and CT revelead cholelithiasis and a 3 cm pancreatic tumor which invaded the peripheral and common bile ducts; and liver metastases. Follow-up 99m Tc-Tektrotide scintigraphy revealed another liver metastasis and hyperfixation in the epigastrium. Therefore, peptide receptor radionuclide therapy (Lu-177-oxodoterotid) was employed, with two sessions so far, in parallel with octreotide between courses, with favorable evolution of tumors marker levels and tumor size.
Conclusion
MEN1-associated neuroendocrine tumors are indolent neoplasms, with a fluctuating evolution over time. A best-case scenario is when they express somatostatin receptors, which allows for treatment with somatostatin analogues, providing adequate tumor control for a long period of time. If they become inefficient, PRRT therapy can be employed alongside, which offers survival and quality of life benefits. All in all, managing these patients requires a multidisciplinary approach, including endocrinologists, surgeons, radiotherapists and oncologists, and management should be individualized on a case-by-case basis.

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EP1200

Insulinoma; a case of misdiagnosed rare tumour

Amina Al-Qaysi[1], Alawia AlBashir[1], Masood Ashraf[1], Harisanth Rajaram[1] & Sherwin Ganegoda[1]
[1]Buckinghamshire Healthcare NHS Trust, United Kingdom

Introduction
Insulinoma is a rare functional pancreatic neuroendocrine tumour affecting 1 in 4 million individuals per year. The inappropriate hyperinsulinemic state in this condition causes hypoglycaemia resulting in a broad spectrum of clinical manifestations including sweating, shaking, confusion, and seizure.
Case report
An 84-year-old lady was admitted to the hospital after sustaining a witnessed generalised tonic-clonic seizure during the early morning hours associated with having capillary blood glucose of 1.8 mmol/l. She had a history of multiple episodes of involuntary arms and legs shaking at night since a year, she was diagnosed with Rapid Eye Movement sleep behaviour disorder for which she was commenced on Clonazepam that failed to improve her symptoms. The patient developed multiple spontaneous hypoglycaemic episodes during this hospital admission and was found to have inappropriately elevated insulin levels (100 pmol/l) and high C-peptide (1048 pmol/l) during one of the episodes when her plasma glucose was 1.6 mmol/l. The urine sulphonylureas screen was negative. A hyper-vascular $1.3 \times 0.9 \times 1.3$ cm tail of the pancreas mass suggestive of insulinoma was detected on the contrast enhanced CT scan of the abdomen with no radiologic evidence of distant metastasis. The patient elected for medical management, Diazoxide was preferred by our patient for its oral route of administration, and was commenced resulting in significant improvement in her symptoms and was well tolerated.
Conclusion
Insulinoma frequently gets misdiagnosed due to its rare occurrence and because of its wide spectrum of neuroglycopenic and autonomic symptoms that could be at times vague in nature mimicking other neuropsychiatric disorders, as highlighted in this case report. Detailed and careful history taking including obtaining a collateral history remains an essential tool allowing early suspicion of this uncommon diagnosis.

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EP1205

Differentiated thyroid cancer in the adolescent population

Hamza Fatma[1], Khouloud Boujelben[2], Hamdi Frikha[2], Ben Salah Dhoha[2], Maalej Souhir[2], Elleuch Mouna[2], Hadjkacem Faten[2], Jardak Issam[1], Mnif Mouna[2], Mnif Fatma[2], Charfi Nadia[2], Guermazi Fadhel[1], Chtourou Khalil[1], Abid Mohamed[2] & Rekik Nabila[2]
[1]Habib Bourguiba Hospital, Department of Nuclear Medicine; [2]Hedi Chaker University Hospital, Department of Endocrinology

Introduction
Differentiated thyroid cancer (DTC) is one of the most prevalent malignant tumors in adolescents and young adults, accounting for 14-15 % of all neoplasms in this population. Patients present commonly with advanced-stage disease. The aim of our study was to highlight clinical and histopathological features of DTC in the adolescent population.
Patients and Methods
This was a retrospective study, performed in the department of nuclear medicine in Habib Bourguiba hospital –Sfax –Tunisia. Twenty patients with DTC, aged between 18 and 30 years old, were recruited between 2019 and 2020.
Results
The mean age of patients was 26.2 years old. The female sex was the most affected with a sex ratio of 1.8. Clinical features leading to the diagnosis of DTC were as follows: thyroid nodule in 11 cases, cervical lymphadenopathy in 5 cases and symptoms of hyperthyroidism in 4 cases. All our patients underwent total thyroidectomy. Cervical lymphadenectomy was performed in 78.5% of patients. Different cytological features were observed. Classic variant of DTC was the most common histological subtype (86.6%), followed by vesicular variant (15.4 %). Multifocality was noted in 54% of patients. Lymph node involvement was identified in 40% of cases. The tumor multifocality was noted in 54% of patients. Lymph node involvement was identified in 40% of cases.
Conclusion
DTC in adolescents and young adults is characterized by an important initial local and distant extension. Papillary carcinoma remains the predominant type. Then, the risk of lymphatic recurrence is high, but remains curable with a combination of surgery and radioactive iodine.

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EP1206

Thyroid papillary microcarcinoma: a tunisian survey

Fatma Hamza[1], Khouloud Boujelben[2], Hamdi Frikha[2], Dhoha Ben Salah[2], Mohamed Khairi Arous[2], Mouna Elleuch[2], Faten Hadjkacem[2], Issam Jardak[2], Mohamed Maaloul[1], Fatma Mnif[2], Nadia Charfi[2], Mouna Mnif[2], Fadhel Guermazi[1], Khalil Chtourou[1], Mohamed Abid[2] & Nabila Rekik Majdoub[2]
[1]Habib Bourguiba University Hospital, Department of Nuclear Medicine; [2]Hedi Chaker University Hospital, Department of Endocrinology

Introduction
Papillary thyroid carcinoma (PTC) is the most common histological form of thyroid neoplasm, increasingly diagnosed at the microcarcinoma stage (tumor diameter $\leq$10 mm). The majority of papillary thyroid microcarcinomas (PTMC) are not recognizable during physical exam and are commonly diagnosed fortuitously during histopathologic analysis of thyroid specimens following surgery for benign thyroid conditions. The aim of our study was to identify different clinical and pathological characteristics of PTMC.
Patients and Methods
A retrospective study including 51 patients who were followed for PTMC, at the department of nuclear medicine at Habib Bourguiba hospital, Sfax-Tunisia. Clinical, pathological and therapeutic characteristics were analyzed.
Results
The average age of patients was 44.6 $\pm$ 8,9 years. There were 46females and only 3 males PTMC was diagnosed after thyroid nodule and nodular goiter surgery in 41.25% and 23,5 % of cases, respectively. Cervical lympadenopathy was found in 25.5% of cases. Only one patient had a lymph node metastasis. All patients underwent total thyroidectomy and cervical lymphadenectomy was performed in 80 % of patients. Pathological examination revealed a vesicular variant in 23.5% of patients and a classic variant of PTC in 76.5% of patients. Multifodality was found in 68% of patients. The mean tumor diameter was of 3.9 mm (1 mm-10 mm). Lymph node involvement was confirmed in 20 % of patients. Lymphocytic thyroiditis was observed in 35.4% of patients. Capsular rupture was found in 43.1% of surgical specimens.
Conclusions
PTMC present various clinical and histopathological features that emplace them on the borderline of benignity. However, regular follow-up is of a great importance in the management of the tumors, as late recurrence may occur.

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Environmental Endocrinology

EP171

Unraveling the connection between celiac disease and autoimmune endocrinopathies: a comprehensive review of 18 cases"

Lamya Echchad[1], Rifai Kaoutar[1], Iraqi Hinde[1] & Gharbi Mohamed El Hassan[1]
[1]Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Celiac disease is an autoimmune disorder related to gluten ingestion in genetically predisposed individuals. Its clinical expression is polymorphic, rendering it a true systemic disease, and its management is based on a gluten-free diet (GFD). Autoimmune endocrinopathies are disorders affecting endocrine glands such as the thyroid or adrenal glands, also stemming from autoimmune reactions with complex pathophysiological mechanisms involving environmental, genetic, and immunological factors. While the impact of celiac disease on the digestive system is well-established, less is known about the connections between celiac disease and autoimmune endocrinopathies.
Patients & methods
This is a retrospective descriptive study which focuses on 18 cases of Celiac Disease presenting with autoimmune endocrinopathies, with follow-up managed by the Endocrinology and Metabolic Diseases Department of Ibn Sina University Hospital of Rabat. The study spans a 4-year period from October 2018 to October 2022. The aim of our study is to assess the prevalence of autoimmune endocrinopathies in patients with celiac disease and to better identify common underlying mechanisms.
Results
The mean age of our patients was 30.6 $\pm$ 12.6 years, with a female predominance. Autoimmune thyroiditis (Hashimoto's) was present in 16 cases (89%), while type 1 diabetes was present in 4 cases (22%). One case (5.56%) had corticotropin deficiency due to autoimmune hypophysitis. Six patients had 2 to 3 autoimmune pathologies associated with celiac disease, representing 33%.
Discussion & Conclusion
Celiac disease and autoimmune endocrine disorders are intricately interconnected medical conditions. Patients diagnosed with celiac disease exhibit an elevated susceptibility to the onset of endocrine disorders such as autoimmune thyroiditis, type 1 diabetes, and Addison's disease. Through our study, we have illuminated this association by examining a series of 18 cases where individuals with celiac disease concurrently presented with autoimmune endocrinopathies. The intricate mechanisms behind this association remain incompletely understood, with suggestions pointing to the potential involvement of genetic, immune, and environmental factors. It has been proposed that gluten ingestion in celiac disease may trigger an inflammatory response, disrupting the immune equilibrium and resulting in endocrine dysfunction. This association emphasizes the critical need for a systematic assessment of endocrine function in individuals with celiac disease. Likewise, individuals diagnosed with autoimmune endocrine disorders should undergo screening for the possibility of celiac disease, facilitating early and effective intervention.

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EP286

An unusual cause of a head and neck mass: about 18 cases

Houas Jihene[1], Heyfa Belhadj-Miled[1], Monia Ghammam[1], El Ghali Wassim[2], Malika El Omri[1], Abir Meherzi[1], Mouna Bellakhdhar[1], Yosra Hasni El Abed[3], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT Department, Sousse, Tunisia, [2], Department of Anaesthesia, Sousse, Tunisia, [3], Department of Endocrinology, Sousse, Tunisia

Introduction
This study aims to investigate the epidemiological, clinical, and therapeutic dimensions of cervicofacial hydatidosis.
Materials and Methods
A retrospective analysis was conducted on 18 patients who underwent surgery for cervicofacial hydatid cysts between 1982 and 2018.

Results
The average age of the patients was 26 years, ranging from 2 to 79 years. The distribution of cysts included cervical muscle in 8 cases, thyroid in 5 cases, parotid in 2 cases, cervicothoracic in 1 case, laryngeal in 1 case, and jugal in 1 case. One case presented with cyst fistulization to the skin. Preoperative suspicion of hydatid cyst was noted in 6 cases. Surgical treatment was tailored to each cyst's location and confirmed intraoperatively based on macroscopic observations and histopathological findings.
Conclusion
Cervicofacial localization of hydatid cysts is a rare occurrence, even in highly endemic regions. Clinical symptoms vary depending on the cyst's location and size, making preoperative diagnosis challenging. Treatment consists exclusively of surgical intervention to excise the cyst without rupture. The prognosis is excellent in hydatid cyst cases treated with total removal of the cyst without rupture.

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EP301

Factitious hypoglycemia: about 16 cases

Rajaa Mashal[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy- University Hassan II – Casablanca-Morocco, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Departement , Casablanca, Morocco

Introduction
Adult factitious hypoglycemia is due to self-administration of insulin or insulin secretagogue, and is the most common cause of Münchhausen syndrome. The objective is to study the epidemiological profile of patients hospitalized for artificial hypoglycemia for better management.
Patients and methods
Retrospective study carried out at the Endocrinology and Metabolic Diseases Department, Ibn Rochd University Hospital - Casablanca, on patients hospitalized from January 2018 to December 2023 for factitious hypoglycemia.
Results
In our study, 16 patients were included, including 4 men and 12 women. Of these, 10 patients (62.5%) were known type 1 diabetics with an average age of 26.1 years (15 years - 35 years) and an average duration of diabetes of 13 years. And 6 patients not known to be diabetic, with an average age of 19.5 years (15 years - 29 years). the 16 patients were admitted to the department with severe hypoglycemia at 0.3 and 0.6 g/l that persisted despite discontinuation of insulin therapy in diabetic patients. all our patients underwent a hormonal work-up with a jeün test. Hormonal assays showed elevated and appropriate cortisol levels in all our patients, with elevated insulin and normal C-peptide levels in 6 patients (3 T1DM and 3 non-diabetic patients), and elevated and inappropriate insulin and C-peptide levels in the other patients. A psychological interview revealed the presence of parental conflicts for our 10 young patients and 6 patients in an anxio-depressive state, with the notion of dummy intake of rapid insulin in 14 patients and dummy intake of gliclazides for 1 non-diabetic patient.
Discussion and conclusion
Factitious hypoglycemia is a difficult-to-diagnose psychiatric disorder. They are most often found in female patients with easy access to hypoglycemic treatments. Psychiatric follow-up is necessary to avoid recurrences, which can be life-threatening in this situation.

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EP332

Can the exposure to the UV-B filter octinoxate modify the response to exogenous triiodothyronine in zebrafish embryos?

Margarida Lorigo[1,2,3], Elisa Cairrao[1,2], Marta Monteiro[3], Luiza Breitenfeld[1,2], Amadeu Soares[3] & Carla Quintaneiro[3]
[1]CICS-UBI, Health Sciences Research Centre, University of Beira Interior, Covilhã, Portugal, [2]FCS - UBI, Faculty of Health Sciences, University of Beira Interior, Covilhã, Portugal, [3]Department of Biology & CESAM (Centre for Environmental and Marine Studies), University of Aveiro, Aveiro, Portugal

The harmful impact of exposure to ultraviolet (UV) filters is a topic of widespread concern due to human toxicological effects. Exposure to these environmental contaminants has emerged due to their extensive use as ingredients in personal care products and their incomplete removal in wastewater treatment plants. Due to their lipophilicity, UV filters are prone to bioaccumulate in aquatic biota, presenting potential adverse effects on both aquatic organisms and humans. The octinoxate (OMC) is one of the most used UV filters as ingredient in the cosmetic industry. Currently, OMC is included in the Community rolling action plan (CoRAP) list (REACH) and List II (EC/List No. 629-661-9) of substances under evaluation for endocrine-disrupting properties under EU legislation. It is known that OMC is an endocrine-disrupting compound (EDC), which interacts with the Hypothalamus-Pituitary-Thyroid (HPT)-axis. Despite this, the toxicological effects induced by OMC on the thyroid hormone (TH) system are not completely understood. Zebrafish (Danio rerio: Cyprinidae, Teleostei) is one of the most widely used model species in developmental biology and biomedicine for endocrine disruption prediction studies. Several studies have reported the crucial role of TH in normal development and physiological homeostasis during the life cycle of zebrafish, including morphogenesis, neurodevelopment, pigmentation, metabolism, and growth. Due to the highly conserved HPT-axis with humans, zebrafish is a promising alternative model for mechanistic studies of TH regulation. Furthermore, zebrafish embryos can be used as a non-animal alternative up to 5-days post fertilization (dpf) (Directive 2010/63/EU, 2010). In this context, this work aimed to understand if and how the exposure to UV-filter OMC modifies the response to exogenous triiodothyronine (T3) and impairs normal zebrafish embryo development. To achieve this, an integrative approach from apical to transcriptional endpoints was used. Zebrafish embryos were exposed to sub-lethal concentrations of OMC (0.04 – 4 mg/l) during 120 hours in binary mixture with T3 (0.02 mg/l). The endpoints evaluated included fish embryo development (hatching and malformations), heart rate, and behaviour. Moreover, the expression of a suite of genes involved in the HPT axis were also assessed as transcriptional endpoint. By unveiling the thyroid-disrupting effects of OMC in zebrafish-developing embryos, we will contribute to increase the knowledge of the OMC mode of action in order to develop measures to promote human thyroid health.

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EP628

Macro-vitamin b12 as a new medical entity

Tamar Peshkova[1], Liana Jashi[2], Koba Kamashidze[3], Irina Nakashidze[1] & Ketevan Dundua[2]
[1]Batumi Shota Rustaveli State University, Batumi, Georgia, [2]David Aghmashenebeli University Of Georgia, T'bilisi, Georgia, [3]The University of Georgia, Tbilisi, Georgia

Introduction
The plasma vitamin B12 (B12) measurement is mainly conducted to detect B12 deficiency. But incidental finding of elevated B12 is not uncommon and may be a sign of serious disease, like solid cancers or caused by over-supplementation. However, there are cases in which high B12 levels are seen in the absence of supplements.
Case
A 57-year-old female presented to our outpatient endocrinology clinic with complaints of headache, hot flashes, dizziness and she was concerned about persistent high level of serum vitamin B12 (2058 pg/ml; 1795 pg/ml; 2521 pg/ml) without supplementation. Her medical history and the documentation she presented revealed that patient was diagnosed with scleroderma, and she has been treated for 25 years. She had autoimmune thyroid disease, impaired glucose tolerance test. In 2023 she had undergone brain aneurysm clipping. At present laboratory investigations, her thyroid function test was compatible with isolated hypothyroxinemia (TSH -2.6 mIU/ml; FT4- 8.98 ng/ml; FT3- 5.88 pmol/l). HbA1c – 5.1%, prolactine 8.33 ng/ml (4.79-23.3), low level of folate – 7.42 nmol/l (10.4-78.9); elevated homocysteine – 14.69 mkmol/l ($<$12.00). Paradoxic combination of hypercobalaminemia and hypercysteinemia got us confused. An MRI scan of the brain as well a CT scan of abdomen, gastroscopy and colonoscopy did not revealed any abnormalities as solid lesions; on an X-ray of chest was shown interstitial opacification suggestive of scleroderma lung disease. We hypothesized the possible pitfalls of measurement and interpretation of vitamin B12. Accordingly, we requested B12 measurement after PEG (polyethylene glycol) precipitation which showed normal concentrations of cobalamin.
Conclusion
Macro-vitamin B12 is an underestimated cause of supra-physiological cobalamin plasma levels and deserves appropriate attention to avoid potential erroneous clinical decisions.

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EP1175

Sodium disturbances in hospitalised patients with COVID-19

Vasiliki Filippou[1] & Rebecca Gorrigan[2]
[1]Queen Mary University of London, United Kingdom, [2]Barts Health NHS Trust, United Kingdom

Background
In March 2020, COVID-19, a disease caused by the coronavirus SARS-CoV-2, was declared a global pandemic, posing a significant threat to global health. Whilst predominantly a respiratory disease, extra-pulmonary manifestations have been reported, including endocrine and electrolyte disturbances. Thus, this study evaluates the incidence of serum sodium testing and abnormalities recorded in patients admitted with COVID-19 infection at the Royal London Hospital (RLH) between 1st March and 1st May 2020.
Methods
This single-centre audit collected retrospective data from 279 patients treated for COVID-19 infection between March 1st 2020 and May 1st 2020 at the RLH. Data on serum sodium testing and abnormalities were obtained from the electronic patient healthcare records.
Results
100% of patients had their sodium level checked and 47.7% had an abnormal result. The commonest sodium disturbance was hypernatraemia. Disease severity, classified according to 4C score, was associated with a statistically significant increase in risk of sodium disturbance. Prolonged hospital stay ($\geq$14 days) was associated with a significantly increased risk of developing an abnormality in serum sodium ($P<0.001$).
Conclusion
Abnormalities in serum sodium are common in patients hospitalised with COVID-19 infection. Incidence of abnormal serum sodium levels was higher in patients with more severe disease as well as longer lengths of hospital stay. These findings suggest that routine evaluation of sodium in COVID-19 inpatients is warranted. It is a frequent occurrence that hospitalised patients develop disturbances in sodium levels, but the relationship between more severe COVID-19 and sodium dysregulation, particularly hypernatraemia should be further investigated. If higher serum sodium levels in COVID-19 patients are linked with higher mortality, closer monitoring and earlier corrections and may aid in preventing disease severity and improve outcomes of hospitalised patients with COVID-19.

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Pituitary and Neuroendocrinology

EP21

Pituitary metastasis from breast cancer: a report of three cases

Andreia Martins Fernandes[1], Leandro Augusto Silva[1], Ana Rita Elvas[1], Joana Couto[1], Raquel G. Martins[1], Jacinta Santos[1], Teresa Martins[1] & Fernando Rodrigues[1]
[1]IPO Coimbra, Endocrinology Department, Portugal

Introduction
Pituitary metastases are rare, accounting for only 1% of intracranial metastases and predominantly originating from breast and lung tumors. Pituitary involvement is observed in only 6–8% of breast cancer cases, with an overall unfavorable prognosis.
Case series
A 53-year-old woman, with a six-year history of breast cancer metastasized to the lungs, presented with a three-month history of headaches, visual disturbances, asthenia, weight loss and polyuria. Head MRI revealed a 20mm lesion in the sellar and suprasellar region, causing obliteration of the suprasellar cistern and compression of the optic chiasm and third ventricle. Assessment of pituitary function revealed low levels of 0800 hours cortisol (0.5 mg/dl), FT4 (0.2 ng/dl), FSH (5.8 IU/l) and LH ($<$0.07 IU/l), and low urine density. Treatment included hydrocortisone 20 mg, levothyroxine 50 µg and desmopressin 0.06 mg. No visual field changes were observed. Transsphenoidal surgery confirmed pituitary metastasis, and she died shortly after due to advancing systemic disease. A 46-year-old woman recently diagnosed with breast cancer presented with dizziness, nausea, somnolence, blurry vision, asthenia, weight loss, and polyuria. Assessment of pituitary function showed low levels of 0800 hours cortisol (0.8 mg/dl), FT4 (0.44 ng/dl) and IGF-1 (37.3 ng/ml). Additionally, she exhibited low urine osmolality (260 mOsm/kg) and a high serum sodium concentration. Head MRI showed a 26mm sellar and suprasellar lesion, obliterating the cisterna and compressing the third ventricle and optic chiasm. Treatment included hydrocortisone 15 mg, levothyroxine 75 µg, and desmopressin 0.06 mg. She died a few months later from disease progression. A 61-year-old woman, with a six-year history of breast carcinoma and subsequent metastatic progression to the liver, bones, lungs, and mediastinal lymph nodes, presented with headache, vomiting, disinhibition, dysarthria, and diplopia. Neurological examination revealed bilateral dysmetria, ataxia, and left lateral rectus paresis. Laboratory tests revealed low levels of FT4 (0.58 ng/dl), FT3 (0.59 pg/ml), FSH ($<$0.3 IU/l), LH ($<$0.07 IU/l) and IGF-1 (52.1 ng/ml). Head MRI revealed left cerebellar and pituitary metastases with optic chiasm compression. Treatment included levothyroxine 100 µg, palliative hormonal therapy, and whole-brain radiotherapy. She died two years later due to neoplastic disease progression.
Conclusion
While pituitary metastases are rare, they should be considered in the differential diagnosis when there is evidence of pituitary involvement in malignant disease. Despite the devastating impact on a patient's survival prognosis, significant potential for symptom relief exists, emphasizing the crucial need for high clinical suspicion for prompt identification and management.

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EP41

The importance of a multidisciplinary approach in the management of glucagonomas. a case report

Ismene Bilbao Garay[1], Nerea Egaña[1], Jorge Rojo[1], Maite Perez de Ciriza[1], Beatriz Sanchez[2], Cristina Garcia[1], Ane Amilibia[1], Amaia Mendia[1] & Alfredo Yoldi[1]
[1]Hospital Universitario Donostia, Endocrinologia y Nutricion, San Sebastian, Spain; [2]Hospital Universitario Donostia, Oncologia Medica, San Sebastian, Spain

Introduction
Glucagonoma is an extremely rare PNET which presenting symptoms can be varied but the most common include necrolytic migratory erythema, diabetes, diarrhea and weight loss. Treatment involves a multidisciplinary approach, as most of them are large and present with metastasis at diagnosis, and would need nutritional support, an expert management of pancreatic exocrine insuffiency and diabetes. The different therapeutic options could potentially also cause nutritional and metabolic disturbances that might need a close monitoring and constant adjusting. We present the case of a patient diagnosed with a stage IVB, glucagon producing GRADE 2 pNET who required a multidisciplinary approach to improve her overall survival and quality of life.
Case report
A 69 year old woman with a new diagnosis type 2 DM and no other previous relevant history, presented with chronic abdominal pain and weight loss. CT scan disclosed a 10$\times$3 cm hypervascular mass in the pancreatic tail, with multiple hypervasular lesions in the liver. A 18FDG PET confirmed abnormal uptake (SUV 4,8) at the distal pancreas, correlating with the CT scan and the Octreo-scan as well (krening 4) Biopsy of the hepatic lesion confirmed metastatic grade 2 PNET. The laboratory values were normal except for an elevated serum glucagon level (830 pg/ml, Ref. 50–150), and increased levels of Cromogranin A 360 (0-108) and NSE 17,20 (0-16,3) accompanied by low levels of Cupper and Zinc. The patient was treated with octreotide lar, which lowered the serum glucagon levels by 73% for 10 months and the tumor size remained stable for 15 months of follow up, but soon after glucagon levels elevated and liver metastases where shown in the MRI. The patient underwent 19 cycles of Everolimus, until progression was assessed and treatment with ^{177}Lu-DOTATATE decided. 6 months after completing the treatment, glucagon levels had gone down by 50% and a 40% reduction in liver metastatic size and a 10% reduction in pancreatic tumor mass were shown by the MRI. The patient had not presented significant treatment-related toxicity and her insulin needs were cut by half. During the whole process the patient's nutrtitional needs, gastric enzymes and insulin requirements were adjusted to ensure the best outcome and improve her quality of life.
Conclusions
Glucagonoma is difficult to diagnose and once diagnosed a challenge to manage. An interprofessional team must work together to monitor the patient as needs as they navigate through the wide range of treatment modalities and their side effects.

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EP50

Delayed diagnosis of pituitary stalk interruption syndrome in a girl with short stature, spaniomenorrhea and normal secondary sexual characteristics: a case report

Soumia Laib[1]
[1]University Hospital Center Touhami Benflis. University of Batna 2, Metabolism, Endocrinology & Diabetes, Batna, Algeria

Pituitary stalk interruption syndrome (PSIS) is a rare developmental defect identified by magnetic resonance imaging and characterized by a thin or interrupted pituitary stalk, aplasia or hypoplasia of the anterior pituitary and absent or ectopic posterior pituitary. The presenting phenotype and symptomatology vary widely. It includes variable degree of isolated or combined pituitary hormone deficiencies with progressive onset, most commonly growth hormone or gonadotropin and extrapituitary malformations. Although PSIS is most frequently diagnosed during childhood and the neonatal period, some individuals may not be diagnosed until adulthood. We report an 18-year-old girl with a history of irregular menstruation that had started 2 years prior to the visit. she born out of non-consanguineous marriage, There was no history of any systemic illness, drug intake or head injury. The pregnancy, labor, delivery and neonatal period had been unremarkable. Family history was not significant. On examination she weighed 75 kg with a BMI of 35.76 kg/m, the waist circumference was 109 cm, and her height was 145 cm (-3SDS, height age 12 years, target height 156,5 cm, upper to lower segment ratio1,13). She had severe proportionate short stature with typical facies of growth hormone(GH) deficiency as a cherubic facial appearance with flat nasal bridge, frontal bossing and midface hypoplasia. She had normal pubertal onset and development without galactorrhea. She had no history of polydipsia, polyuria, headache and visual defects. She had no associated malformations or features of Turner syndrome. After exclusion of systemic disorders, endocrine analysis, showed isolated GH deficiency with hyperprolactinemia. The remainder pituitary evaluation was normal. Others causes of hyperprolactinemia have been excluded. Hand Bone age was ∼17 year and X ray evaluation of iliac apophysis was found in Risser Grade V. Pelvic ultrasound showed no abnormality of pelvic structures and neck ultrasound showed normal thyroid. Magnetic resonance imaging (MRI) of brain showed nonvisible stalk with ectopic posterior pituitary and hypoplastic anterior pituitary. The diagnosis of PSIS was made because of association of physical exam and endocrine findings with magnetic resonance imaging. Late diagnosis of PSIS leads to definitive adult short stature and psychosocial problems. Prompt and appropriate hormone substitution improve final adult height. Our case is interesting because, it highlights the importance of physician clinical awareness and early identification and referral for children with growth disorders to pediatric endocrinologists and because the unique association of GH deficiency and hyperprolactinemia in PSIS with resultant spaniomenorrhea despite having a conserved pituitary gonadal axis and normal pubertal development.

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EP51

Studies on anti-rabphilin-3a antibodies in 15 consecutive patients presenting with central diabetes insipidus at a single referral center

Yoshihisa Sugimura[1], Zenei Arihara[2], Shozo Yamada[3], Naoko Inoshita[3], Naoko Iwata[4], Haruki Fujisawa[1] & Atsushi Suzuki[1]
[1]Fujita Health University, Toyoake, Japan; [2]National Hospital Organization Sendai Medical Center, Sendai, Japan; [3]Moriyama memorial hospital, Edogawa City, Japan; [4]Daido Hospital, Nagoya, Japan

Central diabetes insipidus (CDI) is a rare condition caused by various underlying diseases including inflammatory and autoimmune diseases, neoplasms (such as germinomas and craniopharyngiomas), infiltrative diseases (such as Langerhans cell histiocytosis), neurosurgery, trauma, and genetic defects in vasopressin synthesis. However, up to 15% of CDI causes remain idiopathic, although, a recent report showed idiopathic CDI is a very uncommon condition. An autoimmune process involving destruction of the neurohypophysis may be involved in many patients with idiopathic CDI. When a definitive cause of CDI is not found, most cases of CDI will be labeled idiopathic, but an autoimmune process should always be considered. Lymphocytic hypophysitis, including Lymphocytic infundibuloneurohypophysitis (LINH) accounts for a substantial subset of autoimmune CDI cases and is characterized by lymphocytic inflammation of the posterior pituitary and infundibular stalk. Obtaining an accurate definitive diagnosis of the underlying cause of CDI is difficult. Pathological examination is required for a definitive diagnosis. Recently, anti-rabphilin-3A antibodies were demonstrated to be a highly sensitive and specific marker of LINH. Here, we report a detailed case series, and evaluated the significance of anti-rabphilin-3A antibodies in differentiating the etiologies of CDI. A prospective analysis was conducted in 15 consecutive patients with CDI from 2013 to 2020 at a single referral center. All patients presenting with polyuria and polydipsia underwent endocrinological tests, including the hypertonic saline infusion test, and cranial magnetic resonance imaging. Anti-rabphilin-3A antibodies were measured and the relationship between antibody positivity and the clinical/histopathological diagnoses was evaluated. Among 15 CDI patients, the positive anti-rabphilin-3A antibodies were found in 4 of 5 LINH cases, 3 of 4 lymphocytic panhypophysitis (LPH) cases (including 2 of the 3 biopsy-proven samples), a subtype of lymphocytic hypophysitis that affects both of the anterior and posterior pituitary gland and causes CDI. The positive anti-rabphilin-3A antibodies were found in one intracranial germinoma case, and were negative in two Rathke cleft cyst cases and one craniopharyngioma case. After the treatment with steroid in patient with LPH who were positive for anti-rabphilin-3A antibodies, GH and/or gonadotropin levels were restored. In conclusion, this is the first case series to evaluate the presence of anti-rabphilin-3A antibodies in consecutive patients with CDI. We found that anti-rabphilin-3A antibodies positivity in CDI patients with biopsy-proven LPH and confirm that measurement of anti-rabphilin-3A antibodies may be valuable for differentiating CDI etiologies.

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EP77

Neuroendocrine tumor secreting proinsulin – an overlooked entity

Leandro Augusto Silva[1], Andreia Martins Fernandes[1], Ana Rita Elvas[1], Raquel G. Martins[1], Joana Couto[1], Teresa Martins[1], Jacinta Santos[1], Nuno Cunha[2], Rui Martins[3] & Fernando Rodrigues[1]
[1]IPO Coimbra, Endocrinology; [2]IPO Coimbra, Clinical Pathology; [3]IPO Coimbra, General Surgery

Introduction
Proinsulinoma is an infrequent subtype of pancreatic neuroendocrine tumor (pNET), characterized by the excessive secretion of proinsulin, leading to pronounced hypoglycemia. Clinical manifestations comprise neuroglycopenic and autonomic symptoms, including cognitive impairment, seizures, visual disturbances, diaphoresis, tremors, syncope or coma. Diagnostic modalities involve blood assays and imaging to detect heightened proinsulin production and determine the tumor's location within the pancreas. Surgical intervention stands as the primary modality for curative intent and relief of symptoms in locoregional disease. In scenarios where surgical excision is unfeasible, alternative therapeutic modalities may be explored for symptomatic management.
Clinical Case
A 25-year-old male with normal body weight exhibiting a four-year history of hypoglycemia. Initially asymptomatic, the condition was identified during routine laboratory examinations and subsequently manifesting symptoms such as confusion, fatigue and incoherent speech, all of which were resolved following carbohydrates intake. Relevant medical history includes allergic rhinitis, profilin allergy, and eosinophilic esophagitis. Presently under medication involving proton pump inhibitor (IBP), nasal fluticasone and antihistamine on an as-needed basis. Admitted for elective study of hypoglycemia, underwent a 5-hour fasting test which revealed symptomatic hypoglycemia of 45 mg/dl with confusion, sweating and tachycardia, all resolved after carbohydrates intake. Analytical study during fasting test revealed elevated serum proinsulin (141.4 pmol/l), while serum C-peptide and insulin levels were inappropriately normal (2.41 ng/ml and 10.2 μU/ml, respectively). Beta-hydroxybutyrate was within reference values (0.21 nmol/l). The patient underwent imaging studies (abdomen CT and MRI) identifying an 8 mm hypervascular nodule in the pancreatic body consistent with a pNET. The ^{68}Ga-SSA-PET-CT was negative. The patient underwent surgical resection of tumor. The anatomopathological examination confirmed a 13 mm grade 1 neuroendocrine tumor (the immunohistochemistry study showed strong diffuse positivity for synaptophysin and chromogranin A, with Ki67 $<2\%$, with complete resection (pT1N0), confirming the diagnosis of a proinsulin secreting pNET.
Conclusions
Given the rarity of proinsulinoma, recently recognized as a distinct entity from insulinoma, it is essential to maintain heightened awareness of its nonspecific clinical symptoms. Diagnosing proinsulinoma can be challenging due to its uncommon occurrence and its diagnostic criteria not yet fully defined on a globally agreed-upon basis. Prompt recognition of subtle signs is crucial to prevent delays in diagnosis and ensure accurate treatment.

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EP82

Xanthogranulomatous hypophysitis succesfully treated with rituximab in a teenage female: a case report

Carmen Soriano[1,2], Maria del Carmen Lopez[1,3], María Niveiro[1,4,5], Javier Abarca[1,4,6], Elena García-Garrigos[1,4,7], Joaquín Serrano[1,2,4] & Antonio Pico[1,2,4,8,9]
[1]Hospital General Universitario Dr. Balmis; [2]Endocrinology & Nutrition; [3]Reumatology; [4]Instituto de Investigación Sanitaria y Biomédica de Alicante (ISABIAL); [5]Pathology; [6]Neurosurgery; [7]Radiology; [8]University Miguel Hernandez; [9]CIBERER

Introduction
Hypophysitis, an infrequent inflammatory condition of the pituitary gland, is typically managed with glucocorticoids, reserving surgery for significant mass effects and considering immunosuppressants or radiotherapy for refractory cases. Recent reports indicate positive outcomes with immunosuppressants. Here, we present a case of recurrent xanthogranulomatous hypophysitis in a 16-year-old female successfully treated with Rituximab.
Case Report
A 16-year-old female with no pertinent medical history presented to our emergency department with a severe frontal headache, diplopia, nausea, amenorrhea, polyuria, and polydipsia persisting for 4 months. Physical examination revealed a mild afferent pupillary defect along with complete six-nerve and partial third-nerve palsies. MRI indicated a solid selar mass with a central cystic area, intense peripheral contrast enhancement, and pituitary stalk infiltration displaying intense and homogeneous contrast enhancement. Blood tests revealed deficiencies in corticotroph, gonadotroph, and thyrotroph axis, along with arginine vasopressin deficiency. Somatotroph axis and prolactin levels remained unaffected. Additional tests showed positive antithyroid antibodies, with negative alpha-fetoprotein and Beta-HCG in both serum and cerebrospinal fluid. The patient received high-dose glucocorticoid therapy, leading to significant clinical and radiological improvement. However, after corticosteroid tapering, a relapse occurred, requiring transsphenoidal surgery. Pathological analysis revealed chronic inflammation with predominantly CD20-positive B-cell infiltration, consistent with xanthogranulomatous hypophysitis. Following surgery, a relapse occurred, prompting the use of Rituximab, a monoclonal antibody targeting CD20-positive B cells. The patient received two doses of 1000 mg IV four weeks apart, followed by a single dose of 750 mg IV every 6 months. After four doses, the patient successfully discontinued corticosteroid therapy, experiencing sustained disease remission and excellent symptomatic control.
Conclusion
Rituximab emerges as an effective and sustainable treatment for hypophysitis, providing a valuable alternative to prolonged corticosteroid therapy or surgery.

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EP86

Corticotropic deficiency secondary to wilson disease

Hager Khiari[1], Sabrine Mekni[1], Sawsen Essayeh[1], Imen Rojbi[1], Bennacef Ibtissem[1], Youssef Lakhoua[1], Nadia Mchirgui[1] & Karima Khiari[1]
[1]Charles nicolle hospital, Endocrinology, Tunisia

Introduction
Wilson's disease is a rare and serious genetic disorder. The accumulation of copper in glands causes several endocrine pathologies. Herein, we report a rare case of hypophysitis with corticotropic deficiency caused by Wilson's disease.
Observation
A 33-years-old female patient was referred to the endocrinology department for hypoglycemia. She had a history of Wilson's disease diagnosed at the age of nine complicated by cirrhosis and neurological damage. She presented with fatigue and recurrent hypoglycemia for 3 months and had irregular menses. On physical examination, she had motor incoordination and was in a wheelchair. She was pale. Biological exams revealed corticotropic deficiency with a baseline serum cortisol level of 130 nmol/l and a low serum ACTH (8.62 pg/ml). Liver and renal functions were normal (TP = 80%, Serum creatinine = 60 y mol/l). She had no thyrotropic deficiency (FT4 = 0.76 ng/dl, TSH = 3.11 mIU/l), no gonadotropic deficiency (estradiol = 80 pg/ml, FSH/lH = 6.7/23.63 UI/l) and no somatotropic deficiency (serum IGF1 = 200 yg/l) but had moderate hyperprolactinemia (serum prolactin = 60 ng/ml). Magnetic resonance imaging of the hypothalamo–pituitary region did not show an adenoma and revealed a thickened pituitary stalk. She had no other endocrine disorders related to Wilson's disease like diabetes mellitus (HbA1c = 5%), hypoparathyroidism (serum calcium = 2.27 mmom/l, PTH = 31.6 pg/ml) or peripheral hypothyroidism (TSH = 3.11 mIU/l). The patient was treated by 20 mg of hydrocortisone hemisuccinate daily. The evolution was characterized by an improvement of the fatigue and the disappearance of hypoglycemia.
Conclusion
Wilson's disease is a rare inherited condition. Hypophysitis due to Wilson's disease is rarely reported in the literature. Corticotropic deficiency increases the risk of hypoglycemia and is life-threatening.

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EP87

Growth without growth hormone: an unusual presentation of a pituitary stalk interruption syndrome

Maria Lavinia Popa[1], Preda Diana[1,2], Alexandra Mirica[1,2], Radomir Lidia[3], Enyedi Mihaly[2,4] & Iuliana Gherlan[2,3]
[1]'Grigore Alexandrescu' Emergency Clinical Hospital for Children, Bucharest, Romania, Endocrinology, Bucharest, Romania; [2]'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania, Romania; [3]National Institute of Endocrinology "CI Parhon", Pediatric Endocrinology, Bucharest, Romania; [4]Diagnostic and Treatment Center "Dr. Victor Babes", Radiology, Bucharest, Romania

Introduction
Pituitary Stalk Interruption Syndrome (PSIS) is a congenital developmental anomaly affecting the pituitary gland. Characterized by a triad of features including a thin or absent pituitary stalk, adenohypophysis hypoplasia, and ectopic neurohypophysis on MRI, PSIS can lead to isolated or combined pituitary hormone deficiency. Symptoms may manifest at various life stages, with 70% of cases identified in childhood due to growth retardation. Notably, some patients exhibit normal growth despite growth hormone deficiency.
Case report
A 7 year old boy presented to endocrinology clinic with concerns of genital hypoplasia and a history of bilateral cryptorchidism. Review of the patient's birth history demonstrated an uncomplicated full-term gestation with delivery by cesarean section with a birth weight of 3.2 kg. His motor and language development was normal. Family history was negative. Father's height was 170 cm; mother's height was 173 cm; midparental height was 178 cm (+0.15 DS). Recurrent hospitalisations for pneumonia with dehydration were noted in the past medical history, but no history of seizures. On physical examination, the patient's height was 116.5 cm (-1.26 DS), he had no growth records; his weight was 26.3 kg with a body mass index (BMI) of 19.4 kg/m^2 (at the 96th percentile). He had no signs of thyroid or cortisol deficiency. The sexual maturity rate was Tanner stage I, with a hypoplastic scrotum, a 4.5 cm penile length, covered by suprapubic fat. Laboratory studies demonstrated low free thyroxine (T4) with only slightly above normal thyroid-stimulating hormone (TSH) values. Repeated and extended hormonal analysis demonstrated a pattern of panhypopituitarism with low morning serum cortisol (0.9 µg/dl, normal 5-25), low normal ACTH (12 pg/ml, normal, 7.2-63.3), low freeT4 (0.4 ng/dl, normal 0.65-2.3) with slightly elevated TSH (5.9 µUI/ml, normal 0.5-4.5), normal prolactin, low IGF1 values (18.7 ng/ml and 17.8 ng/ml, -2.81 SDS for Tanner I) and an inhibin B level of 21.7 pg/ml (2.5-10th centile). The diagnosis of GHD (confirmation with stimulation tests) was not extended at that time due to the inability to treat GH as part of the therapeutic program of a patient with a normal height. The bone age was delayed, 3.5 years old, compared to chronological age. MRI confirmed PSIS, revealing hypoplasia of the adenohypophysis, ectopic neurohypophysis, and an absent pituitary stalk
Conclusion
Herein, we report a pediatric obese patient with an unusual presentation and normal growth despite combined pituitary hormone deficiency in the course of pituitary stalk interruption syndrome (PSIS).

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EP88

A case of aggressive corticotropinoma in a patient after combined treatment and bilateral adrenalectomy

Daria Lisina[1], Laura Ebanoidze[1], Ekaterina Pigarova[1], Patimat Khandaeva[1], Larisa Dzeranova[1] & Elena Przhiyalkovskaya[1]
[1]Endocrinology Research Center, Neuroendocrinology, Moscow, Russian Federation

Introduction
Corticotropinomas constitute up to 45% of aggressive pituitary tumors, which characterized by rapid and invasive growth, a high Ki-67 index, resistance to conventional treatments and recurrence in 15-20% of the cases. Progression of corticotroph tumor after bilateral adrenalectomy or Nelson's syndrome is a frequent severe complication and may present with aggressive tumor behavior.

Clinical case
A Cushing disease was diagnosed in a woman of 19 years of age (2010) for which she underwent a transsphenoidal adenomectomy in 2010 and 2011 (immunohistochemical study was not performed) with the development of secondary hypothyroidism and hypogonadism. Then due to persistence of the disease in 2012 a stereotactic radiosurgery (Gamma-knife, 36 Grey) was performed. Due to its absent effect on ACTH secretion (>2000 pg/l) in 2014 the patient had a bilateral laparoscopic adrenalectomy which led in 2017 to development of Nelson's syndrome with right sided diplopia, ptosis, and severe headache; MRI noted a tumor 25x24x38 mm with invasive growth to the right cavernous sinus, spreading forward to the entrance to the right orbit. The patient was treated by repeated transsphenoidal adenomectomy followed by conformal external stereotactic radiotherapy (morphology - pituitary adenoma of oxyphilic cells with a solid alveolar structure; immunohistochemistry - ACTH expression in most tumor cells with uneven nuclear expression of Ki-67 (label index from 3,8% to 9,4%) and negative expression of P53; absent methylation of MGMT gene) with complete elimination of neurophthalmic features. In 2023 these clinical features returned, MRI described tumor measuring $27\times20\times38$ mm in the right cavernous sinus with involvement and narrowing of the right carotid artery, extending to the right orbit and the right contour of the pons. The patient was consulted by a neurosurgeon, however, due to the fact that surgical treatment for this patient seemed overly traumatic and non-radical, by decision of the council temozolomide therapy was prescribed at a dose of 150-200 mg/m^2 daily for 5 days every 4 weeks for 3 courses followed by MRI control in order to determine further treatment tactics. The treatment led to clinically significant reduction in diplopia and headache.
Conclusion
This clinical case demonstrates aggressive corticotropinoma and progression of the rapid and invasive growth despite multimodal treatment even with repetitions. Total adrenalectomy avoided the complications of hypercortisolism for more than 10 years, but the patient needs further treatment of the most aggressive adenoma using oncological therapy methods of which temozolomide is recognized as the first line of therapy.

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EP93

Clinical and paraclinical characteristics of women with sheehan's syndrome

Salma Salhi[1], Ibtissem Oueslati[1], Cyrine Chehaider[1], Anis Grassa[1], Amani Terzi[1], Fatma Chaker[1], Meriem Yazidi[1] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
Sheehan's syndrome is a rare cause of hypopituitarism. It is defined by an ischemic necrosis of the pituitary gland following postpartum hemorrhage. Sheehan syndrome is characterized by various endocrine deficiencies. The aim of the present study was to determine the clinical and paraclinical characteristics of women with Sheehan syndrome.
Methods
This was a monocentric cross-sectional study including 50 women followed for Sheehan's syndrome in the Department of Endocrinology of La Rabta University Hospital of Tunis. Clinical and paraclinical data were collected.
Results
The mean age of participants was 62.2 ± 9.4 years. Diagnostic delay of SS was 11.1 ± 9.4 years [Range: 0-37 years]. The mean duration of the disease was 31.6 ± 9.9 years. Postpartum hemorrhage occurred in all patients, with 12% of them required hysterectomy. The disease was revealed by acute adrenal insufficiency in 86% of patients, secondary amenorrhea in 10%, and secondary hypothyroidism in 4% of cases. Laboratory investigations revealed complete anterior pituitary deficiency in all patients with no case of central diabetes insipidus. Magnetic resonance imaging showed empty sella turcica in all cases. The mean hydrocortisone dose was 20.30 ± 2.75 mg/day. A daily dose >20 mg was prescribed in 10% of cases. The mean levothyroxine dose was 1.60 ± 0.54 µg/kg/day. Only 21 women (42%) received estrogen-progesterone therapy. GH treatment was not prescribed in all participants.
Conclusions
Women with Sheehan syndrome have important exposure to hormonal deficiencies due to the long diagnostic delay, which make them at higher risk of complications compared to other pituitary deficient patients.

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EP96

Evaluation of the clinical and biological profile in patients with congenital pituitary deficiency

Yosra Hasni[1], Hamza Elfekih[1], Oumayma Zarrouk[1], Yasmine Salem[2], Jihene Ben Abdallah[2], Saoussen Mrad[2], Amira Yanes[1], Nassim Ben Hadj Slama[1], Salima Ferchichi[2] & Molka Chadli Chaieb[1]
[1]University Hospital of Farhat Hached, Endocrinology Departement, Sousse; [2]University Hospital of Farhat Hached, Biochemistry Laboratory, Sousse

Introduction
Pituitary deficiency, or hypopituitarism, is defined by insufficient synthesis or secretion of one or more anterior pituitary hormones. These hormones, including growth hormone, are considerably involved, directly and indirectly, in several metabolisms such as hepatic, carbohydrate, lipid metabolisms and the regulation of protein synthesis. The objective of this study was to study the clinical and biological profiles of patients followed for anterior pituitary insufficiency.
Methods
A cross-sectional study was conducted, including patients followed in the Endocrinology department of Farhat Hached University Hospital, Sousse for isolated GH deficiency and/or associated with other anterior pituitary hormonal deficiencies. Data were collected over a period of 9 months from January to September 2022.
Results
Our study included 55 subjects divided into 3 groups: 15 patients followed for an isolated GH deficiency (G1), 20 followed for multiple congenital pituitary deficiencies (G2) and 20 control subjects (control group). The average age of our patients at the time of diagnosis was eleven and a half. A male predominance was noted in G1 (73.3%) and G2 (60%). The evaluation of clinical characteristics such as age, body mass index, blood pressure and waist circumference did not show a statistically significant difference between G1 and G2. The evaluation of metabolic, renal, hepatic, calcium and lipid balance did not show any significant difference between the three groups of the study apart from alkaline phosphatase which was higher in G1 (200.4 ± 106.1 U/l) compared to G2 (169.6 ± 94.1 U/l) and the control group (72.7 ± 23.1 U/l) with a statistically significant difference between the control group and each of the other two groups. Comparing hormonal parameters between G2 and control group, we found a significant difference linked to the male sex in thyrotropic insufficiency, as well as a lower level of sex hormones in both sexes. No significant difference was found between these two groups for gonadotropins, prolactin, and cortisol.
Conclusions
The clinical and biological profile of patients with congenital pituitary deficiency was almost similar between the group with isolated GH deficiency and the group with combined anterior pituitary deficiencies. For hormonal parameters, only TSH, FT4 and sex hormones were different between the two groups.

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EP102

Clinical and paraclinical characteristics of incidentally discovered pheochromocytoma

Abid Arige[1], Mariam Mabrouk[1], Ibtissem Oueslati[1], Elyes Kamoun[1], Faten Cherchir[1], Meriem Yazidi[1] & Melika Chihaoui[1]
[1]RABTA Hospital, Endocrinology, Tunis, Tunisia

Introduction
Pheochromocytoma is a rare tumor originating from chromaffin cells of the adrenal medulla secreting catecholamines. The typical symptoms of pheochromocytoma include hypertension, headache, heart palpitations, anxiety, and profuse sweating. However, some patients with pheochromocytomas remain asymptomatic. The aim of this study was to determine the clinical and paraclinical characteristics of incidentally discovered pheochromocytomas.
Methods
This was a single center retrospective study including patients with confirmed pheochromocytoma. Clinical and paraclinical data were recorder from patients' medical files. Patients were divided into two groups: group 1: patients with incidentally discovered pheochromocytoma and group 2: patients with clinically patent pheochromocytoma.
Results
Fifty-three patients with pheochromocytoma were enrolled in this study. Pheochromocytoma was incidentally discovered in 43 % of cases ($n=23$, 12 women and 11 men). The median age was 51 years (IQR: 36 – 56) in group 1 and 47 years (IQR: 31 – 55) in group 2 ($P=0.271$). There was no statistical difference between the two groups regarding the prevalence of overweight, obesity, and diabetes. Among the clinical findings, the symptom triad made of headache, palpitations and profuse sweating was found in 13% of cases in group 1 and in 57%

of cases in group 2 ($P=0.001$). The prevalence of hypertension was 30% in group 1 and 83% in group 2 ($P<0.001$). Systolic ($P=0.043$) and diastolic ($P=0.029$) blood pressure levels were significantly higher in group 1 than in group 2. The majority of tumors in the two groups secreted normetanephrines only. The blood levels of normetanephrines were 6.5 times the normal range (IQR: 3.5-14.8) in group 1 and 7.15 times the normal range (IQR: 3.6-10.1) in group 2 ($P=0.642$). The median size of the tumor was 50.5 mm (IQR: 38.1-70.5) in group 1 and 49.5 mm (IQR: 37.5-64.7) in group 2 ($P=0.734$). Pheochromocytoma was malignant in 35% of cases in group 1 and 22% in group 2 ($P=0.392$).

Conclusions

It is important to explore all adrenal incidentalomas since some of them turn out to be silent pheochromocytomas and therefore need as much of an urgent management as the clinically patent ones.

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EP103

Acromegaly of immature PIT-1 origin

Aysel Ünver Özkahraman[1], Mert Doğukan[2], Özlem Kandemir Alibakan[1], Burak Koçak[3], Ebubekir Akpınar[4], Mutlu Niyazoğlu[1] & Esra Şüheda Hatipoğlu[1]

[1]Basaksehir Cam and Sakura City Hospital, Endocrine and Metabolism Diseases; [2]Basaksehir Cam and Sakura City Hospital, Pathology; [3]Basaksehir Cam and Sakura City Hospital, Radiology; [4]Basaksehir Cam and Sakura City Hospital, Neurosurgery

Introduction

Acromegaly is a rare pathological condition characterized by excessive growth hormone (GH) secretion, leading to elevated levels of insulin-like growth factor 1 (IGF-1). According to the 2022 World Health Organization classification, GH-secreting pituitary adenomas fall under the PIT1-lineage. Pure GH-secreting adenomas selectively release growth hormone and may exhibit dense or sparse granulation patterns. Other subtypes include mammosomatotroph adenomas, mature plurihormonal adenomas, immature plurihormonal adenomas, and acidophil stem-cell adenomas, all expressing multiple hormones. Immature PIT1-lineage tumors consist of immature cells expressing PIT1 but lack morphologic and immunohistochemical features of fully differentiated cells.

Case report

A 50-year-old male patient reported a chief complaint of escalating joint pain over the past four years. A comprehensive examination revealed distinctive features indicative of acromegaly, including an enlarged nose, prominent forehead, jaw prognathism, widened tooth gap, enlargement of hands, and increase in foot size. The patient's tests IGF-1: 1150 ng/ml (N:76,7-203) GH:5,1 ng/ml (N:0.03-2,47) was detected. Other hormone profiles were normal. During the OGTT test, the values at 60th minute glucose:224,3 mg/dl GH:37.5 ng/ml were pathological. Pituitary MR imaging showed an adenoma with a diameter of approximately 1.8 cm in the left half of the pituitary gland extending to the cavernous sinus and inferior optic chiasm. The visual field test was normal. Transsphenoidal endoscopic pituitary surgery was performed and immunohistochemical findings on pathology were as follows; chromogranin: +, PIT-1: +, SF-1:-, GATA-3:-, Estrogen receptor:-, GH: diffuse +, Prolactin: diffuse +, TSH:-, ACTH:-, LH:-, FSH:-, NKX2.2:-, SSTR2A: Sparse cell +, Ki-67:5%, PHH3:6 mitoses/10 large magnification area, PAS:-. Histomorphologic and immunohistochemical findings were consistent with an immature PIT-1-origin adenoma. In the 3rd postoperative month; IGF-1: 326 mg/ml (N:76.7-203) GH: 0.54 ng/ml (N:0.03-2,47), 75 g OGTT test; 30. min glucose:145 mg/dl GH:0.7 ng/ml was detected. Control pituitary MRI showed no residual and recurrence.

Discussion

Immature PIT1-lineage tumors, displaying lower differentiation levels, present with a variable clinical profile, with approximately 10–20% of affected patients exhibiting GH excess. TSH overproduction is more common, hyperprolactinemia is often attributed to direct tumor secretion. Imaging consistently reveals these as large, invasive tumors, requiring multiple surgeries, radiation, and systemic therapies due to their aggressive nature. In the light of all this information, which class of acromegaly the patient is in may give us crucial clues for the clinical prognosis.

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EP140

Long-term outcomes of non-functioning pituitary macroadenomas following surgery

Mirsala Solak[1], Ivana Kraljevic[1,2], Roman Brekalo[2], Tanja Skoric Polovina[1], Annemarie Balasko[1], Karin Zibar Tomsic[1], Hrvoje Popovac[1], Tina Dusek[1,2] & Darko Kastelan[1,2]

[1]University Hospital Center Zagreb, Department of endocrinology, Zagreb, Croatia; [2]School of Medicine, University of Zagreb, Zagreb, Croatia

Background

Systematic or randomised studies on the natural course of non-functioning pituitary macroadenomas after surgery (NFPA) are lacking.

Objectives

This study aimed to evaluate the long-term outcomes of residual NFPA following pituitary surgery.

Methods

In this retrospective study, we included 130 patients with NPFA who underwent pituitary surgery between 2005 and 2018 at University Hospital Centre Zagreb. The median age of participants was 57 (18-78) years, and 65.4% were male. Data on demographics, surgical outcomes, histology, imaging, and management were collected. The median follow-up time was 90.5 (36-223) months after surgery. Patients with less than three years of follow-up were excluded from the study.

Results

The median adenoma size was 29.2 (10-55) mm, and in 58 (44.6%) cases, infiltration into the cavernous sinus was observed. In the group of patients who had complete tumour resection ($n=45$), ten (22.2%) experienced adenoma recurrence after a median follow-up period of 73.5 (22-216) months. They showed no differences in age, gender, adenoma size, cavernous sinus invasion, or Ki-67 expression when compared to patients without residual adenomas following surgery. Among the 85 (65.4%) patients who had residual adenomas following primary surgery, 13 (15.3%) demonstrated an increase in size after a median follow-up of 44 (16-120) months. These patients tended to be older ($P=0.058$) and exhibited higher Ki-67 expression ($P=0.05$) compared to patients with stable residual adenomas.

Conclusion

Our results emphasize the importance of prolonged post-surgical monitoring for patients with NFPA to promptly detect potential tumour recurrence or an increase in residual tumour size, which are common occurrences in this patient group. Such a proactive approach can significantly impact treatment strategies and improve overall patient outcomes.

Keywords non-functioning pituitary macroadenoma, surgery, residual adenoma, recurrence, long-term

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EP143

Pituitary neuroendocrine tumors in elderly patients: clinical and surgical outcomes in a tertiary hospital

Inés Borrego Soriano[1], Paola Parra Ramírez[1], Patricia Martin Rojas-Marcos[1], Carlos Pérez López[2], Pablo García Feijoo[2], Arturo Lisbona Catalán[1], Paula Vázquez Pérez[1] & Maria Cristina Alvarez Escola[1]

[1]Hospital Universitario La Paz, Endocrinología y Nutrición, Madrid, Spain; [2]Hospital Universitario La Paz, Neurocirugía, Madrid, Spain

Introduction and aim

The current population is experiencing an increase in life expectancy, with a consequent change in the demographic structure of the society. It is common, therefore, to find elderly patients with pituitary neuroendocrine tumors (PitNET) in our usual clinical practice. Currently, there are no specific recommendations for treatment and data of outcomes in elderly are scarce. The aim of our study was to compare the clinical characteristics and surgical outcomes of elderly ($\geq$65 years) and younger patients ($<$65 years) undergoing transphenoidal surgery.

Material and methods

A retrospective study was performed. We included all patients who underwent transphenoidal surgery for PitNET in a tertiary hospital from 2018 to 2023. We stratified the population according to age, considering 65 as the threshold for older age. IBM SPSS26 statistical analysis was used.

Results

124 patients were included. 32 (26%) of them were $\geq$ 65 years old. Most elderly patients had non-functioning PitNET while most young patients had functioning PitNET (15.6% vs 62% $P<0.001$). Besides, most elderly patients had hypopituitarism before surgery (40.6% vs 8.7%, $P<0.001$). Elderly patients underwent surgery more frequently due to visual compromise while young people due to functionality (31.3% vs 51.1% $P=0.012$). Larger pituitary tumors were detected in the elderly patients group (20.5 mm vs 18.1 mm, $P=0.021$). No differences were detected in surgical complications (bleeding, fistula or infection, $P=0.752$) nor hormonal or electrolyte alterations in the immediate postsurgical period ($P=1$) between age groups. However, older patients had a longer hospital stay than younger patients (8 days vs 6 days $P=0.048$). At long-term follow-up (12 months after surgery), no differences were observed between both groups in the rate of biochemical cure of functioning PitNET (60% vs 59.6%, $P=0.988$) and the rate of normal pituitary hormonal profile (34.4% vs 26.1%, $P=0.37$).

There were differences in the rate of hypopituitarism (50% vs 16.3%, $P<0.001$) due to the hormonal situation prior to surgery ($P<0.001$) and not to age differences ($P=0.072$). In addition, improvement of visual disturbances (31.3% vs 12%, $P=0.095$) and persistence of remaining adenoma at radiological follow-up (50% vs 44.6%, $P=0.830$) were similar between older and younger patients.
Conclusions
In our study, older patients with PitNET had a lower prevalence of hormone-secreting tumors, greater prevalence of hypopituitarism, larger tumors and greater visual impairment as an indication for surgery. They had similar surgical outcomes compared to young patients, except for the longer hospital stay.

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EP154

Neuroendocrine involvement in wegener's granulomatosis

Raida Ben Salah[1], Faten Hadj Kacem[2], Siddiqa Saumouro[2], Mohamed Abid[2] & Bahloul Zouhir[1]
[1]Sfax University, Internal Medicine; [2]Sfax University, Endocrinology

Introduction
Wegener's granulomatosis is a necrotizing vasculitis that can affect the central nervous system. Pituitary involvement is exceptional, but may be underestimated. Pituitary involvement in Wegener's disease is rare, and is mainly expressed as diabetes insipidus.
Clinical case
A 33-year-old man was admitted to hospital in 2009 with bilateral optic neuropathy, altered general condition revealing Wegener's disease with rhinosinus involvement, pachymeningitis and pulmonary involvement. The patient was treated with high-dose corticosteroids and monthly boli of Endoxan®, with stabilization of his disease. In 2011, he presented with polyuro-polydypsia. The diagnosis, of central diabetes insipidus, was confirmed by a water restriction test with desmopressin injection. Pituitary MRI showed a disappearance of the usual hypersignal of the post-pituitary on T1-weighted sequences. There was no anteropituitary deficit or hyperprolactinemia. The patient was started on methotrexate 30 mg/week and high-dose corticosteroids, methotrexate and desmopressin. Progression was marked by persistent symptomatology requiring maintenance of desmopressin.
Conclusion
Diabetes insipidus often regresses with general treatment of Wegener's disease. Nevertheless, desmopressin substitution is often necessary, at least initially. Occasionally, pituitary involvement persists despite effective treatment of Wegener's granulomatosis, suggesting glandular destruction.

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EP155

Predicting the development of hyponatremia in patients after transnasal adenomectomy

Khava Fargieva[1], Nino Katamadze[1], Anastasia Milyutina[1], Oksana Ivashchenko[1], Vilen Azizyan[1], Andrey Grigoriev[1], Elena Przhiyalkovskaya[1], Ekaterina Pigarova[1] & Larisa Dzeranova[1]
[1]Endocrinology Research Centre, Moscow, Russian Federation

Introduction
Transsphenoidal surgery is the gold standard of treatment for most masses of the hypothalamic-pituitary region. Given the frequency of its performance in large hospitals, water-electrolyte complications are quite common and are the second most common cause of re-hospitalization of patients. Water-electrolyte disorders after transnasal adenomectomy in up to 30% of cases are associated with the development of severe neurological symptoms, decrease in the quality of life of patients, and increase in the duration of their stay in hospital, thus, the search for ways of early prediction is an extremely urgent task.
Objective
To analyze preoperative patient parameters to develop a prognostic model for the development of hyponatremia in patients after transnasal adenomectomy.
Materials and methods
A total of 117 patients were included in the analysis, 36 of which (31%) were men. Patients were divided into two groups: with developed hyponatremia by the 7th day after surgery and with its absence. Both groups were comparable in sex ($P=0.26$) and age (50.5 years [33.5; 61.5] vs 46 years [36; 57], $P=0.43$). These groups were compared according to 21 characteristics, including hormonal background parameters (ACTH, cortisol, TSH, FT4), presence of cardiovascular diseases, disorders of carbohydrate metabolismand hypogonadism, current drug therapy, as well as tumor characteristics according to MRI and characteristics of the surgical intervention protocol.
Results
According to the analysis performed, no significant differences were found in both groups for any of the input features ($P>0.05$). The same groups were then compared in terms of laboratory parameters depending on the reference interval of the laboratories (TSH/ACTH/cortisol/FT4 above/below/or equal to the reference interval), tumor characteristics (color, consistency, position relative to the pituitary gland, tumor bleeding, etc.) and tumor morphology. No differences were found for any of the characteristics for which the groups were compared (all $P>0.05$). Thus, the groups with hyponatremia on the 7th day after surgery and without hyponatremia on the 7th day after surgery did not differ statistically significantly, which did not allow to build a prognostic mathematical model of this complication.
Conclusions
The inability to predict the development of postoperative hyponatremia on the basis of preoperative parameters, peculiarities of surgical intervention, dictates the necessity of blood sodium monitoring up to 10-14 days after transnasal adenomectomy.

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EP156

Combined endocrine-related adverse effects of immune checkpoint inhibitors in a male patient with advanced cutaneous melanoma and multiple co-morbidities

Irina A. Vaychulis[1]
[1]South-Ural State Medical University, Internal Medicine Department, Chelyabinsk, Russian Federation

A 72-year-old male patient was referred to endocrinologist in June 2023. He had known arterial hypertension, aortosclerosis, ascending aorta and aortic valve replacement, chronic cerebral ischemia. In November 2022 stage IV cutaneous melanoma with lung metastasis had been revealed. For 6 months after tumour resection he received anti-PD-1 immune checkpoint inhibitor therapy which was well tolerated. After the 7th cycle of treatment short-term fever and skin rash had appeared, followed by rapid memory deterioration, progressive asthenia, physical and mental slowness during 2 weeks. On examination no signs of brain metastasis, unremarkable complete blood count, normal fasting blood glucose and serum electrolyte levels, but decreased TSH – 0.02-0.005 (normal range 0.27-4.2) IU/l, increased fT4 – 23.6-29.7 (12-22) pmol/l and fT3 – 11.8 (3.1-6.8) pmol/l, negative TPOAb, negative TRAb were found, and the patient was referred to endocrinologist. He presented with psychomotor sluggishness, traces of skin rash, BMI of 28 kg/m^2, blood pressure of 108/76 mmHg, heart rate of 74 beats per minute, slight hand tremor. No thyroid enlargement or other clinical signs of thyrotoxicosis were revealed. Further testing, administered by endocrinologist, had demonstrated TSH <0.0083 (0.4-4.0) IU/l, fT4 – 17.5 (9-19) pmol/l, fT3 – 6.3 (3.0-5.6) pmol/l, elevated TgAb – 161 (<4.1) IU/ml, low morning plasma cortisol – 34 (101.2 - 535.7) nmol/l and low ACTH (<5 pg/ml) levels with tendency to hypotension. The diagnosis of immunotherapy-induced thyroiditis (hyperthyroid phase) and hypophysitis with the secondary adrenal insufficiency was established. Glucocorticoids (GCs) had been initiated. After 2 months of low-dose GCs treatment his TSH, fT4, prolactin, FSH, LH, K, Na, blood pressure levels were within in the normal range, ACTH remained low – 3.4 (7.2-63.6) pg/ml with improvement in physical and cognitive performance, confirming the diagnosis. GCs treatment and monitoring has been continued. Immune checkpoint inhibitors are increasingly used in cancer therapy. Data accumulation regarding side effects of these drugs is important for early detection and clinical success. Both oncologists and endocrinologists should be aware of various possible endocrine-related adverse effects at any step of treatment, requiring specific individual approach. This case emphasizes that periodic assessment of thyroid and pituitary-adrenal function in such patients is needed because clinical symptoms of endocrine disorders may be unclear, masked, atypical, controversial, or absent, especially in older individuals with multiple co-morbidities.

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EP159

Successful medical management of giant prolactinomas: a comprehensive case report

Carolina Monteiro Antunes[1], Leonor Guia Lopes[1], Paula Sprovera[1], Margarida Oliveira[1], Bruna Pimentel[1], Catarina Gama[1], Francisco Sousa Santos[1] & João Sequeira Duarte[1]
[1]Hospital Egas Moniz, Lisboa, Portugal

Introduction
Giant prolactinomas (diameter >4 cm) account for less than 5% of all prolactinomas and are usually associated with markedly elevated prolactin (PRL) levels. Despite their benign nature, these tumors can be invasive, potentially leading to mass effect symptoms in affected patients.
Case Report
We report a case of a 40-year-old male admitted to the emergency department with a one-week history of headaches, right palpebral edema, and ptosis of the right eye. He had a prior medical history of idiopathic peripheral facial paralysis and was not taking any medication. Upon examination, bitemporal hemianopsia with a deficit of the superior right eye field was evident. A head CT showed a large expansive lesion (41x58x63mm) centered to the sella turcica lateralized to the right side with clivus erosion and invasion of the right carotid canal and foramen oval. The patient was started on dexamethasone and was admitted to the Neurosurgery ward. Laboratory tests showed a PRL of 26,623 ng/ml, TSH 1.54 µU/ml with fT4 10.3 pmol/l (12-22), follicular stimulating hormone (FSH) 1.82 IU/l, luteinizing hormone (LH) 2.36 IU/l, total testosterone 70 ng/dl (249-836), insulin-like growth factor 1 (IGF-1) of 212 ng/ml. He initiated cabergoline 2.5 mg/week, levothyroxine 50 µg/day and switched dexamethasone to hydrocortisone. After discharge, an ambulatory corticotroph axis evaluation ruled out adrenal insufficiency. Three months after starting cabergoline, prolactin levels decreased to 520 ng/ml and testosterone improved to 280 ng/dl. Pituitary MRI confirmed an infiltrative sellar lesion, demonstrating invasion into the cavernous sinus and a suprasellar extension reaching the optic chiasm, with a reduction in size compared to the initial CT scan (27×18 mm). Headaches and ptosis of the right eye lid also improved significantly. The patient continued cabergoline treatment, experiencing a progressive decrease in prolactin levels and further radiological improvement. No side effects were reported. Genetic studies for MEN1 and AIP yielded negative results.
Conclusion
Giant prolactinomas can present as invasive masses giving rise to compressive symptoms such as visual field abnormalities. It is crucial to assess the hypothalamic-pituitary axis for potential hypopituitarism and treatment should be promptly initiated. In this case we highlight that despite its clinical aggressiveness, medical management can be a successful therapeutic option. Close monitoring through imaging and laboratory assessments is essential to evaluate treatment response.

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EP160

High-grade astrocytoma with piloid features: case report

Aicha Lachkhem[1] & Abdelkader Yahi[1], ould kablia samia[1], bensalah meriem[1], abderrahim Derriche[2], Staifi Ahcen[3], Derradji Hakim[4] & Yousfi Yamina[5]
[1]Army Central Army, Endocrinology, Algiers, Algeria, [2]Army Central Army, Radiology, Algiers, Algeria, [3]Army Central Hospital, Ophtalmology, Algiers, Algeria, [4]Army Central Hospital, Neurosurgery, Algiers, Algeria, [5]Anatomopathology, Algiers, Algeria

Introduction
High-grade astrocytoma with piloid features (HGAP) is arecently described brain tumor entity defined by a specific DNA methylation profile. HGAP has been integrated in the World Health Organization classification of central nervous system tumors 2021.
Clinical presentation
A 53-year -old woman was admitted to our department with chief complaints of headache with rapid deterioration in visual acuity over a period of 6 months. During the course of the disease, the patient experienced progressive worsening of symptoms of diabetes insipidus with a daily urine output of approximately 11000 mL. Physical examination revealed thyroid tenderness,decreased visual acuity, bi- temporal visual deficit, and signs of disorientation and memory loss. Laboratory examination revealed TSH (0.69 µIU/ml; reference level: 0.25-5 µIU/ml), decreased FT4 (9.26 pmol/l; reference: 9-20 pmol/l, FSH (2.82 ui/ml; reference level 1.55-9.74), LH (<0.1 ui/ml; reference level 7.7-58.5), Estradiol(<9 nmol/l; reference level 5-54.7), IGF1 (47.1 ng/ml; reference level 71-210). Pituitary function tests revealed markedly elevated serum prolactin level (249 ng/ml; reference: 7-20 ng/ml). There was no significant past history. The MRI brain showed a large ovoid shaped lesion (size: 3.2 cmæ 3.3 cmæ 4.1 cm) involving the intra-sellar and the suprasellar region. The margins of the lesion were not well-defined; the lesion was relatively homogenous with iso-intense T1 and hyperintense T2 signals. Following intravenous Gd-DTPA injection, the lesion showed significant heterogenous enhancement; the lesion had enveloped the internal carotid arteries on both sides and had infiltrated the bilateral cavernous sinuses, the floor of the third ventricle and the hypothalamus region. The sellar floor was mildly enlarged; the imaging of the pituitary gland was unclear. The initial differential diagnosis was between sellar chordoma, pituitary adenoma, lymphoma, glioma and metastatic lesion, a transphenoidal was selected for tumor removal, The histopathological exam showed high histopathological appearance and immunohistochemical profile consistent with a glial morphology process (ATRX lost, Olig 2+) of grade anaplasia, suspicion of a tumor associated with the CMMRE syndrome (constitinal mismatch repair defeciency). The patient was presented in pituitary CPR and a STUPP protocol was decided, The patient died six months after the surgery.
Conclusion
Until larger case series are published allowing better management of these tumors, patients still showed short intervals between diagnosis and tumor progression or death even after extensive multimodal therapy.

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EP161

Kallmann-de morsier syndrome: about a case

Mariem Souissi[1], Boubaker Fadia[1], Houcem Elomma Mrabet[1], Oumaima Dimassi[2], Alaya Wafa[1] & Sfar Mohamed Habib[1]
[1]Taher Sfar University Hospital, the endocrinology department of the Taher Sfar University Hospital of Mahdia, Mahdia, Tunisia; [2]Taher Sfar University Hospital, the endocrinology department of the Taher Sfar University Hospital of Mahdia, Mahdia

Introduction
Kallmann-de Morsier Syndrome is a rare genetic disorder characterized by the combination of hypogonadotropic hypogonadism and anosmia or hyposmia. It is more prevalent in males compared to females. In this case report, we present the case of an adolescent with Kallmann-de Morsier Syndrome.
Case Presentation
An 18-year-old patient was referred to our endocrinology clinic by gynecologists for the investigation of pubertal delay. The patient's parents were not consanguineous. There were not a family history of pubertal delay or infertility. The patient has a history of epilepsy since childhood, managed with medication, and reports a long-standing hyposmia. Upon examination, the patient exhibited facial dysmorphia, including a broad forehead, protruding ears, a flat nose, and full lips. She was at Tanner stage S2P4A2. Neurological examination revealed cerebellar syndrome. Hormonal exploration identified hypogonadotropic hypogonadism and lactotroph insufficiency. Corticotrope and thyrotrope insufficiency were ruled out. Pelvic ultrasound showed an underdeveloped uterus with normal ovaries. The Karyotype was 46 XX. Hypothalamus-hypophysis and olfactory bulb MRI revealed agenesis of the olfactory bulbs, strongly suggesting Kallmann-de Morsier Syndrome. Renal ultrasound showed no anomalies. Hormonal treatment, based on estrogen, was initiated until breast development was complete. Subsequently, a progestin was added to induce menarche.
Discussion
Kallmann-de Morsier Syndrome (KS) or olfacto-genital dysplasia results from prenatal anomalies in the migration of GnRH neurons, often associated with olfactory bulb atrophy. This disease is four times less frequent in females. Primary amenorrhea is the presenting circumstance in over 90% of cases in females. Breast development varies. Diagnosis is confirmed by hypoplasia of olfactory bulbs on MRI. Besides clinical features, it is crucial to explore associated conditions such as renal or dental agenesis, cerebellar syndrome (as observed in this case), cleft lip/palate, or synkinesias. The sporadic form is more common than the familial form, and in 60-65% of patients, no mutations are identified.
Conclusion
Early diagnosis of Kallmann-de Morsier Syndrome is crucial to mitigate the organic and psychological impact of pubertal delay. The clinical and radiological context plays a pivotal role in diagnosis, as genetic studies are often inconclusive. Hormonal treatment facilitates puberty, and long-term fertility can be achieved
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EP169

Lipid profile in women with sheehan's syndrome: a case-control study

Salma Salhi[1], Ibtissem Oueslati[1], Emna Talbi[2], Anis Grassa[1], Kacem Ben Fradj[2], Moncef Feki[2], Meriem Yazidi[1] & Melika Chihaoui[1]

[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia; [2]La Rabta University Hospital, Laboratory of Biochemistry, Tunis, Tunisia

Introduction
Sheehan's syndrome (SS) is a rare cause of hypopituitarism. It results from ischemic necrosis of the pituitary gland following severe postpartum hemorrhage. There is growing interest in understanding the lipid profile alterations in patients with SS, potentially contributing to an increased risk of cardiovascular complications. The aim of this study was to evaluate the lipid profile in women with SS.
Methods
We conducted a cross-sectional study including 50 patients with a complete anterior hypopituitarism secondary to SS and 50 age and body-mass index (BMI) -matched controls. Participants underwent physical examination and laboratory tests including lipid measurements.
Results
The mean age was 62.2±9.4 years in patients vs 60.6±8.4 years in controls ($P=0.385$). The mean BMI was 29.6±6.0 kg/m^2 in women with SS vs 30.0±5.0 kg/m^2 in controls ($P=0.741$). Patients with SS had significantly higher levels of triglycerides (respectively: 1.8±0.8 mmol/l vs 1.4±0.6 mmol/l, $P=0.046$) and triglycerides/HDL-cholesterol ratio (respectively: 1.6±1.2 vs 1.1±0.5, $P=0.016$) compared to controls. The prevalence of dyslipidemia was 66% in patients and 38% in controls ($P=0.005$). SS was positively associated with dyslipidemia with an Odds Ratio of 3.2 (95%-confidence interval (CI): 1.39-7.17, $P=0.005$). Factors associated with dyslipidemia in women with SS included a family history of dyslipidemia (OR=4.4, 95%-CI: 1.2-16.4, $P=0.022$), diabetes (OR=8, 95%-CI: 0.9-68.4, $P=0.031$), and insulin resistance (OR=7.97, 95%-CI: 1.6-40.5, $P=0.006$). However, age, diagnostic delay, disease duration, GH levels, FT4 levels, daily dose of levothyroxine, daily and cumulative dose of hydrocortisone, and estroprogestative therapy were not associated with dyslipidemia.
Conclusions
The prevalence of dyslipidemia was significantly higher in patients with SS than in controls. Its associated factors were family history of dyslipidemia, insulin resistance, and diabetes. Regular lipid profile assessments and lifestyle management are necessary in women with SS.

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EP193

An overview of transsphenoidal surgery in spain from 2018 to 2022

Miguel Paja Fano[1], Betina Biagetti[2], Fernando Guerrero-Pérez[3], Rosa Cámara[4], Dolores Moure[5], Felicia Hanzu[6], M. Angeles Gálvez[7], Andreu Simó[8], Rocío Villar[9], Almudena Vicente[10], Paola Parra[11], Patricia Martin-Rojas[11], Guilermo Serra[12], Anna Aulinas[13], Fernando Muñoz[14], María Calatayud[15], Marta Araujo-Castro[16], Soledad Librizzi[16], Ana Irigaray[17], Dolores Ollero[17], Silvia Aznar[18], Edelmiro Menéndez[19], Tomás González-Vidal[19], Javier Abarca[20], Antonio Pico[21], Johana Sottile[21], Rogelio García[22], Laura González-Fernández[22], Ana Delgado[23], Isabel Ortiz[24], Carmen Tenorio[25], Cristina Novo[25], Jose Recio[26], Nerea Egaña[26], Pedro De Pablos[27], Cristina Crespo[28], David Peñalver[28], Gonzalo Díaz-Soto[29], Aina Raventós[30], Diego Asensio-Wandosell[30], Manel Puig-Domingo[30] & Alfonso Soto[31]
[1]Basurto University Hospital – OSI Bilbao-Basurto, Endocrinology, Spain; [2]Hospital Universitario Vall de Hebron, Endocrinology; [3]Hospital Universitari de Bellvitge, Endocrinology; [4]Hospital Universitari i Politècnic la Fe, Endocrinology; [5]Hospital Universitario de Cruces, Endocrinology; [6]Hospital Clinic Barcelona, Endocrinology; [7]Hospital Reina Sofía, Endocrinology; [8]Hospital Universitario Mutua de Terrassa, Endocrinology; [9]Complejo Hospitalario Universitario de Santiago, Endocrinology; [10]Complejo Hospitalario de Toledo, Endocrinology; [11]Hospital Universitario La Paz, Endocrinology; [12]Hospital Universitarito Son Espases, Endocrinology; [13]Hospital Sant Pau, Endocrinology; [14]Hospital Sant Pau -Hospital del Mar, Neurosurgery; [15]Hospital 12 de Octubre, Endocrinology; [16]Hospital Universitario Ramon y Cajal, Endocrinology; [17]Hospital Universitario de Navarra, Endocrinology; [18]Complejo Hospitalario Universitario de Albacete, Endocrinology; [19]Hospital Universitario Central de Asturias, Endocrinology; [20]Hospital General Universitario de Alicante, Neurosurgery; [21]Hospital General Universitario de Alicante, Endocrinology; [22]Hospital Gregorio Marañón, Endocrinology; [23]Hospital Universitario de Burgos, Endocrinology; [24]Hospital Universitario Virgen de las Nieves, Neurosurgery; [25]Hospital Universitario Virgen de las Nieves, Endocrinology; [26]Hospital Universitario de Salamanca, Endocrinology; [27]Hospital Universitario Doctor Negrín, Endocrinology; [28]Hospital Universitario Río Hortega, Endocrinology; [29]Hospital Clínico Universitario de Valladolid, Endocrinology; [30]Hospital German Trías i Pujol, Endocrinology; [31]Hospital Virgen del Rocío, Endocrinology

Transsphenoidal surgery (TSS) of the hypothalamic-pituitary region is the approach of choice because of its lower morbidity compared to the transcranial approach. However, its results are highly variable and depend on many factors related to the tumor itself, to the medical team, and to technical issues. We review the situation of this procedure in a nationwide retrospective multicenter evaluation. Data were collected from centers participating in the TESSPAIN (TranssphEnoidal Surgery in SPAIN) registry, that included all TSS performed in each center during a 5-year period (2018-2022). Each center recorded the number of neurosurgeons performing TSS, the technical aspects, the number of procedures/year/surgeon, the pathology operated on, the goals set and their achievement, and the occurrence of long-term complications following the procedure. The 29 centers included performed a total of 2815 TSS procedures. Seventeen centers had more than one dedicated neurosurgeon, four of which had one neurosurgeon performing more than 75% of TSS. Twelve centers had one dedicated neurosurgeon (n:9) or two neurosurgeons who always operated together (n:3). An ENT surgeon always performed the nasal phase of the procedure in 21 of 29 centers, while it was performed by the dedicated neurosurgeon in five centers. In the remaining three centers the ENT surgeon was only required for very complex approaches. No one center averaged more than 40 TSS/year. Only six centers averaged more than 25 TSS/year. Only one center did not use an endoscopic approach. Extended approach to the cavernous sinus was reported by 27 centers. The most common pathology was clinically nonproducing pituitary adenomas ($n=1421$;50.5%), followed by producing pituitary adenomas (n: 911 (32.4%): 436 GH-producing, 323 Cushing's disease, 127 prolactinomas and 25 TSH-secreting adenomas). 483 TSS (17.1%) were performed for the treatment of non-adenomatous tumors, usually with extrasellar extension including craniopharyngiomas, RCC, meningiomas, chordomas, and others. The percentage of TSS for nonproducing pituitary adenomas was negatively correlated with the total number of TSS (p:0.016), and the percentage of TSS for non-adenomatous tumors showed a positive correlation with the total number of TSS (p:0.012). TSS in Spain shows an inhomogeneous picture, with a high geographical dispersion and low surgical volume in each center, despite the recommendations of scientific societies. Almost all neurosurgeons use an endoscopic approach and perform a cavernous sinus approach. Centers with higher surgical volume have a higher percentage of TSS for non-adenomatous tumors, while centers with lower surgical volume operate more frequently on nonproducing pituitary adenomas.

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EP208

Oral health-related quality of life in patients with acromegaly vs patients with non-functioning pituitary adenomas

Sandra Blum[1], Linda Daume[2], Rohith Illuri[1], Johannes Kleinheinz[2], Jonel Trebicka[1] & Elena Vorona[1]
[1]Münster University Hospital, Gastroenterology, Hepatology, Endocrinology, Infectiology, Münster, Germany; [2]Münster University Hospital, Cranio-Maxillofacial Surgery, Münster, Germany

Introduction
Acromegaly is a rare endocrinologic disease most commonly caused by an excess of growth hormone (GH) produced by a benign pituitary adenoma. Besides diverse systemic manifestations, acromegaly is also associated with a range of oral-dental problems. To date limited research has been conducted on how oral-dental pathologies affect the oral health-related quality of life (OHRQoL) in patients with acromegaly and growth hormone-producing pituitary adenomas. To our knowledge this is the first study which compares the OHRQoL between acromegaly patients and those with non-functioning pituitary adenomas. The aim of this study is to improve understanding of acromegaly's dental effects and the impact of OHRQoL and to enhance future treatment and patient outcomes.
Methods
41 patients with diagnosis of growth hormone-producing pituitary adenomas and patients with non-functioning pituitary adenoma were included in the study. All participants were asked to complete a german version of the oral health impact profile 14 questionnaire (OHIP-14). For included patients data from the clinical profile were collected. Comparative analysis of both groups were performed. Patients diagnosed with acromegaly and growth hormone-producing pituitary adenomas were additionally examined in regard of their oral-dental health condition by a speacialist and had to answer 3 additional questions referring to their oral-dental care by dentist. Based on the examination, a specialist medical diagnostic of the problem and, if necessary, appropriate treatment is offered.

Results
Mean age of the acromegalic patients was 55,95 years and 26 patients were females. The average OHIP-14 score for an acromegalic patient was 9,95 points. Female acromegalic patients present a higher OHIP-14 Score (12.15 points) than males (6.13 points). The questionnaire domains most affected were psychological discomfort (mean 2.05 ± 2.27) and psychological disability (mean 2.05 ± 2.07) and physical pain (mean 1.53 ± 1.7). 89.7% of acromegalic patients are satisfied with dental care and 95% had no difficulty finding a dentist due to acromegaly. However, 77.4% of acromegaly patients have the impression that the dentist is not familiar with their disease.
Conclusion
the analyses of our data will take a crucial step forward in providing deeper insights into the impact of oral health conditions and associated comorbidities as well as OHRQoL in patients with acromegaly.

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EP210

Pseudoacromegaly – a challenging entity in the endocrine clinic: why you need to know about it?

Pedro Marques[1,2], Inês Sapinho[3] & Marta Korbonits[4]
[1]Hospital CUF Descobertas, Lisbon, Portugal, Endocrinology Department, Lisbon, Portugal; [2]Faculdade de Medicina, Universidade Católica Portuguesa, Lisbon, Portugal; [3]Hospital CUF Descobertas, Endocrinology Department, Lisbon, Portugal; [4]William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, Centre for Endocrinology, London, United Kingdom

Introduction
Pseudoacromegaly encompasses a group of conditions in which patients have clinical features of acromegaly or gigantism, but no GH or IGF-1 excess. With systematically reviewing all published cases ($n = 76$) of patients with pseudoacromegaly who were evaluated due to a clinical suspicion of acromegaly, we identified key distinguishing features which need to be recognized.
Materials and Methods
A systematic search using the terms pseudoacromegaly, acromegaloidism and acromegaloid was conducted. Pseudoacromegaly cases were carefully checked to ensure they met eligibility criteria: 1) presentation suggestive of acromegaly and investigation triggered by acromegaly-related manifestations; 2) acromegaly was excluded based on normal serum GH, IGF-1 and/or GH suppression on oral glucose tolerance test (OGTT-GH); 3) definitive diagnosis of the underlying pseudoacromegaly condition was established.
Results
Of the 76 included cases, 47 (62%) were males, with mean ages at presentation 28 ± 16 yrs (mean ± SD) and at first acromegaloid symptoms 17 ± 10 yrs. Most cases were reported from Asia (42%). Over half 57% were directly referred to Endocrine departments. The most common conditions were pachydermoperiostosis (47%) and insulin-mediated pseudoacromegaly (24%), followed by Cantú (8%) and Berardinelli-Seip (4%) syndromes. Insulin-mediated pseudoacromegaly cases were more often referred to endocrine departments, whereas pachydermoperiostosis to non-endocrine physicians. Acromegaloid facies (75%) and acral enlargement (80%) were the most common features; other prevalent acromegaloid features included hyperhidrosis (36%), pachydermia (32%), arthralgia (29%), macroglossia (25%), prognathism (25%), acanthosis nigricans (25%) and tall stature (20%). Prevalence of acromegaloid physical features and tall stature was higher in cases referred to endocrine specialists (33% vs 6%; $P = 0.003$). GH/IGF-1 axis assessment was heterogeneous: random GH was reported in 65%, IGF-1 in 79%, OGTT-GH in 51%. GH excess was more frequently ruled out based on 2 tests combined (53%); 3 tests were applied in 22%. Pituitary MRI was performed in 30 cases, being normal in 19, while a pituitary adenoma or hyperplasia were reported in 8 and 3 patients, respectively. Investigation patterns differed between cases managed by endocrine and non-endocrine specialists, the former requesting more often IGF-1, OGTT-GH and pituitary MRI.
Conclusions
Pseudoacromegaly is a challenging entity that may be encountered by endocrinologists, with pachydermoperiostosis and insulin-mediated pseudoacromegaly being the conditions most identified as mimicking acromegaly. Adequate assessment of GH/IGF-1 is crucial to rule out acromegaly, which may be better performed by endocrine specialists. Pituitary incidentalomas are common in the pseudoacromegaly setting and require careful judgment to prevent inadequate management.

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EP211

Cannulated prolactin test for the diagnosis of hyperprolactinemia syndrome

Tatiana Mokhort[1], Natalia Karlovich[1], Maryia Malyshko[2], Olga Shishko[3] & Elena Yurenya[3]
[1]Belarusian State Medical University, Endocrinology Department, Minsk, Belarus; [2]16th Outpatient Clinic, Endocrinology Department, Minsk, Belarus; [3]Minsk City Clinical Endocrinological Center, Minsk, Belarus

The aim was to evaluate the results of a cannulated test for prolactin in patients of reproductive age with hyperprolactinemia (HP) and analyze the frequency of specific and nonspecific complaints, the presence of obesity and overweight.
Materials and methods
We examined 120 patients, 93w, 27m; age 31.4 ± 9.0 yrs. After the catheterization of the vein, a venous cannula was installed, blood was taken immediately after the cannulation (P0), then 60 minutes (P1) and 120 minutes (P2). The results of the cannulated prolactin test (CPT) were considered positive - with HP remaining in all three samples (P0, P1, P2), questionable - if HP was retained at P0 and P1, and negative if HP was only at P0. HP was diagnosed in accordance with the recommendations of the Endocrine Society: > 20 ng/ml (424 mU/l) in men and > 25 ng/ml (530 mU/l) in women.
Results
99 patients (87.1% of women and 66.7% of men) had complaints, of them 67 patients (68.8% women and 11.1% men) had specific to HP syndrome (galactorrhea, menstrual disorders, reduced libido, pregnancy-free), 52 patients (39.7% of women and 59.3% of men) had non-specific complaints (breast pain, scrotum pain, weight gain, acne, headache, dizziness, fatigue). Overweight and obesity occurred in 31.8% of patients. Positive CPT was detected in 36.7% of patients. Patients with stress-induced HP (negative CPT) and patients with true HP (positive CPT) had no statistically significant differences in age and frequency of occurrence of specific and non-specific complaints and symptoms for HP. A decrease in serum PRL (P2 vs P0) was found in 113 patients (94.2%), with a median decrease of 158.9 mME/l. Patients with positive CPT had a higher PRL at P0 (888.5 mME/l, $P < 0.001$). Among patients with a negative CPT, i.e. with stress-induced HP, the proportion of overweight and obese was 52.6% vs 22.7% among patients with true HP ($P < 0.001$), and obesity was 21.0% vs 11.3%, $P < 0.05$.
Conclusion
Our results shown that patients with a moderate HP have positive CPT in 36.7% of cases. A negative test, indicating the absence of true HP, is more often recorded in men, as well as in individuals with overweight and obesity. The presence of complaints and symptoms, especially nonspecific ones, does not have a significant impact on the test result. We can assume that CPT is a promising method for excluding physiological (stress-induced) HP in young people of reproductive age with HP.

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EP231

Assessment of muscle hormonal function in adult patients treated with growth hormone (GH)

Magdalena Goralska & Agnieszka Stańczyk, Piotr Wierzbowski, Zbigniew Bartoszewicz, Agnieszka Kondracka, Jarzy Małek, Urszula Ambroziak & Tomasz Bednarczuk Torres
Medical University of Warsaw, Endocrinology and Internal Diseases, Warszawa, Poland

Objective
Growth hormone (GH) is used for metabolic indications in the treatment of adult patients with GH deficiency (GHD). In addition to influencing growth processes in childhood, GH is important in regulating metabolic processes at every stage of life. GH, via insulin-like growth factor (IGF-1), has an anabolic effect on protein metabolism, also in skeletal muscles and cardiac muscle. Moreover, myokines produced by muscle fibers stimulated by muscle contraction, acting in an autocrine and paracrine manner, have a significant impact on metabolism. The most serious consequences of long-term, severe GHD in the adult population are the reduction of muscle and bone mass, which significantly increases the frequency of deaths due to cardiovascular complications and osteoporotic bone fractures, as well asdeteriorates the quality of life. The aim of the study is to assess the hormonal activity of muscles in adult patients treated with growth hormone: with confirmed growth hormone deficiency after a growth-promoting period and with Prader Willi syndrome. The project also aims to assess the impact of treatment on quality of life and physical condition. Patients with GHD who require GH therapy are classified into two groups: GHD that occurred in childhood (childhood-onset GHD - CO-GHD) and GHD acquired in adulthood (AO-GHD, adult-onset GHD).

Design
observational, cohort-prospective
Patients
Study participants: Patients with Prader Willi syndrome, patients with growth hormone deficiency, qualified for recombinant human growth hormone (rhGH) treatment and healthy volunteers.
Measurements
A subjective and physical examination was performed, assessing height, weight, BMI, body composition using the bioimpedance method, and assessing muscle, fat and bone tissue. Quality of life questionnaires, SF-36 and (QoL-AGRDA) were administered. Biochemical and hormonal determinations were made, including (IGF-1) and determinations of myokines like Irisin, Myostatin, IL4, I8, L6, IL15, Apelin and proteins binding insulin-like growth factor (IGFBP-3)
Results
The data obtained in the study allowed us to examine the impact on the hormonal activity of muscles and their function in patients undergoing treatment with human recombinant growth hormone. Hormonal activity of muscles influences metabolic processes and quality of life in patients treated with growth hormone.
Conclusions
Growth hormone deficiency in adults requires precise diagnostics and properly conducted substitution treatment

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EP242

Pancreatic neuroendocrine tumour: from glucagonoma to aggressive insulinoma

Sara Santos[1], Raquel Calheiros[1], Pedro Souteiro[1], Joana Oliveira[1], Isabel Inácio[1], Ana Paula Santos[1] & Isabel Torres[1]
[1]Portuguese Institute Of Oncology of Porto, Endocrinology, Porto, Portugal

Introduction
Pancreatic neuroendocrine tumors (PNETs) originate from neuroendocrine islet cells and can therefore secrete several neuropeptides. Multiple and secondary hormone secretion have been described in a minority of cases, mostly with advanced disease, and it has been hypothesized that this complex secretion pattern can serve as a marker for tumor behavior.
Case report
Male patient, 69 years old, diagnosed with a glucagonoma with pulmonary and hepatic metastasis, in 2009. He was sequentially treated with chemotherapy (gemcitabine and CAPTEM), octreotide, PRRT and everolimus, and lastly with sunitinib. He also had diabetes *mellitus*, likely secondary to the glucagonoma, well controlled with insulin therapy. The patient presented with recurrent symptomatic hypoglycemia that persisted despite insulin suspension. Bloodwork showed glucose 36 mg/dl, C peptide 6,95 (1.1-5.0) ng/ml and insulin 39,2 (2.6-24.9) uUI/ml and the diagnosis of insulinoma was assumed. He started therapy with diazoxide and lanreotide, for hypersecretion control, with a later switch to pasireotide for its hyperglycemic effects. The ^{68}Ga-DOTANOC PET/CT showed hepatic disease progression and he was submitted to 2 additional cycles of PRRNT. None of these measures led to normoglycemia so corticotherapy was introduced. Recurrent severe hypoglycemia with frequent visits to the emergency department led to the patient's hospitalization in our center. Several measures were applied to try to rise his glycemic levels: glucagon perfusion, subcutaneous octreotide 3id, higher steroid doses, 30% glucose perfusion and everolimus (due to its hyperglycemic effect), with little benefit. Considering the hepatic disease progression, (radio) embolization was contemplated, but after discussion with interventional radiology and nuclear medicine, not deemed feasible due to porto-systemic shunt. During the hospital stay, the patient's clinical picture progressively deteriorated, and he passed away shortly after the diagnosis of SARS-COV2 infection.
Conclusion
This case highlights the PNETs ability to change their secretion profile, usually described in the context of advanced and aggressive disease. Several therapeutic lines were used in this patient, with no significant effect, underlying the need for new alternatives for aggressive and refractory insulinomas. Targeted alpha-particle therapies like ^{225}Ac-DOTATATE have been described with great results in this type of patients but, unfortunately, they are still not available in our country.

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EP244

CTGF expression in human pituitary tumors and its association with their aggressiveness: preliminary data from an ongoing study

Rodanthi Vamvoukaki[1,2], Georgios Kyriakopoulos[3], Georgia Ntali[4], Dimitra Vassiliadi[4], Panagiota Vlachou[3], Chrysoula Koukoula[4], Konstantinos Barkas[5], Ioannis Gkalonakis[5], Marinella Tzanela[4], Cynthia Andoniadou[6] & Paraskevi Xekouki[1,2,6]
[1]University General Hospital of Heraklion, Department of Endocrinology Diabetes and Metabolic Diseases, Heraklion, Greece; [2]University of Crete, School of Medicine, Heraklion, Greece; [3]Evangelismos General Hospital, Department of Pathology, Athens, Greece; [4]Evangelismos General Hospital, Department of Endocrinology 'D.IKKOS" - Diabetes Center - Center of excellence for rare endocrine diseases (ENDO-ERN), Athens, Greece; [5]General Hospital of Nikaia - Piraeus "St. Panteleimon", Department of Neurosurgery, Athens, Greece; [6]King's College London, Centre for Craniofacial and Regenerative Biology, London, United Kingdom

Background/Aim
Pituitary neuroendocrine tumors (PitNETs), although usually indolent, may display aggressive behavior. YAP/TAZ signalling has been linked to pituitary development and stem cell regulation, with a preliminary study from our group revealing elevated levels and nuclear localization of YAP/TAZ in non-functioning PitNETs (NF-PitNETs). *CTGF*, a YAP/TAZ target gene, encodes a secreted factor involved in proliferation and angiogenesis, that has been implicated in tumor development. We aim to use specimens of human PitNETs to assess the expression of *CTGF* and correlate with clinical and pathology data.
Material and methods
The clinical and pathology data of 13 patients with PitNETs were initially investigated, including seven patients with functioning and six patients with NF-PitNETs. Their clinical characteristics were analyzed, including age, tumor size, and outcome (remission, recurrence, progression). The 5th edition of WHO classification was used. The expression of *CTGF* in pituitary tumor sections was assessed using RNAscope mRNA *in situ* hybridization (ACDBioTechne). *CTGF* expression was subdivided into four groups based on a semiquantitative scoring system (Very low 0, Low 1, Medium 2, High 3). The tumor subtype, Ki-67 proliferation index, and the MGMT presence ($>50\%$) were correlated with the clinical data and tumor behavior. This study was approved by the Institutional Review Board and all patients provided informed consent.
Results
Our preliminary results showed that *CTGF* is expressed statistically higher (Score 2-3) in patients with Ki-67 above 7% ($P<0.05$). Among six patients with NF-PitNETs, one patient had medium, and three had high levels of *CTGF* (16,6% and 50%, respectively), correlated with Ki-67 above 7% and a recurrence/progression rate of 100%. Interestingly, there was high expression of *CTGF* (Score 3) in two patients with immature POU1F1-lineage PitNETs, which lack terminal differentiation. In patients with functioning PitNETs, 3 out of 7 cases were characterized by medium levels of *CTGF* (Score 2) and were correlated with younger age (<40 years), with high Ki-67 levels above 10% and with MGMT presence (2 out of 3 cases, 66%). None of the remaining four functioning PitNETs with *CTGF* Score 0-1 and low Ki-67 $<3\%$ recurred.
Conclusion
Our preliminary data show increased expression of *CTGF* in NF-PitNETs, particularly in immature subtypes, with high levels of Ki-67 and in functioning PitNETs presenting in younger patients with high Ki-67 and MGMT expression. All patients with high expression of *CTGF* recurred/progressed. Our findings suggest that YAP/TAZ signalling may have a critical role in PitNETs with more aggressive behavior.

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EP246

Sotos syndrome in two generations - a reminder that high suspicion is needed in milder phenotypes

Maria Ponte[1], Andreia Pataco[1], Regina Medeiros[1], Ana Luísa Rodrigues[2] & João Anselmo[1]
[1]Hospital do Divino Espírito Santo de Ponta Delgada, Endocrinologia e Nutrição, Ponta Delgada, Portugal; [2]Hospital do Divino Espírito Santo de Ponta Delgada, Pediatria, Ponta Delgada, Portugal

Introduction
The differential diagnosis of overgrowth includes constitutional tall stature, excess growth hormone (GH) and genetic syndromes. Sotos syndrome generally presents with overgrowth, dysmorphisms and early learning disabilities. Here in, we describe the diagnostic pathway of Sotos Syndrome in an adult male presenting with tall stature and mild morphological and cognitive features, prompted by his son's clear manifestation of the classic triad.
Case report
A male child was born at term and delivered by c-section due to fetopelvic incompatibility, weighing 3460 g (*z*-score 0.2; percentile 59.1), measuring 52.5

cm (*z*-score 1.4; percentile 91.6), with a cephalic perimeter of 38.2 cm (*z*-score 2.9; percentile 99.8). Newborn hearing screening detected congenital conductive hearing loss. Since his 3 months, he has been above the 95th percentile for height and weight. Regarding family history, his father was 2006 cm (*z*-score 4.14; percentile 99.9) and had macrocephaly, elongated face and high forehead. He had refused medical investigation as he always had normal psychomotor development and no clinical symptoms. He concluded high school and works in dust separation. Laboratory study of the son, including IGF-1 and IGFBP-3, was normal. At 18 months, cranial and pituitary CT scans showed only an arachnoid cyst. At 2 years and 6 months, left wrist radiography revealed advanced bone age of 3 years and 6 months. An abdominal echography did not identify any organomegaly or abdominal mass. Genetic karyotype and Fragile X Messenger Ribonucleoprotein (FMR1) gene analysis were normal. Psychomotor retardation was noticed, mainly since he was 3 years old, predominantly in oral communication, locomotor skills and personal-social functions, displaying some autistic-like behaviors. Some dysmorphic features also became evident, such as dolichocephaly, high forehead and ogive palate. Sotos Syndrome was hypothesized and confirmed by identification of a heterozygous variant in Nuclear receptor binding SET Domain Protein 1 (NSD1) gene - c.6604T>C p.(Cys2202Arg). His father was also heterozygotic for this variant. Currently, the child is 9 years old, heights 157.9 cm (*z*-score 3.72; percentile 99.9) and weighs 39 kg (*z*-score 1.37; percentile 91.47). He attends the 3rd year of primary school. Cardiac anomalies were excluded.

Conclusion

Sotos Syndrome may mimic gigantism when intellectual and social impairment are mild. Therefore, it should be considered while approaching overgrowth without GH excess. Recognizing Sotos Syndrome is essential for appropriate surveillance due to increased risk of certain tumors and cardiac and renal anomalies, and for providing genetic counseling.

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EP251

Diagnostic challenges in cyclic cushing's syndrome: a rare case due to ectopic acth secretion by lung carcinoid

Roberto Colle[1,2], Stella Pigni[1,2], Simona Jaafar[1,2], Giacomo Cristofolini[1,2], Maria Francesca Birtolo[1,2], Elisabetta Lavezzi[2], Edoardo Bottoni[3], Silvia Uccella[1,4], Gherardo Mazziotti[1,2] & Andrea Lania[1,2]

[1]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele (MI), Italy; [2]IRCCS Humanitas Research Hospital, Endocrinology, Diabetology and Medical Andrology United Rozzano (MI), Italy; [3]IRCCS Humanitas Research Hospital, Thoracic Surgery Department, Rozzano (MI), Italy; [4]IRCCS Humanitas Research Hospital, Department of Pathology, Rozzano (MI), Italy

Introduction

Cyclic Cushing's syndrome (cCS) is a rare condition characterized by periods of excessive cortisol secretion (peaks), alternating with phases of eucortisolism (through). In most cases, cCS is caused by an ACTH-secreting pituitary tumor, while only few cases of cyclic ectopic ACTH secretion (cEAS) have been described.

Case presentation

In February 2023, a 58-year-old woman was referred to our Endocrine Unit due to a 10-year history of recurring episodes of decompensated diabetes, hypertension, and hypokalemia, coupled with body and facial swelling, and weight gain, occurring approximately once a year and alternated with periods of clinical remission. Physical examination during such episodes was highly suggestive of CS. Remarkably, the patient's family history disclosed several cases of functioning pituitary adenomas. Previous endocrine investigations in different centers had revealed a cyclical adrenocorticotropic hormone (ACTH) -dependent hypercortisolism, with high ACTH and 24h urine free cortisol, and lack of cortisol suppression after dexamethasone suppression test during disease periods, yet the precise localization of the disease remained elusive. Indeed, magnetic resonance imaging had identified a 3-mm 'possible pituitary adenoma', but inferior petrosal sinus sampling had demonstrated no center:periphery ACTH gradient, and 68-Ga-PET-CT had only shown focal uptake in the left thyroid lobe, prompting a subsequent total thyroidectomy with the diagnosis of a follicular adenoma. Upon the recurrence of a peak phase, we performed a corticotropin-releasing hormone test and a desmopressin test, both resulted in inadequate ACTH and cortisol responses suggestive of an ectopic source of ACTH hypersecretion. New 68-Ga-PET-CT and 18-FDG-PET-CT scans during this active period both revealed focal uptake in the middle lobe of the right lung, where a "fungus ball" lesion had been previously described. A pulmonary right middle lobectomy was indicated, while a 'bridge therapy' with Osilodrostat waiting for surgery allowed clinical and biochemical improvement. Histological examination identified a typical ACTH-staining carcinoid (Ki67 1.5%), and the diagnosis was confirmed by post-surgical hypoadrenalism, still persistent.

Conclusion

The diagnosis of cyclic ACTH-dependent hypercortisolism poses major difficulties due to its intermittent nature. Up to now, less than 40 cases of cEAS have been described in the literature, although its actual prevalence may be underestimated. The main pitfalls are the low diagnostic accuracy of both hormonal and imaging procedures, especially if performed irrespective of cortisolaemic status, and the intrisinc challeging diagnosis of ectopic neuroendocrine tumors. Thus, an exhaustive diagnostic work-up during periods of florid disease, as well clinical experience, are paramount to avoid misdiagnoses.

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EP262

Epidemiology, clinical presentation, treatment and outcome of acromegaly in the island of crete, greece: experience of 3 tertiary centers over a four decade period

Maria Chrysoulaki[1], Vasiliki Daraki[2], Maria Sfakiotaki[1], Paraskevi Tzoutzouraki[3], Paraskevi Floroskoufi[4], Grigoria Betsi[2], Rodanthi Vamvoukaki[2], Stavrina Vergou[5], Stefanos Michailidis[5], Artemis Maria Makri[5], Elpida Mpouhlaki[5], Antonela Spanoudaki[5], Georgios Goulielmos[6], Christos Lionis[7], Katerina Stamataki[4] & Paraskevi Xekouki[1,5]

[1]University General Hospital of Heraklion, Endocrinology & Diabetes Clinic, Iraklio, Greece; [2]University General Hospital of Heraklion, Iraklio, Greece; [3]General Hospital St. George, Mournies, Greece; [4]Venizelio Hospital, Iraklio, Greece; [5]Medical School, University of Crete, Giofirakia, Greece; [6]Medical School, University of Crete, Section of Molecular Pathology and Human Genetics, Giofirakia, Greece; [7]Medical School, University of Crete, Clinic of Social and Family Medicine, Giofirakia, Greece

Acromegaly is a rare and insidious endocrine disease, with increased morbidity and mortality mainly due to delayed diagnosis and inadequate control. There are many population studies assessing the epidemiology of acromegaly in Europe while in Greece, there are no published data except for a few small studies regarding treatment outcome.

Aim

To determine the epidemiology, presentation and outcome in patients with acromegaly in Crete, Greece.

Methods

This is a retrospective observational study using data from the archives of three tertiary hospitals from Heraklion and Chania, for the period of 1983 to 2023. Age at diagnosis, estimated delay in diagnosis, clinical, biochemical, imaging data and disease outcome were recorded.

Results

Eighty-five patients were included in the analysis (51 females, 34 males). The mean age at diagnosis was 44.36±13 years and the mean follow-up time was 16±8 years. Forteen patients (16.4%) were younger than 30 years. The time lag from the onset of symptoms to diagnosis was 5.06 years. The most common presenting symptom was suspicious acromegalic features(coarse facial features/acral growth) followed by headaches (23.9%). A metabolic disease (diabetes, dislipidemia, hypertentsion) was present in 41.1% of patients Macroadenomas were found in 40%, while in 15% of patients, size data were missing. Sixty-four (72.41%) patients underwent surgery, 21 patients (27.6%) received medical treatment only (90% somatostatin analogs (SSAs)) and forty-three (50.1%) received adjuvant treatment; SSAs (50.5%), dopamine agonists (10.5%), radiotherapy (10.7%). Six patients had a second operation (7%). Histology reports were available for 28 cases. Tumor subtype analysis available for 16 patients revealed that densely granulated tumors were 1,4 times more frequent than sparsely granulated somatotropinomas (43.75 vs 31.25%), whereas 8.75% were mixed mamosomatotropinomas. A rare case of mixed gangliocytoma/sparsely-granulated somatotrophinoma was recorded as well. Disease remission was observed in 30 patients (35.2%). The mean time interval from treatment to biochemical control was approximately 3 years. Fourteen patients (16,4%) had persistent disease. Three patients died due to malignancies. There was one patient with gigantism in the context of Familial Isolated pituitary adenoma (FIPA) due to *AIP* mutation and one patient with hyperparathyroidism and VIPoma, in the context of *MEN1* syndrome. Genetic testing is ongoing.

Conclusions
Our epidemiological data does not differ from that reported in other published series. Surgery was the main treatment with a cure rate of 46,8% and SSAs the most used medication. The delay in biochemical control indicates suboptimal treatment which can have negative health effects.

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EP265

Radioligand therapy in patients with unknown point of origin, other than gastroenteropancreatic or G3 grading neuroendocrine neoplasms

Grzegorz Kamiński[1], Adam Durma[1], Marek Saracyn[1], Maciej Kołodziej[1], Katarzyna Jóźwik-Plebanek[1], Beata Dmochowska[1], Adrianna Mróz[1], Wawrzyniec Żmudzki[1] & Grzegorz Kaminski[1]
[1]Military Institute of Medicine - National Research Institute, Endocrinology and Radioisotope Therapy, Warszawa, Poland

Background
Neuroendocrine neoplasms (NENs) are rare group of tumors with a different clinical course, prognosis and location. Radioligand therapy (RLT) is currently registered in gastroenteropancreatic (GEP) G1-G2 NENs. Tumors with an unknown point of origin, diagnosed outside the gastrointestinal tract and pancreas, or with Ki-67 > 20%, do not qualify in many countries to standard RLT.
Materials and Methods
48 patients with progressive NENs of unknown primary site, non-GEP-NENs, and G3 with good somatostatin receptor expression were qualified to the study. 32 patients received Lutetium-177 (7.4 GBq), while 16 received tandem therapy with Lutetium-177 and Yttrium-90 with equal activities (1.85 + 1.85 GBq) in 4 cycles every 10 weeks.
Results
Progression-free survival (PFS) before RLT was 34 months (IQR = 36) for the whole study group. In subgroups of patients with an unknown tumor location (n = 25), the median PFS was 19 months (IQR = 23), with 'other' locations (n = 21) 31 months (IQR = 28), and with NEN G3 (n = 7) 18 months (IQR = 40). Just after the RLT, disease stabilization or regression was observed in 42 (87.5%) patients. 43 patients reported to follow-up visit (median time after RLT - 14 months; IQR = 18). In 8 we noted progression, 9 patients died, and stabilization was noted in 26 individuals. PFS and OS probability (%) of surviving 12, 24, 36, 48 months (with 95% CI) were calculated. RLT did not cause statistically significant changes in creatinine or GFR values. Hematological parameters (RBC, WBC, PLT, HGB) as well as chromogranin A concentration decreased significantly during the treatment. There were no statistical differences between both subgroups regarding the type of radioisotope used (177-Lutetium vs 177-Lutetium and 90-Yttrium).
Conclusions
Patients with NENs who do not qualify for standard RLT at this moment due to a lack of registration could benefit from such therapy. There were no significant negative impacts on renal parameters. The reductions in blood counts were noticeably, but not clinically significant, which was acceptable in relation to the positive treatment outcomes.

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EP268

Assessment of the effects of empty or partially empty sella on optic chiasm compression and displacement

Bernadetta Kaluza[1,2], Furmanek Mariusz[3,4], Domański Jan[1,2], Żuk-Łapan Aleksandra[1,2], Babula Emilia[1,2], Poprawa Iga[1,2], Landowska Małgorzata[1,2], Jarząbek Karolina[1,2], Popczyńska Justyna[1,2], Filipowicz Paulina[1,2], Wielglewska Małgorzata[1,2], Walecki Jerzy[5] & Franek Edward[1,2,6]
[1]National Medical Institute of the Ministry of the Interior and Administration, Department of Internal Medicine, Endocrinology and Diabetology, Warsaw, Poland; [2]National Medical Institute of the Ministry of the Interior and Administration, Students Scientific Group of the Medical University of Warsaw at the Department of Internal Medicine, Endocrinology and Diabetology, Warsaw, Poland; [3]National Medical Institute of the Ministry of the Interior and Administration, Department of Radiology, Warsaw, Poland; [4]Medical University of Warsaw, Department of Pediatric Radiology, Warsaw, Poland; [5]Centre of Postgraduate Medical Education, National Institute of Medicine of the Ministry of the Interior and Administration, Warsaw, Poland., Department of Radiology, Centre of Postgraduate Medical Education, National Institute of Medicine of the Ministry of the Interior and Administration, Warsaw, Poland., Poland; [6]Mossakowski Medical Research Centre Polish Academy of Sciences, Warsaw, Poland, Department of Human Epigenetics, Warsaw, Poland

Herniation of the subarachnoid space into the sella turcica results in empty or partially empty sella syndrome. Primary sella turcica syndrome is idiopathic, whereas secondary empty sella is a result of central nervous system pathologies, which may manifest as visual disorders, due to optic chiasm compression or displacement. The purpose of this study was to determine whether empty and partially empty sella—either primary or secondary—are risk factors for optic chiasm compression. The study involved hospital database analysis and selection of 594 patients, who underwent magnetic resonance imaging of the pituitary. Empty or partially empty sella was detected in 136 patients; in 87 patients the condition was primary and in 49 it was secondary. Optic chiasm compression was found in 26 patients. The patients were divided into two groups: patients with empty/partially empty sella (group 1, n = 136) and those with no empty/partially empty sella (group 2, n = 458). Study groups 1 and 2 showed no statistically significant differences in terms of optic chiasm compression rates (6 [4.4%] vs 20 [4.4%], P = 0.98). Univariate logistic regression demonstrated the presence of pituitary macroadenoma to be a statistically significant predictor of optic chiasm compression (OR 20.923, 95% CI 7.166–61.093, P = 0.001); whereas an empty and partially empty sella, either primary (1.351, [0.42-4.342], P = 0.613) or secondary (0.859, [0.174-4.24], P = 0.852); Rathke cleft cyst (OR 0.307 [0.039–2.386, P = 0.259), and pituitary cyst (OR 0.785 [0.168–3.656], P = 0.758) are not risk factors for optic chiasm compression. Empty and partially empty sella have no effect on optic chiasm compression or displacement, which means that they may not manifest with visual symptoms, such as visual field constriction or double vision.

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EP269

Disentangling glucose metabolism during and after pregnancy in women with chronic hyperprolactinemia

Roberta Scairati[1] & Renata Simona Auriemma[1], Sara Di Meglio[1], Guendalina Del Vecchio[1], Rosa Pirchio[1], Chiara Graziadio[1], Claudia Pivonello[1], Rosario Pivonello[1,3,4] & Annamaria Colao[2,3]
[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Naples, Italy, [2]Università Federico II di Napoli, Dipartimento di Sanità Pubblica, Naples, Italy, [3]UNESCO Chair for Health Education and Sustainable Development, University Federico II, Naples, Italy, [4]Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia ed Andrologia, Unità di Andrologia e Medicina della Riproduzione e della Sessualità Maschile e Femminile (FERTISEX-CARES), Università Federico II di Napoli, Naples, Italy

Context
Prolactin (PRL) exerts a crucial role in the regulation of mammalian reproduction and in the promotion of lactation as response to the suckling reflex. Beyond this, it directly modulates gluco-insulinemic metabolism.
Objective
To dissect glucose metabolism during and after pregnancy in patients with chronic hyperprolactinemia (CTPE).
Methods
This longitudinal study included 52 reproductive aged women with CTPE due to pituitary adenomas (43 microadenomas, 9 macroadenomas), chronically treated with cabergoline (CAB) at the mean dose of 0.68 ± 0.6 mg/week for a mean duration of 62.5 ± 52.5 months. 21 out of 52 patients were normal weight (40.3%), 12 overweight (23%) and 8 obese (15.3%). Patients were evaluated before conception, at 12, 24 and 36 weeks of pregnancy and at 1, 2, 3, 4, 5 and 10 years after delivery. CAB was discontinued during pregnancy and restarted in 51.9% of patients after delivery due to recurrent hyperprolactinemia (RH). Anthropometric, hormonal (serum PRL) and metabolic (HbA1c, fasting glucose/FG, glucose tolerance) parameters were assessed.
Results
During pregnancy, serum PRL levels were significantly higher than levels before pregnancy (P < 0.001), while FG remained stable. An inverse correlation between serum PRL and FG was found in the first (P = 0.032) and third (P = 0.05) trimester. The percentage increase in serum PRL levels between first and second trimester

(Δ1, $P=0.048$) and first and third trimester (2, $P=0.001$) were inversely correlated with FG levels at third trimester. Serum PRL before conception emerged as a predictive biomarker of third trimester FG (=2.603; $P=0.048$). Older age was associated with decreased HbA1c in the first trimester ($P=0.048$;), reduced infant birth weight ($P=0.033$), and lower FG at 3 years after delivery ($P=0.025$;). Breastfeeding up to 6 months after delivery correlated with lower FG at 4 and 10 years postpartum. A positive correlation between pre-pregnancy body mass index and FG at 10 years after delivery ($P=0.017$) was observed, particularly in overweight/obese patients requiring higher CAB doses. Patients with RH who had to restart CAB showed shorter breastfeeding duration ($P=0.04$) and higher FG at 2 years after delivery ($P=0.015$).

Conclusion

An appropriate pre-conceptional metabolic management should be recommended in patients with CTPE to reduce the risk of glucose impairment during and after pregnancy. An excessive reduction in PRL levels due to CAB treatment before conception may predict increased blood glucose levels in the third trimester, which may result in an increased risk of GDM.

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EP270

Long-term safety and efficacy of subcutaneous pasireotide in patients with cushing's disease: results from a non-interventional study

Fausto Bogazzi[1], Salvatore Cannavò[2], Carla Giordano[3], Mario Detomas[4], Carla Scaroni[5], Gérald Raverot[6], Jochen Schopohl[7], Carmen Georgescu[8], Andrea Piacentini[9], Arnd Mueller[10], Julia Stermenska[10] & Jérôme Bertherat[11]

[1]University of Pisa, Endocrinology United Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University Hospital of Messina, Unit of Endocrinology, Messina, Italy; [3]University of Palermo, Section of Endocrinology, Dipartimento Biomedico di Medicina Interna e Specialistica (DiBiMiS), Palermo, Italy; [4]University Hospital Würzburg, Department of Internal Medicine, Division of Endocrinology and Diabetes, Würzburg, Germany; [5]Hospital-University of Padova, Endocrinology United Department of Medicine, DIMED, Padova, Italy; [6]Hospices Civils de Lyon and Université Claude Bernard Lyon 1, Lyon, France; [7]Klinikum der Universität München, Medizinische Klinik IV, Munich, Germany; [8]Cluj County Emergency Hospital and Iuliu Hatieganu University of Medicine and Pharmacy, Endocrinology Clinical United, Cluj-Napoca, Romania; [9]Recordati SpA, Milan, Italy; [10]Recordati AG, Basel, Switzerland; [11]Hôpital Cochin, AP-HP, and Université de Paris Cité, Centre de Référence des Maladies Rares de la Surrénale, Paris, France

Introduction

Subcutaneous (sc) pasireotide effectively reduces cortisol levels and is generally well tolerated in Cushing's disease (CD) patients, as demonstrated by a Phase III study (NCT00434148). We report data from a non-interventional, multinational study (NCT02310269) evaluating long-term safety and efficacy of pasireotide sc for CD patients.

Methods

Adults with CD, for whom surgery has failed or is not an option, were analysed by time of pasireotide sc initiation (at study entry: 'new-use' [NU] patients; before study entry: 'prior-use' [PU] patients) and monitored for 3 years. The primary endpoint was incidence of pasireotide-related adverse events (AEs) and serious AEs (SAEs). A key secondary endpoint was the proportion of patients with mean urinary free cortisol (mUFC) ≤ upper limit of normal (ULN) over time.

Results

The full analysis set (FAS) included 152 patients (45 NU, 107 PU); the safety set (SS) included 148 patients (43 NU, 105 PU). In the SS, median (min–max) pasireotide sc exposure was: NU, 7 (0–37) months on study; PU, 34 (0–132) months from drug initiation. 50/105 (48%) PU patients received pasireotide sc for >36 months. Median (min–max) dose on study ($n=148$) was 1200 (300–1800) µg/day. Pasireotide-related AEs occurred in 59.5% ($n=88/148$) of SS patients (NU, 79.1% [$n=34/43$]; PU, 51.4% [$n=54/105$]), mostly (>15%) nausea (16.9% [$n=25/148$]). Hyperglycaemia occurred in 10.1% ($n=15/148$) of SS patients (NU, 23.3% [$n=10/43$]; PU, 4.8% [$n=5/105$]). Pasireotide-related SAEs occurred in 16.2% ($n=24/148$) of SS patients (NU, 25.6% [$n=11/43$]; PU, 12.4% [$n=13/105$]), mostly (>2.5%) hyperglycaemia (3.4% [$n=5/148$]). The only reported grade 4 pasireotide-related SAE was hyperglycaemia (NU, $n=1$). The proportion of patients who discontinued because of pasireotide-related AEs and SAEs were 23.6% ($n=35/148$; NU, 32.6% [$n=14/43$]; PU, 20.0% [$n=21/105$]) and 6.1% ($n=9/148$; NU, 9.3% [$n=4/43$]; PU, 4.8% [$n=5/105$]), respectively. The proportion of patients (FAS) with mUFC ≤ULN (138 nmol/24 h) at baseline and months 12, 24 and 36 were: NU, $n=4/23$ (17.4%), $n=3/10$ (30.0%), $n=5/7$ (71.4%), $n=1/3$; PU, $n=30/45$ (66.7%), $n=31/41$ (75.6%), $n=24/36$ (66.7%), $n=9/15$ (60.0%).

Conclusions

Pasireotide-related AEs and SAEs, including hyperglycaemia, occurred more frequently in NU than PU patients. This suggests that most AEs, including hyperglycaemia, typically occur in the early stages after pasireotide sc initiation and can be effectively managed long term. Most patients achieved/maintained cortisol control over 36 months. Pasireotide sc has a manageable safety profile and is effective for the long-term treatment of CD patients.

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EP295

Sheehan syndrome: about 36 cases

Rajaa Mashal[1], Nassim Essabah Haraj[2], Siham El Aziz[2] & Asma Chadli[2]

[1]Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy- University Hassan II – Casablanca-Morocco, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Departement, CASABLANCA, Morocco; [2]Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy- University Hassan II – Casablanca-Morocco, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Departement, CASABLANCA, Morocco

Introduction

Sheehan syndrome (SS) is a potentially serious complication of the postpartum period, corresponding to ischemic necrosis of the anterior pituitary gland in connection with delivery hemorrhage, and remains a topical issue despite improvements in gyneco-obstetrical management. **The objective** of our study is to investigate the epidemiological, diagnostic and therapeutic aspects of sheehan's syndrome for better management.

Patients and methods

Retrospective study carried out at the Endocrinology and Metabolic Diseases Department, Ibn Rochd University Hospital - Casablanca, on patients hospitalized from January 2000 to December 2023 for partial or complete antehypophyseal insufficiency on sheehan syndrome.

Results

In our study, 38 patients were included. The average age of the patients was 55 years. The etiological factor was delivery hemorrhage, requiring hemostasis hysterectomy in 6 patients.The time to diagnosis was 20 years (40 days - 40 years) . Clinical symptomatology was dominated by the absence of lactation, amenorrhea, axillary or pubic depilation and signs of hypothyroidism. The hormonal assessment including an assay of the cortisolemia of 08h, FSH, LH and TSH was carried out in all our patients, showing a complete deficit of the 3 hormonal axes. Hypohyseal MRI was performed in 18 patients, showing an empty sella turcica in 16 and pituitary apoplexy in 2. Complications in our patients included diffuse bone demineralization in 20 cases and 8 cases of depression. all our patients received hormone replacement therapy with hydrocortisone 20 to 30 mg/d and L-thyroxine 50 to 100 mg/d. 11 patients were put on oestroprogestins, with a good evolution.

Conclusion

Sheehan's syndrome is usually diagnosed late. It should be considered in the case of absence of lactation with amenorrhea after a hemorrhagic delivery, and in the case of chronic asthenia in a woman with a gyneco-obstetrical history.

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EP305

Hypoglycemia revealing an appendicular neuroendocrine tumor

Belhadi Leila[1], Haraj Nassim Essabah[1], El Aziz Siham[1] & Chadli Asma[1]

[1]University Hospital Center Ibn Rochd, Department of Endocrinology and Metabolic Diseases, Casablanca, Morocco

Introduction
Primary neuroendocrine tumors can develop in any organ of the digestive system, most commonly in the small intestine, pancreas, or appendix, followed by the stomach or rectum. Appendiceal neuroendocrine tumors are often discovered incidentally during an appendicular presentation or as part of a carcinoid syndrome, without symptoms of hypoglycemic crises. The association between hypoglycemia and appendicular neuroendocrine tumors remains a subject of debate.
Observation
A 19-year-old patient was admitted for recurrent hypoglycemia, with no specific medical history except for a diabetic mother on metformin and sulfonylureas for the past year. The disease history dates back to one month before admission when a severe hypoglycemic episode occurred with a recorded blood glucose level of 0.5 g/l, accompanied by adrenergic symptoms complicated by a convulsive crisis, which resolved with glucose administration and anticonvulsant therapy. The course was marked by successive hypoglycemic episodes associated with a Whipple triad. Throughout this period, the patient experienced weight loss of 2 kg in one month. Upon admission, the patient presented with a generalized convulsive crisis coinciding with a blood glucose level of 1.03 g/l, leading to status epilepticus and transfer to the intensive care unit. Brain CT and MRI were normal, hile an abdominal CT scan revealed a swollen appendix with a small amount of peritoneal fluid but without infiltration of adjacent fat or pancreatic lesions. An appendectomy was performed, and the pathology report indicated a grade 1 neuroendocrine tumor according to the WHO classification, measuring 2x4 mm, with immunohistochemical expression of chromogranin A and CD56, a Ki-67 proliferation index of 2%, and clear resection margins. Additionally, exploration of thyroid, renal, and hepatic function, cortisol levels returned normal. During post-appendectomy monitoring, the patient normalized blood glucose levels and did not experience further hypoglycemia. As part of the postoperative extension assessment, thoracic-abdominal-pelvic and pancreatic CT scans were performed, and urinary Chromogranin A and 5HIAA levels were negative. An octreoscan conducted 6 months after surgery revealed very moderate hyperfixation in the right iliac fossa.
Conclusion
This observation illustrates the possible endocrine effects of a non-pancreatic neuroendocrine tumor (NET), such as hypoglycemia, which has been described in only one case in the literature. Curative surgery appears to be an effective treatment for these localized tumors.
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EP317

Cyst of the pineal gland: a case report
Redhouane Longo[1], Mourad Benrabah[2], Benabdelatif Katia[3], Abdelkader Yahi[3] & Ould Kablia Samia[3]
[1]Endocrinology department, Regional University Military Hospital of Oran, Algeria; [2]Nuclear Medicine Department, Regional University Military Hospital of Oran, Algeria; [3]Endocrinology Department, Central Military Hospital, Algiers, Algeria

Introduction
Tumors of the pineal region are rare, constitute 0.5% to 1% of intracranial tumors in adults in Europe and the United States. Anatomical location deeply buried under the cerebral hemispheres behind the third ventricle and the brainstem, and the variety of different histological types explain management difficulties. Cysts of the pineal gland, often calcified, may go unnoticed and be discovered during autopsy especially in the elderly, but some cysts are symptomatic and cause signs related to compression of the aqueduct of Sylvius or the tectal blade.
Observation
Patient aged 20, with no particular history, was brought by his father to the psychiatry department for behavioral disorder such as psychomotor instability with subtotal insomnia. During his stay in psychiatry, and given the negative dosage of toxicants, an organic cause was suspected justifying his transfer to our department where a brain magnetic resonance imaging revealed a simple cystic lesion of the pineal gland measuring 18.5 × 13 mm. However, there was no intracranial expansive process or hypothalamopituitary anomaly. 6-sulfatomelatonin in urine (ELISA) returned to 26.4 µg/24 hours (15.6-58.1), which is correct; plasma beta hCG returned to 0.1 mIU/ml (0-1) so normal, and the alpha-fetoprotein returned to 1.01 IU/ml (00-5.8) also normal. A neurosurgical opinion is requested recommending six-monthly radiological monitoring, with possible evacuation puncture at the slightest clinical deterioration or appearance of signs of compression.
Discussion-Conclusion
Epithelial cysts of the pineal region are benign formations with fluid content, asymptomatic in most cases, developed at the expense of the pineal parenchyma. Magnetic resonance imaging most often makes the diagnosis. Some of these cysts increase in size and cause clinical decompensation by compressing the quadrigeminal plate leading to extrinsic stenosis of the aqueduct of Sylvius or by mass syndrome in the posterior fossa.
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EP318

Liraglutide regulates expression of enzymes involved in carbohydrate and lipid metabolism in brain cortex of female rat pups under maternal perinatal food restriction
Zainab Mastoor[1], Lucas Carmelo González-Matías[2], Federico Ferrer[3] & Yolanda Diz-Chaves[3]
[1]Laboratory of Endocrinology Centre for Biomedical Research (CINBIO) University of Vigo, Campus de Vigo, Endocrinology, Vigo, Spain; [2]Laboratory of Endocrinology Center for Research in Nanomaterials and Biomedicine (CINBIO) University of Vigo, Campus de Vigo, Vigo, Spain; [3]Laboratory of Endocrinology Centre for Biomedical Research (CINBIO) University of Vigo, Campus de Vigo, Endocrinology, CINBIO VIGO, Vigo, Spain

Introduction
The regulation of glucose and lipid metabolism in the brain is essential to ensure overall neurological health and proper functioning. Increased glycolysis and lipogenesis, if not properly regulated, can potentially lead to an imbalance between energy production in the brain. Glucose and lipid metabolic dysregulation contribute to the development and progression of various brain diseases. Besides other factors maternal undernutrition may alter glucose and lipid metabolism which persist after birth and might lead to pathogenesis of neurodegenerative diseases in the offspring.
Aim
The aim of the present study was to examine the effect of maternal perinatal food restriction (MPFR) on offspring and also determined the impact of Glucagon-like peptide-1 receptor (GLP-1R) agonist, liraglutide, on the enzymes involve in glucose and lipid metabolism in brain cortex of both male and female rat pups with maternal food restriction compared to control group.
Methods
Sprague-Dawley pregnant rats (300g) were randomly assigned to 50% food restriction (MPFR) or *ad libitum* control groups (CT) at day of pregnancy 12. From GD14 to parturition, pregnant MPFR and CT rats were treated with Liraglutide (100 µg/kg/12 hours, sc.) or vehicle (saline). At postnatal day 21 and before weaning, 16 CT and 16 MPFR male pups and 16 CT and 15 MPFR female pups, half of each group from Liraglutide treated mothers, were sacrificed and brain cortex were analysed by RT-PCR.
Results
Maternal food restriction increased mRNA expression of key enzymes involved in carbohydrate and lipid metabolism in brain cortex of female rat pups: Hexokinase-1, Phosphofructokinase-1, Pyruvate Dehydrogenase Kinase4, 6-Phosphofructo-2-Kinase/Fructose-2,6-Biphosphatase3, Glucose-6 phosphate dehydrogenase, Pyruvate Kinase M, Lactate dehydrogenase A, Fatty acid synthase, Acetyl-CoA carboxylase alpha, Carnitine palmitoyl transferase1. Liraglutide administration significantly reduced or completely restored the expression levels of all those enzymes. In male pups just Glucose-6 phosphate dehydrogenase expression was completely suppressed and levels of 6-Phosphofructo-2-Kinase/Fructose-2,6-Biphosphatase3 prominently increased in MPFR, and Liraglutide had no effect.
Conclusion
1. Maternal perinatal food restriction deeply affected the glucose and lipid metabolic activity in brain cortex of female rat pups but not in males by modifying the expression levels of the majority of key enzymes. As a whole MPFR promotes the increase of both glycolysis and lipolysis in the brain cortex just of females.
2. Liraglutide restored the expression of all those key enzymes and minimizes the effects of maternal food restriction and could offer a promising therapeutic approach for the prevention and treatment of brain diseases.
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EP319

Gender related metabolic differences in hypopituitarism

Dragana Miljic[1,2], Marina Nikolic Djurovic[1,2], Mirjana Doknic[1,2], Sandra Djurdjevic[1,2], Marko Stojanovic[1,2], Zvezdana Jemuovic[1], Ivana Cekic[1], Ivan Jevtic[1] & Milan Petakov[1,2]
[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Center of Serbia, Belgrade, 11 000 Belgrade, Serbia, Neuroendocrinology; [2]University of Belgrade - Faculty of Medicine

Background
Hypopituitarism is characterised by multiple pituitary hormone deficiencies causing adverse metabolic milleu and body composition changes.
Aim
Our aim was to investigate the gender related differences in the prevalence of metabolic syndrome (MetS) and metabolic profiles in patients with hypopituitarism compared to obese controls.
Patients and methods
A retrospective study of 282 patients with hypopituitarism (136 women and 146 men) age 49.2 ± 15.1 years, and body mass index- BMI 27.9 ± 5.8 kg/m^2, has been performed. The most common cause of hypopituitarism was non-functioning pituitary tumor $n = 140$ (49.6%). Group of 246 obese control subjects (115 females, 131 males) age 42.9 ± 14.8 yrs BMI 30.5 ± 5.2 kg/m^2 was used for comparisson. Antropometric, metabolic and clinical parametars were collected and analyzed.
Results
MetS was diagnosed in 48.6% and 57.1% of patients with hypopituitarism using ATPIII and IDF criteria, compared to 35% and 39% prevalence in the control group ($P < 0.05$). Prevalence was higher in female compared to male patients with hypopituitarism according to IDF (63.2 vs 51.4%, $P < 0.05$) and ATP III criteria (54.4 vs 43.2%, $P < 0.05$). However, male patients with hypopituitarism had significantly greater waist circumference (98.6 vs 90.9 cm, $P < 0.001$), lower HDL cholesterol (1.17 vs 1.29 mmol/l, $P < 0.01$) and higher fasting blood glucose (4.72 vs 4.5 mmol/l, $P = 0.046$) than females. Compared to controls significantlly higher cholesterol and triglyceride levels, despite lower BMI and waist circumference in both sexes were found in patients with hypopituitarism (Table 1).

Parameters	Males			Females		
	Hypopit $n=146$	Control $n=131$		Hypopit $n=136$	Control $n=115$	
BMI (kg/m^2)	28.05	**31.77**	$P<0.01$	27.75	**29.00**	$P<0.01$
Waist circumference (cm)	98.65	**108.89**	$P<0.01$	90.92	**92.98**	$P<0.05$
Total cholesterol (mmol/l)	**6.67**	5.59	$P<0.01$	**6.73**	6.12	$P<0.05$
HDL (mmol/l)	1.17	1.07		1.29	1.40	
LDL (mmol/l)	**4.43**	3.35	$P<0.01$	**4.39**	3.93	$P<0.01$
Triglyceridies(mmol/l)	**2.56**	2.20	$P<0.01$	**2.33**	1.71	$P<0.01$

Conclusions
Female patients showed higher prevalence of MetS, while male patients with hypopituitarism had worse metabolic profiles. Compared to obese controls, hypopituitary patients had significantly worse lipid profiles and higher prevalence of MetSy.

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EP320

An open-label long-term Phase 3 study of CAM2029 in patients with acromegaly (ACROINNOVA 2): interim analysis of the subgroup of patients 'new to CAM2029' with controlled or uncontrolled acromegaly on standard-of-care treatment

Diego Ferone[1], Joanna L. Spencer-Segal[2], Guzin Fidan Yaylali[3], Mirjana Doknic[4], Elena Isaeva[5], Alexander Dreval[6], Aleksandra Gilis-Januszewska[7], Emre Gezer[8], Irina Bancos[9], Laurence Katznelson[10], Maria Harrie[11], Agneta Svedberg[11], Alberto M. Pedroncelli[11] & Fredrik Tiberg[11]
[1]Endocrinology United, Department of Internal Medicine, IRCCS Ospedale Policlinico San Martino, Genova, Italy; [2]Department of Internal Medicine and Michigan Neuroscience Institute, University of Michigan, Ann Arbor, MI, United States; [3]Department of Endocrinology, Pamukkale University Faculty of Medicine, Denizli, Turkey; [4]Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Centre Serbia, Medical Faculty of Belgrade, Belgrade, Serbia; [5]Interregional Clinical Diagnostic Center, Kazan, Russian Federation; [6]Endocrinology Department of Moscow Regional Research Clinical Institute, Moscow, Russian Federation; [7]Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [8]Department of Endocrinology and Metabolism, Kocaeli University Faculty of Medicine, Kocaeli, Turkey; [9]Division of Endocrinology, Mayo Clinic, Rochester, MN, United States; [10]Departments of Neurosurgery and Medicine, Stanford University School of Medicine, Stanford, CA, United States; [11]Camurus AB, Lund, Sweden

Background
Acromegaly, a rare, chronic disorder, results from excessive growth hormone (GH) and insulin-like growth factor 1 (IGF-1). The need for convenient therapies that provide effective disease control led to the development of CAM2029, a novel, subcutaneous, octreotide depot designed for convenient monthly self-administration using pre-filled syringes/injection pens. In a 24-week Phase 3 trial (ACROINNOVA 1, NCT04076462) CAM2029 achieved superior IGF-1 control vs placebo (72.2 vs 37.5%; $P = 0.0018$) in patients with acromegaly controlled with standard of care (SoC; octreotide long-acting repeatable/lanreotide Autogel) at screening. Interim data from another CAM2029 Phase 3 trial (52-week, open-label [ACROINNOVA 2; NCT04125836]) are reported here, focusing on patients 'new to CAM2029'.
Methods
ACROINNOVA 2 enrolled patients from ACROINNOVA 1 (reported separately), and 'new to CAM2029' patients with controlled or uncontrolled IGF-1 ($\leq$2x upper limit of normal [ULN]) on stable SoC for $\geq$3 months. New patients received once-monthly CAM2029 20 mg for up to 52 weeks. The primary endpoint was adverse events (AEs). Secondary endpoints included the proportion of patients with IGF-1 $\leq$1x ULN (weeks 50/52 mean); the combined IGF-1/GH response; IGF-1 change from baseline; severity score of acromegaly clinical signs/symptoms, assessed using the Acromegaly Index of Severity (AIS). Baseline values reflect SoC treatment.
Results
Eighty-one 'new to CAM2029' patients were enrolled. At data cut-off (23 May 2023), 61 patients completed treatment at week 52, 15 were ongoing and 5 had discontinued. No new or unexpected safety signals were observed. The most common treatment-emergent AEs were injection-site reactions: 'new to CAM2029', 38.3%; overall population, 43%; none were Grade 3. The proportion of patients achieving IGF/GH control increased during CAM2029 treatment (Table 1). Estimated IGF-1 response (linear probability model, patients with evaluable data at weeks 50/52) increased 21.9% (95% confidence interval [CI]: 9.6, 34.1) from baseline to weeks 50/52. AIS score significantly decreased from SoC baseline to week 52 (mean of –1.3 [95% CI: –2.1, –0.5]).
Conclusions
CAM2029 improved IGF-1/GH control and clinical symptoms in patients 'new to CAM2029'. CAM2029 was well tolerated with a safety profile consistent with SoC. ACROINNOVA 2 reinforces the efficacy and safety of CAM2029 for treating acromegaly, including in patients with uncontrolled disease despite treatment with current SoC.

Table 1. Biochemical endpoints

Endpoint	Baseline n/N$_{all}$(%)	Weeks 50/52
IGF $\leq$1x ULN (weeks 50/52 mean)	12/81 (14.8)	20/60 (33.3)
IGF $\leq$1x ULN (weeks 50/52 mean) and GH $<$2.5 μg/l (week 52)	12/81 (14.8)	18/60 (30.0)

*Patients with evaluable data.

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EP321

An open-label long-term Phase 3 study of CAM2029, an octreotide subcutaneous depot, in patients with acromegaly (ACROINNOVA 2): interim analysis of the ACROINNOVA 1 roll-over patients subgroup

Diego Ferone[1], Julie Silverstein[2], Pamela Freda[3], Laurence Katznelson[4], Federico Gatto[1], Pinar Kadioglu[5], Pietro Maffei[6], Jochen Seufert[7], Joanna L. Spencer-Segal[8], Elena Isaeva[9], Alexander Dreval[10], Maria Harrie[11], Agneta Svedberg[11], Alberto M. Pedroncelli[11] & Fredrik Tiberg[11]
[1]Endocrinology United, Department of Internal Medicine, IRCCS Ospedale Policlinico San Martino, Genova, Italy; [2]Division of Endocrinology, Metabolism and Lipid Research, Department of Neurosurgery, Washington University School of Medicine, St. Louis, MO, United States; [3]Department of Medicine, Vagelos College of Physicians & Surgeons, Columbia University, New York, NY, United States; [4]Departments of Neurosurgery and Medicine, Stanford University School of Medicine, Stanford, CA, United States; [5]Division of Endocrinology-Metabolism and Diabetes, Department of Internal Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey; [6]Department of Medicine, Padua University Hospital, Padua, Italy; [7]Division of Endocrinology and Diabetology, Department of Medicine II,

Medical Faculty, University of Freiburg, Freiburg, Germany; [8]Department of Internal Medicine and Michigan Neuroscience Institute, University of Michigan, Ann Arbor, MI, United States; [9]Interregional Clinical Diagnostic Center, Kazan, Russian Federation; [10]Endocrinology Department of Moscow Regional Research Clinical Institute, Moscow, Russian Federation; [11]Camurus AB, Lund, Sweden

Background
Acromegaly is a neuroendocrine disorder, characterised by growth hormone (GH) and insulin-like growth factor 1 (IGF-1) overproduction. Persistent biochemical control to minimise adverse effects of prolonged excess GH/IGF-1 is a key treatment goal. CAM2029 is a novel octreotide depot, designed for convenient monthly subcutaneous self-administration, using pre-filled syringes/injection pens. A 24-week Phase 3 trial (ACROINNOVA 1, NCT04076462) evaluated CAM2029 in patients with acromegaly, controlled with standard of care (SoC; octreotide long-acting repeatable/lanreotide Autogel) at screening. CAM2029 met the primary endpoint, demonstrating superior IGF-1 control vs placebo (IGF-1 $\leq$upper limit of normal [ULN]: 72.2 vs 37.5%; $P=0.0018$). Interim analysis of patients who completed ACROINNOVA 1 and rolled over to the Phase 3, 52-week, open-label, long-term safety trial (ACROINNOVA 2, NCT04125836) is reported.
Methods
Patients received monthly CAM2029 20 mg for 28 weeks during ACROINNOVA 2. The primary endpoint was adverse events (AEs). Secondary endpoints included the proportion of evaluable patients with IGF-1 $\leq$1x ULN (weeks 50/52 mean); both IGF-1 $\leq$1x ULN (weeks 50/52 mean) and mean GH $<$2.5 µg/l (week 52); acromegaly clinical signs and symptoms severity score, assessed using the Acromegaly Index of Severity (AIS). Data are reported by treatment in ACROINNOVA 1; safety data are reported for the 52-week period.
Results
Of 64 patients completing ACROINNOVA 1, 54 entered ACROINNOVA 2 (prior-CAM2029, $n=36$; prior-placebo, $n=18$). CAM2029 was well tolerated. Fifty percent of patients (prior-CAM2029, 18/36; prior-placebo, 9/18) experienced injection-site treatment-emergent AEs (Grade $\leq$2). One serious treatment-related AE occurred in the prior placebo group (moderately severe cholelithiasis, resolved). In the prior-CAM2029 group, mean IGF-1 remained $<$ULN at weeks 50/52 in 89% of patients (Table 1). In the prior-placebo group, IGF-1 increased $\geq$1$\times$ ULN during ACROINNOVA 1; IGF-1 control was regained after switching to CAM2029. AIS score decreased significantly from SoC baseline to week 52 in prior-CAM2029 patients (–1.3 [95% CI: –2.3, –0.3]); in prior-placebo patients change in AIS score was –0.8 [95% CI: –2.1, 0.5]).
Conclusions
No new safety signals were observed; safety was consistent with SoC. CAM2029 provided persistent control of IGF-1/GH during treatment and improved clinical symptoms. Biochemical control of acromegaly was regained in placebo patients after switching to CAM2029.

Table 1. Biochemical endpoints

Endpoint	Prior-CAM2029	Prior-placebo
	n/N$_{all}$* (%)	
IGF $\leq$1x ULN (weeks 50/52 mean)	25/28 (89.3)	15/15 (100)
IGF $\leq$1x ULN (weeks 50/52 mean) and GH $<$2.5 µg/l (week 52)	23/26 (88.5)	14/14 (100)

*Patients with available data.

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EP322

An open-label long-term Phase 3 study of CAM2029, an octreotide subcutaneous depot, in patients with acromegaly (ACROINNOVA 2): interim analysis of patient-reported outcomes

Diego Ferone[1], Pietro Maffei[2], Julie Silverstein[3], Joanna L. Spencer-Segal[4], Alexsandra Gilis-Januszewska[5], Mirjana Doknic[6], Pinar Kadioglu[7], Pamela Freda[8], Laurence Katznelson[9], Guzin Fidan Yaylali[10], Maria Harrie[11], Agneta Svedberg[11], Alberto M. Pedroncelli[11] & Fredrik Tiberg[11]
[1]Endocrinology United, Department of Internal Medicine, IRCCS Ospedale Policlinico San Martino, Genova, Italy; [2]University of Padua, Department of Medicine (DIMED), Padova, Italy; [3]Division of Endocrinology, Metabolism and Lipid Research, Department of Neurosurgery, Washington University School of Medicine, St Louis, MO, United States; [4]Department of Internal Medicine and Michigan Neuroscience Institute, University of Michigan, Ann Arbor, MI, United States; [5]Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [6]Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Centre Serbia, Medical Faculty of Belgrade, Belgrade, Serbia; [7]Division of Endocrinology-Metabolism and Diabetes, Department of Internal Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey; [8]Department of Medicine, Vagelos College of Physicians and Surgeons, Columbia University, New York, NY, United States; [9]Departments of Neurosurgery and Medicine, Stanford University School of Medicine, Stanford, CA, United States; [10]Department of Endocrinology and Metabolism Diseases, University of Pamukkale, Denizli, Turkey; [11]Camurus AB, Lund, Sweden

Background
Significant treatment-related burdens accompany standard-of-care (SoC) therapies for acromegaly, which typically require healthcare-provider administration. CAM2029 is a novel, subcutaneous octreotide depot conveniently self-administered monthly by pre-filled syringe/injection pen. In a 24-week Phase 3 trial of CAM2029 in patients with acromegaly (ACROINNOVA 1, NCT04076462), insulin-like growth factor 1 (IGF-1) response was 72.2% in patients receiving CAM2029 vs 37.5% with placebo. Interim analysis of overall patient-reported outcomes (PROs) from a 52-week Phase 3 trial of CAM2029 (ACROINNOVA 2, NCT04125836) is reported here.
Methods
ACROINNOVA 2 enrolled patients completing ACROINNOVA 1 (24 weeks; prior-CAM2029 or prior-placebo) and new patients (IGF-1 $\leq$2x upper limit of normal [ULN] during stable SoC [octreotide long-acting repeatable/lanreotide Autogel]) to receive monthly CAM2029 20 mg for up to 52 weeks (28 weeks for prior-placebo group [week 24–52]). The primary endpoint was adverse events. Secondary PRO endpoints included Acromegaly QoL Questionnaire (AcroQoL), EQ-5D-5L visual analogue scale (VAS), Treatment Satisfaction Questionnaire for Medication (TSQM), Patient Satisfaction Scale (PSS) and the Self-injection Assessment Questionnaire (SIAQ v2.0). Higher scores indicate improvement.
Results
Enrolled patients (81 new, 36 prior-CAM2029, 18 prior-placebo) had a mean CAM2029 exposure of 56.3 weeks at data cut-off (23 May 2023). CAM2029 was well tolerated with no unexpected safety signals. From SoC baseline to week 52, mean scores increased for AcroQoL, EQ-5D-5L VAS, and TSQM (Table 1). SIAQ increased from SoC baseline to week 48 during CAM2029 treatment. Mean PSS (scale 0–5) at week 52 was 4.1 (95% confidence intervals [CI] 3.9, 4.3).
Conclusions
PRO scores indicated improvement in patients treated with CAM2029, including those previously controlled with SoC. The safety profile of CAM2029 was consistent with current SoC; no new safety signals were observed. These data support the clinical benefit of CAM2029 and its potential to address unmet needs for patients with acromegaly.

Table 1. PRO endpoints

Assesment	Domain	Mean change from SoC baseline (95% CI) at week 52
QoL: AcroQoL	Total score	3.5 (1.3, 5.7)
	Physical score	1.9 (–0.5, 4.3)
	Psychological total score	4.4 (2.0, 6.8)
QoL: EQ-5D-5L	Visual analogue scale	3.2 (0.5, 5.9)
Treatment satisfaction: TSQM	Convenience	15.6 (11.8, 19.3)
	Effectiveness	6.3 (2.8, 9.8)
	Satisfaction	4.7 (1.1, 8.4)
	Side effects	2.4 (–2.0, 6.8)
		Mean change from SoC baseline (95% CI) at week 48
Self-administration satisfaction: SIAQ	Satisfaction with current way of taking medication	1.6 (0.9, 2.2)
	Feelings about injections	0.8 (0.3, 1.3)
	Self-confidence	0.8 (0.3, 1.4)

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EP323

PET/CT with 68ga-dota-peptides in patients with parathyroid neuroendocrine neoplasms

Uliana Tsoy[1], Karina Pogosian[1], Daria Ryzhkova[1], Olga Yudina[1], Ksenia Yakovenko[1], Pavel Ryazanov[1], Polina Sokolnikova[1], Tatiana Karonova[1] & Elena Grineva[1]
[1]Almazov National Medical Research Centre

Background
Parathyroid tumors are considered to be parathyroid neuroendocrine neoplasia (NEN), according to the recent IARC-WHO classification updates. Primary hyperparathyroidism (PHPT) develops commonly in patients with multiple neuroendocrine neoplasia syndromes (MEN), when it occurs along with pituitary, gastro-entero-pancreatic or other NENs. The latter requires total-body 68Ga-

DOTA-peptides PET/CT. Its major advantage is to detect additional tumors with other localizations, particularly if CT is performed with contrast enhancement. Therefore, simultaneously this technique may reveal parathyroid NENs.
Aims
To determine Ga68-DOTA-peptide PET/CT utilities in parathyroid NENs diagnostics in PHPT patients.
Materials and methods
Sixteen patients with PHPT were included in the study, 11 patients were newly diagnosed, 5 patients had PHPT recurrence. 13 patients were tested for MEN1 mutation, and 7 harbored it. Parathyroid adenomas were localized with neck ultrasound, Tc99m-sestamibi parathyroid scintigraphy or SPECT/CT, CT, PET/CT with 11C-methionine or 11C-choline. Ga68-DOTA-peptide PET/CT was performed in all patients: Ga68-DOTA-TATE PET/CT in 14 patients and Ga68-DOTA-NOC PET/CT – in 2 patients. Parathyroidectomy (PTX) was performed in 10 patients.
Results
16 patients had 27 parathyroid adenomas; 23/27 were found by conventional imaging and 4/27 – through bilateral cervical exploration. Among operated patients ($n=10$) pathology examination revealed 17 parathyroid adenomas, while 6 patients were not operated on due to various reasons. Eight patients harbored single adenomas, five patients – double adenomas, three patients – triple adenomas. Ga68-DOTA-peptide high uptake was found in 18/27 lesions and all of them appeared to be parathyroid adenomas; 12/18 adenomas were verified by the histological examination, the remaining 6/18 – by the conventional imaging since they did not undergo PTX. In five patients 9/27 parathyroid adenomas did not show Ga68-DOTA-peptide uptake and were found by other imaging techniques (5/9) or during PTX (4/9). All these five patients had MEN1 syndrome. Thus, among 27 parathyroid adenomas PET/CT with Ga68-DOTA-peptide revealed 18 lesions, and the sensitivity of the method was 67%. All focuses of Ga68-DOTA-peptide uptake corresponded to parathyroid NENs, hence the specificity was 100%. Therefore parathyroid adenomas' ability to accumulate Ga68-DOTA-peptides during PET/CT is not an exclusive property of MEN1-assosiated parathyroid NENs.
Conclusion
Incidentally localized focuses of high Ga68-DOTA-peptides uptake on PET/CT in the parathyroid glands' allocation may be a reason to exclude PHPT. In case the diagnosis is confirmed, additional conventional imaging may be avoided and patient may be referred directly to PTX, particularly, if PET/CT is performed with contrast enhancement and other PET-negative lesions suspected for parathyroid NENs are not found.

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EP324

AVP-deficiency (central diabetes insipidus) registry in Russia: epidemiology and clinical characteristics

Alexander Lutsenko[1], Daria Sazonova[1], Artem Yu. Zhukov[1], Nino Katamadze[1], Ekaterina Pigarova[1], Larisa Dzeranova[1], Zhanna Belaya[1], Olga Vikulova[1] & Natalia Mokrysheva[1]
[1]Endocrinology Research Center, Moskva, Russian Federation

Background
Epidemiological data on AVP-deficiency is scarce, with non-univocal reported prevalence of 4 per 100.000 for all cases of central and nephrogenic DI without clear gender predominance. Disease registries are major tools for the assessment of epidemiological data, as well as real-life clinical practice, which could be quite valuable for AVP-d.
Aim.
To assess the epidemiological data on ADH-D in Russian Registry for Central Diabetes Insipidus (RCDI)
Materials and method
Database of the Russian Registry for Central Diabetes Insipidus, which includes data from 51 region. Date of analysis – 20-Nov-2023.
Results
Currently, our registry includes information on 3081 patients with AVP-d, from 51 regions of Russia: median age 32.4 years [18.0; 46.8], female-to-male ratio 1786(58%): 1295(42%), age at diagnosis: 32.4 years [18.0;46.8]. The most common causes of AVD-d were postoperative (16.4%), pathology of hypothalamic-pituitary development (9.7%), head trauma (6.6%) and hereditary forms of AVP-d (4.4%). Rare forms accounted for approximately 4% of the patients: neuroinfection, Langergans cell hystiocytosis, sarcoidosis, Sheehan syndrome, DIDMOAD syndrome and hypophysitis. Idiopathic ADH-D was registered in 41.5% of patients. Overall prevalence of AVP-d in Russia according to the National registry is 2.1 cases per 100 000 population. Among participating regions, the highest prevalence is seen in Moscow region (5.4 cases per 100 000 population), which could be attributed to a more thorough registration in tertiary care centers in Moscow. Data on current therapy was available in 2853 patients. Most of the patients receive oral desmopressin ($n=1594$, 55.9%), followed by sublingual ($n=984$, 34.5%) and intranasal ($n=275$, 9.6%) forms.
Conclusions
Russian Registry for AVP-deficiency provides valuable data on demography, etiology, treatment modalities. Continued improvment of the registry will provide more balanced epidemiological data, which is currently lacking worldwide.

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EP340

Bromocriptine test response and its correlation to prolactin levels and MRI characteristics in patients with acromegaly

Shahriar Atai[1,2], Jens Petter Berg[2,3], Jens Bollerslev[2], Kristin Øystese[1,2] & Ansgar Heck[1,2]
[1]Oslo universitetssykehus HF, Rikshospitalet, Endocrinology, Oslo, Norway; [2]University of Oslo, Faculty of Medicine, Oslo, Norway; [3]Oslo University hospital, Oslo, Norway

Introduction
The 2022 WHO classification identifies seven different pituitary tumour subtypes with growth hormone (GH) secretion and/or expression, with or without concurrent prolactin expression. The response to dopamine agonist (DA) treatment in these subtypes requires further investigation. The bromocriptine test has historically been a part of the acromegaly evaluation and may provide insights to DA treatment responsiveness. We aimed to explore the correlations between baseline serum-prolactin concentrations, bromocriptine test response and radiological features in patients with acromegaly to formulate hypotheses for future histological, molecular and clinical studies.
Material and methods
We included patients diagnosed with acromegaly from 2008 to 2017 who underwent a bromocriptine test (2.5 mg). The test was considered positive if the GH levels declined by $>50\%$ at 2, 4 or 6 hours (nadir value) after bromocriptine administration. We correlated baseline serum-hormone concentrations and MR images at diagnosis with test responses. Assessment of MR images included tumour size and volume, invasiveness based on the KNOSP criteria, T1 and T2 intensity and visual assessment of pituitary stalk affection (stalk deviation, dislocation or no visible stalk due to large tumour size).
Results
The study comprised 60 patients (34 males, 26 females) with a median age of 45 years (IQR 34-56). Thirty-five (58%) had a positive and 25 (42%) had a negative bromocriptine test. We found a significant correlation between baseline prolactin above upper reference limit and a positive bromocriptine test ($P=0.02$). The positive test result group also had a significantly higher median baseline prolactin compared to the negative test result group (382 mU/l (IQR 254-727) vs 224 mU/l (IQR 181-475), $P=0.03$). Further, there was a correlation between a positive test and lower invasiveness (KNOSP) ($P=0.02$). There were no significant differences between pituitary stalk affection and test results or prolactin levels.
Conclusions
Patients with $>50\%$ GH decline after a 2.5 mg bromocriptine dose had higher baseline serum-prolactin and less tumour invasiveness. Future studies are warranted to evaluate the association between the bromocriptine test, markers of tumour aggressiveness and treatment response.

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EP341

Volumetric parameters of 68[Ga]Ga-DOTA-TATE PET/CT in the prediction of response to treatment with long-acting somatostatin analogues in patients with well-differentiated NETs

Karolina Morawiec-Sławek[1], Marta Opalińska[1], Wioletta Lenda-Tracz[2] & Alicja Hubalewska-Dydejczyk[1]
[1]Jagiellonian University Medical College, Chair and Department of Endocrinology, Kracow, Poland; [2]Facult, of Health Sciences, Jagiellonian University Medical College, Krakow, Poland

Introduction
Somatostatin analogues (SSA) are recommended as the first-line systemic therapy, to control tumour growth for advanced or metastatic well-differentiated neuroendocrine tumours (WD NET), with good expression of the somatostatin receptors. [68Ga]Ga-DOTA-SSA PT/CT has become the gold standard in the diagnosis, staging and monitoring therapy, of WD NET.
Aim
The aim of the study was to evaluate the predictive role of standardized uptake values (SUVs) and volumetric parameters obtained from pretreatment [68Ga]Ga-DOTA-SSA for response to SSA therapy, in patients with NET.

Material and Methods
42 patients (21 women, 21 men; age range: 46-84 years) with histologicall, confirmed, metastatic, NET (15 pancreatic, 15 small-intestinal, 4 lung, 7 unknow, 1 cecum; WHO G1 13, G2 28, 1 unknown; median Ki-67 index 5%, range 1-16) who received long acting SSA as a first line treatment were included to the study. All of them underwent [68Ga]Ga-DOTA-TATE PET/CT before receiving SSA as a first-line treatment. For each [68Ga]Ga-DOTA-TATE avid lesion, SUVmax and SUVmean were measured as well as TBR was calculated as SUVmean of tumours/metastases divided b, SUVmean of normal spleen. Furthermore, two volumetric parameters were calculated: somatostatin receptor expression tumour volume (STV) and total lesion somatostatin receptor expression (TLD). Finally the sum of STV (total STV, TSTV) and TLD (total TLD, TTLD) was calculated for each patient and used in the analysis.
Results
At the time of the analysis, 14 patients showed stable disease (33,3%), 28 patients were progressive (66,7%); among whom 12 patients died. The median progression-free survival (PFS) and overall survival (OS) were 26.5 and 46.5 months, respectively. The median SUVmax, SUVmean and TBR ratio was 38.5 (range 12.9-99.1), 21.4 (range 10.4-51.9) and 0.93 (range 0.38-3.29), respectively. The median TSTV was 41.4 cm^3 (range 1.0-1446.7) and the median TTLD was 650.7 (range 10.6-16156.8). In the univariate analysis, in the whole population study TBR ratio (HR = 1.96, 95% CI 1.058-3.62, $P = 0.03$) was the only, parameters that was significantly, associated with PFS. Among patients with small intestinal NETs, TSTV (HR = 1.00, $P = 0.023$) and TTLD (HR = 1.00, $P = 0.026$) were significantly, associated with PFS in the univariate analyses. No significant correlation was found between measured volumetric parameters and OS.
Conclusions
>Standardized uptake values and volumetric parameters of pretreatment 68[Ga]Ga-DOTA-TATE PET/CT may, be potentially, useful in prediction of the response to SSA (used in monotherapy, as a first-line therapy,) in patients with NET.

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EP347

Hypogonadotropic hypogonadism, phenotype genotype correlation

Hana Charfi[1], Hamdi Frikha[1], Wajdi Safi[1], Mouna Elleuch[1], Nesrine Dhieb[1], Dhoha Ben Salah[1], Fatma Mnif[1], Nadia Charfi[1], Faten Haj Kacem Akid[1], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker Hospital, Sfax, Tunisia

Introduction
Congenital hypogonadotropic hypogonadism (CHH) of hypothalamic or pituitary origin is a rare condition (1 in 5000 births). Clinical manifestations var, depending on the patient's age and the severity, of the deficiency. CHH is often diagnosed in the context of delayed puberty, without impaired stature, typically, associated with tall stature.
Patients and Methods
This is a bicentric study conducted at the Endocrinology Department of Hedi Chaker University Hospital in Sfax and Fattouma Bourguiba University Hospital in Monastir. It is a retrospective descriptive and analytical study involving 29 cases of CHH, followed between 1991 and 2019. Patients with chronic conditions potentially, affecting pituitary function, those with acquired organic causes of pituitary dysfunction leading to significant hormonal deficiency and those with somatotropic axis deficiency, were excluded.
Results
A clear male predominance was noted with a sex ratio of 2M/1F. The average age at diagnosis was 18.5 years [2-32]. Family, consanguinity, was reported in 62.7% of cases. The most common reason for consultation was delayed puberty, in 73% of cases. The average height of patients was 165.85 cm [123-193]. Sixty, percent of patients had above-average stature at the time of diagnosis, and 16% had a stature delay, between -2 SD and -4 SD, related to molecular abnormalities of sex chromosomes or associated congenital bone anomalies. Ninety, percent of our population reached pubertal bone age at the time of diagnosis. Extra-pituitary involvement was present in 50% of patients: anosmia (30%) and neurosensory impairment (20%). Anterior pituitary exploration revealed corticotrope and lactotrope insufficiency in 5 and 3 patients, respectively. Hypothalamic-pituitary MRI was abnormal in 30% of cases, with pituitary hypoplasia in 6 cases (20%), one of which was associated with corpus callosum atrophy. The posterior pituitary was found in a normal position in all patients. Genetic testing was performed in 9 patients, including 4 relatives, revealing a missense mutation (c.386C > A, p.T129K) in the homozygous state of the KISS1-R gene in 3 relatives.
Conclusion
Although genetic analysis could only, be performed in 9 patients, we attempted to correlate phenotypic aspects with the various biomolecular abnormalities found. The genotype-phenotype correlation for this type of mutation remains challenging due to its modulation by, the cellular and molecular environment.

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EP350

Establishment and representativeness of the stockholm sodium cohort: a laboratorial and pharmacoepidemiologic database covering 1.6 million individuals in the stockholm county

Issa Issa[1], Buster Mannheimer[1], Mikael Franko[1], Jakob Skov[2], Jonatan Lindh[3] & Henrik Falhammar[4]
[1]Södersjukhuset, internal medicine, stockholm, Sweden; [2]Karlstad University Sweden; [3]Tandvårds- & läkemedelsförmånsverket TLV, Sweden; [4]Karolinska Institute, Sweden

Objective
Hyponatremia is associated with considerable morbidity, and mortality but causal links have been difficult to establish. Here, we describe the establishment and representativeness of the Stockholm Sodium Cohort (SSC), designed to study etiologies and outcomes of hyponatremia.
Study, Design and Setting
All residents of Stockholm County, undertaking at least one serum sodium test between 2005-2018 were included in the SSC. Individual-level test results from over 100 Laboratory parameters relevant to hyponatremia were collected and linked to data on demographics, socioeconomic status, healthcare contacts, diagnoses and dispensed prescription medications using national registers.
Results
A total of 1 632 249 individuals, corresponding to 64% of the population of Stockholm County were included in the SSC. Coverage increased with advancing age, ranging from 32% in children and adolescents ($\leq$18 years) to 97% among the oldest ($\geq$80 years). The coverage of SSC included the vast majority of patients in Stockholm County, diagnosed with diabetes mellitus (93%), myocardial infarction (98%), ischemic stroke (97%), cancer (85%), pneumonias requiring inpatient care (95%) and deaths (88%).
Conclusion
SSC is the first cohort specifically, designed to investigate sodium levels in a large, population-based setting. It includes a wide range of administrative health data and Laboratory analyses. The coverage is high, particularly, among elderly, and individuals with comorbidities. Consequently the cohort has a large potential for exploration of various aspects of hyponatremia.

Keywords: Dysnatremia, Stockholm, Sodium, registry SSC, hyponatremia
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EP351

Growth differentiation factor 15 in patients with acromegaly: a case-control study

Hayri Bostan[1], Sema Hepsen[2], Umran Gul[2], Hakan Duger[3], Serdar Kayıhan[2], Aykut Cimsir[2], Özgür Özçelik[2], İlknur Ozturk Unsal[2], Murat Calapkulu[4], Bekir Ucan[2], Erman Cakal[2] & Muhammed Kizilgul[2]
[1]Canakkale Mehmet Akif Ersoy State Hospital, Endocrinology and Metabolism, Turkey; [2]Ankara Etlik City Hospital, Endocrinology and Metabolism, Turkey; [3]Defa Life Hospital, Endocrinology and Metabolism, Turkey; [4]Igdir State Hospital, Endocrinology and Metabolism, Turkey

Background
It was previously shown that the levels of several biomarkers increase due to acromegaly disease-related inflammation and that some markers are parallel to the activity of the disease. It was also known that growth differentiation factor 15 (GDF-15) is increased in several cardiovascular inflammatory and metabolic diseases. The present study aimed to investigate the possible relationship of GDF-15 with acromegaly disease activity by comparing it with healthy individuals.
Methods
This study was designed as a single-center case-control study. A total of 40 acromegaly patients (25 active/15 controlled) (47.7 $\pm$ 9.4 years, 20 female/20 male) and 24 healthy, individuals (49.9 $\pm$ 10.1 years, 13 female/11 male) with age-sex-body mass index (BMI) similar to the patient group were included in the study. Demographic and anthropometric data, metabolic parameters, growth hormone (GH), insulin-like growth factor-1 (IGF-1), and GDF-15 levels of the study population were studied.

Results
The median GDF-15 levels were significantly higher in patients with acromegaly compared to healthy subjects (HS) (280.4 (197.0-553.2) vs 213.3 (179.9-297.2) ng/l, $P=0.01$). Median fasting plasma glucose (FPG), HbA1c, and systolic and diastolic blood pressure levels were significantly higher in patients with acromegaly compared to HS ($P<0.01$). Patients with acromegaly were divided into two groups according to disease control status: active patient group (aPG) ($n=25$) and controlled patient group (cPG) ($n=15$). The duration of symptoms before diagnosis and the frequency of obesity diabetes, and hypertension were similar in both active and controlled acromegaly patients ($P>0.05$). Serum GDF-15 levels of these groups were comparable ($P=0.39$). Interestingly compared to HS, GDF-15 levels were significantly higher in cPG ($P=0.01$), whereas GDF-15 levels tended to be higher in aPG, but did not reach statistical significance ($P=0.06$) (Figure 1). GDF-15 levels were observed to be positively correlated with fasting plasma glucose ($r=0.304$, $P=0.01$) and HbA1c ($r=0.292$, $P=0.02$). In the linear regression analysis, no independent relationship was observed between GDF-15 levels and age, gender, BMI, HbA1c, systolic and diastolic blood pressures, GH, IGF-1, and serum lipid levels ($P>0.05$). When evaluated across the entire cohort, GDF-15 levels were found to be higher in diabetic patients compared to non-diabetic individuals ($P=0.04$).
Conclusions
Plasma GDF-15 levels were increased in the patients with acromegaly compared to healthy subjects. This increment may be due to accompanying diseases such as diabetes rather than a disease-specific effect.

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EP352

Are giant prolactinomas different from macroprolactinomas? The single-centre observation

Maria Aleksandra Komisarz-Calik[1], Anna Bogusławska[1], Aleksandra Gilis-Januszewska[1] & Alicja Hubalewska-Dydejczyk[1]
[1]Jagiellonian University Medical College, Chair and Department of Endocrinology Cracow, Poland

Introduction
The data on giant prolactinomas (the rare (3%) subtype of lactotroph PitNET ($\geq$40 mm)), often causing clinical and therapeutic difficulties are scarce.
Aim
We studied clinical/biochemical and treatment outcomes differences between giant and macroprolactinomas.
Materials and methods
Consecutive patients with giant prolactinomas $\geq$40 mm (GP) and macroprolactinomas $>$10 mm $<$40 mm (MP) treated in the tertiary clinical center in 2022-2023 were included.
Results
There were 41 patients with macroprolactinomas: 15 GP (87% men) and 26 MP (65, 4% men). The age at the diagnosis was 41 in GP vs 48 in MP ($P=0.265$). In GP and MP groups the most frequent symptoms included headaches (10/66, 7% vs 15/57, 7%, $P=0.640$), vision disturbances (10/66, 7% vs 6/23, 1%, $P=0.021$) and hypogonadism (14/93, 3% vs 18/69, 2%, $P=0.267$). Hypogonadism, TSH and ACTH deficiency were significantly more frequent in patients with GP than MP (8/53, 3% vs 5/19, 2%, $P=0.013$). In GP group FSH concentration was markedly lower than in MP (average 1,12 ulU/ml vs 3,09 ulU/ml, $P=0.005$). The baseline prolactin levels were relevantly higher in GP than in MP group (172026 ulU/ml vs 14224 ulU/ml, $P<0.001$). The optic chiasm compression was more common in GP than in MP (12/80% vs 9/34, 6%, $P=0.021$, respectively). The apoplexy occurred only in two patients with GP. Cabergoline was the most common dopamine agonist administered in 24 cases of MP and 12 cases of GP ($P=0.512$). The surgery was performed in 4/26, 8% of GP vs 4/15, 2% of MP ($P=0.565$). Among GP patients one underwent the surgery 2 times and another one 3 times. Other therapeutical options implemented only in GP subgroup included Lanterotide (two cases), with no biochemical and clinical effecty in one case Pasireotide with a remarkable analgetic effect. In one case of aggressive tumour Temozolomide was implemented with a disease stabilization. Cabergoline resistance was observed in 5/33% of GP vs 1/3, 85% of MP, $P=0.327$). The tumour decrease was observed in 11/73, 3% of GP and 13/50% of MP cases. The percentage of tumour shrinkage was significantly higher in patients with GP compared to MP (average 57% vs 32%, $P=0.040$).
Conclusions
The majority of GP and MP patients are men. Pituitary axis deficiencies and visual deficits occur more frequently in GP group. The incidence of tumour shrinkage is similar in GP and MP, however in GP the tumour decrease is higher. Cabergoline resistance and surgery procedures are more common in GP group. Further studies are needed to understand the biology and natural course of GP and MP.

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EP353

Diagnosing acromegaly using artificial intelligence

Sebnem Burhan[1], Mehmet Zahit Yılmaz[2], Benginur Sokmen[2], Dilara Tekin Uzman[1], Zeynep Karaali[2], Mutlu Niyazoglu[1] & Esra Hatipoglu[1]
[1]Basaksehir Cam and Sakura City Hospital, Endocrinology and Metabolic Diseases; [2]Basaksehir Cam and Sakura City Hospital, Internal Medicine

Objective
Even with advancements in diagnostic techniques, acromegaly continues to be diagnosed late. This study aimed to employ deep learning methods to automatically identify acromegaly disease from images of faces, hands, and feet to enhance the efficiency of disease detection.
Design
Cross-sectionaly single-center study with deep learning
Methods
The study included 71 acromegaly patients and 65 healthy controls. All patients had images of their faces and hands; images of the feet were available for 63 acromegaly patients and 48 control patients. The images were processed with TensorFlow to increase the sample size through various transformations such as black and white transformationy rotation, zoom, and shearing. The Convolutional Neural Network (CNN) algorithm was employed across 8 layers in the neural network model. 'Adam' was utilized as the optimizer, and the binary cross-entropy loss function was employed. Early stopping was implemented to monitor the loss.
Results
The average age of the acromegaly group was 46.9 (SD:11.2), while the control group had an average age of 45.2 (SD:13.5). There were 33 males 46.5% in the acromegaly group and 25 males 39.1% in the control group. When the gender distribution and age averages were examined between the groups using the chi-square test and Student t-test, no significant differences were found. In the acromegaly group, the average duration of the disease was 4.12 (SD:4.88), ears, with 28 (39.4%) of them being in remission. The algorithm achieved an accuracy of 69.37% on facial photos, with a sensitivity of 57.14% and specifiCity of 85.42%. For hand photos, the accuracy was 92.79%, sensitivity was 92.06%, and specifiCity was 93.75%. In the case of foot photos, the algorithm demonstrated an accuracy of 70.27%, sensitivity of 49.21%, and specifiCity of 97.92%.
Conclusions
The CNN-based neural network exhibited varying accuracies across facialy hand, and foot photos, with notable accuracy for hands and moderate accuracy for facial photos. However, its performance on foot images was less robust. Incorporating the Random Forest ensemble method significantly boosted the overall accuracy to 94.59%, emphasizing the effectiveness of combining these algorithms for improved performance across diverse image datasets. The study validated the potential of the deep learning model in detecting acromegaly from facial images, highlighting the potential role of artificial intelligence programs in future acromegaly diagnosis.

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EP354

Hypogonadism in acromegaly a single-center experience

Aleksandra Derwich-Rudowicz[1], Nadia Sawicka-Gutaj[1], Kacper Nijakowski[2] & Marek Ruchała[1]
[1]Poznan University of Medical Sciences, Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznan, Poland;[2]Poznan University of Medical Sciences, Department of Conservative Dentistry and Endodontics, Poznan, Poland

Background
Acromegaly is a rare endocrine disorder characterized by excess growth hormone (GH) secretion. GH hypersecretion leads to the overproduction of insulin-like growth factor 1 (IGF-1), which has both somatic and metabolic effects. Hypogonadotropic hypogonadism is present in nearly 30%–50% of acromegaly patients. There is a close correlation between somatotropic axis and gonadal function. The aim of this study was to investigate the prevalence of hypogonadism in male patients with acromegaly and the effect of surgical treatment during follow-up.
Material and methods
The study has a retrospective design. Medical records of patients diagnosed with acromegaly, hospitalized pre- and postoperative between January 2015 and December 2022 have been analyzed. Clinical history, laboratory results and endocrine tests were routinely recorded. All patients underwent a pituitary MRI to determine tumor size and invasion type. The significance level was set at $\alpha = 0.05$ for all analyses. The statistical analysis was performed with Statistica 13.3 (StatSoft, Cracow, Poland).
Results
The analysis involved a total of 62 pre-operative and 60 post-operative male patients. Hypogonadism was diagnosed in 48 males pre-operative (77.42%).

Following surgery, the prevalence of hypogonadism decreased to 60%, ($n=36$). Fisher's Exact Test yielded $P=0.00174$. Most of the patients presented with macroadenoma (53.22%). Postoperative testosterone concentrations increased significantly (8.7 vs 12.0 nmol/l; $P<0.001$), particularly in patients with preoperative hypogonadism (7.2 vs 10.2 nmol/l; $P<0.001$). Gonadotropin levels postoperatively demonstrated a significant elevation (LH: 3.4 vs 3.75 mlU/ml; $P=0.007$; FSH: 5.35 vs 5.90 mlU/ml; $P=0.032$), especially in patients with preoperative hypogonadism (LH: 2.85 vs 3.20 mlU/ml; $P=0.003$; FSH: 5.10 vs 6.05 mlU/ml; $P=0.032$). Testosterone levels were found to be statistically significantly lower in patients with macroadenoma compared to microadenoma (7.2 nmol/l vs 11.05 nmol/l; $P=0.038$). Hypogonadism manifested more frequently in younger patients (<50 years). Prolactin levels were elevated in patients with preoperative hypogonadism and macroadenoma (304 μIU/ml; $P=0.036$). GH and IGF-1 concentrations postoperatively decreased (GH: 3.0 vs 1.4 ng/ml; $P=0.002$; IGF-1: 506 vs 278 ng/ml; $P<0.001$). Patients with preoperative hypogonadism presented higher median baseline values of GH and IGF-1 (GH: 3.74 ng/ml; IGF-1: 556) compared to those without hypogonadism (GH: 1.42 ng/ml; IGF-1: 379.5 ng/ml). Total cholesterol and low-density lipoprotein (Ldl) values experienced a statistically significant reduction post-operatively across all cohorts ($P<0.001$).
Conclusions:
Younger patients diagnosed with macroadenoma, and hyperprolactinemia exhibit a higher predisposition to pre-operative hypogonadism. Neurosurgical treatment can lead to the normalization of GH and IGF-1, but also LH, FSH, and total testosterone.

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EP371

Macroprolactinoma diagnosis and treatment in the setting of schizophrenia

Gabriel Tan[1]
[1]Tan Tock Seng Hospital, Singapore, Singapore

Prolactinomas are the most common pituitary lesion, and respond well to treatment with dopamine agonists. It presents a diagnostic and therapeutic challenge when there is concurrent psychosis, the treatment of which involves dopamine antagonists. A 69-year-old post-menopausal lady with schizophrenia, on olanzapine 5mg ever, evening, presented with unstead, gait. MRI brain scan showed a 3.3 x 1.8 x 2.4 cm pituitary macroadenoma with optic chiasm indentation. Visual field testing showed bitemporal hemianopia. There was marked hyperprolactinemia, low free thyroxine with inappropriatel, normal TSH, inappropriate low FSH and LH for post-menopausal state. Her ACTH stimulation test was robust. She was diagnosed with macroprolactinoma complicated by visual involvement, central hypothyroidism, central hypogonadism. After discussion with psychiatry and neurosurgery olanzapine was stopped and she started on bromocriptine and levothyroxine. She developed giddiness with bromocriptine, hence we switched to cabergoline 0.25mg/week with gradual dose escalation. Follow up showed improvement in her prolactin and free thyroxine. Repeat MRI demonstrated interval decrease in macroadenoma size (2.7 x 2.2 x 1.7 cm) and reduced mass effect on the optic chiasm with clinical improvement in visual fields. This case illustrates diagnostic pitfalls in hyperprolactinemia. Prolactin should be checked in all pituitary lesions. After excluding high dose hook effect, the degree of prolactin elevation can help differentiate between prolactinoma, stalk effect or drug induced hyperprolactinemia. Antipsychotics may worsen hyperprolactinemia, enhance macroprolactinoma growth, and blunt effect of dopamine agonist treatment. Cessation of her antipsychotics needs to be balanced against risk of psychotic exacerbation. Close psychiatry follow-up and cautious uptitration of dopamine agonists is recommended.

Investigations 06/10/2022

Test	Units	Reference
Prolactin (on dilution)	80,370	91–650 mIU/l
ACTH	8.3	1.6–13.9 pmol/l
Cortisol 8am	294	nmol/l
Cortisol 0 min (at 2pm)	194	nmol/l
Cortisol 30 min	509	
Cortisol 60 min	616	
Free thyroxine	7	8–16 pmol/l
TSH	2.02	0.45–4.5 mIU/l
Luteinizing hormone	< 1	11–59 IU/l
Follicular stimulating hormone	1	17–144 IU/l
Estradiol	< 73	pmol/l
IGF-1	67 mg/l	54–163 mg/l
Sodium	145 mmol/l	135–145 mmol/l
Potassium	3.2 mmol/l	3.5–5.1mmol/l
Creatinine	53 umol/l	40-75 umol/l

Follow up

Test	Date	Value	Treatment
Prolactin	06/10/2022	80,370	Bromocriptine 1.25 mg ON then 2.5 mg ON
	03/11/2022	31,658	Bromocriptine 5 mg ON
	28/11/2022	49,352	Cabergoline 0.25 mg once/week then 0.25 mg 2 times/week
	19/01/2023	20,561	
	03/03/2023	5518	
Test	**Date**	**Value**	**Treatment**
Free thyroxine	06/10/2022	7	Levothyroxine 25 mg OM
	03/11/2022	10	
	19/01/2023	10	Levothyroxine 50 mg OM
	09/03/2023	11	

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EP373

Diagnostic mirage: pseudo-cushing's state and the challenges of coexisting pituitary macroadenoma

Nada Aitkassi[1], Essafir Nouhaila[1] & Guerboub Ahmed Anas[1]
[1]Mohamed V Militar, Hospital

Introduction and importance
Pseudo-Cushing's syndrome (PCS) encompasses a spectrum of medical conditions, both physiological and non-physiological, that replicate the clinical features of Cushing's syndrome (CS). In PCS, there is a presence of mild biochemical hypercortisolaemia, which is carefully regulated by physiological feedback hormonal control mechanisms. Physiological conditions contributing to PCS include factors like pregnancy surgical or emotional stress, severe illness, intense chronic exercise, while non-physiological contributors encompass chronic alcoholism, obesity metabolic syndrome, poorly controlled diabetes mellitus, major depression, malnutrition, and anorexia nervosa. The differentiation between pseudo-Cushing's states (PCS) and Cushing's syndrome (CS) presents a significant clinical puzzle, posing a formidable challenge even for experienced endocrinologists.
Case presentation
We present the case of a 46-year-old patient with no History of diabetes mellitus, depression, or excessive alcohol intake. The patient was admitted for the exploration of a pituitary macroadenoma; pituitary contrast-enhanced MRI showed a pituitary tumour ($11\times11\times7.5$ mm). Clinical examination revealed a Grade I obesity (body mass index 33 kg/m^2) with an android phenotype, along with a moon face and a buffalo hump. Secretory assessments were conducted: The midnight cortisol level came back elevated (**67 ng/**dl), a 24-hour urine collection showed a normal level of free cortisol, and overnight administration of 1 mg of dexamethasone reduced the serum cortisol level. And additional investigations have been supplemented by a standard dexamethasone suppression test; the patient demonstrated appropriate suppression during the conducted test.
Conclusion
PCS, a condition mimicking overt hypercortisolism, poses a considerable challenge in the differential diagnosis with Cushing's disease (CD). Patients with obesity metabolic syndrome, polycystic ovary syndrome, chronic alcoholism, depression, and extreme physical stress are recognized as prone to developing PCS. Obese individuals, such as our patient, have been reported to exhibit hyperactivation of the hypothalamus–pituitary–adrenal (HPA) axis in response to both physical and psychosocial stressors. The concomitant discover, of a non-functioning pituitary adenoma added complexit, to the diagnosis in our case.

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EP379

Effective management of SIADH-Induced hyponatremia with tolvaptan: a case report

Besa Osmani[1], Ana Matijaca[2], Dino Kasumović[1] & Ivica Horvatić[1]
[1]Clinical Hospital Dubrava, Department of Nephrology and Dialysis, Zagreb, Croatia; [2]Clinical Hospital Dubrava, Department of Endocrinology and Diabetology Zagreb

We present a case of a 70-year-old female patient without comorbidities who was admitted to our institution following head trauma leading to subsequent subarachnoid hemorrhage and vertigo. Conservative management was

implemented successfully. Throughout the hospitalization, lab monitoring revealed the emergence of hyponatremia which was corrected by fluid restriction and hypertonic solution administration. The patient was discharged without residual vertiginous complications. Shortly post-discharge, the patient presented to the emergency department manifesting severe hyponatremia (116 mmol/l). Diagnostic investigations revealed reduced plasma osmolality alongside normal urine osmolality and normal sodium urine levels with normal TSH and cortisol values. Notably the absence of chronic therapy and urine sodium concentration >50 mmol/l further underscored the diagnosis of Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) due to head injury. Because of prolonged duration of SIADH, which was more than a month since the head injury and without improvement with time which would be expected, we also did thorough work up to exclude other causes of SIADH, including neoplastic process. Patient continued check-ups and despite corrective measures (dietary intervention with increase solute intake and increase of oral sodium chloride) repeatedly had decrease in serum sodium concentration and was repeatedly hospitalized, with the latest admission to the Nephrology Department. Dietary interventions coupled with fluid restriction and parenteral administration of hypertonic solution were implemented in successfully correcting severe symptomatic euvolemic hyponatremia. The follow-ups were then continued via the Nephrology outpatient clinic. Despite adhering to dietary recommendations and fluid intake restrictions, the patient persisted in experiencing hyponatremic episodes with moderate to severe vertiginous symptoms. Consequently a decision was made to introduce a selective Oral Vasopressin V2-Receptor Antagonist into the therapeutic regimen, specifically tolvaptan at 15 mg once daily. The initiation of tolvaptan was conducted with the approval from the Hospital Committee for Medicinal Products. Following the commencement of this targeted therapy normonatremia was consistently maintained, with transient occurrences of mild hypernatremia leading to brief interruptions in tolvaptan administration which then led to hyponatremic relapses. Since the initiation of tolvaptan, the patient has remained free from hospitalization. Regular checkups including electrolyte levels, liver function parameters, renal function and body weight are conducted via Nephrology clinic. To date, the patient has exhibited no noteworth, adverse effects associated with tolvaptan treatment. Despite existing controvers, in using vasopressin receptor antagonists in treatment of chronic hyponatremia we wanted to present case in which prolonged posttraumatic SIADH was successfully managed using tolvaptan.

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EP381

Secondary radiation-induced sarcoma occurring as a rare complication of radiotherapy for a gonadotroph tumour

Prishila Fookeerah[1,2], Angela Bayly[3], Winny Varikatt[3,4], Robert Smee[5,6], Mark Dexter[4,7], Sue Lynn Lau[1,2] & Mark McLean[1,2]
[1]Westmead Hospital, Diabetes and Endocrinology Sydney Australia; [2]Western Sydney University School of Medicine, Sydney Australia; [3]Westmead Hospital, Tissue Pathology and Diagnostic Oncology Sydney Australia; [4]University of Sydney Westmead Clinical School, Sydney Australia; [5]Prince of Wales Hospital, Radiation Oncology Sydney Australia; [6]University of New South Wales, Prince of Wales Clinical School, Sydney Australia; [7]Westmead Hospital, Neurosurgery Sydney Australia

Background
Secondary malignant sarcoma in the sella after radiotherapy for pituitary tumours is rare. Osteogenic sarcoma arising within the fossa after pituitary irradiation has only been described in a few case reports.
Clinical Case
A 31-year-old male patient without significant medical History presented in 2012 with bitemporal hemianopia. There were no associated headaches or clinical features of excess hormone secretion. MRI demonstrated a 26×30×28 mm mass in the pituitary fossay with suprasellar extension and compression of the optic chiasm. There was no invasion of the cavernous sinus. Biochemical investigations showed a mildly elevated serum prolactin of 851 mIU/l (normal range <500), low morning cortisol of 19 nmol/l, low testosterone of 1.8 nmol/l and normal thyroid function- TSH 3.60 mIU/l, free T4 10.4 pmol/l, consistent with a non-functioning pituitary tumour with partial hypopituitarism. He underwent urgent transsphenoidal resection of the tumoury resulting in normalization of vision and a small intrasellar tumour remnant. Three years later repeat surgery was undertaken due to tumour regrowth, now measuring 32×23×30 mm. Histopathological evaluation confirmed a pituitary neuroendocrine tumour of gonadotroph lineage, with expression of SF1 but negative hormonal immunoreactivity. There was no histological invasion or mitoses. Ki-67 was 8%. Because of a significant tumour remnant, he then received postoperative radiotherapy (49.2 G, in 30 fractions). yearly imaging showed stable and asymptomatic residual tumour. 8 years after radiotherapy he experienced worsening visual disturbance and headaches. Repeat MRI showed pituitary mass regrowth to 44×32×44 mm with a large area of unenhanced low T1 and T2 signal intensity and macrocalcification. A third transsphenoidal resection of the recurrent pituitary tumour was undertaken. Histopathology assessment now revealed a gonadotroph tumour seen closely intermingled with a malignant spindle cell component. Focal areas of osteoid production were seen. These cells demonstrated expression of SATB2, loss of H3K27me3 and high Ki67 of 60%. A diagnosis of radiation-induced sarcoma was favoured over sarcomatous transformation in view of the latency period between radiotherapy and the development of this neoplasm in the field of radiation.
Conclusion
This case describes a rare and serious complication of radiotherapy occurring 8 years after treatment of a pituitary gonadotroph tumour, highlighting the need for careful long-term radiological monitoring.

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EP382

Metastasis or macroadenoma – the role of pituitary biopsy in a non-typical clinical presentation – a case report

Olivia Cyran-Stańczak[1], Sonia Kaniuka-Jakubowska[1], Natalia Ostrowska-Mrozowska[1], Tomasz Nowicki[2] & Renata Świątkowska-Stodulska[1]
[1]Department of Endocrinology and Internal Medicine, Faculty of Medicine, Medical University of Gdansk, Poland; [2]2nd Department of Radiology Faculty of Health Sciences with the Institute of Maritime and Tropical Medicine, Medical University of Gdansk, Poland

Metastatic involvement of the pituitary gland is a rare phenomenon with various clinical and radiological manifestations, but it is clinically important and requires appropriate and early diagnosis. The posterior lobe of the pituitary gland is more often involved, so we expect that AVP deficiency would be the most common clinical manifestation of pituitary metastasis. Presentation without involvement of the posterior lobe, without AVP deficiency and with anterior lobe hypofunction is rather an unexpected course. Pituitary biopsy especially when pituitary metastasis is the first detected manifestation of cancer, is an important method for diagnosing metastatic lesions. A 66-year-old female patient with no History of chronic diseases was admitted to the Department of Neurology in March 2023 due to increasing headaches for two months and double vision since the day of admission to the hospital. CT scan and head MR were performed, and a lesion measuring 27×19×25 mm was described in the sella turcica region and part of the posterior sphenoid sinuses; the pituitary infundibulum remained unchanged, moved upwards and forwards. The examination suggested a metastatic involvement of the pituitary gland or a pituitary macroadenoma. Laboratory tests revealed hypofunction of the anterior pituitary lobe in the thyrotropic and corticotropic axes (L-thyroxine substitution and steroid therapy were implemented). In March 2023 the patient was consulted by neurosurgeons to assess the possibility of surgical intervention – however, regarding the risk of metastasis and incomplete resection, they suggested further diagnosis and did not perform adenomectomy. In May 2023, a lesion biopsy using a transsphenoidal approach was performed at the Department of Otolaryngology. Additionally chest CT revealed a tumour in section 3 of the right lung; a biopsy of the lung lesion was performed. The results of the biopsies showed the presence of mucinous adenocarcinoma with primary location in the lung. In June 2023, the patient began palliative radiotherapy in the sphenoid sinus area and passed away in the same month. The described case demonstrates that the clinical and radiological picture of pituitary metastases may be varied and the differential diagnosis is difficult. AVP deficiency is not always a clinical symptom that distinguishes pituitary metastases from PitNET. Our case also highlights the role of pituitary biopsy which should be more common in justified indications, and in this case, performed earlier, could have contributed to earlier implementation of the treatment. This case sustains that a multidisciplinary approach to patients with pituitary lesions is crucial.

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EP383

Challenges in managing acromegaly: choosing the right therapeutic option

Ema Schonberger[1,2], Ines Bilić-Ćurčić[1,2], Romana Marušić[2,3], Kristina Steiner[1], Klara Ormanac[1,2] & Silvija Canecki-Varžić[1,2]
[1]Clinical Hospital Center Osijek, Department of Endocrinology Osijek, Croatia; [2]Facult, of Medicine Osijek, Osijek, Croatia; [3]General Hospital Vukovar, Department of Internal Medicine, Vukovar, Croatia

Introduction
Pituitary tumors leading to acromegaly are typically diagnosed as macroadenomas with the potential to infiltrate nearby tissues. If left untreated, acromegaly can result in systemic complications, such as hypertension, glucose intolerance, type 2 diabetes, and cardiovascular disease, leading to substantial comorbidities and a higher mortality rate.
Case report
We present a case of a 57-year-old patient who initially presented in 1993 with galactorrhea and hyperprolactinemia, treated with bromocriptine. Despite these symptoms, an MRI of the pituitary gland was not conducted. Over the years, the patient developed arterial hypertension and type 2 diabetes mellitus, along with a noticeable increase in shoe size, but did not seek medical help. The diagnosis of acromegaly was ultimately made in December 2020 during hospitalization for neurological symptoms (syncope). Brain MRI revealed an extensive pituitary macroadenoma measuring 50×37×40 mm with bilateral compression of the internal carotid arteries. Initial values of insulin-like growth factor 1 (IGF-1) were 95.9 nmol/l (reference interval 7.2-31.3), and growth hormone (GH) was insuppressible in an oral glucose tolerance test (OGTT). After two months, a partial transsphenoidal resection of the tumor was performed, with which neither clinical nor biochemical control of the disease was achieved. Following the multidisciplinary team's decision, she received adjuvant Gamma-Knife radiotherapy for two months, and treatment with the octreotide was started. Since she was unresponsive to the first-generation somatostatin analog therapy pasireotide was introduced. After the administration of the second dose, symptomatic atrial fibrillation (AF) was recorded in the patient. Although AF is not described as a possible adverse event with pasireotide therapy considering the described prolongation of QT interval and possible worsening of arrhythmiay the therapy was discontinued. Given the circumstances, pegvisomant was considered as the next therapeutic option.
Conclusion
The challenge of achieving complete removal of the GH-producing pituitary macroadenoma during surgery increases the risk of a disease recurrence, and additional treatment methods, such as somatostatin analogs, dopamine agonists, and radiotherapy are often required. However, this population of patients is extremely vulnerable due to the development of complications such as various cardiac conditions and type 2 diabetes, making it difficult to choose the most appropriate pharmacotherapeutic option given their possible side effects and the potential for worsening comorbidities. Nevertheless, it is important to find the best therapeutic option for the patient to improve outcomes and prevent further progression of existing complications.

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EP384

Endocrinologic evaluation in a case series of adult meningiomas: what can we improve?

Miruna-Viorela Nacu[1], Sorina Martin[1,2], Anca Sirbu[1,2], Carmen Barbu[1,2] & Simona Fica[1,2]
[1]"Elias" Emergency University Hospital, Department of Endocrinology Diabetes Mellitus, Nutrition and Metabolic Disorders, Bucharest, Romania; [2]'Carol Davila' University of Medicine and Pharmacy Department of Endocrinology Diabetes Mellitus, Nutrition and Metabolic Disorders, Bucharest, Romania

Introduction
Meningiomas, already one of the most frequent types of primary central nervous system tumors, have been increasing in incidence in the past decade. Considering their location and histologic particularities, radiation therapy (RT), alone or in combination with neurosurgery, is often necessary and can have a negative impact on adjacent structures such as the pituitary gland. More studies investigating the endocrinologic disturbances in this pathology are necessary in order to meet the needs for developing a specific protocol.
Design
We compiled a case series of patients diagnosed with perisellar meningiomas between 2007-2022, who underwent endocrinologic evaluation in our clinic.
Results
Seven cases were found, six females and one male, aged 57-68 years. Onset of symptoms was reported in three cases, one presented with hypopituitarism and two patients with left palpebral ptosis. Six lesions had cavernous sinus invasion and one was located in the left cerebellopontine angle. Tumor dimensions varied from 25/27/25 mm to 22/47/34 mm. Neurosurgery was performed in two cases, one for a parietal lesion in a meningiomatosis patient and one for a sellar meningioma. Histopathologic exam revealed meningothelial meningiomas in both cases. Six patients underwent Gamma Knife radiation therapy. One patient received anti-inflammatory doses of glucocorticoids for almost 2 years prior RT. Hormonal evaluation was performed using basal determinations and no dynamic tests were performed. Endocrinologic assessment prior to RT was available in three cases, one investigating only the adrenal axis, one in the patient receiving glucocorticoids, showing mildly suppressed TSH with normal freeT4, which normalized at the end of the treatment and one in the hypopituitarism case. Mean time from RT until last endocrine workup was 4.8 years (1-11 years). Two patients were on levothyroxine treatment for primary hypothyroidism and apart from the patient with hypopituitarism, the remaining cases had normal thyroid, adrenal and gonadal function. Three patients had elevated prolactin levels, two before treatment and another at one year after RT. Two patients had decreased IGF-1 levels, measured at 2 and 6 years, respectively after RT.
Conclusions
Pituitary disturbances can occur in a wide time frame after RT and active surveillance must be done, balancing over- and under-testing. There is a need for a dedicated protocol for this pathology with adequate selection criteria, adjusted testing intervals and use of appropriate tests in order to identify subclinical deficiencies. Until then, clinicians should aim at correctly documenting radiation therapy dosages, and emphasizing the importance of repeated testing over the years.

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EP386

Atypical dermatological manifestations in cushing's disease: about a case report

Emna Naccache[1,2], Hadami Ben Yamna[1], Ines Kammoun[3] & Radhouen Gharbi[2]
[1]National Institute of Nutrition, Endocrinology Tunis; [2]Tunisia, Endocrinology Tunis; [3]National Institute of Nutrition, Endocrinology Tunis, Tunisia

Introduction
The diagnosis of Cushing's syndrome is frequently invoked by the presence of clincal signs of hypercatabolism. It actually may be associated with a variety of dermatological manifestations which can be atypical. Here, we report the case of a patient having vulvar warts co-occuring with Cushing's syndrome.
Observation
We present the case of a 31-year-old patient presenting with typical signs of Cushing's syndrome: Facial erythrosis, facio-truncular fat distribution, buffalo hump, abdominal obesity with a waist circumference of 98 cm and purple stretch marks on the abdominal and axillary areas, he also had muscular amyotrophy in te lower limbs and BP: 18/10. While examining the patient, we identified atypical dermatological manifestations: vulgar warts on the dorsal surfaces of the both hands simultaneously with the appearance of signs of Cushing's disease. We confirmed a cushing's syndrome by a low-dose dexamethasone suppression test which was positive, an elevated ACTH, the absence of braking in the High-dose dexamethasone suppression Test. The MRI showed a pituitary microadenoma. The other axes were explored and he presented with isolated hypogonadtrophic hypogonadism. As for the complications he presented diabetes, hypertension and osteoporosis.
Conclusion
Long-term exposure to intrinsic corticosteroids during cushing's disease induct immunosuppression which can be the cause of these atypical dermatological manifestations. It is crucial to know how to invoke endocrinopathies like Cushing's syndrome in patients presenting not only the typical signs of the pathology but also atpyical manifestations.

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EP397

Post-operative evaluation of pituitary adenomas operated at the clinical hospital of valladolid

Esther Delgado Garcia[1,2], Juan Jose Lopez Gomez[1,2], Paloma Perez Lopez[1,2], Beatriz Torres Torres[1,2], Laura Herguedas Herguedas[3], Marta Boya Fernandez[3] & Daniel De Luis Román[1,2]
[1]Servicio Endocrinologiay Nutricion, Hospital Clinico Universitario de Valladolid, Valladolid, Spain; [2]Centro de Investigación de Endocrinología y Nutrición Clínica, Facultad de Medicina de Valladolid, Valladolid, Spain; [3]Facultad de Medicina de Valladolid, Valladolid, Spain

Introduction
Pituitary adenomas are neoplasms originating in the pituitary gland. They represent 15.5% of tumor pathology of the central nervous system and their incidence is estimated at 3.4 cases per 100,000 inhabitants/year.
Objective
To evaluate the postoperative results of adenomas operated on at the Hospital Clinico de Valladolid (HCUV)

Material and Methods
Observational, transversal and retrospective study of operated adenoma from 2001 to 2016 in HCUV. Variables studied were epidemiology clinical, radiography pathology surgery radiotherapy and treatment
Results
139 patients were evaluated, 61 (43.9%) being men with a mean age of 51 (42-63) years. The main cause of adenomas presentation was compressive symptoms (41.7%), followed by hormonal excess (26.9%) (table 1) 117 (84.2%) were macroadenomas with a mean size of 17.8 cm^3 and 77.7% had suprasellar or lateral extension. The average reduction in tumor size was 32%. The immunohistochemical phenotype was performed on 64 (38.8%) tumors; the most numerous group was prolactinomas, followed by GH secreters and ACTH secreters. 11 (7.9%) patients had postsurgical complications: 8 diabetes insipidus, 2 SIADH, 1 respiratory distress. 9 patients had to undergo reoperation and 59 required radiotherapy. The long-term patient outcome was cure in 25 (18%) patients; persistence in 111 (79.9%) patients; recurrence in 2 (1.4%) patients and 1 (0.7%) patient died.
Conclusions
Pituitary adenomas are rare lesions that manifest mainly due to compressive symptoms or hormonal hyperproduction. Those who require surgery in the hands of expert surgeons have good results

CLINICAL PRESENTATION	N (%)
Compressive	58 (41,7%)
Hormonal excess	36 (25,9%)
Incidentaloma	25 (18%)
Hormonal deficiency	5 (3,6%)
Compressive/Excess	8 (5,8%)
Compressive/deficit	3 (2,2%)
Excess/deficit	3 (2,2%)
Compressive/deficit/Excess	1 (0,7%)

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EP399

SOX9-positive pituitary stem cells differ according to their position in the gland and maintenance of their progeny depends on context

Karine Rizzoti[1], Robin Lovell-Badge[2], Probir Chakravarty[2] & Daniel Sheridan[1]
[1]The Francis Crick Institute, Stem cell biology and developmental genetics, London, United Kingdom; [2]The Francis Crick Institute, Bioinformatics Core, London, United Kingdom

SOX9-positive pituitary stem cells differ according to their position in the gland and maintenance of their progeny depends on context. We and others have previously characterised a population of adult stem cells (SCs) in the murine pituitary gland. We showed that while these SCs are relatively quiescent in normal conditions, they undergo activation following target organ ablation, providing a well-characterized paradigm to study an adaptative response in the context of the endocrine axes. We have here used single cell technologies to characterize SC heterogeneity and mobilization. We show that the transcriptional profile of SCs varies according to their localization in the gland, revealing different compartemnts and properties. Following target organ ablation, analyses of mobilized SCs reveal that differentiation occurs more frequently than previously thought, and that their progeny is more diverse than demonstrated by the lineage tracing experiments. Comparison of SC progeny following short and long term lineage tracing suggests that maintenance of selected nascent cells underlies SC output, highlighting a trophic role for the microenvironment. Consequently, analyses of cell trajectories further predict pathways and potential new regulators. In conclusion, our data highlight the herogeneity of the adult pituitary SC population while our mobization paradigm provides a valuable model to study the influence of evolving states on the mechanisms of SC mobilization and the role of local interactions.

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EP400

Vasopressin and androgen receptors as potential therapeutic targets in corticotroph pitnets

Maria Francesca Birtolo[1,2], Antoan Stefan Sojat[3], Bertrand Baussart[1,4], Camille Sollier[5], Nesrine Benanteur[1], Xavier Bertagna[5], Anne Jouinot[1,5], Jerome Bertherat[1,5], Guillaume Assié[1,5] & Chiara Villa[1,6]
[1]INSERM U1016, Université Paris Cité, CNRS, Inserm, Institut Cochin, Genomics and signaling of endocrine tumors, Paris, France;[2]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele (MI), Italy;[3]University Clinical Centre of Serbia, National Centre for Infertility and Endocrinology of Gender, Clinic for Endocrinology Diabetes and Metabolic Diseases, Belgrade, Serbia;[4]Hôpital Universitaire Pitié-Salpêtrière, APHP, Sorbonne Université, Department of Neurosurgery, Paris, France;[5]Métabolisme Et Cancer, CHU Cochin, APHP, Université Paris Cité, Département Endocrinologie, Paris, France;[6]Hôpital Universitaire Pitié-Salpêtrière, APHP, Sorbonne Université, Department of Neuropathology, Paris, France

Corticotroph Pituitary Neuroendocrine Tumours (Co-PitNETs) show significant differences in cortisol secretion, responses to existing therapies and gene expression andstill pose a challenge for patient management.
Aim
to explore possible novel therapeutic targets in Co-PitNETs (functioning and silent) through transcriptome analysis (RNA sequencing) and immunohistochemistry.
Methods
Transcriptomic data from a previously reported dataset of 134 PitNETs (T-cohort) (*Neou M, Cancer Cell. 2020*) were used to select potential therapeutic targets that were overexpressed in Co-PitNETs in comparison to other PitNETs types. Among the overexpressed genes, *AVPR1B*, encoding the Vasopressin V1b receptor, and *AR*, encoding the androgen receptor (AR) were validated in two cohorts including all PitNETs types (VI-cohort = 94 PitNETs and ARI-cohort = 66 PitNETs) by immunohistochemical analysis.
Results
In the T-cohort, *AVPR1B* gene was the most differentially overexpressed gene in each transcriptomic group of Co-PitNETs, independent of their clinical presentation (functionning vs silent) and the *USP8* status (Kruskal-Wallis, $P<10^{-14}$). Focusing on hormone receptors, *AR* gene was significantly over-expressed in corticotroph groups when compared to other PitNETs types. The immunohistochemical analysis of the VI-cohort confirmed higher AVPR1B immunostaining in Co-PitNETs than in other PitNET types (Kruskal-Wallis, $P<10^{-6}$). Silent Co-PitNETs largely expressed *AVPR1B* (median 70%), more than functioning Co-PitNETs (median 20%, Wilcoxon $P=0.04$). In the ARI-cohort, *AR* was more expressed in Co-PitNETs, mostly in functioning ones (Wilcoxon, $P=0.04$), and significantly more than in other PitNET types (Kruskal-Wallis, $P<10^{-6}$).
Conclusion
AVPR1B and *AR* are overexpressed in Co-PitNETs representing a possible novel targets for future medical treatments.

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EP401

PAM expression in pituitary neuroendocrine tumors (PitNETs)

Maria Francesca Birtolo[1,2], Bertrand Baussart[1,3], Nesrine Benanteur[1], Anne Jouinot[1,4], Adrian Daly[5], Andrea Lania[2,6], Jerome Bertherat[1,4], Constantine Stratakis[7], Guillaume Assié[1,4], Chiara Villa[1,8] & Giampaolo Trivellin[2]
[1]INSERM U1016, Université Paris Cité, CNRS, Inserm, Institut Cochin, Genomics and signaling of endocrine tumors, Paris, France;[2]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele (MI), Italy;[3]Hôpital Universitaire Pitié-Salpêtrière, APHP, Sorbonne Université, Department of Neurosurgery, Paris, France;[4]Métabolisme Et Cancer, CHU Cochin, APHP, Université Paris Cité, Département Endocrinologie, Paris, France;[5]Centre Hospitalier Universitaire de Liège, University of Liège, Domaine Universitaire du Sart-Tilman, Department of Endocrinology, Liège, Belgium;[6]IRCCS Humanitas Research Hospital, Endocrinology, Diabetology and Andrology United, Milan, Italy;[7]IMBB, FORTH, Heraklion, Greece & NICHD, NIH, Human Genetics & Precision Medicine, Bethesda, United States;[8]Hôpital Universitaire Pitié-Salpêtrière, APHP, Sorbonne Université, Department of Neuropathology, Paris, France

PAM encodes a multifunctional protein recognized as an important regulator of hormone amidation and secretion. Since *PAM* germline mutations have been recently identified in patients with PitNETs, it has been proposed as a candidate gene associated with pituitary hypersecretion.
Aim
To characterize PAM expression in a large cohort of PitNETs through immunohistochemistry and transcriptome analysis (RNA sequencing).
Methods
Immunohistochemistry analysis was performed on FFPE samples from normal pituitary, 102 PitNETs of all hystotypes (16 functioning and 13 silent corticotrophs, 19 somatotrophs, 20 gonadotrophs, 8 null-cell, 19 prolactinomas, and 7 thyrotrophs) and 5 PitNETs with recognized *PAM* variants. PAM immunoreactivity was graded considering the percentage of positive cells and the staining intensity (scored from 0 to 3). The final score was obtained as follow: score = (%x0)+(%x1)+(%x2)+(%x3). PAM expression was assessed through transcriptome analysis on a previously reported dataset of 134 PitNETs (Neou M, Assié G. *Cancer Cell*. 2020).
Results
PAM immunostaining was positive almost in all samples with variable patterns of expression. However, the immunohistochemistry score was lower in corticotroph

tumors with overt Cushing disease compared to the other groups (Kruskal-Wallis, $P=3.69e-05$). Transcriptome analysis confirmed this finding (Kruskal-Wallis, $P=3.888e-10$). Interestingly we found weak and negative staining for PAM in 5 patients (2 acromegalic and 3 with overt Cushing disease) in whom *PAM* variants have recently been identified (Trivellin G, Stratakis CA. *Front Endocrinol*. 2023).
Conclusion
Our preliminary results add to the characterization of *PAM* function in PitNETs. A reduced expression in corticotroph PitNETs with overt Cushing disease opens new insights into the pathogenesis of -and secretion by corticotroph tumor cells.
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EP402

Prolactin impact on aging bone health
Danijela Radojkovic[1,2], Milan Radojkovic[2,3], Milica Pesic[1,2], Vojislav Ciric[1,2], Saša Radenković[1,2], Marija Vukelic Nikolic[2] & Tatjana Jevtovic Stoimenov[2]
[1]Clinical Centre of Niš, Endocrinology Niš, Serbia; [2]University of Niš, Niš, Serbia; [3]Clinical Centre of Niš, Surgery Niš, Serbia

Introduction
The aim of this study was to evaluate potential alterations in prolactin receptor gene expression (*Prlr*) in the duodenum, vertebra, and kidney - key organs in calcium metabolism, across the aging process.
Methods
Wistar female rats were divided into: Group A (10 rats, 5 weeks old), Group B (10 rats, 18 weeks old) and Group C (7 rats, 21 weeks old). Laboratory analysis included: prolactin, serum ionized calcium, phosphorus, urinary calcium and phosphorous excretion, alkaline phosphatase (ALP), osteocalcin (OC) and serum procollagen type 1 N-terminal propeptide (P1NP). Relative quantification of prolactin receptor (*Prlr*) gene expression in duodenum, vertebra and kidney was determined by quantitative real time polymerase chain reaction.
Results
PRL concentrations were significantly higher in group A compared to B and C ($P<0,001$). In the youngest rats (A) serum ionized calcium was significantly decreased compared to B ($P<0,05$) and C ($P<0,01$); serum phosphorus was significantly increased compared to B and C ($P<0,001$); urinary calcium was decreased compared to B and C ($P<0,001$); urinary phosphorous was significantly increased compared to B ($P<0,05$) and without significant changes compared to C. All bone turnover markers, ALP, OC and P1NP, were significantly increased in the Group A compared to B and C ($P<0,001$). In the youngest group of rats (A) expression of *Prlr gene* was higher in the duodenum comperd to the B and C, but without statistical significance. In the kidney there was significantly increased expression of *Prlr gene* in the A compared to C ($P<0,05$). While in the vertebra, significantly dicreased expression of *Prlr gene* was verified in the Group A compared to C ($P<0,01$).
Conclusions
Prlr gene expression undergoes significant changes during aging in tissues critical for calcium homeostasis, potentiall, contributing to adverse effects on bone metabolism. A considerable reduction in *Prlr* gene expression in the kidne, ma, explain the markedl, elevated calciumuresis in older experimental groups. To sustain normal calcium levels, the urinar, loss of calcium is compensated b, extracting calcium from the bones, facilitated b, the heightened expression of the *Prlr* gene, thereb, causing additional harm to the skeletal system in the aging process.
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EP404

Growth hormone deficiency: a series of 102 tunisian observations
Yosra Hasni[1], Hamza Elfekih[1], Oumayma Zarrouk[1], Amira Yanes[1], Amel Maaroufi[1], Wided Debbabi[1] & Molka Chadli Chaieb[1]
[1]University Hospital of Farhat Hached, Endocrinology Diabetolog, Department, Sousse

Introduction
Growth hormone deficiency (GHD) is a rare cause of growth retardation whose diagnosis remains relatively late. Its etiologies are multiple, and its treatment could improve the stature prognosis of the children. The objective of this study was to describe the clinical, biological, radiological, and therapeutic characteristics of GHD, and its outcomes after treatment.
Methods
A cross-sectional study was conducted in the Endocrinology department of Farhat Hached University Hospital in Sousse, between January 2000 and December 2015, collecting 102 patients following for GHD.
Results
The average age at diagnosis was 12 ± 3.83 years with a sex ratio of 1.61. The average height was -3 ± 0.9 SD. The mean bone age was 9.4 ± 3.7 years with an average of 2.7 ± 2 years delay comparing to the chronological age. GHD was associated with other pituitary deficiency in 38.2% of patients and it was complete in 63.7% of cases. A partial GHD (36.3%) was associated significantly with isolated GHD ($P=0.02$) and idiopathic GHD ($P=10^{-3}$). Pituitary MRI was normal in 63.5% of cases, otherwise, it showed an interruption of the pituitary stalk (17.5%), a tumor (12.7%), an empty Sella (3.17%) and hypoplasia of the anterior pituitary (3.17%). Most patients (73.5%) were treated with somatropin with an average dose of 0.7 U/kg/week and an average duration of 3 years. The average height gain under treatment was 1 ± 0.9 SD. Height recovery was significant during the first year of treatment. No side effects of rhGH were observed. A statistically significant negative correlation between height gain and chronological age, height in SD and bone age at the start of treatment were found. Also, there was a statistically significant positive correlation between the height gain and the therapeutic compliance as well as an injection rhythm at 5/7 days, and especially the duration of the treatment.
Conclusions
Our study revealed a diagnostic delay in children with GHD. We insist on early diagnosis and treatment to improve the stature prognosis of these children. We must improve therapeutic compliance, necessary for a better response to treatment, through regular monitoring and good education of the child and those around him.
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EP444

Utility of the Metoclopramide Test in the Differential Diagnosis of Hyperprolactinaemia
Estíbaliz Alegre[1], Álvaro González[1], Marta Zaballos[2], Henar Casal[2], Javier Salvador[2] & Juan Carlos Galofré[21]
[1]CIÚnica Universidad de Navarra, Biochemistry, Pamplona, Spain, [2]CIÚnica Universidad de Navarra, Endocrinology, Pamplona, Spain

Introduction
In addition to physiological causes, the hyperprolactinemia spectrum includes iatrogenesis, pituitary adenomas, various diseases and functional disorders. Hyperprolactinemia accurate etiological diagnosis is essential for appropriate treatment. Non-functioning pituitary incidentalomas occur in approximately 10% of the population and tiny microprolactinomas could be elusive to imaging by magnetic resonance (MRI). Therefore, the coincidence of hyperprolactinemia and a pituitary mass does not necessarily mean that the patient has a prolactinoma and vice-versa. Dynamic testing with dopamine antagonists to distinguish adenoma-related hyperprolactinaemia from other causes, such as metoclopramide test (MCPT), were described several decades ago. Although their use is not universal, they have been shown to be useful in the differential diagnosis of hyperprolactinemia. The MCPT protocol includes a fasting serum sample drawn to determine prolactin (PRL) and TSH at baseline (PRL0), taken 30' and 60' after 10 mg MCP IV injection. The relative PRL increase is calculated as (PRL_{max}-PRL0)/PRL0 expressed as percentage (%PRL). PRL_{max} is the highest PRL post-infusion. An absolute >2.1 mU/l increase in TSH_{max} over TSH0 indicates a high dopaminergic tone. Although there may be overlapping, generally a $>100\%$ increase in PRL_{max} over PRL0 is considered a normal response. Prolactinomas typically display a flat PRL response (usually $<100\%$ increase) with a >2.1 mU/l TSH_{max} increase.
Material and Methods
We selected 98 patients (80% female) with hyperprolactinemia who had undergone MCPT and pituitary MRI. Patients were divided into three groups according to PRL_{max} response: Group A ($<100\%$) (N=35), Group B ($\geq$100-300%) ($n=16$) and Group C ($\geq300\%$) ($n=47$).
Results
Mean (range) PRL0, PRL_{max} (ng/dL) and%PRL increase were: GrA: 153 (41-1246), 171 (72-1214) and 45.5% (-7.1-97.8%); GrB: 123 (19-141), 281 (49-461) and 178.0% (106.9-272.8%); GrC: 31 (3-75), 257 (93-498) and 1470.8% (324.3-15224.0%). Mean (range) TSH_{max} (mU/mL) were: GrA: 2.4 (-2.2-11.2); GrB: 1.9 (-0.1-5.1); GrC: 0.5 (-1.9-3). A positive MRI pituitary image was found: GrA: 28/35 (80%); GrB: 9/16 (56%); GrC: 3/47 (6%). All 3 GrC microadenomas behaved like non-secreting incidentalomas.
Conclusion
In prolactinomas, the PRL_{max} after MCPT usually exhibits an increase $<300\%$. Therefore, MCPT is superior to baseline PRL in accuracy regarding the origin of hyperprolactinaemia. MCPT results guide the therapeutic intervention and may reduce the need for a pituitary MRI.
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EP445

Assessment of gonadotropic and lactotropic function in patients previously infected with SARS-COV-2

Nassim Ben Hadj Slama[1], Taieb ACH[1], Ghada Saad[1], Asma Ben abdelkrim[1], Molka Chaieb[1] & Koussay ACH[1]
[1]Farhat Hached University Hospital, Endocrinology, Soussa, Tunisia

Introduction
The most recent declared pandemic is attributed to COVID-19, caused by the novel coronavirus SARS-CoV-2. The angiotensin-converting enzyme 2, the principal receptor for SARS-CoV-2, exhibits expression in various tissues, prominently within gonadal and hypothalamo-hypophyseal domains. Long COVID, characterized by persistent symptoms post-infection, manifests in certain individuals and includes manifestations associated with the genitourinary system, such as sexual and menstrual dysregulation. The objective of this study is to systematically evaluate the gonadotropic and lactotropic functions in individuals with a history of SARS-CoV-2 infection.
Patients & Methods
This prospective study, conducted from January to December 2022, was carried out at the Endocrinology Department of Farhat Hached University Hospital in Sousse. The study included patients with a history of SARS-CoV-2 infection, categorized into those who had fully recovered (G1) and those experiencing Long COVID (G2). Gonadotropic function was systematically assessed through the measurement of gonadotropins (FSH and LH), Prolactin (PRL), and Estradiol (E2) levels in women, and Testosterone levels in men.
Results
A cohort of 64 patients underwent hormonal evaluation. Each group was composed of 32 patients. The median duration for hormonal exploration was comparable between G1 and G2 with respective values of 11.5 months [Q1–Q3]=[9-14] and 11 months [Q1–Q3]=[6-14] ($P=0.498$). Predominant symptoms in Long COVID patients included asthenia (84.4%) and cognitive disturbances (93.8%). Sexual disorders were reported by only 9.3% of G2 patients. The mean prolactin levels were 243.25 ± 223.71 mIU/l for G1 and 212.46 ± 135.48 mIU/l for G2 ($P=0.508$). Across all groups, 6.3% exhibited moderate hyperprolactinemia ($P=0.88$). In male patients, the mean testosterone levels were 5.25 ± 1.25 ng/ml for G1 and 6.45 ± 3.39 ng/ml for G2 ($P=0.269$). Female patients displayed average estradiol levels of 62.94 ± 68.46 pg/ml for G1 and 88.59 ± 89.05 pg/ml for G2 ($P=0.314$). Hypogonadotropic hypogonadism was observed in 4.6% of the overall study population, with a comparable distribution between G1 and G2 ($P=1$). No cases of peripheral hypogonadism were detected.
Conclusion
Despite reports in the literature documenting gonadal dysfunctions linked to COVID-19, our findings indicate that gonadotropic function remains intact in the majority of Long COVID patients. However, a notable 9.3% of our cohort presented with sexual disorders. Comprehensive studies focusing specifically on the gonadotropic and lactotropic axes in Long COVID patients with sexual dysfunctions are imperative to deepen our understanding of the endocrine intricacies associated with this lingering condition.

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EP449

Patient reported perspectives of disease burden in acromegaly: data from the acromegaly community patient-focused drug development meeting

Nidhi Agrawal[1], Kevin CJ Yuen[2], Vivien Bonert[3], Wenyu Huang[4] & Jill Sisco[5]
[1]NYU;[2]Barrow Pituitary Center;[3]Cedars Sinai Medical Center;[4]Northwestern University;[5]Acromegaly Community

Acromegaly is a rare disease most commonly caused by benign pituitary adenomas producing excess growth hormone. A profound mismatch between biological control and symptom control creates a high disease burden despite optimal disease management. To learn more about the patient experience, Acromegaly Community hosted a virtual Externally Led Patient-Focused Drug Development meeting in January 2021. There were 304 registered attendees, including 128 people with acromegaly and their family members, caregivers, and friends; industry, advocacy, and regulatory representatives; scientists; and healthcare providers. A >90-page report[1] prepared by Acromegaly Community captures participants' input on acromegaly symptoms and daily impacts and on current and future approaches to treatment, providing a valuable opportunity to learn about acromegaly directly from those most affected by it. We hereby summarize the key findings of the report. Overall acromegaly negatively impacts all aspects of daily living (Table 1). Fatigue/muscle weakness (reported by 92% of respondents) and joint problems/arthritis (90%) are the most commonly experienced and most troublesome symptoms (a top health concern of 63% and 65% of respondents, respectively). Some insightful statements pa include: 'I struggle with simple tasks… lifting laundry, carrying groceries, or mowing my lawn and doing simple housework' 'Living with acromegaly affects patients' mental health'.'Mental illness tore apart my family.' Anxiety/depression is experienced by 75% and is a top concern of 33% of respondents. acrorage and mo relationships. Most patients underwent pituitary surgery (83%) had with a wide range of surgical outcomes. Many require ongoing medical therapy, which is expensive, inconvenient, and frequently painful and can have severe side effects. Most patients have tried medications that reduce growth hormone secretion (71%), block its action (43%), or lower hormone levels (38%). Many patients use other medications to treat secondary symptoms such as diabetes and hypothyroidism (35%) and/or depression or anxiety (37%). Patients fail various combinations of medications before finding the right regimen. In the future, patients aspire more effective treatments for fatigue/muscle weakness and joint issues; more effective, tolerable, and easily administered drugs for biological and symptom control that shrink tumors; and effective treatments for hunger and weight gain, along with dietary advice and physical therapy.

1. Acromegaly Community. Voice of the Patient: Living with Acromegaly. 20 October 2021.

Table 1. Acromegaly impacts on daily living.

Aspect	Respondents
Social interaction	49%
Exercising	42%
Sports/recreation	39%
Household (e.g., cleaning, cooking)	38%
School, job	38%
Family	33%
Walking	26%

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EP450

Routine monitoring for acromegaly-associated complications and recurrence: a single-centre audit

Asif Nawaz[1], David Williams[1], Fiona Guy[1], Thinzar Min[1,2] & Win Yin[1]
[1]Swansea Bay University Health Board, Endocrinology and Diabetes, Swansea, United Kingdom;[2]Diabetes Research Group, Swansea University Medical School, Endocrinology and Diabetes, Swansea, United Kingdom

Introduction
Endocrine society guidelines advocate early colonoscopy and monitoring for acromegaly-associated complications and recurrence. We aimed to establish whether people with acromegaly under our care received appropriate monitoring.
Methods
Patients under follow-up with acromegaly diagnosed 1989-2021 were included. Electronic health records were accessed for clinic letters, colonoscopy reports, blood and imaging results from the diagnosis to recent follow-up.
Results
Twenty-two patients are included, with a mean age 47.5 ± 17.1 years at diagnosis, mean disease duration 15.3 ± 10.5 years, 2 (9.1%) had pre-existing type 2 diabetes (T2D), and 11 (50.0%) are male. Surgery was undertaken in 18 (81.8%), of whom 2 developed recurrent disease, and 4 managed medically from diagnosis. Five (22.7%) patients had colonoscopy within 12 months of diagnosis and a total of 11 (50.0%) patients had a colonoscopy since their diagnosis of acromegaly. Of these, three demonstrated colonic polyps of whom one had repeat colonoscopy within 5 years, one declined further endoscopy, and the other had no repeat endoscopy in 6 years. Over follow-up, 4 (18.2%) developed new T2D. In the last year, 18/22 (81.8%) had a serum IGF-1, 12/22 (54.5%) had HbA1c, and in the last 3 years 16/22 (72.7%) had repeat pituitary imaging. Of the 6 patients on somatostatin analogues or growth hormone antagonists, 4 (66.7%) had liver function tests in the last 6 months.
Discussion
Patients with acromegaly under our care infrequently had colonoscopy surveillance, and almost half did not have diabetes screening in the last year. We will develop local practice standards for annual review, and re-audit.

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EP459

Clinical presentation and comorbidities in hyponatremia: a key to the diagnosis of endocrine cause

Sanja Borozan[1], Dragana Miljic[2], Marina Nikolic Djurovic[2], Mirjana Doknic[2], Sandra Pekic Djurdjevic[2], Marko Stojanovic[2],

Zvezdana Jemuovic[3], Ivana Cekic[3], Ivan Jevtic[3], Snezana Vujosevic[1] & Milan Petakov[2]
[1]Clinical Centre of Montenegro, Faculty of Medicine, University of Montenegro, Montenegro;[2]Faculty of Medicine, Belgrade University, Serbia; Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Center of Serbia, Belgrade, 11 000 Belgrade, Serbia;[3]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Center of Serbia, Belgrade, 11 000 Belgrade, Serbia

Introduction
The aim of the study was to establish the predictive factors for endocrine disease-induced hyponatremia.
Patients and methods
Fifty-two patients with hyponatremia (Na <135 nmol/l) were referred to Department of Neuroendocrinology, University Clinical Center of Serbia from January 2015 to March 2023 ($n=52$; 31 females, 60%) mean age 60.5 ± 14.1 years, mean serum sodium level 124.9 ± 9.0 mmol/l. Seven patients (13.4%) with translocational hyponatremia, caused by hyperglycemia were excluded from the analysis.
Results
No significant differences between the non-endocrine (NEhypoNa) and endocrine hyponatremia (ENhypoNa) group was detected regarding the age ($P=0.439$), gender ($P=0.899$), body mass index ($P=0.236$) and smoking habits ($P=0.668$). Compared to patients in NEhypoNa group ($n=27$, 60%), patients with ENhypoNa ($n=18$, 40%) more frequently presented with rapid-onset hyponatremia (77.8% vs 25.9%, $P<0.05$). Although mean serum Na was not significantly different between groups (122.8 vs 124.4 mmol/l; $P=0.583$), severe symptoms were predictive factors for endocrine cause, found in 77.7% of ENhypoNa patients vs 37% in NEhypoNa group ($P=0.05$). Hypertension was associated with non-endocrine causes of hyponatremia (66.7% in NEhypoNa vs 27.8% in ENhypoNa group; $P=0.011$), most commonly caused by syndrome of inappropriate diuresis (SIAD). Chronic comorbidities like type 2 diabetes, obesity and osteoporosis were more frequently present in NEhypoNa, but the sample was small so the statistical significance was not reached. In 2/3 of patients in ENhypoNa group hyponatremia unmasked previously unrecognized primary or secondary adrenal insufficiency and hypopituitarism, diagnosed in 6 (13.3%) and 12 (26.7%) patients respectively.
Conclusion
Acute and severe hyponatremia on admission with less chronic comorbidities (diabetes, obesity, hypertension, osteoporosis), more frequently reflected underlying endocrine cause of hyponatremia.

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EP460

Bone health and skeletal fragility in second- and third-line medical therapies for acromegaly: preliminary results from a pilot monocenter experience

Sabrina Chiloiro[1], Antonella Giampietro[2], Amato Infante[3], Pier Paolo Mattogno[4], Consolato Gulli[3], Liverana Lauretti[4], Alessandro Olivi[4], Alfredo Pontecorvi[2], Laura De Marinis[2], Francesco Doglietto[4] & Antonio Bianchi[2]
[1]Università Cattolica del Sacro Cuore, Dipartimento di Medicina e Chirurgia traslazionale, Rome, Italy;[2]Fondazione Policlinico Universitario A. Gemelli IRCCS, Dipartimento di Medicina e Chirurgia traslazionale, Rome, Italy;[3]Fondazione Policlinico Universitario A. Gemelli IRCCS, Department of Diagnostic Imaging, Oncological Radiotherapy, and Hematology, Rome, Italy;[4]Fondazione Policlinico Universitario A. Gemelli IRCCS, Department of Neurosurgery, Rome, Italy

Introduction
Skeletal fragility is a relevant and not-reversible complication of acromegaly, involving around 30-40% of patients since the disease diagnosis. Few studies have investigated the effects on skeletal health of medical therapies for acromegaly. We aim to investigate the frequency of incident vertebral fractures (i-VFs) in patients treated with Pasireotide Lar + Pegvisomant (study group), after at least 24 consecutive treatment months and to compare the i-VFs frequency in the study group with controls: patients treated with Pasireotide Lar, Pegvisomant in monotherapy (m-Peg-V), and in association to first-generation somatostatin receptor ligands (fg-SRLs + Peg-V).
Subjects and methods
A retrospective, longitudinal, observational was designed. For the study cohort, inclusion criteria were: (1) ascertained diagnosis of acromegaly; (2) age older than eighteen years; (3) not-controlled acromegaly during treatment for at least 12 consecutive months with fg-SRLs and further 12 consecutive months of treatment with Pasireotide Lar or Pegvisomant in monotherapy or in combination with fg-SRLs; (6) treatment with Pasi-Lar + Peg-V for at least 24 consecutive months. For the control groups, inclusion criteria were: (1) ascertained diagnosis of acromegaly; (2) age older than 18 years; (3) not-controlled acromegaly during treatment for at least 12 consecutive months with fg-SRLs; (4) controlled acromegaly after at least twelve consecutive months with Pasi-Lar or Pegvisomant in monotherapy or in combination with fg-SRLs. The exclusion criteria (both for the study cohort and for the control groups) were: (1) diagnosis of active neoplasia; (2) previous or current treatment with drugs known to cause fragility fractures, except for glucocorticoid replacement therapy for central adrenal insufficiency; (3) history of spine surgery or trauma.
Results
Six patients were treated with Pasi-Lar + Peg-V, 6 patients with Peg-V in monotherapy (m-Peg-V), 16 patients with fg-SRLs + Peg-V and 10 patients with Pasi-Lar. Eight patients experienced i-VFs. None Pasi-Lar + Peg-V treated patient experienced i-VFs. The i-VFs frequency was lower in Pasi-Lar + Peg-V treated patients (0/8; 0%), as compared to those observed in m-Peg-V treated patients (4/8; 50%, $P=0.03$). The i-VFs frequency was slightly higher in Pasi-Lar treated patients (1/8; 12.5% $P=0.062$) and in fg-SRLs + Peg-V treated patients (3/8; 37.5% $P=0.364$), concerning those treated with Pasi-Lar + Peg-V (0/8; 0%). I-VFs occurred more frequently in patients with higher GH levels at acromegaly diagnosis ($P=0.04$), and in patients who experienced a BMD worsening ($P=0.005$).
Conclusion
Our preliminary data suggested that in conventional and multi-drug resistant acromegaly, the combination therapy Pasi-Lar + Peg-V may prevent the i-VFs occurrence. Prospective studies should further validate these results and ascertain underlying physiopathology mechanisms.

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EP462

Difficulties in treating acromegaly: what treatment? when to start?

Esra Eraslan Aydemir[1], Sinem Başak Tan Öksüz[1] & Sevim Güllü[1]
[1]Ankara University Hospital, Endocrinology and Metabolism, Turkey

Introduction
Acromegaly is a disorder caused by excessive secretion of growth hormone, often due to pituitary masses. The first step in treatment is transsphenoidal surgery. Cabergoline, somatostatin receptor ligands or pegvisomant may be used in patients with an inadequate response after surgery. Finally, radiotherapy may be used in patients with inadequate response to medical treatment.
Methods
In this retrospective study, data of 89 patients (59 females, 30 males) diagnosed with acromegaly in Ankara University Hospitals between 2002 and 2024 were analysed.
Results
The mean age at diagnosis was 40.2 ± 11.4 years and the mean follow-up was 97.6 ± 77.9 months. Pituitary surgery was performed in 82 of 89 patients and the postoperative remission rate was 31.7% ($n=26/82$). Patients ($n=62$) who did not achieve remission or who relapsed during follow-up underwent reoperation ($n=22/62$, 35.4%) and/or radiotherapy ($n=17/62$, 27.4%) and/or medical therapy ($n=54/62$, 62%). Of the 60 patients treated with medical therapy, 36 (60%) received monotherapy and 24 (40%) received combination therapy. Remission was achieved in 38 (63.3%) patients. Of the 60 patients, 33 (55%) were treated with somatostatin receptor ligand (SRL) monotherapy, 3 (5%) with dopamine agonist (DA) monotherapy, 16 (26.6%) with SRL and DA combination, 5 (8.3%) with SRL, DA and pegvisomant combination, 3 (5%) with SRL and pegvisomant combination. When analysing the patients who were receiving medical treatment, it was observed that there was a delay in treatment change in 6 patients. The mean delay in switching treatment was 61.5 months. The economic status of the patients, the Covid pandemic, referrals to different and inappropriate centres and patient non-compliance were found to be the reasons for this delay.
Conclusion
Despite many advances in medical and surgical treatment, some patients with acromegaly are not adequately treated. In cases SRLs are insufficient, switching to pegvisomant or a combination therapy of pegvisomant and SRLs is recommended.[1] Switching to new treatment regimens based on patient characteristics in all patients who do not achieve remission will increase the success of acromegaly treatment. The success of acromegaly treatment can also be increased by evaluating patients in experienced centers.
Reference
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EP463

A retrospective evaluation of operated non-functional pituitary adenomas over four decades in the maltese population

Jessica Mangion[1,2], Josanne Vassallo[1,2] & Mark Gruppetta[1,2]
[1]Mater Dei Hospital, Neuroendocrine Clinic, Msida, Malta;[2]University of Malta, Faculty of Medicine and Surgery, Msida, Malta

Introduction
Surgery in nonfunctional pituitary adenomas (NFPAs) is usually indicated when there is mass effect or progressive increase in size. Our study aims to analyze NFPAs which were operated until the end of 2023 in a well-defined population.
Methods
A retrospective analysis of 128 operated patients with NPFAs, diagnosed at the only central national service hospital in Malta, between January 1980 and December 2023, was performed. Detailed clinical data was obtained for each patient and the pre- and post-operative MR pituitary scans were analysed. Univariate and multivariate analyses were done to establish which variables can predict the presence of residual and/or recurrence post-operatively.
Results
72 (56.3%) were males and the median age was 56 years (IQR 42.5-64.5). The median tumour size was 27.6mm (IQR 21.5-35.1) with giant macroadenomas making up 10.2%. The median follow-up was 10.5 years (IQR 5-17). Most patients were operated once, 11 were operated twice, and only 2 thrice. During the study period 24 (18.8%) patients passed away. 103 patients (80.5%) had an accessible baseline MR pituitary, of which 95 (74.2%) tumours had chiasmal compression, 120 (93.8%) had suprasellar extension and 56 (43.8%) had cavernous sinus invasion. A residual post-operatively was detected in 80 (62.5%) patients. During follow-up, regrowth was detected in 25 (19.5%) patients with a median of 38 months from surgery (IQR 17-60). Univariate analysis revealed a statistically significant association between tumour residual and cavernous sinus invasion ($P<0.001$), largest tumour diameter ($P<0.001$), tumour volume ($P<0.001$), suprasellar extension ($P=0.04$) and infrasellar extension ($P<0.001$). The largest tumour diameter remained an independent predictor of having a residual post-operatively after logistic regression ($P=0.008$; OR 1.34 95% CI 1.08-1.68). Using ROC analysis to predict the presence of residual post-operatively, an infrasellar dimension of 5.2 mm was 80% sensitive and 70% specific (ROC-AUC 0.786, $P<0.001$). Tumour regrowth was statistically significantly associated with cavernous sinus invasion ($P=0.002$), tumour residual ($P=0.003$), largest tumour diameter ($P=0.032$) and transverse dimension ($P<0.001$). The transverse dimension remained an independent predictor of regrowth after logistic regression ($P=0.005$ OR 1.24 95% CI 1.07-1.44). There was no significant association between mortality and tumour residual or regrowth post-operatively.
Conclusion
The majority of operated NFPAs have good prognoses with few having significant regrowth despite residual tumours. An infrasellar dimension of 5.2mm was 80% sensitive and 70% specific to predict tumour residual post-operatively whilst the transverse dimension preoperatively was found to be independently associated with risk of regrowth.

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EP464

TSHoma: mapping the indolent journey

Tala Nasrini[1] & Adnan Ajmal[2]
[1]Koc University Hospital, Istanbul, Turkey; [2]Cleveland Clinic Abu Dhabi كلينك أبوظبي مستشفى كليفلاند, Abu Dhabi, United Arab Emirates

Background
Thyroid stimulation hormone producing pituitary adenomas [TSHoma] are very rare and present a diagnostic and management challenge due to limited clinical guidance. Indolent presentations such as multinodular goiter and mild hyperthyroidism can easily mislead the management. Moreover, we would also like to emphasize limitations of TSH with a reflex free T4 [FT4] test in such scenarios.
Clinical Presentation
Forty-three years old female was experiencing mild hyperthyroid symptoms and progressively enlarging multinodular goiter for few years. She was advised to get thyroidectomy after biopsy proven benign nodules. Interestingly, free thyroid hormones were mildly higher than ULN of 19.8 pmol/l for FT4 and 6.8 pmo/l for free T3 over last 5 years with inadequate TSH suppression with TSH between 1.4-2.1 mIU/l. Presurgical CT neck showed incidental sellar mass with subsequent MRI showing a 1.8 cm pituitary adenoma invading the right cavernous sinus and almost encircling the right cavernous carotid. Additional biochemical work up including elevated alpha subunit 2.7 ng/ml, SHBG 194.5 nmol/l with high alpha subunit/TSH ratio strongly suggested TSHoma. Due to invasive nature of the tumour, we employed primary pharmacotherapy with somatostatin receptor ligand (SRL) which holds promising potential, with reported instances of tumour regression in ~ 40% of cases. She was treated with octreotide LAR 20 mg every 4 weeks with subsequent follow ups over last 6 months showing very significant clinical, biochemical and radiologic improvement in goiter and pituitary tumour. Thyroid hormone levels are completely normalized now with resolution of hyperthyroid symptoms. Six months follow up pituitary MRI shows pituitary adenoma size is significantly decreased from 1.8 cm to 1.1 cm with regression of invasion.
Conclusion
TSHoma compromise 0.5-3% of pituitary adenomas. Majority of the cases come to attention as sellar mass affect so high index of suspicion is warranted especially when presentation is more indolent. High free hormones with inadequate TSH suppression should raise suspicion also highlighting the limitations of TSH with reflex FT4 test employed at many practices. TSH remained completely normal during her clinical course. Trans-sphenoidal resection is the most common primary treatment, but primary pharmacotherapy with SRL is also employed in select cases with limited success. Patient preference, lack of chiasmal compression, Knosp 3B-4 cavernous sinus invasion with gross total resection unlikely and progressively enlarging multinodular goiter were the factors that guided us to resort to SRL as primary treatment. Subsequent significant improvement highlights the importance of considering such therapy in carefully selected patients.

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EP465

Magnetic resonance imaging of pituitary formations diagnostics using neural networks

Elena Brutskaya-Stempkovskaya[1], Yulia Dydyshka[1], Siarhei Kavetski[2], Volha Shyshko[1,3], Ivan Vasilevich[1] & Artsiom Alperyn[4]
[1]Belarusian State Medical University Minsk, Belarus; [2]Republican clinical hospital of medical rehabilitation, Belarus; [3]Minsk City clinical Endocrinology center, Belarus; [4]Belarusian State University Belarus

The introduction of the brain magnetic resonance imaging (MRI) of into routine clinical practice has led to a significant increase of pituitary masses detection, including as incidental findings. An increase in the frequency of detection of pituitary gland formations entails a significant increase in costs for clinical and hormonal examination, MRI monitoring and dynamic observation by an endocrinologist. However, only a small number of identified formations require radical treatment. An important clinical problem is to determine the malignancy, predictors of potential growth and hormonal activity of pituitary incidentalomas. The development of an automated algorithm for diagnosing pituitary formations to identify groups of patients for priority examination is of great practical importance.
Materials and methods
A cross-sectional study of 746 patients was conducted for development a neural network program for automated MRI pituitary formations screening. All patients underwent the pituitary MRI without contrast at the Republican Clinical Hospital of Medical Rehabilitation in 2019-2022, coronal (T1, T2) and sagittal (T1) projections were studied. The MRI assessment was carried out by a radiologist; the clinical diagnosis was verified by endocrinologists.16 000 (30%) MR images from the original sample were manually labeled. Neural network architecture has been developed that is capable of performing multi-class classification using segmented images of the pituitary gland obtained as the output of the Faster-RCNN neural network (pretrained model) with a ResNet 50-FPN framework. The ratio of the intersection area of the predicted area and that obtained as a result of manual marking to their merging area, averaged over all images, was used as a metric. The test sample size was 25% of the original one.
Results
The average age 40.9 ± 16.5 years. Structure of diagnosis: 176 – normal, 336 – microadenoma, 68 – macroadenoma, 108 – postoperative changes, 58 – other pathology of the pituitary gland. A trained neural network analyzed MRI of pituitary formations.
Results
Accuracy (proportion of correct answers) by class: normal – 84%, microadenoma – 77%, microadenoma – 90%, postoperative changes – 91%, others – 91% (total – 86%). Precision (accuracy)$=0.63$, Recall (completeness)$=0.7$, F1-measure$=0.66$. Thus, the efficiency of predictions is sufficient for automated screening of the proposed groups of pituitary formations.
Conclusions
The results of the study prove the possibility of MRI pituitary formations automated screening using a developed neural network with a high degree of reliability.

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EP466

Incidence of neoplasia in acromegaly in Polish centre – retrospective study

Aleksandra Jawiarczyk-Przybyłowska[1], Justyna Kuliczkowska-Plaksej[1], Martyna Strzelec[1], Łukasz Gojny[1], Małgorzata Rolla[1], Anna Brona[1] & Marek Bolanowski[1]
[1]Wroclaw Medical University Endocrinology Diabetes and Isotope Therapy Wrocław, Poland

Introduction
Acromegaly is a rare, chronic and progressive disease caused by a pituitary adenoma. Excessive secretion of growth hormone (GH) and insulin-like growth factor-I (IGF-I) leads to cell proliferation and differentiation, which results in changes in external appearance and causes various systemic complications. Elevated levels of GH and IGF-I are also thought to promote the development of cancer and some studies have shown that acromegaly is a disease with a high risk of developing cancer. The aim of our study was to assess the incidence of benign and malignant neoplasms among patients with acromegaly and the relationship between their prevalence and disease activity, the time of diagnosis of acromegaly and the time of occurrence of the first symptoms of this disease.
Materials and Methods
The retrospective study included a statistical analysis of the medical records of 230 patients with acromegaly treated at the Department of Endocrinology, Diabetes and Isotope Therapy in Wroclaw (Poland) in 1990-2023 in order to estimate the incidence of neoplasms among them. Statistical analysis was performed using Statistica for Windows, version 13.1 by StatSoft (USA).
Results
We observed 171 cases of neoplasms, including 144 benign tumours and 27 malignant tumours. Among the malignant tumors, the most common were breast cancer, thyroid cancer and hematologic cancer, and among benign tumors, colorectal polyps. Both neoplasms and benign tumors were diagnosed both in the short and long term after the diagnosis of acromegaly, but in the longer term only malignant tumors were diagnosed. Both types of tumors occurred more frequently in controlled acromegaly than in cured acromegaly. The incidence of cancer, regardless of type, was higher in patients with active acromegaly compared to cured patients.
Conclusions
This study confirmed the association between the activity of acromegaly as well as the time from diagnosis of the disease with the prevalence of neoplasms. For this reason, oncological vigilant and active search for cancer among patients with acromegaly at every stage of the disease are necessary.

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EP467

Morphology and function of reproductive system in women with hyperprolactinemia in chronic treatment with cabergoline

Guendalina Del Vecchio[1], Roberta Scairati[1], Fabiana Gallo[1], Rosa Pirchio[1], Sara Di Meglio[1], Luigi Carbone[2], Carlo Alviggi[3], Annamaria Colao[1,4], Rosario Pivonello[1,5,6] & Renata Simona Auriemma[1]
[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Naples, Italy;[2]Università Federico II di Napoli, Dipartimento di Neuroscienze, Scienze Riproduttive ed Odontostomatologiche, Naples, Italy;[3]Università Federico II di Napoli, Dipartimento di Sanità Pubblica, Naples, Italy;[4]UNESCO Chair for Health Education and Sustainable Development, Federico II University, Naples, Italy;[5]UNESCO Chair for Health Education and Sustainable Development, Federico II University, Naples, Italy;[6]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia ed Andrologia, Unità di Andrologia e Medicina della Riproduzione e della Sessualità Maschile e Femminile (FERTISEXCARES), Naples, Italy

Purpose
The present study aimed at investigating the morphology and function of reproductive system in women with hyperprolactinemia (HPRL) receiving chronic treatment with cabergoline (CAB)
Methods
Twenty-three women(aged 34.21 ± 10.09 yrs) with HPRL, including 17 with microprolactinoma, 3 with macroprolactinoma and 3 with iatrogenic HPRL, entered the study. All patients were well-controlled with CAB treatment (medium dose 0.46 ± 0.45 mg/week). In population study, PRL at diagnosis (PRL0), PRL at evaluation (PRL1), FSH, LH,17B-estradiol (E2) and AMH in the early follicular phase(2°-5° days), and PRL(PRL2) and progesterone(PRO) in luteal phase(16°-25°day) were evaluated. Age at diagnosis(A0), age at evaluation(A1), CAB dose at evaluation (CE), mean (CM) and cumulative CAB dose (CD) and treatment duration (TD) were also evaluated. In both follicular and luteal phases, a transvaginal ultrasound was performed to evaluate: hysterometry (HS), endometrial thickness (ET), ovary length(dl), height (DAP), width (DT) and volume (OV), uterine volume (UV), right (AFR) and left (AFL) antral follicles count, right(RRI) and left (LFI) uterine artery resistance index, right (RPI) and left (LPI) pulsatility index. Based on CM, patients were stratified in Group 1 ($CM < 0.35$ mg/week) and Group 2 ($CM > 0.35$ mg/week). Based on TD, patients were stratified in Group 3 ($TD < 62$ months) and Group 4 ($TD > 62$ months).
Results
In Group 1, right DL ($P = 0.04$), DT ($P = 0.016$), DAP ($P = 0.023$) and OV ($P = 0.002$) during follicular phase were significantly higher than in Group 2. In Group3, right DL ($P = 0.004$), DAP ($P = 0.023$), DT ($P = 0.016$) and OV ($P = 0.002$) during follicular phase, and LPI ($P = 0.004$) in luteal phase were significantly higher than in Group 4. In Group1, LH ($P = 0.044$) and estradiol ($P = 0.023$) during luteal phase were significantly higher than in Group 2, while no significant differences were found in hormonal profile between Group3 and Group4. In whole study population ($n = 23$), PRL0 directly correlated with AMH ($P = 0.01$) and PRO ($P = 0.002$), whereas PRL1 with RRI ($P < 0.001$) and PRL2 with AMH ($P = 0.02$). TD indirectly correlated with ET ($P = 0.007$), right DT ($P = 0.05$) and DL ($P = 0.01$), LPI ($P = 0.05$) and RPI ($P = 0.0033$), and directly with UV ($P = 0.02$). CD indirectly correlated with LH ($P = 0.05$) and right DL ($P = 0.048$). A0 correlated indirectly with AFR ($P = 0.002$), AFL ($P = 0.002$) and AMH ($P = 0.012$), and directly with UV ($P = 0.027$) and CE ($P < 0.001$). Similarly, A1 indirectly correlated with AFR ($P = 0.027$), AFL ($P = 0.039$) and AMH ($P = 0.003$). E2 correlated directly with HS ($P = 0.044$) and RRI ($P = 0.003$), and indirectly with CD ($P = 0.036$). In turn, AMH directly correlated with CE ($P < 0{,}0001$), LPI ($P < 0{,}0001$), and left DT ($P = 0.031$).
Conclusion
CAB might have a direct beneficial effect on uterine and ovarian morphology and function, mainly improving uterine vascular flow parameters.

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EP468

Pasireotide as first line medical therapy for treatment of selected patients with acromegaly

Nicoleta Olarescu[1,2,3], Jens Bollerslev[1,2], Anders Jørgensen[1,2] & Ansgar Heck[1]
[1]Section of Specialized Endocrinology, Department of Endocrinology, Oslo University Hospital (OUS), Oslo;[2]Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway;[3]Research Institute of Internal Medicine, Oslo University Hospital (OUS), Oslo, Norway

Objective
Pasireotide is a second-generation somatostatin receptor ligands (SRLs) with highest affinity for somatostatin receptor (SST)5, followed by SST2. It is considered, so far, in patients resistant to first-generation SRLs, after surgical failure. Histological characteristics and T2-weighted MRI can predict resistance to first-generation SRLs in patients with somatotroph adenomas. Previous studies primarily assessed efficacy of pasireotide as 2nd or 3rd line medical treatment. However, pasireotide might be an option in patients expected to be resistant to first-generation SRLs (e.g. hyperintensity T2-weighted MRI signal and/or sparsely granulated immunohistochemical pattern). We describe the efficacy of pasireotide as the first pharmacological treatment.
Methods
Clinical and biochemical parameters, T2-weighted MRI signal intensity, histological diagnosis and efficacy of pasireotide treatment on GH and IGF-1 levels, and tumour volume (by ellipsoid formula), were recorded in four patients (two treated as primary treatment, two after debulking surgery), expected to be resistant to first-generation SRL.
Results
Table 1 presents age, GH and IGF-1 levels, and tumour volume before and after treatment with pasireotide median 5.6 (range 4.5-6.6) months. All tumours were hyperintense on T2-weighted MRI and sparsely granulated somatotroph adenomas were identified in the operated patients. Variability in GH and IGF-1 reduction was observed. Tumour volume decreased at least with 31% and the effect occured early. One patient started ad-on cabergoline therapy two months after pasireotide. At last visit, 18-58 months after treatment initiation, all patients still received pasireotide, two in combination with pegvisomant, one with cabergoline and one patient was additionally treated by radiotherapy. Two patients had normalised IGF-1, two patients further improved IGF-1. HbA1c remained stable in two patients and worsened in two patients with further need of anti-diabetic treatment.

Table 1. Patients' characteristics before and after treatment with pasireotide

	Baseline					Follow-up				Change (%)		
sex	Age yrs	GH µg/l	IGF-1 nmol/l	IGF-1/ ULN	Tumour volume cm^3	GH µg/l	IGF-1 nmol/l	IGF-1/ ULN	Tumour volume cm^3	GH	IGF-1	Tumour volume
#1_female	31	4.0	68	2.3	7447	2.1	26	0.9	4556	47	62	39
#2_male	51	2.9	60	2.7	47158	2.7	58	2.6	28540	7	3	39
#3_female	35	1.6	55	1.9	5457	1.5	39	1.3	3749	6	29	31
#4_female	30	200.0	114	3.9	7758	3.8	81	3.8	3360	98	29	56

Conclusions
In patients with T2-hyperintense MRI adenomas and presumed resistance to first-generation SRLs, pasireotide may be considered as first line medical treatment, facilitating rapid tumour control and decreased disease activity.

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EP469

Congenital growth hormone deficiency associated with hypopituitarism: experience from the endocrinology department of hedi chaker university hospital in sfax

Hamdi Frikha[1], Mouna Elleuch[1], Nesrine Dhieb[1], Dhoha Ben Salah[1], Wajdi Sefi[1], Faten Haj Kacem Akid[1], Fatma Mnif[1], Nadia Charfi[1], Mouna Mnif[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology

Introduction
Congenital hypopituitarism is considered a study model to understand the mechanisms of development and the physiological functioning specific to the pituitary gland. Its exact prevalence is challenging to establish. In this report, we present the experience of the endocrinology department at Hedi Chaker University Hospital in Sfax regarding the diagnosis and management of patients with antehypopituitarism associated with growth hormone deficiency (GHD).
Methods
A retrospective descriptive and analytical study was conducted, collecting data from patients with antehypopituitarism and GHD who were followed at the endocrinology department of Hedi Chaker University Hospital in Sfax.
Results
We included 87 patients with antehypopituitarism and GHD. The median age at diagnosis in our cohort was 14 years, with a gender ratio of 1 female to 2 males. Growth projection on the growth curve indicated severe growth retardation of more than -3 standard deviations (SD) in 73.5% of cases. In 25.9% of cases, two or three pituitary axes were affected, while four axes were involved in 17.6% of patients. Finally, 10.6% of our patients had involvement of all antehypopituitary axes. Hypoplastic pituitary was the most frequent morphological anomaly, found in 48% of cases on pituitary imaging. In our study, a positive correlation was found between the early discovery of hypopituitarism and the presence of pituitary hypoplasia, as well as with the severity of growth retardation and the number of affected axes ($P=0.009$; 0.016; 0.02, respectively). Therapeutically, our study highlighted heterogeneity in the response to growth hormone treatment, with an average statural gain of 1.4 ± 1.2 SD (0, +4 SD). The target height was reduced by an average of 17.4 ± 14.8 cm in boys and 10.3 ± 4.6 cm in girls. Molecular analysis revealed mutations in exon 2 of the ProP-1 gene in all familial cases and two sporadic cases with highly heterogeneous phenotypic expression.
Conclusion
These results are consistent with existing literature on antehypopituitarism with growth retardation. They highlight the importance of early diagnosis, clinical and genetic variability of the disease, and the variable response to growth hormone treatment. These findings contribute to a better understanding of GHD and can help optimize the clinical management of these patients. The mutations in exon 2 of the ProP-1 gene identified in all familial cases and two sporadic cases in our cohort emphasize the genetic complexity of isolated growth hormone deficiency.

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EP470

Infundibuloneurohypophysitis in sjögren's syndrome: a case report

Ameni Terzi[1], Jemel Manel[1], Chehaider Cyrine[1], Adel Meriem[1], Chiboub Marwa[1], Kandara Hajer[1] & Kammoun Ines[1]
[1]National Institute of Nutrition, Endocrinology department, Tunis

Introduction
Infundibuloneurohypophysitis (INH) is an autoimmune disease that typically presents as central diabetes insipidus (CDI). It is often more common in women with an autoimmune background. Here, we have the opportunity to describe an unusual case of a female patient who developed Sjögren' syndrome (SJS) following CDI.
Case presentation
A 55-year-old female was admitted to our department for exploration of polyuoropolydipsic syndrome evolving for 8 years, of abrupt onset, estimated at 12L per day and associated with nyctiuria. The urine density was low at 1005. The urinary osmolarity was 60 mosml/l. The patient underwent the two-stage water deprivation test that strongly indicated the presence of CDI. After hydric restriction, the antidiuretic hormone vasopressin level was low (0.5 pmol/l). The pituitary MRI displayed the absence of classical posterior pituitary lobe hyperintensity in T1 and a decrease in anterior pituitary gland height with partial intrasellar arachnoidocele. Further endocrinological assessment did not reveal any pituitary axes impairement. The patient started oral desmopressin, experiencing a marked relief of polyuria, as well as polydipsia. After 2 years, the patient developed dry eye and mouth syndrome that were explored. She presented pulmonary and central neurological involvement characterized by demyelinating encephalic lesions. Immunological tests revealed positive antinuclear, antiSSA52 and antiSSA60 antibodies. The diagnosis of primary SGS was established based on 4 out of the 6 American-European criteria. She was treated with corticosteroids.
Conclusion
The diagnosis of the underlying condition of CDI is challenging and raises several concerns for patients as it requires long-term follow-up. This report outlines the notably rare association between INH, an inflammatory disorder of the pituitary gland revealed herein by CDI and primary SJS. The pathogenesis is poorly understood. However, the autoimmune origin is strongly suggested by its association with connective tissue disorders, particularly SJS.

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EP471

Diseases of the pituitary stalk

Hana Charfi[1], Dhoha Ben Salah[1], Mouna Elleuch[1], Yesmine Elloumi[1], Fatma Mnif[1], Nadia Charfi[1], Mouna Mnif[1], Faten Haj Kacem Akid[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker Hospital, Endocrinology-Diabetology Departement, Sfax, Tunisia

Introduction
The pituitary stalk (PS) can be the target of various congenital or acquired pathologies. These conditions are increasingly encountered with the advent and development of magnetic resonance imaging (MRI). Clinically, PS pathology is often revealed by the occurrence of diabetes insipidus. However, other clinical manifestations related to hypothalamo-hypophysial involvement may also be variably associated.
Objective
To identify the circumstances of discovery, clinical features, hormonal aspects, and radiological findings related to pituitary stalk pathology.
Materials and Methods
A retrospective study of 34 patients with pituitary stalk anomalies, hospitalized at the Endocrinology Department of Hedi Chaker University Hospital in Sfax over a 24-year period.
Results
The average age of our patients at the time of diagnosis was 28 years. A male predominance was noted with a sex ratio of 1.2. The most common circumstances of discovery were polyuro-polydipsic syndrome and growth delay in 41% of cases each. Anterior pituitary insufficiency was present in 73% of patients. Diabetes insipidus was diagnosed in 52% of cases. Pituitary stalk hypertrophy, described in 44% of cases, was secondary to granulomatosis (40%), metastatic origin (26.66%), lymphocytic hypophysitis (13.33%), and idiopathic (20%). Pituitary stalk interruption, present in 56% of patients, was post-surgical, post-traumatic, and idiopathic in 21%, 10.5%, and 68.5%, respectively.
Conclusion
The spectrum of pituitary stalk pathologies is extensive, posing a diagnostic challenge. Knowledge of the main differential diagnoses is crucial for better management.

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EP472

Standing balance control in patients with acromegaly

Michaela Title[1], Yuqi Wang[1], Melanie Posiewko[1], Lisa Tramble[2], Syed Ahmad[2], David Clarke[3], Syed Imran[2] & Michel Ladouceur[1]
[1]Dalhousie University Kinesiology Halifax, Canada; [2]Dalhousie University Endocrinology Halifax, Canada; [3]Dalhousie University Neurosurgery Halifax, Canada

Patients with acromegaly (PWA) experience higher rates of falls and fall-related injuries than age-matched Canadian adults. Previous studies of standing balance revealed increased sway in PWA compared to healthy controls but failed to control for the effects of the pituitary adenoma. Therefore, the aim of the present study was to determine if acromegaly influenced the neuromuscular control of standing balance. Bipedal standing balance was evaluated in PWA ($n=13$) in biochemical remission and a control group of patients with non-functioning pituitary adenomas (PNA, $n=13$). The groups were of similar age, sex, and BMI and all participants underwent surgery to remove the pituitary adenoma. Self-reported survey data was used to compare joint pain, functional disability scores, and history of joint surgery between groups. PWA reported significantly higher back ($P=0.004$), hip ($P=0.007$), and knee ($P=0.007$) pain and greater functional disability of the hip ($P=0.041$) and knee ($P=0.041$) than PNA. However, the history of joint surgery did not significantly differ between groups. Bipedal standing balance trials were repeated with eyes open, and eyes closed. Bipedal centre of pressure (COP) was measured using two AMTI force plates with one underneath each foot. Centre of mass (COM) was measured using a 14 body segment model with anatomical 3D positions recorded using a 14-camera OptiTrack motion capture system. The force plates and motion capture systems were synchronized and sampled at 200 Hz. Primary outcome measures included COP 95% prediction ellipse area and anteroposterior (AP) and mediolateral (ml) components of COP range, COP mean velocity, COP median frequency, root mean square (RMS) difference between COP and COM, cross-correlation between COP and COM, and time lag between COP and COM. PWA exhibited significantly greater RMS difference of COP and COM than PNA in both the AP ($P=0.042$) and ml ($P=0.006$) axes. No other balance measures were significantly different between the groups. There was no significant interaction between vision and acromegaly for any of the balance outcome measures. In conclusion, the larger RMS difference between COP and COM may indicate impaired sagittal plane ankle stiffness and impaired frontal plane hip mechanics in PWA.

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EP473

Walking balance in patient with acromegaly

Yuqi Wang[1], Michaela Title[1], Melanie Posiewko[1], Lisa Tramble[2], Syed Ahmad[2], David Clarke[3], Syed Imran[2] & Michel Ladouceur[1]
[1]Dalhousie University Kinesiology Halifax, Canada; [2]Dalhousie University Endocrinology Halifax, Canada; [3]Dalhousie University Neurosurgery Halifax, Canada

Acromegaly triggers, and is associated with, peripheral nervous system modifications and joint degenerations, which are considered to impact the walking balance of patients with acromegaly (PWA). Therefore, to better understand if these systemic degenerations impact the transitory adaptations in locomotor patterns of these patients, this study aims to establish the walking balance deficits of PWA. Walking balance was evaluated in PWA ($n=8$) in biochemical remission and a control group of patients with non-functioning pituitary adenomas (PNA, $n=8$). The groups were of similar age, sex, and BMI and all participants underwent surgery to remove the pituitary adenoma. Self-reported survey data was used to compare joint pain, functional disability scores, and history of joint surgery between groups. PWA reported significantly higher back, hip, and knee pain and greater functional disability of the hip and knee than PNA. However, the history of joint surgery did not significantly differ between groups. Walking balance was assessed using the Timed Up and Go (TUG) test, the Dynamic Gait Index (DGI) score, and muscle energy patterns during obstructed walking (10% leg length obstacle). The kinematics and kinetics of walking were calculated by measuring bipedal ground reaction forces and centre of pressure (COP) using two AMTI force plates with one underneath each foot. Lower limb kinematics were measured using a 7-body segment model with anatomical 3D positions recorded using a 14-camera OptiTrack motion capture system. Force plate and motion capture systems were synchronized and sampled at 200 Hz. Lower limb kinematics and kinetics were calculated using Visual 3D. The outcome measures of the study consisted of TUG time, DGI score, and differences in joint power during obstructed walking. PWA took more time to complete the TUG task but did not have a lower DGI score (ceiling effect). There was no significant difference found in obstructed walking speed or obstructed walking stride length between the PWA and PNA groups. The muscle energy pattern adaptations required for crossing obstacles show a possible trend with a decrease in frontal plane energy generation by the hip abductors of the support leg and sagittal plane energy absorption by the knee extensors of the passing leg. These findings suggest that PWA may employ a different strategy to control hip abduction when adapting to an obstacle compared to PNA. These results show that changes in the mechanics of walking in PWA may indicate a potential alteration in muscle activation strategies.

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EP474

GH and ACTH co-secretion by two pituitary microadenomas

Dominika Ondruskova[1], Peter Vanuga[2] & Anna Pávaiová[2]
[1]National Institute of Diabetes and Endocrinology, n.o., endocrinology, Lubochna, Slovakia;[2]National Institute of Diabetes and Endocrinology, n.o., endocrinology, Lubochna

Introduction
Pituitary ACTH-dependent Cushinǵs disease and acromegaly are rare conditions. Pituitary adenomas co-secreting GH and ACTH are even more unusual.
Case report
A 29-year-old patient, mother of three children, long-term follow-up by an endocrinologist for a thyroid struma without an autoimmune basis, was sent in April 2023 for further examination for detection of hypercortisolemia and insufficient suppressibility in the overnight 1 mg dexamethason test. The patient reported irregular menstruation, slight weight gain, intense sweating, swelling of her hands and feet. From objective symptoms facies lunata was noticeable, without other remarkable features. According to the diurnal profile of cortisol, the patient did not have preserved circadian variability of cortisolemia, we detected an elevation of cortisoluria, ACTH was within the normal range. On the basis of dexamethasone suppression test, we repeatedly confirmed the diagnosis of ACTH dependent Cushing syndrome, Cushing's disease. Due to the high level of IGF-1, we repeatedly performed the oral glusoce tolerance test with STH, in which up to the 120th minute there was insufficient suppression of STH. This condition was evaluated as hypersomatotropism. Other pituitary functions were normal. We completed an MRI examination of the pituitary gland because of the suspicion of pathology in this area, which verified two 2 and 4 mm large microadenomas. Than we started treatment with a steroidogenesis inhibitor and a somatostatin analogue before neurosurgery. On 27th of August 2023, transsphenoidal extirpation of both pituitary microadenomas was performed. Histologically, in both material fragments a corticotroph PIT NET, Crookés cell adenoma was verified. Immunohistochemically, growth hormone overproduction was not detected. Four months have passed since the time of diagnosis until the date of the operation. The patient noticed an increase in the size of foot by 1 number. After surgery, there was a remission of acromegaly and Cushing's disease. Central hypocorticism was newly developed, therefore we started replacement therapy with Hydrocortisone. Subsequently, the patient reported a regular menstrual cycle, less intense sweating, reduction of swelling on the hands and feet. We objectively observed a weight loss of a total of 3 kg in 3 months.
Conclusion
Early detection of two pituitary hormone overproductions and a quick neurosurgical solution protected the patient from the possible development of a number of comorbidities associated with GH and ACTH overproduction. Due to the aggressive variant of corticotroph adenoma, intensive monitoring of the patient will be necessary.

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EP475

A rare case of partial hypopituitarism secondary to hereditary hemochromatosis presenting as unexplained hypotension

Mohamed Mortagy[1], Thake Kaung[1] & Frank Murphy[1]
[1]Hampshire Hospitals NHS Foundation Trust, Gastroenterology Winchester, United Kingdom

Introduction
Hereditary hemochromatosis is a common disorder in white population with a prevalence of 4-6.4%. It is a systemic disorder that affects multiple organs. It could affect the pituitary gland leading to hypogonadotropic hypogonadism and could affect other pituitary hormones to a lesser extent. We present a rare case of hereditary hemochromatosis leading to hypotension most likely due to iron infiltration of the pituitary gland.

Case presentation
A middle aged male presented to the emergency department with a gradual onset of progressive dyspnoea, abdominal distension, bilateral leg swelling and jaundice. His past medical history is remarkable for alcohol related liver cirrhosis. He cut off his alcohol 3 months prior to this presentation and last alcohol intake was 2 weeks prior. He was afebrile, tachycardic, on oxygen with normal blood pressure. He had jugular venous distension, bilateral crackles, ascites, and bilateral lower limb oedema. Chest Xray showed right sided pleural effusion. Echocardiography was unremarkable with normal ejection fraction. Abdominal ultrasound and CT were only remarkable for liver cirrhosis with minimal ascites. He had very high ferritin levels (4059 mg/l) and transferrin saturation (89%). He became hypotensive (systolic blood pressure <80) for a few days despite stopping furosemide, giving IV fluids and albumin. With his prolonged persistent hypotension, there was a question whether he has developed hypopituitarism secondary to hemochromatosis. His Serum FSH (1.0 u/l), LH (<1.0 u/l), testosterone (3.2 nmol/l), and AM cortisol were low (104nmol/l). Prolactin (454 mu/l) was high. TSH (2.04 mu/l) and Free T4 (18.9 pmol/l) were normal. He was suspected to have partial hypopituitarism secondary to hemochromatosis. Hydrocortisone was started and his blood pressure improved significantly.
Discussion
Hereditary hemochromatosis causes iron deposition in many organs specially the liver, the heart and the pancreas leading to multi-system affection and consequently liver cirrhosis, heart failure and diabetes. This patient had only liver cirrhosis with no other known organ affection. He was hypotensive despite appropriate treatment. His pituitary hormonal profile showed low gonadotropins, low cortisol despite normal thyroid function. This implies that he had partial hypopituitarism secondary to iron deposition in the pituitary gland secondary to his hemochromatosis. His hypotension resolved once hydrocortisone was started.
Conclusion
Clinicians should be aware that hypopituitarism should be suspected in patients with unexplained hypotension with history of hemochromatosis.

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EP476

Sellar and supra-sellar cavernous hemangioma: a rare case report

Zineb Ait Si Ali[1], Nada El Idrissi Dafali[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Centre Hospitalo-Universitaire Mohammed VI Marrakech, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction
Sellar and supra-sellar hemangioma is a very rare, benign tumor, presenting a differential diagnostic difficulty with pituitary adenomas, especially as its imaging aspects are non-specific. We report an unusual case of an intrasellar and suprasellar cavernous hemangioma that was initially thought to be an invasive pituitary macroadenoma.
Case report
A 65-year-old female patient presented with headaches and visual disturbances that had been evolving for 10 years, in a context of preserved general condition. The evolution of the symptoms had been marked by a worsening for the last 3 months. Clinical examination was unremarkable. Work-up: hypothalamic-pituitary MRI visualized a voluminous expansive sellar and supra-sellar lesion measuring $68\times57\times44$ mm, consistent with an invasive macroadenoma. Cortisolaemia: 5.3 mg/dl Prolactinaemia: 10.7 ng/ml, T4l: 8 pmol/l. The patient was started on hydrocortisone and L-thyroxine replacement therapy. She underwent an initial biopsy, the anatomopathological study concluded to a vascular tumor proliferation in favor of a cavernous hemangioma with no sign of malignancy. The patient was scheduled for trans-sphenoidal tumor resection.
Discussion and conclusion
Hemangioma is a benign vascular tumor, arising preferentially in the liver and skin. Cerebral localization is rare (0.5%), and sellar and supra-sellar involvement is extremely rare, with a slight female predominance. The clinical and radiological presentation is not characteristic enough to differentiate cavernous hemangiomas from other pathologies more frequently encountered in the sellar and supra-sellar region, such as pituitary adenomas, meningioma, optic glioma, craniopharyngioma, germinoma... It is important to differentiate sellar cavernous hemangioma from pituitary tumors because of the risk of severe hemorrhage during operation, as these tumors are vascular lesions and postulated to be dural based, and the possible complications in the postoperative period Diagnosis of certainty remains the prerogative of anatomopathological examination. Given the high risk of bleeding, subtotal tumor resection with decompression of surrounding tissue, followed by radiotherapy, may be considered the safest and most effective strategy.

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EP477

Clinical characteristics of acrmegaly in men

Souleima Trigui[1], Dhoha Ben Salah[1], Mouna Elleuch[1], Kouloud Boujelben[1], Mouna Mnif[1], Elleuch Mouna[1], Nadia Charfi[1], Mohamed Abid[1] & Nabila Mejdoub[1]
[1]Chu Hedi Chaker, Endocrinology Sfax

Introduction
Acromegaly is a rare pathology characterized by chronic hypersecretion of Growth Hormone (GH) and Insulin-like Growth Factor-1 (IGF-1) that causes somatic, metabolic, and systemic changes. There are few data in the literature on the impact of the disease in male.
Patients and methods
Retrospective descriptive study including 15 adult males with acromegaly hospitalized in the endocrinology department of the Hedi Chaker Sfax university hospital over the period from 1998 to 2020. Acromegaly was diagnosed at an average age of 46.6 years with a peak incidence between the ages of 40 and 59 years. Acromegaly was revealed at an age beyond 60 years in 3 patients (20%). The diagnosis time was, on the average of 7.2 years ±6.1 with extremes ranging from 2 days to 17 years. Acrofacial dysmorphic syndrome was the most common discovery circumstance (53.3% of cases, $n=8$). Two patients among these 8 were diagnosed with diabetes mellitus during follow-up (13.3%). The tumor mass syndrome was the revealing symptom of the adenoma in 5 cases (33.3%) and antepituitary insufficiency was the revealing symptom in 2 cases. Decreased libido and erectile dysfunction were reported during the interview by 33.3% and 26.6% of patients respectively. Joint manifestations were found in 7 patients (46.6%) such as paresthesias in 4 patients (26.6%) and carpal tunnel syndrome in 3 patients (20%). Hypertension was observed in 5 patients (33.3%) and hypertrophic cardiomyopathy in 3 patients (20%). Sleep apnea syndrome (SAS) was diagnosed in 4 patients (26.6%). A homogeneous multinodular euthyroid goiter was observed in 2 patients (20%). Digestive colonoscopy showed colonic polyps in 2 patients (20%). One patient had segmental and focal hyalinosis and one patient had Wolf Parkinson's white syndrome. A gonadotropic deficiency was noted in 26.6% of patients ($n=4$), a thyrotropic deficiency in the same percentage and a corticotropic deficiency in 13.3% of patients ($n=2$). Carbohydrate tolerance disorders were noted in 7 patients (46.6%): prediabetes in 2 cases (13.3%) and diabetes in 5 cases (33.3%). Macroadenomas were the most common (73.3%). However, We did not detect giant somatotropic adenomas.
Conclusion
Production of GH has deleterious effects on many aspects of male sexuality. It induces hypogonadism through mass effect and through increase of prolactinemia. Moreover, hypogonadism is also one of the factors linking acromegaly to erectile dysfunction (ED), and metabolic complications of acromegaly.

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EP478

Sheehan syndrome and thyrotropic insufficiency

Ismail Sid Ahmed[1], Amal Ourdi[1], Khawla Rhouzali[1], Abdessamad Malki[1], Siham Rouf[1,2] & Hanane Latrech[2]
[1]Endocrinology-Diabetology and Nutrition Department Chu Mohamed VI Oujda, Faculty of Medicine and Pharmacy, Mohammed First University Oujda, Morocco, Oujda, Morocco;[2]Endocrinology-Diabetology and Nutrition Department Chu Mohamed VI Oujda, Faculty of Medicine and Pharmacy, Mohammed First University Oujda, Morocco, laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy, Mohammed First University Oujda, Morocco, Oujda, Morocco

Introduction
Sheehan Syndrome can be determined as partial or complete hypopituitarism occurring after massive postpartum uterine hemorrhage leading to pituitary infarction. The first symptom classically described is the absence of milk flow. It is a rare and lethal condition, especially in underprivileged countries around the world. The resulting hypothyroidism is often diagnosed late, involving long-term complications. The aim of this study is to determine the prevalence of thyrotropic insufficiency associated with Sheehan Syndrome.
Methods
This is a retrospective descriptive study, including 5 patients with Sheehan Syndrome involving thyrotropic insufficiency, hospitalized in the Department of Endocrinology, diabetology and nutrition at the University Hospital of Oujda-Morocco during the period of October 2015 to December 2023. Data were analyzed by SPSS V 21.

Results-Discussion
The average age was 41.6 ± 15.14 years with an average diagnosis time of 11.5 years. Delivery hemorrhage was observed in 3 patients (60%), while the absence of milk flow was observed in 2 patients (40%). The clinical signs were dominated by secondary amenorrhea in 60% of cases. All patients expressed signs of hypothyroidism. The TSHus varied between 0.17 mIU/l and 2.88 mIU/l, and FT4 was low in all cases, with an average of 4.28 pmol ± 4.56 pmol/l. Hypothalamic-pituitary MRI imaging was in favor of an arachnoidocele in all our patients. All patients were treated with levothyroxine with good clinical improvement.
Conclusion
Thyroid insufficiency is one of the most important endocrine disorders, due to its cardiovascular risk. Furthermore, in the presence of massive post-partum haemorrhage, strict surveillance is required to early detection of Sheehan syndrome.

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EP479

New onset pituitary adenoma after cushing's disease: recurrence or coincidence

Ana Quítalo[1], Francisca Leitão[1], Sara Franco[1], Margarida Lagarto[2], Henrique Vara Luiz[1] & Luísa Raimundo[1]
[1]Hospital Garcia de Orta, Almada, Portugal;[2]Hospital de São Francisco Xavier, Lisboa, Portugal

Introduction
Multiple pituitary adenomas (PA) have a prevalence of 0.2-2.6% of all resected PAs. However, most of them are simultaneously diagnosed and in the setting of acromegaly. In a 2019 surgical series with 22 cases of multiple PAs, only one case was asynchronous and all of them had a positive immunohistochemical staining.
Case report
A 32-year-old woman (1996) was referred to na Endocrinology appointment with amenorrhea and weight gain for the last 6 months and recent diagnosed hypertension. Central obesity, moon facies, hirsutism and violaceous abdominal striae were present at physical examination. The initial evaluation revealed serum cortisol 28 mg/dl (6.24-18), ACTH 151 pg/ml (9-50) and urinary free cortisol (UFC) 3 times the upper limit of normal. No suppression was found after 2 and 8mg dexamethasone tests and the CRH test was negative. Pituitary MRI showed a left inferolateral microadenoma (8 mm) and the inferior petrosal sinus sampling confirmed the ACTH gradient. After transsphenoidal surgery, histology confirmed the diagnosis of Cushing's disease. UFC levels normalized and the patient needed hydrocortisone for a year. The 6-month post operation MRI showed no evidence of residual lesions. Tem years later (2006), a follow up MRI described a median PA with 8x9x10mm, protruding to the suprasellar cistern. The patient reported symptoms of new weight gain and easy bruising. UFC levels were persistently elevated with no suppression in the 2 mg dexamethasone test, but serum ACTH was normal with a peak $<50\%$ in the CRH test. However, by this time, the patient was taking antiepileptic drugs. With the suspicion of recurrent Cushing's disease, a second transsphenoidal surgery was performed. Histology revealed a null cell adenoma with negative immunostaining. Fifteen years later (2015), the residual lesion increased in size with $21 \times 14 \times 12$ mm and invasion of the left cavernous sinus. With no evidence of hypercortisolism, she underwent fractionated stereotaxic radiotherapy. The most recent blood work showed normal pituitary function and the last MRI (2021) described a residual lesion with $9.7 \times 3.5 \times 4$ mm.
Conclusion
Double PAs are a very rare entity that can pose a significant challenge. Detailed hormonal assessment and immunohistochemical staining are essential for correct diagnosis. This case illustrates a rare diagnosis of a corticotroph and a null cell adenoma. However, molecular analysis is currently in charge of providing a more accurate characterization of the last PA.

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EP543

Dynamic changes of fibroblast growth factor 21 levels in response to acute and chronic alcohol consumption

Cyril Vogel[1], Clara Sailer[1], Christ-Crain Mirjam[1], Bettina Winzeler[1] & Julie Céline Refardt[1]
[1]Universitätsspital Basel, Basel, Switzerland

Background
Fibroblast growth factor 21 (FGF21) is a hormone induced in the liver by metabolic stressors including starvation, sugars, and ethanol. Alcohol consumption increases endogenous FGF21 levels in humans while administration of FGF21 has been shown to reduce alcohol consumption in non-human primates. The effect of acute moderate alcohol consumption and long-term alcohol cessation on FGF21 levels in humans is controversial. We hypothesize that even moderate alcohol consumption increases FGF21 levels and that reduced long-term alcohol consumption lowers FGF21 levels.
Methods
We included data from two prospective intervention studies: first, a randomized, crossover design with 10 healthy men consuming beer (goal blood alcohol concentration of 0.8‰) or water. Blood samples were collected at six time points over the observation period of 720 minutes. The primary endpoint was difference in FGF-21 levels following both interventions. Second, 147 alcohol-drinking individuals participating in a randomized, placebo-controlled trial investigating the effect of glucagon-like peptide 1 (GLP-1) receptor agonist dulaglutide on smoking cessation. Alcohol consumption was assessed at baseline and after 12 weeks of treatment. The primary endpoint was change in FGF21 levels in persistent drinkers and those who had stopped drinking.
Results
In healthy volunteers, blood alcohol concentration peaked at 90 min and FGF21 levels increased from 125.5 pg/ml to 3149.6 pg/ml at 240 min after beer intake and from 142.0 pg/ml to 184.8 pg/ml after water intake (estimated difference 1386.0 (95% CI 934.55, 1837.44), $P<0.001$). FGF21 levels remained elevated at 720 min after beer intake (525.3 pg/ml vs 302.7 pg/ml, $P=0.028$). In the individuals striving for smoking cessation, median (IQR) baseline alcohol consumption was 3 glasses/week (2, 7) and median (IQR) FGF21 levels were 458.87 pg/ml (278.81, 779.81). At 12 weeks, 27 had stopped drinking alcohol which correlated with lower FGF21 levels (356.18 pg/ml (228.17, 720.75) vs 413.07 pg/ml (223.58, 717.83), estimated difference 228.65 pg/ml (95% CI 14.57, 440.35), $P=0.03$). The results were independent of age, sex, BMI, or smoking status. There was no difference in FGF21 levels between intervention ($P=0.3$) or smoking status ($P=0.1$).
Conclusions
Our findings suggest a dynamic response in FGF21 levels, with moderate acute alcohol consumption inducing elevated FGF21 levels, reflecting metabolic liver stress. In contrast, the reduction in long-term moderate alcohol consumption was associated with lower FGF21 levels, indicative of potential liver recovery These insights contribute to our understanding of the interplay between alcohol consumption and FGF21 dynamics, emphasizing the importance of both short and long-term considerations in liver health.

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EP564

Evaluation of serum prolidase levels in acromegaly patients

Cansu Bezgincan Cayli[1], ÖZGE ÖZER[2], Huseyin Kayadibi[3], Aysen Akalin[2], Medine Nur Kebapci[2], Ozben Ozden Isiklar[3] & Goknur Yorulmaz[2]
[1]Eskisehir Osmangazi University, Meselik Campus, İnternal Medicine, Eskisehir, Turkey;[2]Eskisehir Osmangazi University, Meselik Campus, Endocrinology, Eskisehir, Turkey;[3]Eskisehir Osmangazi University, Meselik Campus, Medical Biochemistry, Eskisehir

Introduction
Acromegaly is a rare disease with high morbidity and mortality rates that occurs due to growth hormone (GH) hypersecretion from adenoma in somatotroph cells in the pituitary gland. It is thought that chronically high GH and Insulin-like Growth Factor-I (IGF-1) levels in its pathogenesis increase tissue collagen synthesis due to fibroblast activation. Prolidase enzyme is also the catalyst of the rate-limiting step of collagen synthesis. In our study, we planned to investigate prolidase enzyme levels in acromegaly patients who applied to our clinic.
Patients and Methods
31 acromegaly patients and 26 healthy volunteers were included in the study. The patients' age, gender, age at diagnosis, disease duration, diagnosis and current GH and IGF-1 levels, sedimentation, CRP, white blood cell values, serum prolidase enzyme level, imaging, and medical treatments were scanned from their files.
Results
The average age at diagnosis of the acromegaly group was 44.64 ± 11.58. The lowest age at diagnosis was 19, and the highest age at diagnosis was 72. The average disease duration was 6.8 ± 4.77 years. While the average prolidase level in the patients was 1111 ± 179.5 U/l, it was 1270.5 ± 282 U/l in the control group. There was no statistically significant difference between the acromegaly group

and the control group ($P=0.17$). There was no correlation between acromegaly disease duration and prolidase level ($r=0.938$). It was observed that there was a correlation between the development of visual field defect and prolidase level ($P=0.019$).
Conclusion
There is a few study in the literature evaluating prolidase enzyme activity in the acromegaly patient group. The results in our study may be related to the effect of examining a limited patient group. Further studies are needed to examine different parameter dynamics with long-term follow-up in large patient groups to elucidate the relationship between acromegaly and prolidase enzyme.

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EP565

Hyperprolactinaemia as a reason for referral to specialist consultation

Jose Alvaro Romero Porcel[1], Celia Gallego Díaz[1], Sara Hami Gil[1], Pavle Puzigaca[1] & María Victoria Cózar León[1]
[1]Hospital Virgen de Valme, Endocrinología, Nutrición, Sevilla, Spain

Objective
Analysis of referrals from Primary Care to the Endocrinology Department for analytical findings of elevated prolactin levels and their subsequent management after initial assessment.
Material and methods
Retrospective descriptive study of 118 patients who were referred to the Endocrinology and Nutrition department of the Dos Hermanas Peripheral Specialities Centre between October 2020 and December 2022. Patients already diagnosed with hyperprolactinaemia who were lost to follow-up and those who did not carry out the requested tests and could not be re-evaluated after the first consultation were excluded from the analysis.
Results
Most referrals were women (95.8%) with a peak age between 18 and 25 years (40.7%). The most frequent reason for requesting the initial blood test by their primary care physician was oligomenorrhoea (35.6%), followed by those with no stated or confirmed reason (22%). The prolactin levels for which they were referred were less than 100 pg/ml (mean value 65.3 ± 40.4 pg/ml) in 92.3%, with the smallest proportion (37%) being performed correctly (in follicular phase, at rest and with extraction 30 minutes after venipuncture). Of this total, 76% were normalised following our extraction recommendations. These non-pathological results were reported telematically in 47.9% of cases.
Conclusions
Most referrals for hyperprolactinaemia could be avoided with a correct blood collection, given the high rate of normalisation in this way, without requiring referral to a specialist clinic. For this reason, and once referred, the telematic review of results is an effective option for informing patients, avoiding the need to be present in person and the associated waiting time.

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EP566

Body composition in patients with acromegaly: the impact of disease control and medical treatment

Dario De Alcubierre[1], Tiziana Feola[1], Ludovica Vincenzi[1], Lucrezia Lamorgese[1], Valentina Sada[1], Giulia Puliani[2], Alessia Cozzolino[1], Emilia Sbardella[1], Marie-Lise Jaffrain-Rea[3] & Andrea Isidori[1]
[1]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy;[2]IRCCS Regina Elena National Cancer Institute, Rome, Italy;[3]Neuromed Institute, IRCCS, Neuroendocrinology, Pozzilli, Italy

Background
Acromegaly is associated with increased lean mass (LM) and reduced fat mass (FM), therefore body mass index is not a reliable parameter of body composition in this context. Moreover, the contributing factors to these alterations, along with their potential reversibility after achieving disease control, remain poorly understood. This study aimed to detect body composition alterations, as well as to investigate the impact of biochemical control and different medical treatments, in patients with acromegaly.
Methods
In this cross-sectional, case-control study, consecutive patients with active acromegaly (ACRO) were compared with age and sex-matched healthy controls (CTRL). Anthropometric and hormonal parameters were recorded. Total and region-specific body composition parameters were assessed via dual-energy x-ray absorptiometry (DEXA) scanning, measuring visceral adipose tissue (VAT), LM, and FM percentages. Appendicular lean tissue (ALT) and overall skeletal muscle index (SMI) were then calculated according to standardized *formulae*. Disease control of acromegaly was defined by IGF1 levels per upper limit of normal (IGF1 $\times$ ULN) <1.2. Statistical analysis was performed with parametric and non-parametric tests, as appropriate. Data are expressed as mean $\pm$ standard deviation or median (interquartile range) according to data distribution. Statistical significance was set at $P<0.05$.
Results
40 patients with active acromegaly (ACRO) [22 males, median age 56.5 (41-64)] and 20 matched controls were enrolled. Among ACROs, 23 patients presented with biochemical control, 23 were on somatostatin analogs (SSAs), 9 were on pegvisomant (PEG), either as monotherapy or in combination with SSAs, and 8 patients were naïve to medical treatment. ACROs exhibited higher ALT ($P=0.032$) and a trend towards higher SMI ($P=0.065$) compared to CTRLs. In ACROs, no differences in body composition parameters were detected based on disease control status, except for a trend towards lower trunk fat ($P=0.056$) and higher total lean mass percentage ($P=0.070$) in poorly controlled patients. GH negatively correlated with VAT ($r=$-0.404, $P=0.016$), total ($r=$-0.486, $P=0.003$) and trunk ($r=$-0.564, $P<0.001$) fat percentage; IGF1xULN positively correlated with total lean mass percentage ($r=0.312$, $P=0.050$). Lastly, after stratifying ACROs according to type of medical treatment, no significant differences in body composition parameters were observed among SSA-treated, PEG-treated, and naïve patients.
Conclusions
Our analysis revealed increased lean tissue and skeletal muscle mass in patients with acromegaly compared to matched controls. These changes seem, in part, linked to the direct impact of hormonal excess; however, the role of different medical treatments requires further clarification.

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EP567

Measurement of visceral fat area in women with hypopituitarism receiving conventional hormone replacement therapy: a case-control study

Salma Salhi[1], Ibtissem Oueslati[1], Seif Boukriba[2], Elyes Kamoun[1], Meriem Yazidi[1], Nadia Khessairi[1], Fatma Chaker[1], Habiba Mizouni[2] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia;[2]La Rabta University Hospital, Department of Radiology, Tunis, Tunisia

Introduction
Visceral fat area (VFA) represents the amount of fat stored in the abdominal cavity around internal organs. It is increasingly recognized as a crucial marker of metabolic health and cardiovascular risk. The aims of the present study were to measure VFA and to assess its associated factors in women with complete anterior hypopituitarism.
Methods
We conducted a cross-sectional study including 50 patients with a complete anterior hypopituitarism secondary to Sheehan syndrome, receiving conventional hormone replacement therapy, and 50 age and body-mass index (BMI)-matched controls. Participants had a clinical examination, laboratory tests and an abdominal computed tomography scan to calculate the VFA.
Results
The mean age was 62.2 ± 9.4 years in the patients and 60.6 ± 8.4 years in controls ($P=0.385$). The mean BMI was 29.6 ± 6.0 kg/m^2 in patients and 30.0 ± 5.0 kg/m^2 in controls ($P=0.741$). Patients had a significantly higher waist circumference than controls (respectively: 101.3 ± 10.2 cm vs 95.7 ± 10.5 cm; $P=0.007$). Parietal fat area was comparable between the two groups (patients: 270.2 ± 97.7 cm^2; controls: 242.7 ± 107.3 cm^2; $P=0.154$). However, VFA was significantly higher in patients (170.6 ± 58.8 cm^2) than in controls (148.8 ± 73.8 cm^2) ($P=0.030$). Visceral adiposity, defined by a VFA ≥ 150 cm^2, was observed in 64% of patients and 39% of controls ($P=0.014$). Sheehan syndrome was positively associated with visceral adiposity (Odds Ratio $=2.78$, 95%-Confidence interval: 1.21-6.37; $P=0.014$). Age ($P=0.022$) and sedentary ($P=0.010$) were associated with visceral adiposity. However, diagnostic delay, duration of the disease, family history of metabolic disorders, as well as GH and FT4 levels, and hormone replacement therapy were not associated with visceral adiposity.
Conclusions
VFA was significantly higher in women with hypopituitarism than in controls. Visceral adiposity was more prevalent in patients compared to age and BMI matched controls. Its associated factors were age and sedentary.

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EP568

Diagnostic discordance of osteoporosis in acromegaly: a comparison of quantitative computed tomography and dual-energy X-ray absorptiometry

Chen Shuaiming[1], Li Jing[2], Yu Yerong[2] & Li Jianwei[2,2]
[1]West China Hospital, Sichuan University, Department of Endocrinology & Metabolism, Chengdu;[2]West China Hospital, Sichuan University, Department of Endocrinology & Metabolism, Chengdu, China

Background
Patients with acromegaly have an increased risk of vertebral fractures, yet normal or elevated bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA). This suggests that DXA may not be a reliable tool for assessing BMD in acromegalic patients. Multiple studies have suggested that patients with acromegaly have compromised trabecular bone but not cortical bone. Quantitative computed tomography (QCT) represents a three-dimensional technique for quantifying volumetric trabecular bone density, which is not affected by osteophytes and scoliosis commonly seen in acromegalic patients.
Objective
To examine the diagnostic discordance of osteoporosis between QCT and DXA in patients with acromegaly, and explore influencing factors of BMD in spine by DXA and QCT, separately.
Methods
We enrolled patients diagnosed with acromegaly consecutively at West China Hospital between January 2021 and December 2023, and excluded patients with plurihormonal PIT-1 positive pituitary adenoma. The diagnostic criteria established by the World Health Organization in 1994 for DXA were employed to diagnose osteoporosis and osteopenia, while the criteria endorsed by the International Society of Clinical Densitometry were utilized for QCT. Minor discordance was defined as the presence of adjacent diagnostic classes between the two techniques, whereas major discordance arose when one method diagnosed osteoporosis while the other indicated normal bone health.
Results
We enrolled 53 participants (28 females/25 males), with a median age of 44 years old. Three participants were diagnosed with osteoporosis/low bone mass by DXA, and 5 with osteoporosis by QCT. Major discordance, minor discordance, and concordance in diagnoses between the two techniques were 3.8%, 18.9%, and 77.4%, respectively. Patients consistently diagnosed with osteoporosis had higher age (59 vs 42 years old, $P<0.005$) and lower BMD by QCT (110.1 g/cc vs 153.8 g/cc, $P<0.005$) compared to patients without discordant diagnoses. Multiple linear regression analyses showed that age ($\beta=-0.516$, $P<0.005$), body mass index ($\beta=-0.209$, $P=0.024$), growth hormone ($\beta=0.187$, $P=0.023$), and female ($\beta=-0.178$, $P=0.039$) were independent factors of BMD by QCT, while none of them were independent factors of BMD by DXA. The adjusted R2 of this model was 0.429.
Conclusion
Our study demonstrated that QCT might be a more sensitive tool to assess bone health in patients with acromegaly, especially in those who are younger and have less severe bone loss. BMD data by QCT can be largely explained by clinical features of acromegalic patients but not by DXA, which suggests that QCT may be a superior diagnostic tool in this population compared with DXA.

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EP569

Neurosteroids and cognition in cushing disease

Sebnem Burhan[1], Ebubekir Akpınar[2], Sevim Eyupoglu[3], Buruç Erkan[2], Mutlu Niyazoglu[1] & Esra Hatipoglu[1]
[1]University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Department of Endocrinology and Metabolism Diseases, Istanbul, Turkey;[2]University of Health Sciences, Basaksehir Cam ve Sakura City Hospital, Department of Neurosurgery, Istanbul, Turkey;[3]Brain 360 Special Psychology Laboratory, Psychology

Objective
Neurosteroids, a unique hormone group, are recognized for their impact on cognitive processes. The primary objective is to assess the correlation between cognitive function and NS levels in cases of Cushing's disease and a control group of nonfunctional pituitary adenoma (NFPA).
Design
The study comprised 26 individuals diagnosed with Cushing's disease (CDG), while a control group (CG) consisted of 14 age-gender matched participants with NFPA. Eighteen different neurosteroid levels were investigated. Montreal Cognitive Assessment Test (MoCA) to evaluate attention, sustained attention, information processing speed; Selective Recall Test (SRT) to evaluate verbal learning and delayed recall; Spatial Recall Test (SPART) to evaluate visuospatial learning and delayed recall; Symbol Digit Modalities (SDM) to evaluate attention and processing speed; Animal Naming Test (ANT) to evaluate verbal fluency and semantic memory, Verbal Fluency Test (FAS) for evaluate verbal fluency.
Results
There was no statistically significant difference in age between CDG and CG ($P=0.918$). The median age of the CDG was 49.5 years and the median age of the CG was 44 years. (IQR: 40.5-58.0, IQR: 34.5-64.0) There were 5 males, 19.2% and 21 females, 80.2% in CDG, and 4 males, 28.6%, and 10 females, 71.4% in CG. There was no difference between the sexes ($P=0.5$). There was no difference in cognitive function tests in patients with CDG and CG. In CG, there was a negative correlation between verbal memory performance measured by SRT test and aldosterone level ($r=-.667$, $P=.009$). In CG, there was a positive correlation between FAS and corticosterone, 7-OH-Pregnenolone, and dihydrotestosterone ($r=.731$, $P=.003$, $r=.738$, $P=.003$, $r=.969$, $P=.031$). In CG, ANT was positively correlated with corticosterone and 7-OH-Pregnenolone ($r=.787$ $P=.001$, $r=.767$ $P=.001$). In CG, there was a positive correlation between the SDM and corticosterone and 7-OH-Pregnenolone ($r=541$ $P=.046$, $r=.545$ $P=.044$). In CDG, there was a positive correlation between learning verbal memory, corticosterone, and deoxycorticosterone ($r=.401$ $P=.042$, $r=.446$, $P=.043$). In CDG, MoCA scores tend to be negatively associated with aldosterone levels ($r=-405$ $P=.062$). There was a negative correlation between the visuospatial attention test and allopregnanolone($r=-.571$, $P=.021$). In CDG, deoxycortisol levels were positively correlated with ANT($r=.391$, $P=.048$), and cortisol, corticosterone, and deoxycorticosterone levels tended to be associated with ANT ($r=.385$, $P=.052$, $r=.361$ $P=0.070$, $r=.423$, $P=.056$). Visio-spatial memory and allopregnanolone levels tend to be negatively correlated ($r=-467$, $P=.068$).
Conclusion
Some particular neurosteroids could potentially influence certain cognitive abilities in cases with CD.

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EP595

Prolactinomas and macroprolactin: the complexity of interpreting macroprolactin data

Sjana Kos[1] & Jorn Assmann[1]
[1]Maasstad Hospital, Clinical Chemistry Rotterdam, Netherlands

Hyperprolactinemia is a condition that can present itself in many different contexts ranging from physiological during pregnancy, pharmacological (e.g., due to antidepressants or antipsychotics) or truly pathological. Pathological mechanisms of hyperprolactinemia include pituitary tumors, tumor metastases, autoimmune diseases and ectopic prolactin producing tumors. In addition, prolactin values may be elevated due to macroprolactin. Detection of macroprolactin through PEG-precipitation is performed under various conditions in different laboratories and reporting of post PEG-prolactin is performed through different approaches. Also, prolactin assays have distinct sensitivity towards macroprolactin. We show the impact of switch from one prolactin measuring method (Siemens Immulite XPi) to another (Roche Cobas Pro®). Should gender specific prolactin monomeric reference values be used, on average approximately 25% of all hyperprolactinemic samples are deemed hyperprolactinemic measured by both methods (Table 1). When adding $<50\%$ recovery (Percent recovery = (post-PEG prolactin ÷ pre-PEG prolactin) × 100; $<50\%$ Recovery means that more than 50% of the measured pre-PEG prolactin comprises of prolactin adducts (e.g., macroprolactin).) to the abovementioned rule of leveling within the monomeric reference intervals, a substantially smaller percentage of Siemens and Roche samples would be assumed to be macroprolactinemic with 10.8% and 2.3% respectively. This would especially be impactful if no post-PEG prolactin value would be reported along with the%-recovery and exemplifies the importance of being acquainted with the rules a laboratory sets for the presence of macroprolactin, but also the assay the lab utilizes. Unfortunately, such technicalities can impossibly be captured in guidelines and might be unknown to the clinician even though they could potentially impact decision making (especially when the post-PEG prolactin value is not reported and laboratory reports only recovery value). Thus, in final reporting, it is very important to define laboratory specific monomeric reference intervals when the presence of macroprolactin is defined by normalizing within monomeric reference intervals. In addition, post-PEG prolactin values should be reported when utilizing recovery as a defining factor for the presence of macroprolactin in order to prevent misdiagnosis. Differences between both reporting strategies might be smaller or larger depending on the assay used and its sensitivity to macroprolactin. Therefore, the likelihood of the presence of true pathological hyperprolactinemia always needs to be assessed in the context of the assay used, the sensitivity of the assay to prolactin adducts, type of PEG polymer used and the manner in which prolactin adducts are reported by the laboratory.

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EP597

Hormonal implication in pediatric intracranial hypertension

Rekik Mona[1], Kammoun Sonda[1], Jallouli Aida[1], Nabila Rekik Majdoub[2] & Trigui Amira[1]
[1]Habib Bourguiba Hospital, Department of ophthalmology; [2]Hedi Chaker Hospital, Department of endocrinology

Introduction
Pediatric intracranial hypertension (PIH) refers to increased pressure within the skull in children. While it is less common than in adults, hormonal factors can play a role in certain cases. Changes in hormone levels during puberty, particularly in girls, may contribute to this condition. This form is sometimes referred to as Idiopathic Intracranial Hypertension of Adolescence. We report a case of bilateral papilledema revealing idiopathic intracranial hypertension related to puberty
Observation
A 13-year-old patient, with no medical history, presented with complains of headache and diplopia for 3 days. The ophthalmological examination found visual acuity at 10/10 in both eyes, left VI nerve palsy, and bilateral papilledema. Goldman visual field testing revealed an enlargement of the blind spot in both eyes. Body mass index, brain magnetic resonance imaging, and laboratory tests including endocrine assessment were normal. Lumbar puncture showed an intracranial pressure of 50 mmHg. The diagnosis of idiopathic intracranial hypertension related to puberty was established. The patient was treated with acetazolamide and underwent depletive lumbar puncture. Outcome was favorable with complete regression of headaches, oculomotor disorders and normalization of intracranial pressure. After 5 years of follow-up, the patient remained stable without any recurrence
Conclusion
PIH is a rare condition, sometimes leading to severe visual involvement. The pathogenic mechanisms of this condition remain poorly understood. The association between PIH and puberty has been demonstrated. Indeed, puberty is characterized by an increase in growth hormone (GH) levels that crosses the blood-brain barrier and enhances cerebrospinal fluid production by the choroid plexus.

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EP600

Hypogonadism in male patients with cushing's syndrome: prevalence and outcome

Elisabeth Nowak[1], Frederick Vogel[1], Leah Braun[1], Stephanie Zopp[1], German Rubinstein[1], Pia Adam[1], Junia Schweizer[1], Katrin Ritzel[1], Felix Beuschlein[2] & Martin Reincke[1]
[1]Department of Medicine IV, LMU University Hospital, LMU Munich, Germany;[2]Department of Endocrinology, Diabetology, and Clinical Nutrition, University Hospital Zurich, Zurich, Switzerland

Background
Secondary hypogonadism (SH) is a common comorbidity of Cushing's syndrome (CS) in men. There is a large overlap in associated symptoms and comorbidities between hypogonadism and hypercortisolism. To date, the influence of coexistent SH on clinical and biochemical parameters in CS is largely unknown and longitudinal data investigating its recovery during the remission phase are scarce.
Hypothesis
We hypothesized that SH is a frequent and important risk factor for adverse outcomes of myopathy and osteoporosis.
Participants and Methods
We included 30 treatment-naïve adult men with overt CS diagnosed since 2012 with available baseline testosterone data. Hypogonadism was diagnosed based on age-specific cut-offs of total testosterone (TT). Outcomes were compared to 30 age- and BMI-matched male controls. In a subgroup of 20 men with CS, a longitudinal analysis after remission was conducted at 6, 12, and 24 months.
Results
Men with CS had significantly lower levels of TT, bioavailable T, and free T compared to controls ($P<0.0001$) with lowest levels in ectopic CS. At baseline, 16 (53%) men with CS had SH: 9/21 (42%) with pituitary, 5/6 (83%) with adrenal, and 2/3 (67%) with ectopic CS. Glucocorticoid excess measured by late night salivary cortisol was weakly but significantly inversely correlated with bioavailable T ($r=-0.396$, $P=0.0499$) and other reproductive hormones and there was a similar trend for serum cortisol ($r=-0.373$, $P=0.0605$). As expected, muscle function, both self-reported and confirmed by hand-grip strength, was significantly lower in men with CS ($P<0.0001$ and $P=0.0482$), whereas osteoporosis was more frequent in men with CS vs controls (50% vs 7%, $P<0.0001$). However, when stratified according to presence or absence of SH there was no significant difference in signs and symptoms of CS. SHBG correlated negatively and significantly with red blood cell (RBC) parameters (Haemoglobin, haematocrit, erythrocytes, and MCH, $r=-0.42$ to $-0,47$, $P<0.05$), with a similar trend for related reproductive hormones. Following successful surgery, testosterone levels increased significantly ($P=0.0010$), reaching normal levels six months after remission. Despite normalisation of SHBG levels, RBC parameters remained lower in men with CS even two years after remission.
Conclusion
SH is a common comorbidity in men with all types of endogenous CS and is reversible in most patients after six months of successful therapy. Despite being related to glucocorticoid excess, SH was not directly associated with myopathy. However, there seems to be a correlation with RBC parameters, some of which do not normalise even two years after remission.

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EP601

Personalized dosimetry as a key for optimizing radioligand therapy (RLT) with 177Lu- or 177Lu/90Y-DOTA-TATE in patients with well-differentiated neuroendocrine tumors – an update on the initial results of the DUONEN multicenter study

Marta Opalinska[1], Grzegorz Kamiński[2], Marek Dedecjus[3], Aldona Kowalska[4], Maciej Kolodziej[2], Marek Saracyn[2], Piotr Garnuszek[5], Wioletta Lenda-Tracz[6], Danuta Gąsior-Perczak[4], Anna Borkowska[6], Joanna Januszkiewicz-Caulier[3], Joanna Długosińksa[3], Anna Sowa Staszczak[1], Anna Budzyńska[7], Agata Kubik[7], Krzysztof Kacperski[7], Wioletta Chalewska[3], Paulina Cegła[3], Alicja Hubalewska-Dydejczyk[1] & Renata Mikolajczak[5]
[1]Jagiellonian University Medical College, Chair and Department of Endocrinology, Krakow;[2]Military Institute of Medicine - National Research Institute, Department of Endocrinology and Isotope Therapy, Warsaw;[3]National Institute of Oncology, National Institute of Oncology, Warsaw;[4]Jan Kochanowski University in Kielce, Collegium Medicum, Kielce, Poland;[5]National Centre for Nuclear Research, Radioisotope Center Polatom, Otwock-Swierk;[6]Jagiellonian University Medical College, Faculty of Health Sciences, Kraków, Poland;[7]Military Institute of Medicine - National Research Institute, Department of Nuclear Medicine, Warsaw

Aim/Introduction
Peptide Receptor Radionuclide Therapy (PRRT) is an effective treatment for disseminated neuroendocrine tumors (NETs) expressing somatostatin receptors. Despite many published studies, the consensus on the optimal PRRT treatment algorithm has not been reached yet. The main objective of the DUONEN multicenter, randomized, phase III study (EUDRACT No: 2020-006068-99) is the development of a dosimetry-based personalized PRRT algorithm. The second goal includes the assessment of the efficacy of dosimetry-based personalized therapy with mixed [^{177}Lu]Lu- and [^{90}Y]Y-DOTA-TATE in comparison to [^{177}Lu]Lu-DOTA-TATE in standard radioactivity doses (7400 MBq). The personalized dosimetry is designed to deliver maximal radiation dose to the tumor tissue while maintaining the safety of critical organs.
Materials and Methods
Adult patients with advanced, unresectable well-differentiated (G1 and G2) NETs, progressing on long-acting somatostatin analogues are randomized into four arms: A - treated with [^{177}Lu]Lu -DOTA-TATE with constant radioactivity of 7400MBq per cycle B - treated with mixed [^{177}Lu]Lu-DOTA-TATE and [^{90}Y]Y-DOTA-TATE, initially at a ratio of 3700:1850MBq/MBq. The [^{177}Lu]Lu-DOTATATE radioactivity remains constant in all cycles, and the [^{90}Y]Y-DOTA-TATE radioactivity is adjusted in the next cycles, based on bone marrow and kidney dosimetry to the highest radiation dose in the tumor tissue C - analogous to arm B, except that here the radioactivity of [^{90}Y]Y-DOTA-TATE remains constant and the radioactivity of [^{177}Lu]Lu-DOTA-TATE is adjusted depending on the dosimetry results D – first dose analogous to arm A and individualized in the next cycles based on dosimetry results. The treatment efficacy is evaluated on morphological imaging (CT or MR) according to RECIST 1.1 criteria. The safety of PRRT is assessed by the kidney and bone marrow biochemical function.
Results
35 patients have been enrolled to the study (arm A-9, arm B-9, arm C-9, arm D-8). Six patients discontinued therapy due to disease progression or its side effects. By now 94 cycles of PRRT were administered, including 57 fixed doses (first doses or arm A). Out of the 37 doses adjusted based on personalized dosimetry, the radioactivity dose was increased in 16 and decreased in 21. The first eight patients were evaluated post-PRRT according to RECIST 1.1 criteria achieving stable disease in 3 cases, and partial and complete response in 4 and 1 case, respectively.
Conclusions
Personalized renal and bone marrow dosimetry affects individual PRRT doses in each subsequent treatment cycle. Acknowledgments: The study is funded by the Medical Research Agency (Project number 2019/ABM/01/00077-00).

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EP677

Imaging the sella turcica in sheehan syndrome: is there a correlation with clinical presentation?

Sawsen Nouira[1], Hamza Elfekih[1], Amel Maaroufi[1], Koussay Ach[1], Yosra Hasni[1] & Molka Chaieb[1]
[1]University Hospital Farhat Hached, Endocrinology Sousse

Introduction
Few studies have considered the natural history of pituitary anatomy in Sheehan syndrome (SS), as seen on magnetic resonance imaging (MRI) or CT scan. An imaging study of the sella turcica was carried out in patients with SS. The aim was to look for correlations between radiological findings and the degree of endocrine insufficiency on the one hand, and diagnosis delay on the other.
Methods
This is a retrospective study carried out between 1977 and 2021 on patients with SS followed at the endocrinology department of the Farhat Hached Hospital in Sousse, Tunisia. Clinical and radiological findings were documented and reviewed.
Results
Fifty-four patients diagnosed with SS were included. The mean age at diagnosis was 47 ± 14 years. The mean diagnostic delay was 15 years. Twenty patients had complete anterior hypopituitarism, 34 with at least one preserved pituitary function. Pituitary imaging was normal in 7 cases. The sella turcica was totally empty in 15 patients, partially empty in 32 cases. A remnant of pituitary tissue was found more frequently (56%; $n=22$) in those with dissociated hypopituitarism ($P \leq 0.005$). Patients with an empty sella turcica at the time of diagnosis had a longer diagnostic delay (18vs14 years; $P \leq 10^{-3}$).
Conclusion
The presence of a pituitary remnant is inversely correlated with the duration and extent of the disease. The empty sella should be the end point of the process, indicating the necrosis that has occurred. In women whose diagnosis has been delayed, the discovery of an empty sella is frequent.

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EP679

Oral mucosal lesions and dental hygiene assessment in acromegaly patients

Burak Can Cengiz[1,1], Sefika Polat[2], Elif Yildizer[3] & Ihsan Ates[1]
[1]Ankara Bilkent City Hospital, Internal Medicine, Ankara, Turkey;[2]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara, Turkey;[3]Ankara Yildirim Beyazit University, Oral, Dental and Maxillofacial Radiology, Ankara, Turkey

Aim
There is a lack of studies in the literature evaluating the relationship between oral health, oral mucosal lesions, dental hygiene status, and disease prognosis in acromegaly patients. Our study aimed to assess oral mucosa in acromegaly patients, predict dental problems that may develop, correlate oral lesions and mucosal status with patients' IGF-1 levels, investigate the relationship with the treatment method used, and evaluate the oral mucosal damage caused by concomitant and secondary chronic diseases accompanying acromegaly
Methods
The study includes acromegaly patients aged 18-65 and a control group of healthy volunteers with similar demographics. Data collection involves demographic information, clinical history, laboratory findings, and a 6-item questionnaire. Intraoral examinations are conducted by an experienced specialist using dental tools and probes.
Results
Results reveal no significant age difference between patients and the control group. TSH values are lower, while HbA1c and fasting glucose values are higher in patients. Tongue lesions are significantly more prevalent in patients. However, periodontal and plaque indices, as well as oral dryness scores, are similar between the groups. No correlation is found between disease duration, hormonal levels, and oral hygiene parameters.
Discussion
In our study, we found that oral mucosal lesions in acromegaly patients increased significantly compared to the control group. Especially, tongue lesions and the rate of having tongue lesions were observed to be higher. These results suggest that oral health status in acromegaly patients might reflect the disease's specific nature. Additionally, an impact on glucose metabolism and potential increased diabetes risk in acromegaly patients was observed. However, these effects were not considered clinically significant. The findings highlight the importance of regularly monitoring oral health status in acromegaly patients.

Keywords: Acromegaly, Oral Mucosal Lesions, Dental Hygiene
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EP681

Ophthalmological complications during acromegaly: about 76 cases

Alida Mireille Uwimana[1], Nassim Essabah Haraj[1], Siham El aziz[1] & Asma Chadli[1]
[1]CHU Ibn Rochd, Department of Endocrinology and Metabolic Diseases, Casablanca, Morocco

Introduction
Acromegaly is a rare disease with an insidious course characterized by several complications that determine its prognosis. This is a case study about 76 patients treated at CHU Ibn Rochd to evaluate the ophthalmological impact of this disease.
Material and methods
This is a retrospective study of 76 cases of acromegaly followed in the endocrinology department of Ibn Rochd University Hospital from January 2005 to October 2023. All our patients benefited from an ophthalmological evaluation and visual field. The statistical analysis was done by EXCEL software.
Results
The average age was 49 years with a sex ratio F/M of: 0.33. The average BMI rate was 29 kg/m^2 with overweight in 12 patients (20.8%), and obesity in 23 patients (41.6%). The average duration of the disease was 9 and a half years; The average IGF1 level was 2.3 times normal and the etiological diagnosis was a pituitary adenoma in all patients. Pituitary tumor syndrome (THS) (96%) and acro -facial dysmorphia (93%) were the main reasons for consultation. Visual disturbances linked to STH were noted in 50% of our patients, including blindness ($n=2$), diplopia ($n=9$) and visual blur ($n=38$). A decrease in visual acuity was observed in 91.2%. Ophthalmological examination detected papillary pallor in 30%, glaucoma in 6.5% and diabetic retinopathy in 7.8%. The visual field showed bitemporal hemianopia in 40.35%, diplopia in 1.75%, amputation of the visual field in 10.52%, a slight bitemporal deficit in 14.9%, a slight peripheral deficit in 8, 77% Bitemporal hemianopia and visual field amputation were the most common visual field alterations
Discussion
Somatotropic adenomas are characterized by an insidious evolution and a generally late diagnosis during a tumor syndrome and visual disturbances which reflect tumor invasion at the expense of the cavernous sinus and the optical pathways.
Conclusion
Preserving the visual prognosis remains one of the major objectives of treatment. It is therefore important to evaluate the visual impact by an ophthalmological and visual field examination during the initial diagnosis and during the follow-up of acromegaly. Close collaboration between endocrinologist, neurosurgeon and ophthalmologist is necessary.

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EP683

Cured by apoplexy-a case series

Stefanie Gross[1], Ionut Petre[1], Theodora-Mădălina Pavel[1], Dan Alexandru Niculescu[1,2], Cristina Capatina[1,2,3], Constantin Cucu[1,2] & Catalina Poiana[1,2]
[1]"C.I. Parhon" National Institute for Endocrinology, Endocrinology I, Bucharest, Romania;[2]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania;[3]

Pituitary apoplexy, a rare but impactful complication of pituitary adenomas, involves sudden hemorrhage or infarction within the pituitary gland, leading to diverse clinical presentations and complications, ranging from severe headaches to panhypopituitarism. This case series explores the intersection of pituitary apoplexy and the subsequent cessation of tumor secretion in five patients with various secreting pituitary adenomas, offering unique insights into potential curative effects. In the first case, a male with a 6 mm ACTH-secreting microadenoma experienced one year of remission post-apoplexy, only to face a subsequent relapse necessitating enrollment in a cortisol receptor blocker clinical study. In the second case, the patient experienced a critical episode characterized by intense headache, vomiting, and loss of consciousness two months prior to presenting at our department. Upon examination, the patient displayed acromegaloid clinical features and presented with newly discovered diabetes type 2. However, blood tests indicated panhypopituitarism, marking a significant clinical paradox. The MRI findings further substantiated the diagnosis, revealing signs of necrosis that strongly suggested the occurrence of pituitary apoplexy. This case underscores the complexity of pituitary apoplexy's clinical manifestations, where symptoms spanning acromegaly and panhypopituitarism coexist, necessitating a meticulous diagnostic approach for appropriate management In another case, an acromegaly patient with modest symptoms but biochemical evidence encountered pituitary apoplexy just before scheduled neurosurgery, subsequently considered cured. The final patient, diagnosed with a GH and prolactin secreting adenoma, experienced pituitary apoplexy resulting in a cure. Remarkably, in this case, a patient with a prolactin and GH-secreting macroadenoma showed GH secretion cessation post-apoplexy, managed with dopamine agonists, with a notable tumor volume reduction

two weeks later. This series collectively highlights the complex and variable outcomes associated with pituitary apoplexy, emphasizing its potential curative impact on different types of secreting pituitary adenomas. The observed changes in hormonal secretion and tumor volume provide valuable insights into the dynamic nature of these adenomas post-apoplexy. If patients successfully overcome the acute phase, pituitary apoplexy may play a beneficial role in achieving a cure for hypersecretion in pituitary adenomas.

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EP687

Differences between genders in acromegaly

Plotuna Iulia-Ştefania[1,2], Melania Balas[1,2], Ioana Golu[1,2], Daniela-Georgiana Amzar[1,2] & Mihaela Vlad[1,2]
[1]"Victor Babeş" University of Medicine and Pharmacy, 2nd Department of Internal Medicine, Endocrinology, Timişoara, Romania;[2]Timiş County Emergency Clinical Hospital, Enocrinology, Timişoara, Romania

Background
Acromegaly is a rare condition associated with increased secretion of growth hormone (GH), most frequently from a pituitary adenoma. Gender can influence the secretion of growth hormone and insulin growth factor 1 (IGF-1). Healthy females appear to have higher spontaneous GH levels. In comparison, active acromegaly is associated with lower IGF-1 levels, possibly due to the inhibitory influence of circulating estrogen on the hepatic production of IGF-1.
Objectives
Our study aimed to evaluate gender-specific differences in patients diagnosed with acromegaly.
Material and Method
The study group included 23 acromegalic patients, aged between 20 and 72 years, 9 men (39.13%) and 14 women (60.85%). The mean age at diagnosis was 55 for females and 43.5 years for males. Data was collected retrospectively, including personal history, clinical examination, laboratory assessment, and magnetic resonance imaging results.
Results
In our cohort of patients, the female sex was predominant. Women were older than men at diagnosis ($P<0.05$) and had a longer estimated disease duration, an aspect that was not statistically significant. The duration of the disease was comparable between groups. GH and IGF-1 were similar between groups, as well as the size of the adenoma. Disease control was achieved in 78% of male and 71% of female patients. The prevalence of pituitary insufficiency was similar between groups. Hypertension was more frequent among women, while obesity and sleep apnea were diagnosed predominantly in men, but without statistical significance. Diabetes mellitus and malignancies were present only in women, but probably due to the small sample size, the results did not reach significance.
Conclusions
Disease control, GH, IGF-1, and disease duration were similar between females and males. Women were older at diagnosis and were more prone to develop DM and malignancies. Men were diagnosed more frequently with sleep apnea, these results are consistent with the fact that they were also more prone to developing obesity.

Keywords: Acromegaly, Pituitary, Gender, Comorbidities
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EP688

Apoplexy of microprolactinoma after cabergoline therapy: rare situation but big emergency

El Jadi Hamza[1] & Moustaghit Imane[2]
[1]Oued Eddahab Military Hospital, Endocrinology, Agadir, Morocco;[2]Oued Eddahab Military Hospital, Endocrinology, Agadir, Morocco

Summary
Pituitary apoplexy (PA) is a rare clinical situation caused by pituitary infarction with or without hemorrhage. Although it is usually spontaneous, dopaminergic agonists (DA) are known to be predisposing factors, particularly Bromocriptine, more rarely Cabergoline. We report the case of a 31 years old female patient, with no notable pathological history, consulted for headaches and menstrual irregularities. Pituitary hormone levels were normal except for hyperprolactinemia at 110 ng/ml (<25). MRI showed a pituitary microadenoma of 7x3 mm. Cabergoline was started at a dose of 0.5 mg per week, which brought the prolactin level down to the normal range (21 ng/ml). Five months later, the patient presented to the emergency room with a sudden headache and decreased visual acuity. The physical examination revealed a patient in good general conditions without shock, the ophthalmological examination showed bilateral papilledema and preserved visual acuity. The visual field showed bilateral scotomas and the brain MRI revealed a necrotic-hemorrhagic transformation of the adenoma with an empty sella turcica. The endocrine work-up did not reveal any hormonal dysfunction. The patient was put on high doses of corticosteroids. The evolution is marked by a clear improvement of the visual field and papillary oedema. PA is a rare situation. The management of apoplexy is multidisciplinary, with hospitalization in a neurosurgical or endocrinological setting in close proximity to a neurosurgical center recommended. Glucocorticoid treatment should be started immediately in case of (near constant) corticotropic insufficiency, hemodynamic instability and altered consciousness. Decompression surgery is indicated in cases of impaired consciousness, recent or worsening severe visual impairment. Isolated oculomotor damage may be an indication for surgery for some teams but not for others. Conservative treatment is considered under the cover of corticosteroid therapy and clinical and ophthalmological monitoring. It is indicated in cases of contraindication to surgery (when the benefit/risk balance is against surgery), stable or long-standing moderate visual disorders or isolated oculomotor paralysis. Often reported with Bromocriptine, PA can also occur with Cabergoline. Due to the high mortality and morbidity of apoplexy, it should be borne in mind that close monitoring is necessary when treatment with DA is prescribed and the patient should be informed of this risk. Although DA precipitate risk, treatment can be continued for hormonal and anti-tumor remission.

Keywords: pituitary apoplexy prolactinoma, Cabergoline.
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EP689

Acromegaly and morris syndrome: description of a clinical case

Simone Antonio De Sanctis[1,2], Sabrina Chiloiro[1,2], Antonella Giampietro[1,2], Liverana Lauretti[3], Marco Gessi[3], Guido Rindi[4], Alessandro Olivi[3], Alfredo Pontecorvi[1,2], Laura De Marinis[1,2], Francesco Doglietto[3] & Antonio Bianchi[1,2]
[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Endocrinologia e Diabetologia, Rome, Italy;[2]Fondazione Policlinico Universitario A. Gemelli IRCCS, Dipartimento di Medicina Traslazionale, Rome, Italy;[3]Fondazione Policlinico Universitario A. Gemelli IRCCS, Neurosurgery, Rome, Italy;[4]Fondazione Policlinico Universitario A. Gemelli IRCCS, Department of Life Sciences and Public Health, Section of Anatomic Pathology, Rome, Italy

Introduction
The Morris syndrome, is a rare X-linked disorder in which patients with XY chromosomal makeup (corresponding to a male genotype) develop female sexual characteristics. Acromegaly is a rare disease related to excessive production of growth hormone (GH) and insulin growth factor-I (IGF-I). Rarely, acromegaly was reported to be associated to a chromosomal microduplications of Xq26.3, responsible for early onset form of acro-gigantism. However, cases of acromegaly associated with Morris syndrome have never been documented in the literature.
Case-report
We present the case of a 49-year-old woman with Morris syndrome, diagnosed in 1992 and undergoing gonadectomy and hormone replacement therapy for about 15 years, who came to our attention in June 2022 after removal of a somatotropinoma. The diagnosis of acromegaly was suspected by finding typical facies and acral extremity growth, reported to have arisen from 10 years. The patient underwent mandibular reduction surgery and removal of tubular adenoma of the colon in 2010. In June 2021, the patient performed random GH, IGF-I and prolactin (PRL) dosages which was found to be altered (GH: 7.14 mg/l, IGF-I: 686 ng/mL, PRL: 17.9 ng/ml). The GH dosages after 75 grams oral glucose tolerance test showed a GH paradoxical response (60 minutes after glucose administration GH was 8.99 mg/l, after 120 minutes GH was 13.40 mg/l). A contrasted pituitary MRI showed the presence of an 8 mm intrasellar lesion. Therefore, a transsphenoidal resection of the pituitary tumor was conducted in September 2021. The histological examination proved the diagnosis of somatotropinoma, with diffuse positive immunohistochemistry for GH and weak and focal positive immunohistochemistry for prolactin, also expressing Pit-1, p53, SSTR2A, synaptophysin and CAM5.2 and with Ki-67 = 1%. The patient also reported in previous clinical history: multinodular thyroid goiter, primary hypothyroidism under treatment with levothyroxine, hypovitaminosis D under cholecalciferol replacement therapy, hypertension being treated with beta-blockers and thiazide diuretic, obesity (BMI 40). At the last follow-up at our center in June 2023, the patient presented in fair general clinical condition, with improvement of related acromegaly symptoms, normalized baseline GH (0.1 ng/ml) and IGF-I (84 ng/ml) values, and negative pituitary MRI for signs of

somatotropinoma recurrence. The clinical, laboratory and morphological picture documented remission from acromegaly.
Conclusions
Our clinical case describes for the first time to our knowledge the clinical association between Morris syndrome and acromegaly. Although this condition is rare, further genetic studies are needed to demonstrate a genetic association between these two conditions.

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EP690

Mutation of the kiss-1 gene responsible for combined hypopituitarism: a report of 3 cases

Hamdi Frikha[1], Mouna Elleuch[1], Hana Charfi[1], Nesrine Dhieb[1], Dhoha Ben Salah[1], Mariam Moalla[2], Wajdi Sefi[1], Faten Haj Kacem Akid[1], Fatma Mnif[1], Nadia Charfi[1], Mouna Mnif[1], Hassen Hadjkacem[3], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology;[2]Center of Biotechnology of Sfax, Laboratory of Molecular and Cellular Screening Processes;[3]College of Sciences, University of Sharjah, Department of Applied Biology, United Arab Emirates

Introduction
The KISS1 gene codes for the G protein-coupled receptor 54 (KISS1R) and plays a crucial role in the regulation of reproduction and pubertal maturation. Mutations in the KISS1-R gene are extremely rare and usually implicated in isolated hypogonadotropic hypogonadism. Here, we report three cases of a familial mutation in the KISS1 gene responsible for combined hypopituitarism.
Observations
Three related patients (including two twins) from a first-degree consanguineous union presented with delayed puberty at the ages of 15 and 16, respectively. Clinical examination revealed growth retardation and the absence of pubertal development signs without anosmia. Exploration confirmed combined hypopituitarism in all three patients (complete growth hormone deficiency, gonadotropin deficiency, and corticotropin deficiency). Magnetic resonance imaging was normal for all patients. Genetic study showed a non-stop mutation c.1195T>C, p.X399R in the KISS1 gene.
Conclusion
This mutation was absent in 100 controls from the Tunisian population, as well as in all accessible international genomic databases, indicating a de novo character. These observations challenge the distinction between different forms of hypopituitarism, suggesting instead a phenotypic continuum and a multifaceted pathology.

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EP691

Immunohistochemical staining patterns of non-functioning pituitary adenomas and presentation of secondary hormonal deficiencies

Alex Corriveau[1], Andrea Hebb[2], Lisa Tramble[3], David Clarke[2] & Syed Imran[4]
[1]Dalhousie University, Pathology;[2]Dalhousie University, Division of Neurosurgery, Canada;[3]Dalhousie University, Division of Endocrinology & Metabolism, Canada;[4]Dalhousie University, Halifax, NS, Division of Endocrinology & Metabolism, Canada

Introduction
Secondary hormonal deficiencies (SHD) are frequently observed in patients with pituitary adenomas. We previously reported that pituitary tumour clinical subtypes were associated with specific patterns of SHD, and nonfunctioning adenomas (NFAs) were more likely to present with multiple SHD. We extended our work to examine if the immunohistochemical staining patterns of NFAs impacted SHD.
Methods
All clinically NFAs surgically removed between November 2005 to December 2018 were identified through the Halifax Neuropituitary database. A total of 135 patients met the inclusion criteria and their pathology specimens were analyzed. NFAs were classified based on those without any hormonal staining or those staining with either/or growth hormone (GH), adrenocorticotropin (ACTH), thyroid stimulating hormone (TSH), luteinizing hormone (LH), follicle stimulating hormone (FSH) and prolactin (PRL). We reviewed their pattern of SHD at presentation.
Results
Of the 135 patients, 78 showed positive immunoreactivity to at least one of the above pituitary hormones while 57 showed no staining; 75 patients had SHD, while 60 patients had no evidence of SHD at presentation. As expected, macroadenomas were more likely to be associated with SHD than microadenomas ($P<0.001$). When comparing SHD patterns, tumors with and without any staining there were significant differences in the patterns of SHD regardless of tumour size ($P<0.01$). Patients with TSH staining tumors were overall more likely to experience SHD ($P<0.01$).
Conclusion
This novel study will allow us to understand the relationship between tumor pathology and SHD. The analyzed data suggests that SHD patterns vary based on the immunohistochemical profile of NFA.

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EP692

Lymphocytic pituitary revealed by diabetes insipidus

Hana Charfi[1], Fatma Mnif[1], Dhoha Ben Salah[1], Mouna Elleuch[1], Mouna Mnif[1], Nadia Charfi[1], Faten Haj Kacem Akid[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker Hospital, Sfax, Tunisia

Introduction
Lymphocytic hypophysitis (LH) is most likely of autoimmune origin, as it is associated with other autoimmune diseases in 20 to 25% of cases, with the most common being lymphocytic thyroiditis. It is common in young women in late pregnancy or postpartum. Diabetes insipidus (DI) occurs in approximately 35% of patients with LH. To link DI to LH, we investigated the clinical, biological, and radiological characteristics of patients with DI.
Patients and Methods
A retrospective and monocentric descriptive study conducted in the Endocrinology Department of Hedi Chaker University Hospital in Sfax over a 20-year period (2000-2020). We identified 44 cases of DI, examined the records, and selected 6 cases of DI secondary to LH.
Results
All our patients were female with an average age of 36.16 years [22-47]. The discovery circumstance was secondary polyuria and polydipsia (SPUPD) in all patients. Family autoimmunity (AI) was reported in 33.33% of cases. Personal AI was described in 50% of cases, with Hashimoto's thyroiditis in two patients. Water deprivation test was performed in all patients, except one who underwent an initial pituitary MRI, leading to the diagnosis of partial central diabetes insipidus (DIC) in 20% of cases and complete DIC in the remaining cases. Pituitary hypertrophy was described in 33.33% of patients, initially suggesting a diagnosis of granulomatosis, eliminated by the negativity of specific investigations.
Conclusion
Recognition of LH in the context of DI is crucial for prompt diagnosis and appropriate management, particularly given its potential autoimmune origin and frequent association with other autoimmune conditions. This insight can guide clinicians in refining diagnostic approaches and optimizing patient care for individuals presenting with DI.

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EP693

Predictive factors determining adequate response during insulin tolerance test

Sahar Abidi[1], Nadia Khessairi[1], Sabrina Ayari[1], Kammoun Elyes[1], Ibtissem Oueslati[1] & Melika Chihaoui[1]
[1]Endocrinology department, Rabta Hospital, Tunis, Tunisia

Introduction
The insulin tolerance test (ITT) is the gold standard for hypothalamic-pituitray adrenal axis assessment. An adequate response of serum cortisol level above or equal to 18 µg/dl confirms the integrity of the adrenal axis. Otherwise, it confirms adrenal insufficiency (AI). The aim of our study was to investigate clinical and biological factors for the prediction of an adequate response during the ITT.
Methods
We conducted a cross-sectional descriptive study. It involved 100 patients with suspected AI. The ITT protocol consisted of blood samples for fasting blood glucose and baseline cortisol, followed by intravenous injection of rapid insulin at a dose of 0.1 to 0.2 IU/kg. A second sample was taken at the time of hypoglycemia, followed by blood samples every 10 minutes for 60 minutes after hypoglycemia. An adequate response was defined as a serum cortisol level above or equal to 18 µg/dl after a serum glucose level below 0.40 g/l.
Results
The mean age was 41.4 ± 15.12 years and the gender ratio (F/H) was 0.2. Forty-two patients (42%) had an adequate response and 58 patients (58%) had an inadequate response. There was no difference of the mean age between the two

groups ($P=0.94$). Anorexia and orthostatic hypotension were more frequent in patients with AI. ($P=0.028$; $P<10^{-3}$). Weight and BMI were comparable between the two groups. Fasting blood glucose and nadir blood glucose were comparable between the two groups (0.91 ± 0.14 g/l vs 0.92 ± 0.14 g/l; $P=0.91$) and (0.29 ± 0.01 g/l vs 0.29 ± 0.01 g/l; $P=0.84$). Basal cortisol level in the group with normal axis were significantly higher than in the AI group (11 ± 4.1 µg/dl vs 8.3 ± 2.4 µg/dl; $P<0.001$). A basal cortisol of 9.75 µg/dl had a sensitivity of 59% and a specificity of 73% to predict an adequate response. On the other hand, a cutoff point of 13.3 µg/dl had a sensitivity of 100% but a specificity of 26%.

Conclusions

Dynamic test is required to assess the integrity of the adrenal axis. Our study suggests that a basal cortisol of 9.75 µg/dl reliably predicts adequate cortisol response.

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EP694

Giant pituitary adenomas: therapeutic and prognostic complexities

Hind Ouakrim[1,2], Salsabil Haouach[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]

[1]Chu Mohamed Vi Marrakesh - Drh, Marrakech, Morocco; [2]Chu Mohamed Vi Marrakesh - Drh, Marrakech

Introduction

Giant pituitary adenomas are defined as tumors with a largest diameter of ≥ 40 mm. They are characterized by high invasiveness, causing compression of adjacent structures and hormonal dysfunction. The aim of this case report is to highlight the diagnostic, therapeutic, and prognostic challenges associated with this rare entity.

Case report

A 35-year-old male, diagnosed with diabetes under insulin therapy, along with Hashimoto's thyroiditis managed with levothyroxine, presented urgently with a sudden onset of headache, vomiting, and a decline in bilateral visual acuity. Magnetic Resonance Imaging (MRI) of the head revealed a substantial 60x34 mm lesion in the sellar and suprasellar regions, causing compression of the optic pathways and V3, accompanied by active hydrocephalus. Laboratory investigations indicated gonadotropin deficiency, a slightly elevated prolactin level of 39.9 ng/mL, and cortisol at 15 µg/dl. Visual field examination revealed a complete loss of vision in both eyes. The patient underwent surgical removal of the cerebral lesion via a trans-sphenoidal approach. Histopathological examination identified a pituitary adenoma (PA) expressing growth hormone (GH), prolactin, and thyroid-stimulating hormone (TSH). Postoperatively, the patient developed diabetes insipidus and corticotrope deficiency. The patient is under hormonal medical treatment, including hydrocortisone (15 µg/day), levothyroxine (100 mg/day), desmopressin (60 µg, 2 tablets/day), and androtardyl. At the three-month follow-up, imaging revealed a sellar and suprasellar lesion involving both cavernous sinuses, measuring $44.3\times36\times36.4$ mm. Repeat surgery was indicated, with treatment plans incorporating dostinex and somatuline 120 mg LP. Unfortunately, the patient died immediately post-operatively.

Discussion

Giant pituitary adenomas are uncommon tumors, with a prevalence estimated at 6-10% of all pituitary adenomas. They present a therapeutic challenge due to their size, invasiveness, and frequent extrasellar extensions. The initial presentation is determined by the lesion's mass effect and hormonal dysfunction. Surgery remains the treatment of choice, although achieving complete tumor excision in such large tumors is challenging. Histopathological study with immunostaining is crucial to confirm the diagnosis and define medical therapy. The literature reports high mortality rates following excision of giant pituitary adenomas.

Conclusion

Giant pituitary adenomas represent a challenge in clinical endocrinology, requiring multidisciplinary management in diagnosis, therapeutic management, and long-term follow-up.

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EP695

An artificial intelligence system for estimating the improvement of clinical and paraclinical parameters after therapy in pituitary tumors

Ana-Silvia Corlan[1], Babuc Diogen[2], Costi Flavia[2], Mihaela Vlad[1], Melania Balas[1], Ioana Golu[1], Daniela-Georgiana Amzar[1] & Onchis Darian[2]

[1]University of Medicine and Pharmacy Timisoara, Endocrinology, Timisoara, Romania; [2]West University of Timisoara, Computer Science, Timisoara, Romania

Pituitary tumors usually have an excellent prognosis after targeted treatment involving surgery, radiotherapy and medical therapy. Metabolic abnormalities are encountered in 22.3-52.5% of pituitary adenoma patients and are correlated with disease progression and prognosis. Therefore, in this study, we propose an artificial intelligence system for estimating the improvement of clinical and paraclinical parameters for patients undergoing therapy. The patient cohort is made out of 107 patients with a panel of clinical and paraclinical parameters recorded before (for 45 patients) and after therapy (for 62 patients). We first made a classification of tumor activity in case of functioning pituitary tumors. Secondly, we made a classification, distinguishing between symptomatic and asymptomatic patients for non-functioning pituitary adenomas. We trained a supervised deep neural network having as input the variable parameters of remaining tumor size after therapy, total volume and the clinical (systolic, diastolic blood pressure and body mass index) and paraclinical parameters (fasting plasma glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, uric acid, aspartate aminotransferase, alanine aminotransferase and C-reactive protein serum levels), and the fixed parameter treatment. Our target was the estimation of a cut-off value for symptomatic pituitary tumors. The versatile artificial intelligence system reached an accuracy of 85.71% for the patients after treatment, giving to the patient and the attending physician, valuable information regarding the prospective success of the treatment.

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EP696

A pituitary metastasis from occult neuroendocrine carcinoma

Luigi Demarchis[1], Sabrina Chiloiro[2], Pier Paolo Mattogno[3], Antonella Giampietro[2], Maria Grazia Maratta[4], Liverana Lauretti[3], Giovanni Schinzari[4], Rosalinda Calandrelli[5], Simona Gaudino[5], Guido Rindi[6], Alessandro Olivi[3], Giampaolo Tortora[4], Francesco Doglietto[3], Laura De Marinis[2], Alfredo Pontecorvi[2], Antonio Bianchi[2] & Marco Gessi[6]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, Pituitary United; [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, Pituitary United; [3]Fondazione Policlinico Universitario A. Gemelli IRCCS, Neurosurgery; [4]Fondazione Policlinico Universitario A. Gemelli IRCCS, Medical Oncology; [5]Fondazione Policlinico Universitario A. Gemelli IRCCS, Radiology; [6]Fondazione Policlinico Universitario A. Gemelli IRCCS, Anatomic Pathology Section

Background

Pituitary metastases are rare findings and account for 1% of surgically treated pituitary lesions. Despite the low incidence, given the frequent compression exerted on surrounding structures, pituitary metastases can present with major symptoms such as headache, visual disturbances and visual field. Ultimately, damage to the pituitary gland may be associated with electrolyte disturbances.

Clinical case

A 57-year-old male patient was admitted to our hospital for ptosis, lacrimation and diplopia, previously treated with corticosteroids without benefit. A brain contrasted MRI examination showed a sellar lesion, in contact with the optic chiasma, infiltrating the right cavernous sinus, the clivus and the clinoid. Biochemical and hormone examinations showed slight hyperprolactinemia (47 ng/ml) in absence of electrolyte disturbances and deficits of pituitary hormones. The visual field examination detected a left superior-temporal campimetric deficit. Pre-surgery chest X-ray was negative. A sub-total transsphenoidal excision of the lesion was conducted and histologic examination identified a 'neoplasm with well-differentiated neuroendocrine morphology, relatively monomorphic round cells, intense expression of synaptophysin, chromogranin, 2A-somatostatin receptor, insulinoma-associated protein-1 (INSM1), thyroid transcription factor-1 (TTF1). Neoplastic cells were Pit1-, Tpit-, GATA3-, SF1-, CDX2-, ISLET1-, CAM5.2- and AE1/AE- negative. Proliferative index (MIB1) was 5-7%. Comment: localization of a neuroendocrine tumor (NET). Immunohistochemical pattern suggests a pulmonary origin (possible atypical carcinoid, NET G2)'. The patient underwent a 68-Gallium-DOTA-TOC Positron Emission Tomography/-computed tomography (PET-CT) showed the residual sellar tumor with increased SSTR expression. A contrasted total body CT confirmed the residual neoplasia of maximum diameter of 24 millimeters in the right lateral and posterior sellar region, eroding the lamina quadrilateralis and the ipsilateral posterior clinoid process, extending extra compartmentally into the cavernous sinus, encompassing the intracranial portion at the internal carotid artery. Finally, the patient underwent 18-F-fluorodeoxyglucos PET-CT, which detected a more functionally active area in the right parasellar region. All radiological investigations did not reveal the primary tumour and other metastasis. Therefore, according to NET grading, non-detection of primary tumor and persistence of local disease, it is decided to treat the patient with somatostatin receptor ligand and to re-evaluate the status of disease, also considering the possibility of radiotherapy on the residual tumor.

Conclusions

Our case is intended to emphasize the importance of considering the pituitary not only as a site of primary tumor but also as a possible site of metastasis, mainly from

breast, lung, and colon cancers, without excluding firstly possible rarer primaries as occult or other side of NETs.

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EP698

Clinical presentation and MRI findings in patients with hypophysitis - a single center experience

Izabella Czajka-Oraniec[1], Karolina Cylke-Falkowska[1], Maria Stelmachowska-Banas[1] & Wojciech Zgliczyński[1]
[1]Centre of Postgraduate Medical Education

Introduction
Hypophysitis is a very rare and heterogenous condition characterized by pituitary inflammation that leads to hypopituitarism, diabetes insipidus and symptoms associated with mass effect such as headaches and visual disturbances. Studies on large groups of patients with hypophysitis are scarce. The aim: We performed an analysis of clinical symptoms, pituitary function, and management of patients diagnosed with hypophysitis.
Material and Methods
This was a retrospective single-centre study of 30 consecutive patients diagnosed with hypophysitis in the Department of Endocrinology at Bielanski Hospital in Warsaw for the last 10 years (between 2014 and 2023). We evaluated medical records of the patients, hormonal and MRI results, and treatment outcomes.
Results
Patients with hypophysitis represented 0.38% of all patients admitted to the Department during this period. Female gender was predominant (78.1%) but the association with pregnancy occurred only in one case. The mean age at diagnosis was 41.9 ± 15.5 years and ranged from 15 to 71 years. The most common symptoms at diagnosis were headache (43.8%) and diabetes insipidus (56.3%). The gonadotropic, thyrotropic and corticotropic axis were affected in 65.6%, 56.3% and 59.4%, respectively. The most typical MRI findings were infundibular thickening (65.6%), enlarged pituitary gland (56.6%) and the lack of typical posterior pituitary signal in T1-weighted images (25.0%). Diagnosis of hypophysitis was mostly based on clinical presentation, laboratory and imaging results, and the response to glucocorticoid treatment. Histopathological diagnosis was confirmed in 4 patients (13.3%). There were 6 cases of secondary hypophysitis - 2 sarcoidosis, 1 Langerhans's cell histiocytosis and 3 induced by immune checkpoint inhibitors. The remaining cases were diagnosed as primary hypophysitis. Nine patients (30.0%) had positive anti-thyroid antibodies and the autoimmune thyroid disease was the most common autoimmune disease in a family history. Twelve patients (37.5%) received high-dose glucocorticosteroid therapy with prompt improvement of symptoms. However the relapse of the disease was observed in 4 of them. Two patients with a recurrent hypophysitis received a second line treatment with azathioprine and mycophenolate mofetil and they have remained in remission.
Conclusions
The diagnosis of hypophysitis is commonly made based on the clinical, radiological, and hormonal picture. It typically occurs in middle-aged women but pregnancy does not seem to be a risk factor. Our results confirmed that the gonadotropic axis was the most frequently affected. Treatment with high-dose glucocorticosteroids had a beneficial effect in terms of at least partial relief of symptoms, especially headaches.

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EP701

TSH and GH co-secreting macroadenoma: a case report

Meriem Adel[1], Radhouen Gharbi[2], Emna Naccache[1], Manel Jemel[1], Hajer Kandara[1] & Ines Kammoun[1]
[1]National institute of nutrition and food technology, Endocrinology, Tunis;[2]Tunisia, Endocrinology, Tunis

Introduction
Thyroid-stimulating hormone-secreting pituitary adenomas (TSH-omas) are infrequent, constituting 0.5%-3.0% of pituitary adenomas (PAs). Additionally, the co-secretion of growth hormone (GH) and TSH in PAs is notably rare, accounting for only 16% to 19.7% of TSH-producing PAs. Limited cases have been reported.
Observation
We report the case of a 59-year-old woman who presented with asthenia and weight loss; she was referred to the endocrinology department for further investigation as a dysmorphic syndrome suggestive of acromegaly was noted. She had no previous medical or surgical history. On physical examination she has an enlargement of hands and feet, enlarged tongue and thickened lips, enlarged and protruding mandible. Blood pressure was 130/80 and pulse was 65 bpm. Laboratory results showed: IGF-1, 397.9 ng/ml; non-suppressible GH levels after oral glucose loading; free thyroxine (FT4), 61.47 pmol/l (12-22 pmol/l); TSH, 0.41 µU/ml. Adrenocorticotropic hormone (ACTH), <1.5 ng/l; cortisol 918.4 nmol/l; follicle stimulating hormone (FSH), 22.72 mU/l; PRL, 116 mUI/l; estradiol, 26 pg/ml; Alpha subunit was 0,87 mUI/ml with elevated α-TSH/TSH molar ratio at 3.48. Magnetic resonance imaging showed a macroadenoma measuring 10 mm × 11 mm. The patient was prescribed 30 mg of methimazole. Follow-up thyroid assessments one month later indicated a TSH level of 0.19 mIU/ml and an FT4 level of 44.07 pmol/l. After restoring FT4 to normal levels, a transsphenoidal excision surgery for the pituitary adenoma is planned.
Conclusion
This is a rare case of a pituitary macroadenoma producing both GH and TSH. This may be due to the fact that Pit-1-producing cells have been shown to be the source of both somatotrophs and thyrotrophs during differentiation into mature pituitary cells. Early diagnosis, multidisciplinary management and vigilant surveillance are essential to improve the prognosis of this co-secreting PAs.

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EP702

Long-term exposure of corticotroph pituitary tumor cells to glucocorticoid results in resistance to its anti-proliferative effect

Ticiana Silva[1], Fadime Dogan[2], Anand Iyer[2], Peter van Koetsveld[2], Richard Feelders[2] & Leo Hofland[2]
[1]Erasmus MC Cancer Institute, Erasmus MCy; [2]Erasmus Mc, Department of Internal Medicine, Division of Endocrinology Rotterdam, Netherlands

Background
Cortisol has a suppressive effect on corticotroph proliferation. In Cushing's disease (CD), the relative resistance to glucocorticoid (GC) action may favor corticotroph tumor formation and autonomous ACTH secretion.
Objective
To analyze the consequences of long-term GC exposure on corticotroph tumor cell proliferation and to evaluate the modification of gene expression attributable to prolonged GC treatment.
Methods
Mouse AtT20 corticotroph pituitary tumor cells were used. Cells were treated continuously with dexamethasone (DEX) for 10-weeks at a dose of 10nM which is supraphysiological and achievable in the case of CD. Subsequently, cells were cultured in DEX-free medium for up to 5-weeks (washout period). AtT20 cells cultured only in DEX-free medium served as control. After 1- and 5-week of washout, dose-response experiments were performed to determine cell sensitivity to DEX. Quantitative PCR was performed on control cells and cells previously treated with DEX at 1- and 5-week washout periods (DEX-treated cells). mRNA analysis was performed at 72-hr of DEX (100 nM).
Results
DEX inhibited the proliferation of control AtT20 cells in a dose-dependent manner. In long-term DEX-treated cells, DEX failed to inhibit cell growth despite 1- and 5-week washout period. No differences were observed between control and DEX-treated cells regarding DEX-induced effects on mRNA expression of the glucocorticoid receptor, *Pomc* and *Fkbp5*. However, DEX induced expression of the proapoptotic *Bid* gene in control cells but had no effect in DEX-treated cells. DEX did not affect *Bad* gene expression in control cells but suppressed its expression in DEX-treated cells. For cell cycle related genes, DEX induced a strong upregulation of *Cdkn1a*, a cell cycle inhibitory gene, in control cells, whereas this induction was lower in DEX-treated cells.
Conclusion
Long-term treatment of corticotroph tumor cells with GC results in cells resistant to the growth inhibition by GC, despite an unchanged sensitivity of genes directly related to GR activation indicating differential effects on (long-term) gene expression. Continued exposure of GC may thus superimpose adaptive changes, in which acute GC challenge elicit a different pattern of gene expression less committed to cell growth inhibition, such as lower expression of proapoptotic genes and less induction of the cell cycle inhibitor *CDKN1a*.

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EP706

Historic unveiling; ground breaking encounter of non-functioning pituitary macroadenoma coexisting with myasthenia gravis- debut case report

Umer Qazi[1] & Molly Scott[1]
[1]Watford, Diabetes, Watford, United Kingdom

Background
The correlation linking Myasthenia Gravis (MG) and pituitary adenomas is exceedingly uncommon. Our thorough investigation of medical literature uncovered merely eight documented cases showcasing this association. Notably, five of these cases specifically involved adenomas that secreted prolactin[1]. Two instances implicated a non-functional pituitary adenoma in this rare association[2]. Solely one case was identified involving a growth hormone (GH)-secreting adenoma in this context[3]. So, to our knowledge, this marks the inaugural documentation of a non-secreting adenoma detected in a patient diagnosed with myasthenia.
Case detail
A 72 years of age gentleman, Mr X, was admitted to the hospital on 8/11/23 due to eye symptoms and was found to have both a pituitary macroadenoma and myasthenia gravis. He had a medical history including retinopathy, cataract surgery, YLC procedure, hypertension, type 2 diabetes, prostate cancer, and bowel cancer. Over two months, he experienced double vision and eyelid drooping, worsening by the end of the day and more pronounced in the left eye. Additionally, he reported dull eye discomfort intermittently. Mr X also had new-onset breathlessness and fatigue for about three weeks, worse with exertion and at day's end. He felt more tired than usual but had no issues with swallowing, breathing, or speech. Physical examination revealed bilateral ptosis with equally sized pupils reacting to light. An incidental finding of a $13\times12\times16$ pituitary macroadenoma was discovered on MRI orbit without compressing the optic chiasm or optic nerve abnormalities. His CT head (19/10/23) showed no significant intracranial issues, and subsequent imaging ruled out thymus malignancy. Blood tests indicated acetylcholine receptor antibodies at a level of 292, TSH receptor antibodies <0.3, TPO <4, random cortisol 775, and ACTH 54, Prolactin of 158 mu/l (normal), growth hormone level of 0.74 mg/l (Normal), IGF-1 is 20.9 nmol/l (Normal) and with normal FSH. LH and testosterone levels. He commenced IVIG treatment followed by an up-titrating course of prednisolone under neurology guidance, monitoring CBGs. He will receive continued care from neurology and endocrine clinics, with a follow-up contrast MRI scheduled in six months.
Conclusion
In conclusion, the simultaneous presentation of myasthenia gravis and pituitary macroadenomas represents an exceedingly rare occurrence. This unique co-occurrence underscores the complexity and diversity of potential medical conditions and highlights the importance of comprehensive assessment and collaborative multidisciplinary care for such exceptional cases. Continued research and clinical observation are essential to better understand the underlying mechanisms linking these two distinct conditions when they occur together

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EP709

A rare cause of gonadotropic insufficiency

Raida Ben Salah[1], Seddiqa Somauroo[2], Faten Hadjkacem[2], Mohamed Abid[2] & Zouhir Bahloul[1]
[1]Sfax University Internal Medicine; [2]Sfax University Endocrinology

Introduction
The causes of gonadotropic insufficiency are many and varied. Pituitary lymphomas are a rare and difficult-to-diagnose cause.
Case report
We report the case of a 30-year-old female patient who was admitted to the internal medicine department for an altered general condition with febrile headache. She reported secondary amenorrhea evolving for three months. The pregnancy test was negative. On physical examination, the patient was cachectic and pale. She had ptosis of the right eye, associated with extrinsic nerve III paralysis and anesthesia of the right hemiface. Specialized biology of the hypothalamic-pituitary axis showed gonadotropic insufficiency, with follicle-stimulating hormone at 1.2 mIU/l (1.5-2.4) and luteinizing hormone below 0.1 mIU/l (1.7-8.6), with moderate hyperprolactinemia at 26 ng/ml ($n<15$). The corticotropic, thyrotropic and somatotropic axes were normal. Pituitary MRI revealed a voluminous 21 mm long axis T1, T2 iso-signal sellar process with heterogeneous enhancement after gadolinium injection associated with diffuse pachymeningeal enhancement. Abdominal CT showed infiltrative pancreatic, lymph node and bone involvement. A diagnosis of lymphoblastic B lymphoma was made on peritoneal CT biopsy with multiple localizations: abdominal, bone and pituitary. The patient was treated with chemotherapy.
Conclusions
Lymphomas of the pituitary stem are extremely rare tumours, with symptoms dominated by headache, asthenia and diplopia. Imaging can determine whether this thickening is isolated or associated with other lesions, which are more easily accessible to biopsy.

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EP711

Panhypopituitarism revealing pituitary tuberculosis: a case report

Redhouane Longo[1], Mourad Benrabah[2], Abdelkader Yahi[3], Benabdelatif Katia[3] & Ould Kablia Samia[3]
[1]Endocrinology department, Regional University Military Hospital of Oran, Algeria;[2]Nuclear Medicine Department, Regional University Military Hospital of Oran, Algeria;[3]Endocrinology Department, Central Military Hospital, Algiers, Algeria

Introduction
Tuberculosis is a serious disease which is on the increase worldwide, particularly in poor and developing countries, killing 3.000.000 people every year. Preferential localization is lungs, kidneys and the bones. Rare at the brain, it's exceptional at the pituitary gland. Diagnosis is usually very difficult, even simulate a pituitary adenoma, thus imposing a surgical treatment, and it is the pathologist who will rectify the diagnosis.
Observation
This is a 23-year-old patient admitted with anterior pituitary insufficiency with palpebral ptosis and polyuropolydypsia syndrome. Patient had a history of tuberculous meningoencephalitis for 05 months still under treatment. Endocrine assessment revealed global anterior pituitary insufficiency with hyperprolactinemia, associated with post pituitary insufficiency. Hypothalamohypophyseal magnetic resonance imaging revealed a suprasellar collection centred on the pituitary stalk measuring $10\times11\times18$ mm in diameter with a liquid signal. Patient was put on hormone replacement therapy, which is currently being monitored.
Discussion
Pituitary tuberculosis remains an exceptional pathology, frequency is difficult to determine because only a few rare sporadic cases have been published in the literature. Clinical symptomatology mimics that of a non-secreting pituitary adenoma. Damage to the cavernous sinus is very frequently observed. Diagnosis is difficult when a late complication of a primary tuberculosis infection that goes unnoticed, less after tuberculosis meningitis.
Conclusion
Common challenge for clinician and radiologist is to determine which patients are likely to have a tuberculoma, diagnosis must be rapid, given the possibility of cure through early and well-conducted medical treatment.

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EP712

Rheumatological diseases and acromegaly: a clinical case

Margarita Perepelova[1], Larisa Dzeranova[1], Taras Panevin[1], Elena Przhiyalkovskaya[1], Ekaterina Pigarova[1], Ekaterina Troshina[1] & Evgeny Zotkin[1]
[1]Endocrinology Research Centre

Background
Acromegaly is a chronic endocrine disease characterized by excessive secretion of somatotropic hormone (GH), which in turn leads to increased secretion of insulin-like growth factor 1 (IGF-1) in the liver. Many cells in the body are targets for these hormones. Excess of GH, in the vast majority of cases caused by hormone-producing pituitary adenoma, and IGF-1 leads to cellular and tissue growth of practically all organs and systems, including the bone and joint apparatus.
Case presentation
Patient A., 56 years old, since 2021 was observed for diabetes mellitus by an endocrinologist, subsequently the doctor paid attention to the enlargement of feet, joint pains. Examinations showed GH, IGF-1 elevation, and pituitary adenoma was visualized on MRI which led to diagnosis of acromegaly. In March 2023 a transnasal adenomectomy was performed. A dynamic examination after 6 months confirmed the absence of remission of acromegaly - IGF-1 498.5 ng/ml (82-283), and therefore therapy with octreotide 20 mg once every 28 days was initiated. During the examination, attention was drawn to complaints of pain in large joints, according to the results of a blood test: rheumatoid factor 37.7 IU/ml (0-30),

antistreptolysin O 50 IU/ml (0-200), C-reactive protein 1.5 mg/l (0.1-5). Consulted with a rheumatologist, taking into account the clinical picture (Raynaud's phenomenon, swelling of the hands, arthritis, arthralgia and myalgia) and laboratory and instrumental examination (immunological disorders, primary muscular process without exacerbation according to ENMG, synovitis according to ultrasound of the hands), the diagnosis was verified - mixed connective tissue disease tissues: arthritis, arthralgia, proximal muscle weakness, swelling of the hands, Raynaud's phenomenon, Gottron's papules, immunological disorders (antinuclear factor 1/2560, AT to RNP-70 >300.0, rheumatoid factor 85.0). Due to the presence of articular syndrome, methotrexate 15 mg/week and methylprednisolone 8 mg/day were initiated. During treatment, the patient noted a significant decrease in joint pain.

Conclusions

Thus, the presented clinical case emphasizes the importance of differential diagnosis of articular syndrome in acromegaly at the initial stage, since the identification of an immunoinflammatory rheumatic disease requires a completely different tactic that helps improve the patient's well-being and relieve pain. Particular attention should be paid to patients who continue to have joint pain after achieving biochemical remission of acromegaly. In this regard, it is necessary not only to carry out a differential diagnosis of acromegalic arthropathy and rheumatological diseases, but also to provide multidisciplinary monitoring, in particular by a rheumatologist and an endocrinologist.

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EP713

Challenges in diagnosis and management of silent corticotroph adenomas: insights from three case studies and literature review

Xinyi Zhao[1,2], Zhenyi Li[1] & Chun Wang[1]
[1]West China Hospital, Sichuan University Department of Endocrinology and Metabolism, Chengdu, China; [2]Chengdu First People's Hospital, Department of Endocrinology and Metabolism, Chengdu, China

Silent Corticotroph Adenomas (SCAs) are a type of pituitary tumor that is discovered without obvious clinical symptoms. SCAs are considered to be one of the five "high-risk" tumors due to their aggressive behavior, characterized by high levels of proliferation, rapid progression, and recurrence. Unlike functional corticotropin adenomas, SCAs do not exhibit any clinical or biochemical signs of hypercortisolemia. When the tumor is detected, it often exhibits invasive growth and poses a challenge for complete surgical excision. Positive immunoreactivity for ACTH or/and T-PIT in the pathological examination of the resected tumor after surgery may be the only evidence for the diagnosis of SCAs. The introduction of pituitary-restricted transcription factor (T-PIT) has enhanced the diagnostic precision of SCAs. Even cell lineage-specific pituitary transcription factors are the only diagnostic basis, as shown in case 3, ACTH expression is negative and finally diagnosed by positive T-PIT expression. Currently, the management of intractable SCAs remains an active subject of investigation. This article discusses three clinical cases and conducts a literature review to underscore the significance of timely radiotherapy after surgical intervention for residual or recurrent tumors. Therefore, our patients in this article received adjuvant radiotherapy after surgery. Unfortunately, the patient of case 1 could not be relieved even after surgery and twice gamma knife treatment and required a second operation. Nevertheless, the prognosis of case 3 was better than that of the first two patients after radiotherapy because early intervention was determined once diagnosis of SCA was confirmed. The management of refractory SCAs remains an area of ongoing exploration. Aggressive macroadenomas usually have low expression of O6 -methylguanine-DNA methyltransferase in Cushing's Disease. Therefore, temozolomide (TMZ) may be a novel therapeutic option to treat invasive pituitary tumors. The European Society of Endocrinology has adopted TMZ as the primary therapy for invasive pituitary tumors that have not responded to conventional treatment. In case 1, there was no significant tumor growth after TZM treatment. This article underscores the potential of TMZ as an alternative in cases resistant to conventional therapies.

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EP714

Pituitary stalk interruption syndrome: a case report

Redhouane Longo[1], Mourad Benrabah[2], Benabdelatif Katia[3], Abdelkader Yahi[3] & Ould Kablia Samia[3]
[1]Endocrinology Department, Regional University Militar, Hospital of Oran, Algeria; [2]Nuclear Medicine Department, Regional University Militar, Hospital of Oran, Algeria; [3]Endocrinology Department, Central Militar, Hospital, Algiers, Algeria

Introduction

Pituitary stalk interruption syndrome is a congenital anomaly of the pituitary gland responsible for GH deficiency or global pituitary insufficiency, characterized by abnormalities visible on Magnetic Resonance Imaging (MRI) associating a thin or interrupted pituitary stalk, ectopic posterior pituitary, and hypoplastic anterior pituitary. Mutations in the HESX1 transcription factor or the LHX4 gene may be the cause of this anomaly, but a prenatal origin cannot be ruled out. This syndrome is often revealed during the neonatal period and childhood, but sometimes the symptoms can be overlooked and the diagnosis will therefore be delayed. We report a case of this syndrome diagnosed at a late stage.

Observation

17-year-old patient admitted for failure to thrive and delayed puberty. Clinical examination reveals a harmonious dwarfism, a height of 156 cm (−2 standard deviation), a weight of 56 kg, the patient is classified G1P1 according to the Tanner classification, and the bone age was 13 years according to the Atlas of Greulich and Pyle. Hormonal assessment reveals a complete GH deficiency (following an insulin hypoglycaemia test), associated with hypogonadotropic hypogonadism. There was no corticotropic or thyrotropic deficit. Hypothalamohypophyseal MRI reveals a pituitary stalk interruption syndrome with ectopic posterior pituitary. Scrotal ultrasound concludes bilateral testicular hypotrophy. The patient is currently undergoing growth hormone replacement and regular monitoring.

Discussion

Pituitary stalk interruption syndrome is defined by morphological abnormalities on MRI: Pituitary stalk not visible, pituitary hypoplasia and ectopic post-pituitary. Stature prognosis remains pejorative if the diagnosis is late, hence the need for early detection of staturo-puberty delay.

Conclusion

Pituitary stalk interruption syndrome is a rare congenital malformation that must be considered in the presence of combined or isolated hypopituitarism. MRI is currently the most effective means of imaging for the diagnosis of this malformation.

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EP715

Deep vein thrombosis unmasking the diagnosis of Sheehan syndrome

Rada Sparavalo[1], Sanja Borozan[2] & Sanja Vrbica[3]
[1]General Hospital, Internal medicine, Department of Endocrinology, Endocrinology, Nikšić, Montenegro;[2]Clinical Centre of Montenegro, Endocrinology, Podgorica, Montenegro;[3]General Hospital Nikšić, Radiology, Nikšić, Montenegro

Sheehan syndrome (SS) caused by postpartum hemorrhage leads to varying degrees of pituitary insufficiency. With improved obstetrical care, ischemic pituitary necrosis is less common and, as a consequence, most cases of SS are being overlooked and diagnosis is delayed for years due to its nonspecific signs and symptoms. Data regarding the relationship between hypopituitarism and increased risk of venous thrombosis are inconsistent and need to be elucidated further. A 41-years-old woman presented with swollen leg and profound fatigue. Venous doppler revealed left crural deep vein thrombosis and the treatment with anticoagulants was started. Initial laboratory analysis suggested hypothyroidism with TSH 5.76 IU/ml, free T4 <5.15 ng/dl, free T3 <2.30 ng/dl with negative thyroid-specific antibodies so the patient was placed on levothyroxine (100 mg daily) and referred to endocrinologist. Further evaluation was obtained two months after and revealed the presence of iatrogenic hyperthyroidism (TSH 0.10 IU/ml, free T4 19.44 ng/dl) together with secondary adrenal insufficiency and growth hormone deficiency (GH <0.1 ng/ml). Endocrinology review showed a past history of postpartum hemorrhage after third delivery 6 years ago. Pituitary magnetic resonance imaging (MRI) revealed an empty sella. A diagnosis of SS was made and patient placed on oral glucocorticoid therapy together with modified dose of levothyroxine. A typical presentation of SS include a long period of time between the puerperal hemorrhage and the diagnosis of hypopituitarism. A detailed obstetrical history is needed in order to recognize the pattern and avoid the initiation of thyroid hormone replacement before complete evaluation of pituitary function.

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EP716

Acromegaly and adrenal myelolipoma - Is there a connection?

João Menino[1], Inês Meira[1], Sara Ribeiro[1], Juliana Gonçalves[1], Jorge Pedro[1] & Joana Queirós[1]
[1]São João Universitary Hospital Center, Endocrinology Department, Porto, Portugal

Introduction
Adrenal myelolipomas are rare benign tumors. There has been an association of adrenal myelolipomas with other pathologies with hormonal hypersecretion, such as hypersecretion of adrenocortical hormone (ACTH) in Cushing's Disease and Congenital adrenal hyperplasia. We report a case of acromegaly with co-existent large adrenal myelolipoma.
Case Report
A 48-year-old caucasian male was referred to our Endocrinology consultation for an adrenal incidentaloma. His past medical history was relevant for dyslipidemia, with no medication. He was asymptomatic. On examination, his blood pressure was within normal range and there were no alterations compatible with acromegaly. His previous CT scans revealed a mass in the right adrenal gland that had grown from 40×44 mm to 59×51 mm in 2 years. An adrenal CT scan in our institution described the mass as a myelolipoma with 50×65×69 mm. The analytical studies revealed a negative 1 mg dexamethasone suppression test (0.6 µcg/dl), no elevation in 24 h urinary metanephrines (64.72 µcg/24 h) or normetanephrines (269.98 µcg/24 h), and a normal ionogram (Na 142 mEq/l, K 4.0 mEq/l, Cl 104 mEq/l) with no hypertension history. During the follow-up, the patient suffered a cranial trauma, and a pituitary adenoma was identified in a CT scan. Further analytical studies revealed an elevated IGF-1 (387 ng/ml), normal prolactin levels (4.5ng/ml), and normal thyroid function (TSH 0.92 µUI/ml, fT4 1.03 ng/dl). A pituitary MRI confirmed the presence of an adenoma with 10mm. An Oral glucose tolerance test confirmed the diagnosis of acromegaly, with a nadir of 1.39 ng/ml. The patient is currently awaiting pituitary surgery.
Conclusion
There is evidence that acromegaly is associated with increased incidence of several types of tumors, including colon polyps and thyroid nodules. To our knowledge, there are no reported cases in literature of large adrenal myelolipomas in patients with acromegaly. Our patient presented with a large myelolipoma, with no known etiology, and further studies and case reports are needed to ascertain their correlation.

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EP718

Acromegaly and multiple myeloma: a case report

Ruxandra Paula Ristea[1], Teodora Puşcaş[1], Claudiu Zaharia[2], Serghei Tutovan[1] & Mihaela Stanciu[1,2]
[1]County Clinical Emergency Hospital of Sibiu, Endocrinology, Sibiu, Romania;[2]Lucian Blaga' University of Sibiu, Faculty of Medicine, Endocrinology

Introduction
Acromegaly is a progressive disorder caused by excess growth hormone (GH), usually due to a GH-secreting pituitary adenoma, associated with an increased risk of cancer-related mortality. Insulin-like growth factor 1 (IGF-1) has been involved in tumor development by promoting cell proliferation and inhibiting apoptosis. Multiple myeloma (MM), a plasma cell neoplasm, has been suggested to have a potential link to IGF-1 in its pathogenesis.
Case report
This paper presents the case of a 51-year-old male diagnosed with acromegaly in 2018, with a pituitary macroadenoma (12/11/10 mm) that was surgically removed via a transsphenoidal approach. Postoperatively, the patient developed adrenal insufficiency and central hypothyroidism, necessitating corticosteroid and thyroid hormone substitution. Octreotide effectively controlled GH and IGF-1 levels until March 2022, when the treatment was switched to Lanreotide. Later, the patient experienced nonspecific thoracic pain, the thoracic radiography revealing a 7.3 cm mass in the right superior lateral-thoracic region. A thoracic MRI confirmed a 9 cm mass, later diagnosed as plasmacytoma following biopsy. Radiotherapy was initiated, and a bone marrow examination performed one month later revealed a cytological profile of a grade III A Durie Salmon multiple myeloma. The patient was treated with lenalidomide, low-dose dexamethasone, and bortezomib (VRd regimen) and was proposed for a bone marrow transplant.
Conclusions
Although acromegaly is associated with malignancy, its association with MM has not been thoroughly investigated. This case highlights the need for increased awareness of the potential association between these two conditions. Long-term surveillance and close monitoring of acromegaly patients are essential to detect and manage the development of secondary malignancies. This enables early intervention and improved patient outcomes, especially given the current lack of consensus on therapeutic guidelines and recommended prognosis for multiple myeloma coexisting with acromegaly.

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EP719

A rare case of SIAD in unique association with the rare lesion of a pituicytoma

Sonia Kaniuka-Jakubowska[1], Maria Maksymowicz[2], Grzegorz Zielinski[3], Małgorzata Zdrojewska[4], Nicole Kaźmierczak[1], John Wass[4], Federico Roncaroli[5] & Renata Świątkowska-Stodulska[1]
[1]Facult, of Medicine, Medical University of Gdansky Department of Endocrinology and Internal Medicine, Gdansk, Poland; [2]Maria Sklodowska-Curie National Research Institute of Oncology Department of Cancer Pathomorphology Warsaw, Poland; [3]Militar, Institute of Medicine, Department of Neurosurgery Warsaw, Poland; [4]Oxford University Hospitals NHS Foundation Trust, Department of Endocrinology at the Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, United Kingdom; [5]Facult, of Biology Medicine and Health, University of Manchester, Division of Neuroscience, Manchester, United Kingdom

Introduction
AVP secretion disturbances in pituitary lesions usuall, present as AVP deficienc, due to compression of the posterior pituitary lobe. Excessive secretion of AVP (syndrome of inappropriate antidiuresis) (SIAD) is ver, uncommon in patients with pituitary tumor. A few cases of non-functionating adenoma, prolactinoma, and even pituitary apoplex, were described to present with SIAD. Pituicytoma is a rare tumor of the neurohypophysis. The, usuall, present with visual defects, hypopituitarism, headache, and fatigue. Rarel, the, are associated with Cushing's disease or acromegaly. We present a patient with pituicytoma with SIAD.
Case presentation
A 45-year-old female was admitted with hyponatremia. Low sodium levels were first noted six months before knee replacement surgery. There was no hyponatremia 2 years before, in random check. The patient onl, complained with muscle cramps. The Laboratory results were compatible with SIAD: hyponatremia, plasma hypoosmolality urine hyperosmolarity and increased urinar, sodium excretion, without an, features of adrenal, thyroid or renal disturbances. She underwent detailed screening for malignanc, and the onl, finding was pituitary mass. Pituitary MRI revealed a 6x9x13mm lesion in the left-lateral part of the pituitary with involvement of the pituitary stalk. The patient refused fluid restriction and insisted on surgical treatment. After surgery she presented with AVP deficienc, on graduall, decreasing doses of desmopressin. Histopathological results revealed pituicytoma.
Conclusion
To our knowledge, this is the first documented case of pituicytoma presenting with SIAD. SIAD associated with pituitary lesions is ver, uncommon. A common mechanism causing AVP oversecretion irrespective of the type of lesion is possible including AVP secretion b, the pituitary mass.

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EP722

Pituitary apoplexy presenting with altered level of consciousness, in a normal pituitary gland

Eni Celo[1], Megi Lekbello[2], Erion Spaho[3], Bariola Duro[4], Marsida Kasa[3], Grisilda Gjana[3] & Eriselda Taulla[3]
[1]Trauma University Hospital, Albania;[2]Mother Theresa University Hospital; [3]Trauma University Hospital; [4]Public Medical Center Paskuqan, Paskuqan, Albania

Introduction
Pituitary apoplexy is a rare, potentially life-threatening syndrome caused by ischemic infarction or hemorrhage, generally into a pituitary tumor. The clinical manifestations of PA usually manifest suddenly and include headache, nausea/vomiting, altered awareness and visual abnormalities. Regarding endocrine deficiencies, signs and symptoms of cortisol deficiency are generally observed in the early stage after apoplexy onset, as occurred in our patient. Hypothyroidism, hypogonadism, and growth hormone deficiency are frequent and may occur progressively during weeks, months, or years. In cases with severe, visual or neurological manifestations, surgical decompression is indicated; patients with mild, stable clinical picture can be managed conservatively.
Case presentation
We describe the case of a 67-year-old man with spondylolisthesis L5-S1 who was admitted to Trauma University Hospital in preparation for a scheduled surgery. His medical history included type 2 Diabetes, arterial hypertension, dyslipidemia. In 2020 he was hospitalized with inferior paraplegia and his head CT was normal. He was dismissed from the hospital with some diagnosis including diabetic polyneuropathy and anxiety disorder. The patient appeared to be recovering well until two days later, when it was noticed that he was lethargic and disoriented. His examination resulted in low blood pressure 86/60 mmHg, regular pulse rate of 113 bpm. During the

neurological examination he was unresponsive of verbal stimulations, but responsive of dolent stimuli. His pupils were equal in size and both had normal direct and consensual responses to light. The neurologist recommended a head MRI in which resulted in pituitary apoplexy. In his blood work resulted glycemia – 68 mg/dl, normal BUN, sodium - 120 mmol/l (136-145), potassium – 4.5 mmol/l (3.5-5.1), TSH -1.6 mUI/ml (0.4-4), prolactin – 8.5 ng/ml (3.5-19.4), LH – 4.1 mUI/ml (1.6–15.2), FSH – 2.9 IU/ml (3- 8.1), ACTH – 5.5 pg/ml (6-50), cortisol – 1.8 mg/dl (3.7-19.4). Management included hemodynamic stabilization, correction of electrolyte disturbances and corticosteroid administration: intravenous hydrocortisone was administered with the dose of 100 mg every 8 hours for 24 hours, then transitioned to oral hydrocortisone 20 mg in the morning (08.00) and 10 mg at noon (16.00). After hydrocortisone admission the patient regained his normal mental status with no further episodes of confusion. On the ophthalmologic examination the patient had no visual deficits so a conservative approach was considered safe. After 6 days he was dismissed from the hospital on glucocorticoids replacement.

Discussion

This case illustrates the prompt and accurate diagnosis of pituitary apoplexy after a major surgery leading to optimal patient outcome.

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EP724

Anterior pituitary insufficiency, diagnosis and etiology: about 43 cases

Zaynab Hifdi[1], Saloua Elamari[1], Soukaina Laidi[1] & Marouan Fatima[1]
[1]Cheikh Khalifa Bin Zayed Al Nahyan Hospital, Casablanca, Morocco

Introduction

Pituitary insufficiency results from the failure of the anterior pituitary gland to secrete hormones, and has many causes. Nonspecific clinical manifestations can delay the diagnosis. Our study aims to detail the clinical, biological, radiological, and etiological aspects of pituitary insufficiency, evaluate treatment and identify factors associated with complications.

Material and methods

This retrospective study includes patients over 18 years of age with biologically confirmed pituitary insufficiency. We describe in detail demographic, clinical, paraclinical, etiological and therapeutic aspects. An in-depth analysis identifies factors contributing to diagnostic delays and complications.

Results

The mean age of patients was 59 years, with a sex ratio (M/F) of 0.79. Pituitary insufficiency was often discovered by signs of hyposecretion (27.9%), complications such as pituitary apoplexy, hyponatremia and acute adrenal insufficiency (34.88%), or during a systematic work-up for pituitary adenoma (37.2%). Clinically, 74.4% showed signs of corticotropic insufficiency, 55.8% of gonadotropic insufficiency, and 27.9% of hypothyroidism. Hormonal investigations revealed corticotropic (88.4%), thyrotropic (62.8%), gonadotropic (55.8%), somatotropic (13.95%) and lactotropic (13.95%) deficiencies. Imaging showed abnormalities in 83.72% of cases, including macroadenoma (51.6%), craniopharyngioma (7.1%), inflammatory pathology (11.9%), Sheehan syndrome (7%), empty sella turcica (4.8%), and genetic pathology (9.5%). Iatrogenic, infectious and microadenoma causes have a prevalence of 2.4% each.

Conclusion

Our study highlights an increased prevalence of pituitary insufficiency in women. Vague clinical signs often lead to late diagnosis. A thorough diagnostic approach and individualized therapeutic management are crucial to optimize clinical outcomes in patients with pituitary insufficiency.

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EP725

Inhabitual presentation of parathyroid adenoma

Amel Elkorbi[1], Nawres Bouaziz[1], Mahdi Ferjaoui[1], Rachida Bouatay[1], Naourez Kolsi[1], Harrathi Khaled[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction

Spontaneous extracapsular hemorrhage of a parathyroid adenoma causing cervico-mediastinal hematoma is a rare but life-threatening manifestation. Our objective is to present a rare case of cervico-thoracic hematoma secondary to a spontaneous rupture of a parathyroid adenoma and to specify its clinical, radiological, therapeutic and evolutionary features.

Case report

This is a 50-year-old woman with no significant pathological history who presented to the emergency department for cervico-thoracic ecchymotic lesions associated with upper dysphagia. History evoluted for five days. There was no context of trauma or anticoagulant treatment. The patient complained from generalized bone pain. Physical examination find no cervical mass. A cervico-thoracic scan was showed an extended retropharyngeal hematoma extended to the posterior mediastin associated with signs of compression. We noted also an inferior right retro-thyroid nodule. Parathormone levels was elevated PTH, malignant hypercalcemia and hypophosphoremia were also observed. The diagnosis of symptomatic primary hyperparathyroidism was concluded. Cervical ultrasound and MIBI scintigraphy confirmed the parathyroid nature of this nodule. A lower right parathyroidectomy was performed after correction of serum calcium. The evolution was marked by the normalization of the phosphocalcium balance and the absence of recurrence of the hematoma with a follow-up of one year.

Discussion/Conclusion

The parathyroid origin should be evoked in the presence of any spontaneous cervico-thoracic hematoma associated with compressive signs. The association, although rare, is still possible.

Disclosure of interest: none declared

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EP761

Development of transition readiness assessment questionnaire for patients with rare endocrine diseases

Savi Shishkov[1], Janeta Yaneva[1], Radina Dimitrova[1], Maria Zlateva[2], Mira Siderova[1] & Violeta Iotova[2]
[1]Medical University "Prof. Dr. Paraskev Stoyanov ", Second Department of Internal Medicine, Varna, Bulgaria; [2]Medical University "Prof. Dr. Paraskev Stoyanov", Department of Paediatrics, Varna, Bulgaria

Introduction

Transition readiness is important for adolescents with chronic diseases. Health deterioration in this age may have long-lasting negative effects. Concerning rare endocrine disease, proper knowledge of the condition and treatment is required for optimal disease management.

Aim

The aim of the current study was to develop transition readiness assessment questionnaire suitable for use in pediatric patients and young adults with chronic endocrine diseases.

Methods

A 16 item long questionnaire was developed with similar questions in two variants – one for self-assessment and the other for health care professional (HCP) assessment. In the self-assessment scale, the options were no/I don't know/yes respectively valued as 0/1/2 points. Depending on the level of knowledge each item in the HCP variant was marked with 0 to 2 points. In total, 32 points yielded a 100% score.

Results

The pediatric patients scored on average 54% in the HCP assessment scale compared to 65% for the adults. In 2/10 adult patients' the self-assessment and HCP assessment matched. In the rest (8/10) there was a large discrepancy between self and HCP assessment, with higher result in the latter. The two patients with matching results scored 100% indicating that well educated patients are also more self-responsible In all cases the transition readiness questionaries led to discussion with the patient and/or the parent. A second simplified version of the questionaries was developed that reflects the recommendations given by patients and HCPs. After applying corrections to the initial variant, the second version was evaluated as appropriate by the HCPs.

Conclusion

In the majority of patients HCP assessment scored superior compared to self-assessment tool. A second version of the questionnaire was developed for further testing and validation. Transition readiness assessment with tailored tools is useful in initiating discussions with the adult HCP. This facilitates further preparation for the transfer to adult-centered health care.

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EP764

Reactional pituitary hyperplasia in a young turnerian girl

Rahal Amel[1]
[1]Bologhine Hospital, Endocrinology, Algiers, Algeria

Introduction

Pituitary hyperplasia, defined as an increase in the size of the pituitary gland, is rare in children; the main etiology is the onset of puberty. We report the case of a

15-year-old girl with Growth retardation and amenorrhea. The exploration of the pituitary region revealed pituitary hyperplasia measuring 18 mm x 13 mm. Karyotype revealed Turner mosaic syndrome.
Discussion
In our patient, the hyperplasia was secondary to thyroid cell proliferation secondary to prolonged poorly controlled peripheral hypothyroidism; however, an autoimmune origin cannot be ruled out. It was the response to treatment with Levothyrox, which led to a net regression of hyperplasia of more than 80% after regular treatment with thyroid hormones, which confirmed our diagnosis.
Conclusion
The prevalence of pituitary hyperplasia secondary to peripheral hypothyroidism varies from 21 to 85% and is 70% in patients with TSH levels exceeding 50µUI/ml. The diagnosis of thyrotropic hyperplasia is certain once the process has regressed after hormone replacement, and if this does not occur, the diagnosis should be reconsidered.

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EP765

Diagnosis and management of cervical paragangliomas: a report of six cases

Rachida Bouattay[1], nawres bouaziz[1], Emna Bergaoui[1], Mahdi Ferjaoui[1], Amel El Korbi[1], Nawrez Kolsi[1], Khaled Harrathi[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction
Paragangliomas are rare tumours that arise from paraganglia of neural crest origin. They have an incidence of approximately 1:300,000 and a third arise in the head and neck. A significant number of cervical paragangliomas are relatively asymptomatic, causing little more than a lump in the neck. The rest can cause cranial nerve palsies and infiltrate the skull base. Surgical treatment may cause the same deficits and, in some, risks more serious neurological deficits. The aim of this study is to review our experience in the management of these tumours.
Methods
This is a retrospective study involving cases of cervical paragangliomas, taken care of in our department, over a period of 10 years (2012-2021).
Results
A total of 6 cervical paragangliomas were identified in 5 patients. There were 3 women (60%) and two men (40%) with a mean age of 53.4 years (range: 32-68 years). There was not a family history for paragangliomas. A slow growing, painless neck mass was the main clinical presentation in all cases. There was no evidence of a functional tumor. Physical examination revealed a firm lateral cervical swelling. There were no cervical lymphadenopathy or nerve palsy in all cases. In preoperative imaging, neck ultrasound was performed for all patients. Computed tomography was performed in 4 cases and imagnetic resonance imaging in 3 cases. Of these 5 cases, 4 patients had carotid body paragangliomas, one of which is bilateral. Only one patient had vagal paraganglioma. We did not observe any malignant tumor. Secretory activity was studied in all cases an all patients had normal level of metanephrines. In our study, 3 patients were treated with surgery without postoperative complication in follow-up. One patient was treated with radiotherapy, while there was a patient who was not followed up.
Conclusions
Cervical paragangliomas are slow-growing tumours. Due to its localization near large vascular structures and cranial nerves, the surgical treatment is challenging. The surgery should be as conservative as possible to minimize the complications. In that aspect, preoperative embolization was mainly advised in large and hyper-vascularized tumors. However, in some parts of the world, radiotherapy (whether conventionally fractionated or as a single treatment from the 'gamma knife') or a watchful waiting policy is preferred.

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EP770

Neuroprotective steroids in patients with multiple sclerosis

Radmila Kančeva[1,1], Martin Hill[1], Marta Velíková[1], Lyudmila Kancheva[1], Josef Včelák[2], Radek Ampapa[3], Michal Židó[4], Ivana Štětkářová[4], Anna Libertinová[5] & Eva Havrdová - Kubala[6]
[1]Institute of Endocrinology, Steroid Hormones and Proteohormones, Prague, Czech Republic;[2]Institute of Endocrinology, Molecular Biology and Genetics, Prague, Czech Republic;[3]Jihlava Hospital, MS center, Jihlava, Czech Republic;[4]3FM CU and UHKV, Neurology, Prague, Czech Republic;[5]Faculty of Medicine, Charles University and University Hospital Motol, Neurology, Prague, Czech Republic;[6]General Faculty Hospital, Clinic of Neurology, Prague, Czech Republic

Multiple sclerosis (MS) is a common inflammatory autoimmune and demyelinating disease of the central nervous system (CNS) that compromises health and leads to disability. Sex differences in the prevalence and progression of MS suggest the involvement of sex steroids in the pathophysiology of MS. In late pregnancy, at the highest levels of progesterone and estradiol, the number of relapses decreases and increases again after delivery due to changes in steroid levels. In addition, dehydroepiandrosterone (DHEA) and its derivatives may also influence the development of MS. Therefore, the correlations between circulating steroid levels in MS patients were evaluated with respect to the pathophysiology of MS. The levels of endogenous steroids ($n=85$) (quantified using the GC-MS/MS platform) in serum samples from 23 fertile-aged follicular menstruating women with multiple sclerosis and 7 premenopausal women ($n=7$) before treatment were simultaneously compared with age-matched controls ($n=16$) using a multivariate regression with dimensionality reduction (orthogonal projection to latent structure, OPLS) including the age of the volunteers. The presence of MS was negatively correlated with serum endogenous steroid levels, with steroid levels explaining 29% of the presence of MS. The analytes included sulphates of Δ^5 pregnanes (glutamate and negative $GABA_A$ receptor modulators) and androstanes, their free analogues, neuroprotective and immunoprotective 7α-hydroxy, 7-oxo-, 7β-hydroxy and 16α-hydroxy-metabolites of Δ^5 androstanes, progestogens (bioactive progesterone, 20α-dihydroprogesterone, 17-hydroxyprogesterone, its free and conjugated 20α-dihydrometabolite, 16α-hydroxyprogesterone) inactive Δ^4 androgen androstenedione, bioactive Δ^4 androgens testosterone and 5α-dihydrotestosterone including its conjugated form, estrogens estrone sulfate and bioactive estradiol, a variety of 5α/β reduced free and conjugated 20-oxo and 20α-dihydropregnanes (including GABAergic positive modulators with hydroxyl in the 3α-position, glutamate receptor modulators). Furthermore, the analytes measured included 5α/β-reduced free and conjugated androgens also including a number of neuroactive steroids and finally the active corticosteroids cortisol and corticosterone as well as the inactive cortisol metabolite cortisone and finally 11β-hydroxy-androstanes. It was found that 28 steroids were significantly negatively correlated with MS. These steroids included a number of bioactive substances including five neuroprotective and immunoprotective 7α-hydroxy, 7-oxo-, 7β-hydroxy-Δ^5 androstanes, a number of GABAergic positive modulators with a hydroxyl at the 3α-position, and two 11β-hydroxy androstanes. Thus, it is likely that lower serum levels of a number of bioactive steroids in MS patients could be related to the pathophysiology of this disease. Grant NU20-04-00450 from the Ministry of Health of the Czech Republic supported the study.

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EP879

Pituitary stalk interruption syndrome – a rare case of delayed onset adrenal crisis

Huajing Ni[1], Denuka Kankanamge[1], Martina Preda[2], Antonio Di Ieva[1] & Veronica Preda[1]
[1]Faculty of Medicine and Health Sciences, Macquarie University, Macquarie Park, Australia;[2]I-MED Radiology, Sydney, Australia

Background
Pituitary stalk interruption syndrome (PSIS) is a rare congenital condition characterised by the triad of thin or absent pituitary stalk, hypoplasia of the adenohypophysis, and ectopic neurohypophysis. PSIS has multifactorial aetiology with highly heterogenous clinical manifestations, usually diagnosed in early infancy or childhood. There have been previous reports of untreated panhypopituitarism diagnosed in adulthood, indicating preservation of some pituitary function. Nearly all patients had normal posterior pituitary function. It is difficult to predict the onset of hormonal crisis, making routine surveillance of critical importance. We present an unusual case of a 31-year-old male who has been off hormonal supplementation for at least a decade with an acute hypoadrenal crisis. Our case highlights the challenges in transition of care from paediatric to adult services and the importance of long-term follow-up of PSIS patients.
Clinical Case
Our patient presented following an acute episode of collapse in the context of a recent viral infection, with profoundly hyponatremia (98 mmol/l) and seizure. Congenital hypopituitarism was diagnosed at 10 days of age and managed with hydrocortisone, thyroxine and growth hormone replacements under paediatric endocrinology care, reaching predicted height of 170 cm . After a brief period of testosterone therapy at age 18, he was lost to follow-up and had been on no replacement between age 18–30. He was able to maintain a physically demanding job without any significant adrenal crises or hospitalisation until his recent presentation. Physical examination revealed no dysmorphic features. His biochemistry during admission was consistent with central hypothyroidism (TSH 0.81 mIU/l, FT4 7 pmol/l, FT3 $<$ 1.5 pmol/l) with non-detectable growth hormone and gonadotropins. Cortisol was measured post stress doses of hydrocortisone and ACTH was 1.9 pmol/l. Prolactin was 300 mIU/l. MRI pituitary confirmed extremely thin stalk with small residual pituitary gland, an

area of T1 brightness representing probable ectopic pituitary tissue, and posterior bright spot was not present. He was recommenced on glucocorticoid and thyroxine replacement with normalisation of serum sodium, and will continue to follow up with an adult service.

Conclusion

The present case aims to raise awareness of PSIS, a rare condition predominantly diagnosed in the paediatric population with lasting impact into adulthood. It should be emphasised to patients as they enter adolescence the importance of ongoing hormone replacement, and active efforts should be made to facilitate transition of care to an adult service along with medical alerts, sick day management and family awareness of the condition.

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EP880

Acromegaly complicated with hypercortisolemia

Saori Kitayama[1], Yasufumi Seki[1], Satoshi Morimoto[1], Noriyoshi Takano[1], Kaoru Yamashita[1], Daisuke Watanabe[1], Kanako Bokuda[1], Kosaku Amano[2], Takakazu Kawamata[2], Takashi Komori[3], Tatsuo Sawada[3] & Atsuhiro Ichihara[1]

[1]Tokyo Women's Medical University Hospital, Department of Internal Medicine, Tokyo, Japan;[2]Tokyo Women's Medical University Hospital, Department of Neurosurgery, Tokyo, Japan;[3]Tokyo Women's Medical University Hospital, Department of Pathology, Tokyo, Japan

Introduction

Acromegaly hardly complicates hypercortisolemia due to co-over-secretion of ACTH from the pituitary tumor. Herein, we present a case of acromegaly with hypercortisolemia.

Clinical case

A 68-year-old woman visited a local clinic due to bitemporal visual field defects. A magnetic resonance imaging scan of the pituitary gland showed a 25 mm-sized mass extending from the sellar to the suprasellar region, and she was referred to our hospital for further evaluation. Physical examination revealed combined features of acromegaly and Cushing's disease including cranial ridges, macroglossia, enlargement of the nose and lips, moon face, and central obesity. Her body mass index was 23 kg/m^2. Serum levels of hemoglobin A1c, low-density lipoprotein cholesterol, and triglyceride were 5.3%, 104 mg/dl, and 133 mg/dl, respectively. Serum GH and insulin-like growth factor (IGF)-1 levels were 2.59 ng/ml and 238 ng/ml (+2.2 SD) (reference, 60-180), respectively. Serum GH levels were not suppressed (1.77 ng/ml) during a 75 g oral glucose tolerance test. Morning plasma ACTH and cortisol levels were 55.9 pg/ml (reference, 7.2-63.3) and 13.5 μg/dl (reference, 4.0-18.3), respectively. Plasma cortisol levels were suppressed not by 0.5 mg of dexamethasone but by 8.0 mg of dexamethasone, suggesting a coexistence of acromegaly and Cushing's disease. Transsphenoidal surgery was performed, and the immunostaining of the excised tumor cells was positive for GH but negative for ACTH. GH and IGF-1 levels were normalized just after the surgery. Although the cortisol levels remained unsuppressed by 0.5 mg of dexamethasone 8 years after the surgery, the case had not exhibited metabolic abnormalities associated with Cushing's disease.

Discussion

The co-secretion of GH and ACTH from the pituitary tumor is extremely rare because the expressions of the two hormones are regulated by different transcription factors. However, the endocrinological tests suggested a coexistence of acromegaly and Cushing's disease in our case. Pseudo-Cushing's syndrome, a condition accompanied by physiologic overactivity of the hypothalamic-pituitary-adrenal axis, displays signs of Cushing's disease. The absence of pathological evidence and metabolic impairment of Cushing's disease suggested this case as acromegaly with hypercortisolemia associated with pseudo-Cushing's syndrome.

Conclusion

We present a case of acromegaly with hypercortisolemia associated with pseudo-Cushing's syndrome. The significance of hypercortisolemia might need to be carefully interpreted in patients with acromegaly.

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EP882

Pituitary microadenoma in children and adolescents: minireview of the literature

Ashraf Soliman[1], Noor Hamed[1], Nada Alaaraj[1], Fawzia Alyafei[1], Shayma Mohamed[1] & Sohair Elsiddig[1]

[1]Department of Pediatrics Hamad Medical Centre, Pediatric Endocrine, Doha, Qatar

Background

Pituitary tumors are uncommon in childhood and adolescence, with a reported prevalence of up to 1 per million children. Only 2 - 6% of surgically treated pituitary tumors occur in this age group. Although these tumors are almost never malignant and hormonal secretion is rare, they can cause significant morbidity. Pituitary microadenomas, though rare, pose unique challenges due to their potential hormonal activity and growth during a critical developmental period. Microadenomas are defined as those smaller than 10 mm, while those larger are classified as macroadenomas.

Methods - Literature Search

We conducted a search of the medical literature using Pubmed, Google Scholar, and Scopus, focusing on research articles about pituitary microadenomas in children and adolescents. A total of 33 articles met our search criteria and were analyzed for this mini review.

Results and discussion

Prevalence: Pituitary adenomas constitute about 3% of all intracranial neoplasms in children and account for 5% of all pituitary adenomas. A 60-year study on pediatric pituitary adenomas revealed a small percentage of microadenomas, underscoring their rarity.

Clinical Presentations

In a study of 20 microadenomas, 75% occurred in girls, with an average age at diagnosis of 14.4 years. Common symptoms included amenorrhea (53.3%) and galactorrhea (42.8%) in girls, and gynecomastia in boys.

Pathological types

Prolactinomas, corticotrope, and somatotroph adenomas are the most common types. Among 42 pituitary adenomas studied, 33% were macroadenomas, and 21% were microadenomas, with prolactin-secreting and ACTH-secreting adenomas being the most prevalent.

Management

Treatment strategies are guided by the tumor's functionality and size. Medical management is typically the first choice for functioning microadenomas that secrete excess hormones. Surgical intervention, primarily transsphenoidal surgery, is reserved for symptomatic or functioning tumors unresponsive to medical therapy. Radiotherapy and radiosurgery are considered in refractory cases or when surgery and medical therapy fail.

Outcomes

The prognosis for children with pituitary microadenomas is generally favorable. For instance, in medically managed prolactinomas, many patients achieve normal prolactin levels and tumor shrinkage. Success rates for surgically treated cases vary based on tumor type and the extent of its removal.

Conclusion

Pediatric pituitary microadenomas, while rare, require a nuanced approach to diagnosis and management. Advances in diagnostic techniques and treatment protocols have improved outcomes. Ongoing research and vigilant long-term follow-up are crucial for optimizing patient care and outcomes, particularly due to the potential for recurrence and long-term endocrine effects.

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EP883

Sheehan syndrome in a tunisian hospital: a clinical experience of 123 cases

Sawsen Nouira[1], Hamza Elfekih[1], Amel Maaroufi[1], Yosra Hasni[1], Molka Chaieb[1] & Kussay Ach[1]

[1]University Hospital Farhat Hached, Endocrinology, Sousse

Introduction

Sheehan's syndrome (SS) results from severe post-partum hemorrhage leading to necrosis of the pituitary gland. Here we describe the clinical characteristics of patients with Sheehan syndrome.

Methods

We conducted a 44-year cohort study (1977 to 2021) of patients with SS followed at the endocrinology department of Farhat Hached Hospital in Sousse, Tunisia. Medical history, physical examination findings and laboratory investigations were documented.

Results

One hundred and twenty-three patients diagnosed with Sheehan syndrome were included. The mean age at diagnosis was 43 ± 12 years [21-78]. The mean delay between the previous obstetrical event and the diagnosis of SS was 11 years. Thirty-four patients (28%) gave birth at home. All patients had a history of obstetric hemorrhage, 79 cases (64%) had blood transfusion and 16 cases (13%) had undergone peripartum hysterectomy. The most frequent symptoms were asthenia in 108 cases (87%), amenorrhea in 106 cases (86%), agalactia in 102 cases (86%) and loss of pubic and axillary pilosity in 44 cases (36%). At diagnosis, 93% (n = 115) had corticotropic deficiency, 93% (n = 104/112) had gonadotropin deficiency, 91% (n = 113/123) had thyrotropic deficiency, and 86%

($n=112$) had lactotropic deficiency. The somatotropic axis was investigated in 42%($n=51$) of patients, and somatotropic deficiency was found in all of them. Sheehan's syndrome was diagnosed relatively late (>1 year) in 100 patients. We found that the majority of multiparous patients 83%($n=83$) consulted late ($P=10^{-3}$). More than half the patients who consulted early ($n=17/23$) had a history of blood transfusions ($P=10^{-3}$).
Conclusions
Early diagnosis of SS based on our clinical findings is important for proper management of these patients through multidisciplinary collaboration between obstetricians and endocrinologists. In addition, special attention and strict follow-up are required for all women presenting with massive hemorrhage in the last trimester, in order to identify cases of SS.

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EP885

Silent gonadotroph adenomas and platelet dynamics

Ekin Yiğit Köroğlu[1], Gülsüm Karaahmetli[1], Didem Özdemir[2], Servet Güreşçi[3], Denizhan Divanlıoğlu[4], Fatma Dilek Dellal Kahramanca[1], Oya Topaloğlu[2], Reyhan Ersoy[2] & Bekir Çakır[2]
[1]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yıldırım Beyazıt University Faculty Of Medicine, Endocrinology and Metabolism, Ankara; [3]Ankara Bilkent City Hospital, Pathology, Cankaya; [4]Ankara Bilkent City Hospital, Neurosurgery, Cankaya

Objective
Gonadotroph adenomas are the most common subtype of pituitary adenomas. Rarely, clinical findings may occur due to the secretion of high amounts of biologically active gonadotropins. It may affect platelet activity if there is an excessive increase in the release of estrogen and testosterone or if it is used in pharmacological doses. In this study, we aimed to investigate whether platelet activity indices and coagulation parameters were affected in silent gonadotroph adenomas.
Methods
Patients who operated for a pituitary adenoma in our center between March 2019 and July 2023 were recruited for the study. Presence of thromboembolic disease history, preoperative and postoperative (after the first month) follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone, free testosterone, estradiol (E2), platelet count, mean platelet volume (MPV), platelet distribution width (PDW), international normalized ratio (INR) and activated partial thromboplastin time (aPTT) levels of the patients were recorded.
Results
25 female patients and 32 male patients were included in the study. We found no statistically significant difference between FSH, LH, testosterone, and E2 levels in both genders' preoperative and postoperative periods. No statistically significant difference was observed in MPV, PDW, INR, and aPTT in both genders. None of the patients in the study had a history of thromboembolic events. No thromboembolic event was observed in any patient within the first year of the postoperative period.
Conclusion
Silent gonadotroph adenomas do not affect platelet activity in male and female patients.

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EP887

Overview of pituitary malignancies

Hassan Heshmati[1]
[1]Endocrinology Metabolism Consulting, LLC, Hassan Heshmati and Valerie Shaw Endocrine Research, Anthem, AZ, United States

Introduction
Pituitary malignancies include pituitary carcinomas and pituitary metastases. These malignancies are ver, rare and create important diagnostic and therapeutic challenges. This review presents an update on pituitary malignancies.
Methods
A systematic search of literature was conducted using the search terms pituitary carcinoma, pituitary metastasis, prevalence, management, and survival.
Results
Pituitary carcinomas are tumors of adenohypophyseal origin that have craniospinal and/or systemic metastases. They are denominated metastatic pituitary neuroendocrine tumors and represent around 0.1%-0.2% of all pituitary tumors. The affected patients are mainly males. The diagnosis of pituitary carcinomas is often delayed, and several cases are only diagnosed at autopsy. The clinical and biochemical features of pituitary carcinomas are usually similar to those of benign pituitary tumors. Most pituitary carcinomas are hormone-secreting tumors (mainly prolactin- and adrenocorticotropic hormone-secreting tumors) but some pituitary carcinomas develop in the setting of silent pituitary tumors. There are no well-established histopathologic, molecular, or genetic distinctions between benign pituitary tumors and pituitary carcinomas. The diagnosis of pituitary carcinomas cannot be made until metastases are identified. The metastases can be in the central nervous system (e.g., brain, spinal cord, dura, and leptomeninges) and/or distant organs (e.g., bone, liver, and lungs). The treatment of pituitary carcinomas includes surgery (e.g., gross total or subtotal resection), radiotherapy, and medical therapy (e.g., suppression of excess hormonal secretion, correction of hormonal deficiencies, chemotherapy, and immunotherapy). Although the prognosis is relatively poor, the survival of pituitary carcinomas has significantly improved since the introduction of temozolomide, a drug used as a first-line chemotherapy. Patients with metastases to the central nervous system have also a longer survival than those with distant organs metastases. Pituitary metastases account for approximately 1% of all pituitary tumors. They invade mainly the posterior lobe of the pituitary gland. Breast, lung, kidney, and prostate are the most common primary cancers. In several patients, the primary cancer remains unknown. Most cases are asymptomatic and often diagnosed at autopsy. Symptomatic patients present with diabetes insipidus, hypopituitarism associated with hyperprolactinemia, and visual impairment. The treatment of pituitary metastases includes surgery, radiotherapy, and medical therapy (e.g., correction of hormonal deficiencies, chemotherapy, and immunotherapy). The prognosis is poor. The median overall survival is approximately 1 year.
Conclusions
Pituitary carcinomas and pituitary metastases are rare malignancies that are difficult to diagnose and treat. They have poor prognosis. Most pituitary carcinomas are hormone-secreting tumors. The main cancers metastasizing to the pituitary gland are breast and lung cancers.

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EP888

A male case of autoimmune hypophysitis

Oumaima Dimassi[1,2], Najwa Lassoued[1,2], Nada Hassairi[2], Maryem Souissi[1,2], Wafa Alaya[1,2] & Habib Sfar[1,2]
[1]Mahdia, Tunisia; [2]Taher Sfar University Hospitaly Endocrinology departement, Mahdia, Tunisia

Background
Hypophysitis is a heterogeneous condition that leads to inflammation of the sella and/or suprasellar region, potentially resulting in hormonal deficiencies and/or mass effects. The overall incidence and prevalence of hypophysitis has dramatically increased over the past decade, mainly due to increased awareness of the condition in the medical community. The clinical presentation varies from an asymptomatic condition to a fatal disease often as a result of electrolyte abnormalities due to glucocorticoid deficiency in the context of adrenal crisis from central adrenal insufficiency. A presumptive diagnosis can be made often without biopsy. Hormone replacement and, in selected cases, careful observation is advised with imaging follow-up.
Case presentation
A 47-year-old male patient with a history of dyslipidemia and smoking habit, presented with muscle cramps, paresthesias, profound fatigue, constipation, and significant weight loss over a year. Initial diagnostic tests revealed primary hypothyroidism due to Hashimoto's thyroiditis. Upon admission, clinical signs included low blood pressure and episodes of hypoglycemia. Laboratory findings indicated corticotropic insufficiency, gonadotropin deficiency, and normal prolactin. Cerebral MRI findings were pivotal in the diagnostic process, revealing no abnormalities in the anterior pituitary, homogeneous enhancement and a normal pituitary stalk. The diagnosis of autoimmune hypophysitis was made due to the association of anterior pituitary insufficiency and Hashimoto's thyroiditis. Treatment was initiated promptly, incorporating levothyroxine, oral hydrocortisone, and testosterone injections. Despite the severity of the initial presentation, significant improvement was observed with no reported functional complaints.
Conclusions
Although the diagnosis of hypophysitis ultimately requires a biopsy, the presumptive diagnosis based on clinical manifestation in conjunction with magnetic resonance imaging (MRI) and laboratory findings is typically made in clinical settings. Milder forms of hypophysitis are treated with replacement of deficient hormones. Timely diagnosis and interventions are keys to prevention of the lethal complications of this disease.

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EP889

Cyclic cushing's syndrome: understanding the patterns of a complex endocrine disorder

Beatriz Tavares da Silva[1], Andreia Martins Fernandes[2], Raquel Almeida[3], Maria Teresa Pereira[1] & Cláudia Amaral[1]
[1]Porto, Porto, Portugal; [2]Coimbra, Coimbra, Portugal; [3]Santa Maria da Feira, Santa Maria da Feira, Portugal

Introduction
Cyclic Cushing's Syndrome is an uncommon disorder characterized by recurrent episodes of elevated cortisol levels, alternating with periods of normal cortisol secretion. These cycles of hypercortisolism can occur at regular or irregular intervals, ranging from days to years between episodes.
Case presentation
A 57-year-old woman evaluated at the Endocrinology Outpatient Clinic because of symptoms of hypercortisolism with 18 months of evolution: unexplained weight gain (15 kilograms), worsening blood pressure control, thin arms and legs, a moon face and proximal muscle weakness. On physical examination, the patient presented a cushingoid facies without facial plethora, cervical fat accumulation and centripetal obesity. Her medical history included hypertension since 2019 with optimal control using two antihypertensive drugs. She underwent laboratory investigation to document the presence of hypercortisolism and was diagnosed with ACTH-dependent hypercortisolism, evidenced by elevated midnight salivary cortisol levels (37.9 nmol/l; n <7.6) and 24-hour urinary free cortisol (UFC) (4485.3 nmol/day; NR: 11.8-485.6), as well as elevated ACTH (137.4 pg/mL; n <60). Pituitary MRI confirmed the presence of a microadenoma with 7mm. Although she was proposed for bilateral inferior petrosal sinus sampling (BIPSS), in the days preceding the procedure, she presented significant improvement of her symptoms. Cortisol levels dropped significantly: 0800 hours serum cortisol of 4.5 ug/dl (NR: 6.2-19.3) measured twice and a 24-hour UFC of 18.7 ug/day (NR: 4.3-176). Subsequent MRI failed to definitely demonstrate pituitary apoplexy and there were no clinical evidence suggesting this diagnosis. The diagnosis of Cyclic Cushing's Syndrome was assumed to be the most likely and BIPSS was not performed. One month later, she was evaluated for generalized fatigue and there was again evidence of hypercortisolism with elevated midnight salivary cortisol levels (63.0 nmol/l; n <7.6) and a 24-hour UFC of 2540.6 nmol/day (NR: 11.8-485.6), confirming recurrent cortisol secretion in favour of the diagnosis of Cyclic Cushing's Syndrome. BIPSS is scheduled to be performed later this month, despite the increased probability of Cushing Disease.
Conclusion
Cyclic Cushing's Syndrome poses a unique challenge in the realm of endocrine disorders. Unlike its more predictable counterpart, this syndrome involves intermittent hormone level fluctuations, complicating both diagnosis and treatment. The diagnosis remains a complex task and demands continuous patient follow-up. This case emphasize the importance of optimizing confirmation of hypercortisolism at the time of BIPSS.

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EP890

Temozolomide therapy in an aggressive ACTH-producing pituitary tumour

Inês Redondo de Carvalho[1], Gonçalo Fernandes[2] & Francisco Sobral do Rosário[1]
[1]Hospital da Luz Lisboa, Endocrinology Lisbon, Portugal; [2]Hospital da Luz Lisboa, Oncology Lisbon, Portugal

Introduction
Aggressive pituitary tumours are rare (<2% of pituitary macroadenomas) and are characterized by local invasiveness, progressive growth, and multiple recurrences despite conventional treatments. Approximately 30-40% of these tumours are functioning corticotroph adenomas. Diagnosis relies on clinical, imaging evaluation with magnetic resonance imaging (MRI), hormonal, and pathological assessments. Its therapeutic approach is challenging.
Clinical Case
A 53-year-old woman diagnosed in 2015 with Cushing's disease due to a pituitary macroadenoma underwent transsphenoidal resection, with no apparent residual lesion and normalization of ACTH levels. Histology identified a corticotroph pituitary adenoma with a low Ki67 (<3%) and p53+ in more than 50% of cells. One year later, she experienced a significant tumour recurrence, leading to a second surgical intervention where complete tumour resection was impossible. Therapy with cabergoline and gamma-knife radiosurgery was conducted, resulting in residual tumour. Elevated ACTH levels and hypercortisolism persisted, and therefore metyrapone was initiated. The clinical picture of hypercortisolism worsened, leading to the development of diabetes mellitus, vertebral osteoporotic fractures, and retinal detachment. In 2020, she underwent bilateral adrenalectomy. Since then, there has been a gradual rise in ACTH levels with persistent lesions. In 2023, she experienced a sudden episode of ophthalmoplegia and left eyelid ptosis, consistent with homolateral cavernous sinus syndrome. MRI confirmed left cavernous sinus invasion by the pituitary tumour, prompting urgent transsphenoidal surgery with subtotal lesion resection. Histology revealed a corticotroph pituitary tumour with Ki67 15% and an increased number of mitoses. Postoperative imaging control showed residual intra-sellar lesion with bilateral cavernous sinus involvement. Genetic testing (FoundationOne) did not identify any mutation considered a therapeutic target. Following multidisciplinary discussion, chemotherapy with temozolomide was initiated (administered every 3 weeks, with a dose of 150mg/m^2 in the first cycle and 200 mg/m^2 in the following). The treatment was well-tolerated, without hematological complications. An initial reduction in ACTH levels was observed, as well as lesion stability at the end of the 6th cycle.
Conclusion
This case presents an aggressive corticotroph adenoma, illustrating the complexity of its treatment, which requires a multimodal and multidisciplinary approach. Due to tumour progression despite various interventions, temozolomide therapy was initiated.

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EP891

Mucocutaneous diathesis in severe cushing disease

Inês Redondo de Carvalho[1], José Carda[2], Carlos Tavares Bello[1], Isabel Esperança[3] & Francisco Sobral do Rosário[1]
[1]Hospital da Luz Lisboa, Endocrinology Lisbon, Portugal; [2]Hospital da Luz Lisboa, Haematology Lisbon, Portugal; [3]Hospital da Luz Lisboa, Intensive Care Medicine, Lisbon, Portugal

Introduction
Cushing syndrome is a complex disease with multisystemic manifestations. It includes skin and connective tissue abnormalities, in which glucocorticoids reduce the synthesis and production of collagen, resulting in skin thinning, subcutaneous vascular tissue frailty and mucocutaneous bleeding.
Case report
A 59-year-old woman with history of hypertension, type 2 diabetes, hypercholesterolemia, and chronic kidney disease, was admitted to the Intensive Care Unit due to severe hypokalaemia. In the past months, she referred muscle weakness, asthenia, weight gain, and more recently elevated blood pressure with headaches. Physical examination at admission revealed a cushingoid phenotype and haemorrhagic diathesis (petechiae on the abdominal girdle and lower limbs). Blood work-up was consistent with ACTH-dependent hypercortisolism and MRI showed a pituitary macroadenoma invading adjacent structures. Unexpectedly, the patient developed subconjunctival haemorrhage, epistaxis, bleeding at puncture sites, and diffuse petechiae. No menorrhagia, haematuria, gastrointestinal bleeding or hemarthrosis occurred. The patient was not taking acetylsalicylic acid, non-steroidal anti-inflammatory drugs, or anticoagulants. Considering the mucocutaneous diathesis, the patient was submitted to an extensive diagnostic study which included grade I thrombocytopenia (100-110$\times$10^9/l) (reference range: 170-430$\times$10^9/l), normal coagulation time (PT, aPTT and TT), increased fibrinogen level, normal platelet aggregation studies by Platelet Function Analyser (PFA-100) and Aggregometry test, increased Von Willebrand factor and activity, and increased VIII factor. Given the absence of platelet or coagulation abnormalities that could justify the haemorrhagic diathesis, it was assumed to be related with vascular and subcutaneous fragility secondary to hypercortisolism. A skin biopsy was not carried out because of the established skin diathesis and since it would not change the therapeutic attitude. The bleeding diathesis did not allow for surgical intervention. Following multidisciplinary discussion, mifepristone was initiated at 200mg/day, leading to significant improvement in the haemorrhagic diathesis. The patient underwent bilateral adrenalectomy due to the risk of a neurosurgical procedure. However, postoperatively, the patient developed multisystem organ failure of unknown origin resulting in the patient's demise.
Conclusion
The authors report on a case of severe Cushing disease, whose main clinical manifestations were the hypokalaemia and haemorrhagic diathesis. Mucocutaneus haemorrhage is not usually severe in Cushing's, often being the thromboembolic events the clinician's major concern from the haematological standpoint. Medical treatment with mifepristone rapidly improved both conditions and can be considered a treatment option in this setting. Clinical heterogeneity in Cushing disease is very wide and a multidisciplinary approach should be undertaken to improve patient care.

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EP892

Cardiac arrest as a presentation of hypophysitis-induced hypopituitarism developed following a COVID-19 infection

Nino Tedoradze[1], Mariam Pailodze[1], Ann Kobaidze[1], Meri Davitadze[2], Sophio Tsikarishvili[1], Nino Akiashvili[1] & Lika Jajanidze[1]
[1]Caucasus Medical Centre, Endocrinology Tbilisi, Georgia; [2]Universit, of Birmingham, Institute of Applied Health REsearch, Birminghem, United Kingdom

Background
Hypophysitis is a rare inflammatory condition of the pituitary gland, speculated to have autoimmune aetiology. The diverse clinical presentations rely on hormonal deficiencies and the pathophysiological impact on the target organs. This condition may give rise to life-threatening complications. MRI is the best imaging modality for diagnosis and the conclusive diagnosis necessitates a biopsy of the affected tissue. The optimal management approach remains a subject of controversy. Herein, we describe a case of hypophysitis with sudden cardiac arrest.
Case Report
An 18-year-old female was admitted to the hospital due to loss of consciousness during swimming, and involuntary movements. Cardiopulmonary resuscitation was performed successfully with restoration of cardiac function. Further investigation revealed mitral valve abnormalities, systemic inflammatory syndrome, and severe metabolic acidosis. Laboratory tests showed: pH=6.5, PcO2=34, Po2=275, Hco3=2.9 mmol/l, lac=22. Cardiac catheterization ruled out significant coronary stenosis, pinpointing the cause of cardiac arrest to ventricular fibrillation. Four months prior, patient had a Covid-19 infection, and a month later she developed visual disturbances, transient blindness, hearing loss episodes, and menstrual irregularities. laboratory tests showed slightly elevated TSH, and pituitary hyperplasia on brain MRI. Medications were not prescribed. On the 3rd day of hospitalisation, patient developed polyuria and hypernatremia, plasma and urine osmolarity were normal, ACTH=9.0 0 pg/ml, Cortisol=16.320 μg/dl (5.27-22.4), TSH=0.10 μIU/ml (0.35-5.5), FT4=0.59 pg/ml (0.83-1.43), FT3=0.7 pg/ml (3-4.74). Considering the previous MRI findings, hypophysitis was suspected and the diagnosis of hypopituitarism with hypothyroidism and hypocortisolism was established. The patient was commenced on replacement therapy with hydrocortisone and levothyroxine sodium, alongside desmopressin for fluid and electrolyte balance. For cardiac rhythm disturbances, antiarrhythmic medication was started, the patient underwent an implantation of a cardioverter-defibrillator. Currently the patient on levothyroxine sodium 50 mg daily, Hydrocortisone 20mg daily, metoprolol 100mg twice weekly, levetiracetam 500 mg twice daily. Follow-up assessments demonstrated improvement in cardiac function and normalisation of hormone levels. In 6 months, the patient failed short Synacthen test and was continued on replacement.
Conclusion
Making an accurate and timely diagnosis of hypophysitis still remains a challenge. It is possible that Covid-19 was the reason of hypophysitis. Recognizing and addressing early symptoms and signs of hypopituitarism can be potentially life-saving, in particular when it is masked with cardiac disorders. Additionally, detailed history-taking may play a key role in establishing the diagnosis. Addressing hormonal deficiencies early on not only prevents potential life-threatening events but also improves the overall quality of patient care.

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EP893

Macroprolactinemia and empty sella syndrome

Oumayma Zarrouk[1], Taieb Ach[1], Rihab Kochtali[1], Ghada Saad[1], Asma Ben Abdelkrim[1], Molka Chadli Chaieb[1] & Koussay Ach[1]
[1]University Hospital of Farhat Hached, Endocrinology Departement, Sousse

Introduction
Macroprolactinemia is a polymeric form of prolactin release that leads to clinically paucisymptomatic presentations. It can be isolated or associated with other causes of hyperprolactinemia. We report the case of macroprolactinemia discovered in a patient being treated for an empty sella turcica.
Case report
This concerns a 47-year-old patient, monitored since the age of 31 for moderate idiopathic hyperprolactinemia discovered following bilateral galactorrhea and amenorrhea. There was no associated medication use. Her exploration revealed a prolactin level of 635 mIU/l. Thyroid function tests were normal (T4=10.2 ng/l, TSH=1.76 mIU/l). A brain CT scan showed an empty sella turcica. The patient's evolution under 5 mg/day of dopamine agonists was marked by the occurrence of pregnancy with persistent moderate hyperprolactinemia in the postpartum period. The patient reached menopause at the age of 47, with elevated gonadotropins (FSH=78 mIU/ml, LH=33 mIU/ml, and estradiol: 35 pg/ml). Consequently, the treatment was discontinued, and regular clinical monitoring was initiated. Chromatography revealed a predominance of the macroprolactin form with 4.8% monomeric prolactin, 5% big prolactin, and 83% big big prolactin.
Conclusion
Our observation suggests that macroprolactinemia can be associated with classical etiologies of moderate hyperprolactinemia, such as an empty sella turcica. Detecting it could potentially avoid the need for dopamine agonist treatment.

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EP895

Delayed puberty due to pituitary tumours (macroprolactinomas) is rare, a case report

Furhana Hussein[1], Gideon Mlawa[2], Zahid Khan[2], Belayet Hossain[2], Muhammad Saleem[2] & Man-Yan Cheung[2]
[1]Queen's Hospital, Endocrinology and Diabetes/Acute Medicine, London, United Kingdom; [2]Queen's Hospital, London, United Kingdom

Introduction
There are multiple causes of delayed puberty including constitutional delay in growth and puberty, chronic diseases, hypothyroidism, and pituitary tumours (e.g. craniopharyngioma). Delayed puberty due to macroprolactinoma is rare.
Case Presentation
A 23-year-old male was reviewed in the Endocrine clinic after presenting with headaches and generally feeling unwell. Blood test showed a high prolactin level of 84637, low FT 7.7, low testosterone level 0.1 with low LH 1.5 and FSH 0.5. IGF-1 was 58. MRI pituitary showed Pituitary Macroadenoma (3.0×2.7×2.2 cm). X-ray of left wrist revealed bone age of 14-15 years old. During his clinic review, he was found to have a high-pitched voice, pre-pubertal hair, pubic hair distribution Tanner stage 2, and micropenis. He was started on cabergoline 250 micrograms twice a week and his prolactin level improved to 15325 after 1 month of therapy then later to 1975. The cabergoline dose was increased/escalated to 500 micrograms twice a week
Discussion
Delayed puberty is diagnosed when there is a lack of secondary sexual characteristics at the age of 14 years in boys and the age of 13 years in girls. Some of the causes of delayed puberty include constitutional delay of growth and puberty, poor nutrition, hypothyroidism, and chronic diseases. The above causes are for patients with intact Hypothalamic-pituitary axis. The causes of delayed puberty may also be due to impaired hypothalamic-pituitary axis. These include tumours such as craniopharyngioma, astrocytoma, and impaired development of hypothalamic-pituitary axis in septo-optic dysplasia. Irradiation, trauma, or surgery to the hypothalamic-pituitary region may contribute to delayed puberty as well. This case demonstrated that the patient most likely developed the pituitary macroprolactinoma before puberty and it has been slow growing. Medical therapy with dopamine agonist has produced improvement in prolactin levels but the patient will need small dose of testosterone 50mg once a month to induce puberty.
Conclusion
Here we present a rare cause of delayed puberty caused by macroprolactinoma. Medical management is first line treatment with dopamine agonist such as cabergoline. It is also important in these cases to consider hereditary macroprolactinomas causes such as multiple endocrine neoplasia type 1 (MEN 1) and Familial isolated pituitary adenoma (FIPA) syndrome especially if two or more cases of pituitary adenomas appear in the same family in the absence of MEN 1 and Carney complex.

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EP903

Craniopharyngioma in children: a therapeutic challenge! (about 2 cases)

Ahmed Boukhalfa[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Mohamed VI University Hospital Center, Marrakech, Morocco, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Introduction
Craniopharyngioma (CP) is a rare epithelial tumor of the sellar and suprasellar region, histologically of low grade (WHO grade I). Significant locoregional invasion explains the frequency of recurrence, mainly due to incomplete surgical resection. We report two cases of craniopharyngioma in children, in order to outline the therapeutic difficulties encountered during management.
Case 1
Eleven years-old patient reported frontal headache with asthenia and chills, followed by vomiting. Examination BP 11/6 cmhg, HR 95 bpm, Tanner S2P3. Workup: TSH 3.3 mIU/l, fT4 10 pmol/l, fT3: 3.24 pmol/l, FSH 5.5 IU/l, LH: 2.1 IU/l, PRL 12.58 ng/ml, Cortisolaemia 12.64 ug/dl, Na+ 133, K+ 5.3. MRI: median intra- and suprasellar mass 16*19*20 mm, polymicrocystic. Fundus: no abnormalities. Patient underwent surgery, histology: craniopharyngioma. Post-

operative MRI showed persistent lesional process of 16×17×12 mm, indicating incomplete surgical resection.
Case 2
Patient aged 21, followed for sellar and suprasellar lesional process of 22.4×30×37 mm. Examination BP 126/72 mmHg, HR 76 bpm, Tanner S2P2. Work-up: Cortisol 14.61 µg/dl; TSH 1.71 mIU/l; fT4 17.53 pmol/l, Prolactin 8.8 ng/ml; estradiol <5 ng/l; FSH 4.86 IU/l; LH 0.98 IU/l. Tumour resected, histology showed a craniopharyngioma. At 18 months post-op recurrence with signs of compression of the anterior quadrigeminal tubercles, visual field: OD concentric narrowing and OG temporal superior quadranopsia. Several repeat operations performed (6 times), with installation of bilateral blindness. At last checkup, intra- and suprasellar process with polylobed contours and dual cystic and fleshy components, 49×46×48 mm.
Discussion
The most common symptoms in children prior to CP diagnosis are headache (68%), visual disturbances (55%), growth retardation (36%), nausea (34%), neurological deficits (23%), polydipsia/polyuria (19%) and weight gain (16%). Hypothalamic-pituitary MRI is the gold-standard imaging modality. The type of surgical resection depends on locoregional invasion and determination of the primary origin of the prostate cancer (ventricular, suprasellar, etc.). Over two-thirds of patients treated with surgery and radiotherapy (RTH) in childhood have a satisfactory outcome. Current radiotherapy techniques include 3D fractionated radiotherapy, intensity-modulated HBRT, steriotactic HBRT and, more recently, proton therapy.
Conclusion
Le CP is a locally aggressive, low-grade tumor with high morbidity in children and adults.
Keywords: craniopharyngioma, children, surgery, invasion, recurrence.
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EP908

Cardiovascular complications of acromegaly: about 76 cases

Alida Mireille Uwimana[1], Nassim Essabah Haraj[2], Siham El Aziz[2] & Asma Chadli[2]
[1]CHU Ibn Rochd, Casablanca, Morocco; [2]CHU Ibn Rochd, Department of Endocrinology and Metabolic Diseases, Casablanca, Morocco

Introduction
Acromegaly is a rare disease with an insidious course characterized by several complications that determine its prognosis. This is a case study to evaluate the cardiovascular impact on 76 patients treated at CHU Ibn Rochd Casablanca.
Material and methods
This is a retrospective study of 76 cases of acromegaly followed in the endocrinology department of Ibn Rochd University Hospital from January 2005 to October 2023. All our patients had an ECG; Heart echo and metabolic assessment. The statistical analysis was carried out using EXCEL software.
Results
The average age was 49 years with a sex ratio F/M of: 0.33. The average BMI rate was 29 kg/m^2 with overweight in 12 patients (20.8%), and obesity in 23 patients (41.6%). The average duration of the disease was 9 and a half years; The average IGF1 level was 2.3 times normal and the etiological diagnosis was a pituitary adenoma in all patients. Hypertension was found in 33%, rhythm and/or conduction disorders were observed in 52 % of patients, hypertensive cardiomyopathy in 16%. Metabolic assessment: pre-diabetes in 10 patients (17.8%) and diabetes in 28 patients (50%). Dyslipidemia was observed in 20 patients (35.7%).
Discussion
Among the cardiovascular complications, hypertension is frequently found; it is more frequent as the disease is older, the GH is higher and the age of the patients is greater. 26 % patients had at least 2 risk factors and 9 % were affected by 4 risk factors These complications are the consequences of the effects of permanent hypersecretion of growth hormone and growth factor (IGF-1) as well as late treatment
Conclusions
Cardiovascular complications of acromegaly are common and must be screened systematically in order to prevent the morbidity and mortality of this disease.
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EP909

Lower limb kinetics during walking in patient with acromegaly

Yuqi Wang[1], Michaela Title[1], Melanie Posiewko[1], Lisa Tramble[2], Syed Ahmad[2], David Clarke[3], Syed Imran[2] & Michel Ladouceur[1]
[1]Dalhousie University, Kinesiology, Halifax, Canada; [2]Dalhousie University, Endocrinology, Halifax, Canada; [3]Dalhousie University, Neurosurgery, Halifax, Canada

Acromegaly, characterized by growth hormone excess, adversely affects the patients' musculoskeletal and neural systems, consequently impairing physical function. Previous studies have noted walking impairments in patients with acromegaly (PWA). This study aimed to characterize the kinematic and kinetic changes during walking in PWA. Kinematics and kinetics of walking were evaluated in PWA ($n=8$) in biochemical remission and a control group of patients with non-functioning pituitary adenomas (PNA, $n=8$). The groups were of similar age, sex, and BMI and all participants underwent surgery to remove the pituitary adenoma. Self-reported survey data was used to compare joint pain, functional disability scores, and history of joint surgery between groups. PWA reported significantly higher back, hip, and knee pain and greater functional disability of the hip and knee than PNA. However, the history of joint surgery did not significantly differ between groups. Bipedal ground reaction forces and centre of pressure (COP) were measured using two AMTI force plates with one underneath each foot. Lower limb kinematics were measured using a 7-body segment model with anatomical 3D positions recorded using a 14-camera OptiTrack motion capture system. Force plate and motion capture systems were synchronized and sampled at 200 Hz. Lower limb kinematics and kinetics were calculated using Visual 3D. The outcome measures of the study consisted of walking speed, stride length, angular excursion, joint moments and joint power. Group differences were found in lower limb kinematics and kinetics during the stance phase. PWA exhibited increased hip and knee flexion, decreased hip adduction, and decreased ankle plantar flexion at push-off. Hip flexion moments were reduced, and hip abduction, knee extension, and knee abduction moments were elevated in PWA. There were no differences in ankle joint moments between groups. These kinematic and kinetic modifications during the initial stance phase resulted from a higher energy generation by hip extensors but lower energy absorption by hip abductors and knee extensors in PWA compared to PNA. In the midstance phase, PWA demonstrated lower energy absorption by hip flexors compared to PNA. Furthermore, PWA revealed lower energy generation by hip flexors, energy absorption by knee extensors, and energy generation by ankle plantar flexors during push-off. These results show that changes in the mechanics of walking in PWA are similar to those observed in patients with hip and knee osteoarthritis. However, some differences in the energy distribution pattern indicated a potential alteration in muscle activation strategies compared to patients with osteoarthritis.
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EP913

HTA and hypokalemia: always think of cushing's disease

Talbi Dounia[1], Elmoatamid Kaoutar[1], Sebbar Ghizlane[1], Rifai Kaoutar[1], Iraqi Hinde[1] & Gharbi Mohamed El Hassan[1]
[1]Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Arterial hypertension of endocrine origin remains a rare and curable cause of hypertension. The association of hypertension and hypokalemia should always prompt us to consider cushing's disease.
Case Report
A 39-year-old female patient, followed for 9 years for hypertension on dual therapy. Clinical examination was unremarkable, in whom the diagnosis of ACTH-dependent cushing's syndrome was made on the basis of clinical and biological criteria with elevated ACTH at 52 pg/ml and hypokalemia at 3.2 mEq/l. Hypothalamic-pituitary MRI showed a 6-mm pituitary microadenoma.
Discussion and Conclusion
Hypokalemia is a frequent finding in patients with cushing's disease. In the presence of hypercortisolism, the conversion of cortisol to cortisone may be saturated by a decrease in 11B-hydroxysteroid dehydrogenase (type 2) activity, so cortisol has an affinity for the mineralocorticoid receptor identical to that of aldosterone, leading to stimulation of the mineralocorticoid receptor in the renal tubules, inducing an increase in mineralocorticoid activity, with increased sodium reabsorption and potassium excretion, increased bicarbonate reabsorption and higher blood pressure. Consequently, this combination of hypertension and hypokalemia should suggest cushing's disease in particular, when other causes have been ruled out.
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EP914

Recurrence and predictive factors of the same in the endogenous cushing syndrome

Raúl Rodríguez Juárez[1], Maria Dolores Aviles Perez[1], Elena Martínez Silla[1], Javier García Sanchez[1], Laura Cánovas Noguera[1] & Juan Luis Delgado Montoya[1]
[1]Granada, Granada, Spain

Objective
Endogenous cushing syndrome (ECS) is a complex and rare disease. After treatment, 50% of cases have recurrence. The objective is to evaluate the prevalence of recurrences in patients diagnosed of ECS and its predictive factors.
Materials and Methods
Analytical retrospective observational study with 19 ECS diagnoses cases followed-up from January 1999 to December 2023. Demographic (sex, age), clinical (cause, face plethora, fragile capillary, reddish-purple stretch marks, high blood pressure, diabetes mellitus, obesity, osteoporosis) and biochemical (plasma cortisol (PC), nocturnal salivary cortisol (NSC), urinary free cortisol (UFC) before treatment) variables were collected, and recurrence frequency and relationship with the previously mentioned variables. The statistical analysis was performed with the IBM SPSS v.25 program (Statistical significance $P < 0.05$).
Results
19 patients were analyzed, 16 females and 3 males. Mean age 41 ± 10.8 years. ECS's cause was 52.6% cushing's disease, 36.8% adrenal cause and 10.5% ectopic cause. The 89.5% of the cases had high blood pressure, 73.7% facial plethora, 57.9% capillary fragility and obesity and 52.6% reddish-purple stretch marks. Diabetes mellitus was observed in 36.8% and osteoporosis in 26.3%.
Conclusions
In our study, there's a recurrence of 42.1% of the cases, most frequently in those of pituitary origin. Despite observing a similar percentage in clinical variables, the means of the biochemical variables before treatment are higher in those patients who presented recurrence, although these differences were not statistically significant, probably related to the presence of a small sample size. This increases the possible usefulness of this variables as predictors of disease recurrence.

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EP924

Experiences with pasireotide treatment in subjects with acromegaly

Martin Kužma[1,2], Peter Vanuga[1,3], Peter Jackuliak[1,2] & Juraj Payer[1,2]
[1]Faculty of Medicine (University of Comenius), Bratislava, Slovakia; [2]Hospital Bratislava Ružinov, Bratislava, Slovakia; [3]National Institute of Endocrinology and Diabetology, Lubochna, Slovakia

Currently, acromegaly is treatable by 3 groups of drugs available for the treatment of acromegaly: dopamine agonists (DA), somatostatin analogues (SRL) and a growth hormone receptor blocker (GH receptor antagonist GHRA). More recently, pasireotide and pasireotide-LAR were developed as multi-receptor targeted SRLs with higher potency than 1st generation SRLs/octreotide-LAR and lanreotide/and until now were considered second generation SRLs. Pasireotide, unlike first-generation SRLs, has good affinity for both SST2 and SST5. One of the pasireotide monotherapy groups are non-diabetic patients sufficiently controlled for 1st-generation SRL therapy in combination with low-dose pegvisomant. Pasireotide can also be used in combination with pegvisomant, if the combination of drugs does not sufficiently control the biochemical activity or symptoms of the disease. Short-acting pasireotide demonstrated tumor reduction of at least 20% in 56% of patients after 6 months of treatment. Pasireotide-LAR shows a good tolerability profile, like SRL. The worsening of acromegaly symptoms has been reported to be better with pasireotide than with first-generation SRLs. Hyperglycemia is seen as one limiting factor for its use in acromegaly and Cushing's disease, especially in diabetic or prediabetic patients at the beginning of treatment. However, all that is achieved is that glycemic control is achieved with good standard antidiabetic treatment, only a small proportion of patients require interruption of treatment and hyperglycemia is induced after the end of reversible treatment. In this abstract we share our experiences with pasireoitde treatment in 5 acromegaly subjects. Overall, it could be assessed that pasireotide treatment is sufficiently effective in inducing biochemical control and at the same time a safe treatment modality in terms of adverse effects and hyperglycemia.

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EP926

Secondary amenorrhea revealing a giant hamartoma of the tuber cinereum

Hayfa Farid[1], Taieb ACH[1,2], Sawsen Nouira[1], Hamza Elfekih[1,2], Yosra Hasni[1,2], Amel Maaroufi[1,2] & Molka Chedli Chaieb[1,2]
[1]Farhat-Hached University Hospital, Department of Endocrinology-Diabetology, Sousse, Tunisia; [2]Faculty of Medicine of Sousse, University of Sousse

Introduction
Hamartomas are benign tumors that occur in many different parts of the body. Brain locations of hamartoma are rare but still reported in few cases such as the tuber cinereum (TC) location. Children with hypothalamic hamartomas develop precocious puberty generally associated with gelastic seizures. However, TC hamartomas do not necessarily induce clinical symptoms. Amenorrhea has never been reported as a revealing symptom of TC hamartomas. Here we describe an atypical discovery of a giant hamartoma of the TC in a young woman who presented for a secondary amenorrhea.
Case Presentation
A 23-year-old woman presented to our department for a secondary amenorrhea associated with recurrent headaches. The past history revealed that the patient had her first periods at the age of 19-year-old, and presented one year after a spaniomenorrhea. On examination, there was no hirsutism, no galactorrhea no signs of hypothyroidism or hypogonadism with a normal neurological examination. Her body mass index was 30 kg/m^2. Pelvic exam was normal. Laboratory data revealed a negative Human Chorionic Gonadotropin level, normal thyroid function and normal serum levels of Growth hormone and ACTH. Serial hormone tests including serum concentration of luteinizing hormone, follicle stimulating hormone, estradiol, and progesterone, indicated normal cyclical ovarian activity. A moderate hyperprolactinemia after dilution was identified (=33 ng/ml [3–20 ng/ml]). There were no other medications intakes explaining the hyperprolactinemia. Synacthen testing showed normal adrenal response. A luteinizing hormone-releasing hormone test showed a normal gonadotrophin response excluding the pituitary cause of the secondary amenorrhea. Hyperprolactinemia was the selected diagnosis to secondary amenorrhea. A magnetic resonance imaging revealed a homogeneous suprasellar hamartoma of the TC of 20 mm, with sellar extension. The hyperprolactinemia was explained by the mechanical compression on the pituitary stalk. The patient was started on cabergoline with an improvement of the prolactin levels and had a natural pregnancy 6 months later.
Conclusion
The hamartoma of the TC is a rare, non-neoplastic heterotopic mass of normal nervous tissue. In contrast, during early life, the diagnosis is made of clinical symptoms such as precocious puberty and/or gelastic seizures. Works on clinical manifestations in the adult life are rare. In our case the main symptom was a secondary amenorrhea. More detailed imaging techniques and new molecular methods may, in future, provide further insight into the pathogenesis of either sexual impairment or seizure activity in TC hamartoma.

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EP927

A case of inappropiate secretion of thyrotropin-to be or not to be a TSHoma

Cristina Stancu[1], Vlad Radulescu[2], Andreea Cristina Bordeianu[2] & Corin Badiu[2,3]
[1]National Institute of Endocrinology Endocrinology IV, Bucharest; [2]National Institute of Endocrinology Endocrinology IV, Bucuresti; [3]Carol Davila University of Medicine and Pharmacy Endocrinology Bucuresti

A 39 years old pacient presented for the first time in may 2023 with altered vision, dizziness, tachycardia and palpitations with paraclinical investigations suggestive for inappropiate TSH secretion: TSH=5.31 μUI/ml (NR: 0.27-0.42), fT4=56.8 pmol/l (NR: 11.9-21.6), fT3=17.4 ng/dl (NR: 3.1-6.8), ATPO <9 UI/ml, ATG=12.7 UI/ml (NR: 0-115). He has been treated with antithyroid drugs (Thiamazole 10 mg per day). The thyroid ultrasound and ophthalmological exam were normal. Additional laboratory testing showed elevated level of prolactin=919 μUI/ml (NR: 86-324) and SHBG=141 nmol/l (NR: 18.3-54.1), IGF-1=126.5 ng/ml (NR: 83-238). We repeated the thyroid function which revealed: TSH=4.71 μUI/ml (NR: 0.35-4.94), fT4=24.69 pmol/l (NR: 9-19), T3=208.26 ng/dl (NR: 35-193). He never experienced galactorrhea or symptoms of low libido. The MRI exam revealed a sellar gadolinophilic tumor with suprasellar extension, having contact with the optic chiasm and the left optic nerve, extended at the level of the right cavernous sinus measuring approximately 20/28.1/24 mm (AP/lL/CC) concordant with clinical manifestations and laboratory results. The tumor ablation was performed through transsphenoidal approach endoscopic assisted. The histophatological and immuno-histochemistry results proved that it was a plurihormonal macroadenoma prolactin and GH secreting but with negative staining for TSH (repeated twice), ACTH, LH, and FSH. Given all the information, we could not exclude an immature adenoma of PIT1 line which requires additional genetic testing. After surgery, at 3 months apart, the pacient presents central hypothyroidism, central adrenal insufficiency, confirmed with the insulin tolerance test (basal cortisol=0.62 μg/dl, maximum cortisol=8.79 μg/dl) and somatotroph insufficiency (maximum GH=0.16 ng/ml) but with normal pituitary-gonadic axis and prolactin slightly above the upper limit of normal. We substituted the thyroid and the adrenal function. At 5 months post-surgery we obtained optimal thyroid and adrenal substitution, and partial stimulation after 1 μg of Synachten i.v with the highest cortisol level=17.58 μg/dl with normal somatotroph and gonadal axis (we considered optimal stimulation if cortisol >18 μg/dl, partial response 12-18 μg/dl and diagnostic for insufficiency <12 μg/dl). In conclusion, particularity of the case is the initial clinical and biochemical setting of the patient which is in contrast with the histopathological exam of the macroadenoma and also the partial recovery of the adrenal axis, especially after pituitary surgery.

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EP928

A rare case of transient central hypothyroidism

Zora Lazurova[1], Juraj Semancik[1] & Martin Javorsky[1]
[1]University of PJ Safarik, 4th Department of Internal Medicine, Kosice, Slovakia

We report a case of 48 years old female with history of arterial hypertension and breast cancer in long term remission. She was admitted to the hospital due to strong headache. MRI of the brain revealed spontaneous intracranial hypotension caused by the cerebrospinal fluid (CSF) leak in left fronto-parietal region, thickening of pachymeningeal tissues, distension of sinus transvs and cranial buldging of the pituitary gland with non homogenous structure. Although patient did not present any clinical symptoms suspicious for hypopituitarism, the hormonal profile was performed and the central hypothyroidism was found (TSH less then 0.005 mIU/l; $n=0.3$-4.2 mIU/l, fT3 4.06 pmol/l; $n=$ 3.1-6.8 pmol/l, fT4 11.02 pmol/l; $n=$ 11.9 – 21.6 pmol/l), while all other axes were intact. Thyroid hormones were mildly decreased, therefore no substituion therapy was indicated. Patient underwent the procedure using epidural blood patch, with excellent clinical outcomes, CSF leak disappeared right after procodure. Hormonal tests one month after procedure found mild improvement of central hypothyroidism (TSH 0.03 mIU/l, fT3 4.6 pmol/l, fT4 11.2 pmol/l), other axes remained normal. Three months after procedure the MRI check up revealed complete resolution of the signs of intracranial hypotension, also pituitary gland turned to be homogenous and not enlarged. Laboratory tests shown normalization of thyroidal axis function (TSH 2.1 mIU/l, fT3 4.9 pmol/l, fT4 14.6 pmol/l). This case presents a rare cause of transient central hypothyroidism due to a spontanoues intracranial hypotension. To the best of our knowledge, only few cases of hypopituitarism in patients with this rare condition have been described to the date.

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EP932

Psychological aftermath of acromegaly: a case report

John Warner-Levy[1] & Adrian Heald[1]
[1]Salford Royal Hospital, Salford, Department of Endocrinology and Diabetes, Salford, United Kingdom

Case

Acromegaly is associated with osteoarthritis due to soft tissue swelling. Our patient was first diagnosed with acromegaly in 2001 at the age of 51, subsequently undergoing a transsphenoidal pituitary adenoma resection in 2002, followed by postoperative radiotherapy in 2003, with subsequent development of anterior hypopituitarism. He has comorbidities of osteoarthritis, (having previously undergone bilateral total hip replacements and a left total knee replacement), bunionectomy with pinning of the right great toe in 2014, well-controlled T2DM, and a colonic polyp. He currently takes Hydrocortisone/levothyroxine/Tostran gel/Pegvisomant(*GH receptor antagonist*)/Omeprazole/Tramadol/Calcichew/Rosuvastatin/Metformin/Naproxen, and Lanreotide(*somatostatin analogue*). Although his acromegaly remains well controlled with a normal IGF-1, he still suffers from significant joint pain and experiences limited mobility as sequelae of his acromegaly. Due to his joint problems as a result of his acromegaly, he unfortunately had to stop working as a warehouse operative in 2011. Since leaving work, he has felt anergia and a lack of motivation. In an attempt to overcome this, between 2011 and 2020, he was volunteering regularly. On days when he was volunteering, he felt engaged and well, but on days when he was not working as a volunteer, he would find himself sleeping excessively with an absence of purpose. All of these activities finished with the Covid-19 pandemic, and since then, he has not been able to perform any voluntary work. His symptoms have since worsened, with a pronounced feeling of 'pointlessness' and continuing weariness. He believes his motivation would return if he regained structure to his life. Frustrations have also arisen due to no longer being able to perform simple 'DIY' household tasks, due to difficulty bending over and balancing on ladders. In January 2024 he was seen by an endocrinologist in a regional chronic fatigue syndrome clinic. It was felt that he did not have chronic fatigue syndrome but rather was experiencing reactive low mood as a result of a major change in his functional level over the last decade or so. On consultation with a clinical psychologist, it was felt that a referral to his local Social Prescribing Team would facilitate some low-intensity cognitive behavioural therapy while also putting him in touch with organisations who could potentially provide him with some structured and meaningful voluntary work. He continues to follow up with his endocrinologist.

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EP933

Radiation-induced hypopituitarism: a case report

Yelena Aghajanova[1,2] & Sona Maghakyan[1,3]
[1]Yerevan State Medical University after Mkhitar Heratsi, Department of Endocrinology, Yerevan, Armenia; [2]Muratsan University Hospital, Department of Endocrinology; [3]Mikaelyan Institute of Surgery, Department of Endocrinology, Yerevan, Armenia

Introduction

Radiation treatment is used for patients with secreting and non-secreting pituitary adenomas, residual pituitary adenomas, or recurrent pituitary adenomas to achieve long term disease control. The hypothalamic–pituitary unit is a particularly radiosensitive region in the central nervous system and pituitary hormone deficiencies are the commonest late complication of radiotherapy, which usually occur after several years. The development of hormone deficiencies with time varies in the published literature. We report a patient with hypopituitarism who developed clinical manifestations 2 years after radiation therapy.

Case Presentation

A 59-year-old man, who complained of general weakness and shortness of breath for the past 1-month, lost consciousness, had cardiac arrest. Ambulance was called, CPR was performed and the patient was transferred to the ICU of the hospital. There he was treated with infusion therapy, inotropic therapy, water-electrolyte balance treatment (KCl 4%), oxygen, insulin therapy, anticoagulants, gastroprotective therapy. Patient had a history of Lymphoblastic leukemia, which has been diagnosed 5 years ago, he underwent chemotherapy, radiation therapy and has been in remission for the past 2 years. He also had Type 2 Diabetes for 15 years, and was on insulin therapy for past 6 years. He had history of acute respiratory infection 1 month before current admission. On admission, examination revealed Ps=62 bpm, BP=106/65 mmHg, T=36.5^{0}C, SpO_2 95 % (7 liter/min O_2+), SpO2 80% (O_2-), BMI=33.6 kg /m^2. Daily diuresis 8000 ml, urine specific gravity-1005-1002-1004. Fasting glucose -10.4-9.8-6.8 mmol/l. Chest X-Ray, ECG and Echo were normal. Hormonal tests: LH-<0.100 mIU/ml (N 1.7-8.6), FSH- 0.457 mIU/ml (N 1.5-12.4), TSH-<0,009 uIU/ml (N 0.3-4.5), FT4-0,899 pg/ml (N 8.9-17.2), ACTH-2.14 pg/ml (7.2-63.3), Cortisol-21.89 nmol/l (171-586), Prolactin-4.07 ng/ml (4.6-21.4), Testosterone-<0.025 ng/ml (2.8-8), HbA1C -6.6% (4.8-5.9). Brain MRI was without features. He was diagnosed with Panhypopituitarism. Secondary hypocortisolism, Secondary hypothyroidism, Secondary hypogonadism, Central diabetes insipidus. Type 2 diabetes mellitus. The patient was given Oxygen, Infusion therapy, Levothyroxine 25 mg (2 days), then 50 mg (5 days) and 75/50 mg every other day, Hydrocortisone 10/5/10 mg 3 times daily, then 10/10/10 mg and 15/10/15 mg doses, Desmopressin at first 2 drops, then 3 drops daily. Dose adjustments were made with blood pressure, pulse and diuresis monitoring. The patient improved on treatment, he was discharged in good general health condition and was advised to continue hormonal therapy with the same doses and see endocrinologist regularly.

Conclusion

According to literature, clinical evaluation, baseline pituitary hormone assessment, and dynamic testing for growth hormone and adrenocorticotropic hormone (ACTH) deficiency (because they are the most sensitive) should begin one year after radiotherapy to prevent these life-threatening complications.

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EP934

Endolymphatic sac tumor with von hippel–lindau disease: report of a case

Rachida Bouattay[1], Nawres Bouaziz[1], Mehdi Ferjaoui[1], Elkorbi Amel[1], Naourez Kolsi[1], Harrathi Khaled[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction

Endolymphatic sac tumors (ELSTs) are very rare and locally aggressive low-grade neoplasm of endolymphatic system origin, which can arise sporadically or in association with von Hippel–Lindau (VHL) disease. It is an autosomal dominant multisystem disorder with a prevalence of 1 in 39 000 people that predisposes the patients to clear cell neoplasms of various organs. Herein, we report a rare case of an ELST in a patient with VHL disease, in order to describe the clinicopathologic features of the case.

Case presentation

A female, 58-year-old patient was referred to our Otolaryngology Department with one-year history of progressive sensorineural hearing loss in the left ear and non-pulsatile tinnitus. The family medical history disclosed the presence of symptoms of von Hippel–Lindau disease. Her mother, brother and three nephews had history of resection of cerebellar hemangioblastomas and evidence of genetic

VHL disease. A complete otorhinolaryngological examination was performed and it was normal. Pure tone audiometry showed left side mild sensorineural hearing loss. Computed tomography (CT) scan done primary without contrast then injected in second time showed a low-density lesion with enhancement on contrast arising from the left side of the cerebellopontine angle region. Erosion of the left petrosal bone and mastoid air cells was observed, extending to the internal auditory meatus. On magnetic resonance imaging (MRI) study, a 3.2×1.8×2.6 cm hyper vascular lesion was detected in the petrous part of the left temporal bone and mastoid air cells. Moreover, a work-up was performed to confirm the VHL syndrome. An ophthalmologic examination done detected multiple hemangioblastomas of the retina and an ultrasonography of the abdomen revealed bilateral renal cysts. Genetic study was not performed on our case. With these findings a provisional diagnosis of ELST associated with VHL disease was made. Therefore, the patient was treated with intensity modulated radiotherapy. She is followed regularly for 36 months with routine MRI surveillance. There were no several complaints and MRI display no radiological signs of progression.

Discussion & Conclusion

Endolymphatic sac tumors are rare neoplasm of the petrous temporal bone that has a slight female predominance. The association between ELST and VHL disease has increased our knowledge of this rare tumor. Approximately 10% of patients with VHL disease have ELSTs. Early surgery resection is the best treatment strategy of this tumour and radiotherapy is used almost exclusively as palliative treatments for tumors that cannot be resected completely.

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EP935

A rare association of insulinoma in tuberous sclerosis complex patient

Muhammad Tahir Chohan[1], Davis Ogeto[1], Kamal Abouglila[1], Irfan Khan[2], M Shafie Kamaruddin[2], Anna Mitchell[3], Earn Gan[3], Manu Nayar[4] & Wasfi Alrawashdeh[4]

[1]University Hospital of North Durham, United Kingdom; [2]Darlington Memorial Hospital, United Kingdom; [3]Royal Victoria Infirmary, United Kingdom; [4]Freeman Hospital, United Kingdom

Introduction

Tuberous sclerosis complex (TSC) is a multisystem inherited disease associated with neurocutaneous manifestations and multiple hamartomas but rarely associated with neuroendocrine tumours (NETs). The current TSC guidelines do not recommend routine screening for NETs in TSC.

Case report

21 year old male with genetically confirmed tuberous sclerosis (TSC-2 mutation) with intellectual disability, epilepsy with previous episodes of status epilepticus and stable subependymal giant cell astrocytoma. Medications included Sodium valproate, Clobazam, Lamotrigine, Perampanel, Cenobamate and buccal midazolam as needed. His usual seizure frequency was several absence seizures throughout the day but only 1-2 generalised tonic-clonic seizures per month. He was admitted with increased frequency of generalised tonic-clonic seizures over the preceding few weeks and was found to have spontaneous hypoglycaemia (1.9 mmol/l). Subsequent investigations confirmed endogenous hyperinsulinism (fasting laboratory blood glucose 1.9 mmol/l, C-peptide 0.56 (0.34-1.8 nmol/l) insulin 43.7 (12-150 pmol/l)). Short synacthen test, thyroid function tests and antiepileptic drug levels were satisfactory. CT of the chest, abdomen and pelvis did not reveal any concerning abnormalities; neuro-imaging showed a stable astrocytoma. A Tektrotyd scan did not reveal any Tektrotyd avid pancreatic lesion. Given high suspicion of underlying insulinoma clinically, he underwent endoscopic ultrasound which revealed an 18 mm hypoechoic lesion close to the tail of pancreas and splenic hilum. A biopsy confirmed well differentiated pancreatic NET with expression of insulin (Ki-67 $<2\%$)

Management

His blood sugars were managed with a combination of diazoxide, subcutaneous octreotide and intravenous dextrose infusions. After the biopsy confirmed pancreatic insulinoma, he underwent laparoscopic spleen preserving distal pancreatectomy with complete excision of underlying insulinoma. After surgery, his diazoxide, octreotide and dextrose infusions were stopped and he did not have any further hypoglycaemic episodes.

Conclusion/learning points

Insulinoma is an uncommon pancreatic NET. It is rarely associated with TSC but should be considered in people with TSC who have spontaneous hypoglycaemia or increased seizure frequency, as early diagnosis and surgical management results in better treatment outcomes.

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EP936

Cardiovascular complications in acromegaly

Zahra Ismail[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]

[1]University Hospital Center Mohamed VI, Departement of Endocrinology, Diabetes and Metabolic Disease, Marrakech, Morocco

Introduction

Chronic excess of growth hormone is responsible for numerous cardiovascular, respiratory, metabolic and neoplastic complications, leading to significant morbidity and mortality. The aim of this study is to analyze the different cardiovascular manifestations and cardiovascular risk factors in acromegaly.

Methods

A retrospective descriptive study including 44 patients hospitalized in the endocrinology department of University Hospital Mohamed VI of Marrakech, from October 2006 to February 2022. Data were collected from medical records.

Results

the sex ratio is 1, mean age of 46.7 years [15-68]. GH hypersecretion was related to a pituitary adenoma in all cases. The IGF-1 measured in 32 patients, was elevated in 31 (96.87%), GH was elevated under OGTT in 1 patient, and in 12 patients, the diagnosis was made retrospectively based on pathology results (27.3%). Cardiovascular risk factors: hypertension was present in 27.3% of cases, diabetes in 34% and dyslipidemia in 2.2%. thirty four percent of patients was overweight and 9% obese. None of the patients had a coronary syndrome or stroke. The ECG found electric left ventricular hypertrophy in 34% of cases. Chest X-rays showed cardiomegaly in 27.2% of cases. Echocardiography was performed in 29 patients, and showed abnormality in 4 cases (9%): left ventricular hypertrophy in 2 patients, hypertrophic dilated cardiomyopathy in one patient and stage 3 tricuspid valve disease in 1 patient.

Conclusion

Cardiovascular complications are very common in acromegaly (20-50% of cases), dominated by hypertension and hypertrophic heart disease. Compared with the general population, the risk of death in patients with acromegaly is increased to 61%, The main cause of mortality is cardiovascular complications. The higher the level of GH and the longer the course of the disease, the more serious these complications become. The evolution of cardiovascular complications during acromegaly management appears to vary greatly according to the disease history and the degree of control of GH excess. Some studies have shown that the cardiac structure and function improve significantly after the disease is controlled.

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EP937

Vagal paraganglioma miming a lymph node metastasis of papillary thyroid cancinoma

Amel Elkorbi[1,2], Nawres Bouaziz[2], Mahdi Ferjaoui[2], Rachida Bouatay[2], Naourez Kolsi[2], Harrathi Khaled[2] & Jamel Koubaa[2]

[1,2]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction

Vagal paragangliomas are rare tumors that developed from paraganglionnar tissue. They are relatively easy to diagnose. They have benefited from advances in diagnostic imaging, particularly angiography and magnetic resonance imaging (MRI). We aim to study the particularities of clinical findings in a vagal paraganglioma miming a lymph node metastases in patient with a history of papillary thyroid carcinoma.

Case report

We report the case of a 66-year-old woman treated for lymph node tuberculosis eight years ago, with a discovery on a cervical ultrasound monitoring of an infracentimetric left thyroid nodule staged EU-TIRADS 4 with lymph node metastases. The patient underwent a total thyroidectomy with bilateral mediastinal lymphadenectomy for multifocal papillary carcinoma associated with lymph node metastases in recurrent chains. The patient was treated by complementary iratherapy with no fixation on technetium scintigraphy. However, thyroglobulin remained at high levels. A cervico-thoracic computed tomography was performed concluding to a vascularized sized 18x30 mm in relation to the left carotid glomus, suggesting lymph node metastases in the context. The patient underwent left functional lymphadenectomy. Per-operatively, we observed a high bleeding lesion closed to the vagal nerve. The extemporaneous examination confirmed the diagnosis of a vagal paraganglioma. Definitive pathology did not show any lymph node metastases. The postoperative period was marked by the

occurrence of a recurrent left paralysis with a good course after speech therapy. There were no recurrence of paraganglioma and thyroid carcinoma after six years of fellow-up.
Discussion/Conclusion
Paragangliomas are usually benign tumors. They are rare and slow in evolution. Management is well codified included imaging for the diagnosis of the tumor and its extensions, surgery as standard treatment and radiotherapy is an alternative in non-operable cases. Nevertheless is not usually the rule, as in our case we misdiagnosed the paraganglioma on the CT scan, as it highly mimed a lymph node metastasis.
Disclosure of interest
none declared
Keywords: paraganglioma, thyroid cancer, lymph node, metastasis, surgery
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EP950

Body mass index in patients with prolactinoma
Hind Ouakrim[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Chu Mohamed Vi Marrakesh - Drh, Marrakech, Morocco

Introduction
Hyperprolactinemia may be associated with weight gain, metabolic syndrome, and insulin resistance. Treatment with dopamine agonists (DA) has been shown to reduce body weight and improve metabolic parameters. The objective of our study is to confirm weight gain secondary to hyperprolactinemia and analyze the evolution of weight in patients under dopaminergic antagonists.
Materials and Methods
This is a prospective cross-sectional analytical study conducted over an 8-year period involving 88 patients aged $\geq$18 years, followed for prolactinomas who adhered to medical treatment with DA.
Results
The average age was 35 years, with most females (70.5%). The mean BMI was 28 kg/m^2, and the average abdominal waist circumference was 106 cm. The prevalence of overweight was 36.4%, and obesity was 34.1%. The average treatment duration was 6 years. Weight reduction was observed in 29.5% of patients.
Discussion and Conclusion
Patients with prolactinomas have a higher prevalence of obesity or overweight compared to normal individuals. The mechanism by which hyperprolactinemia induces weight gain is not fully understood, but the blockade of dopaminergic tone may play a significant role. Studies have shown that hyperprolactinemia affects the expression of genes involved in appetite regulation, contributing to increased fat mass in these patients. Normalizing prolactin levels can improve body composition. It is crucial to monitor BMI in patients with hyperprolactinemia and take measures to maintain an ideal weight and reduce the risks of associated diseases.
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EP976

Unusual revelation of a pheochromocytoma with neurofibromatosis type 1
Souleima Trigui[1], Dhoha Ben Salah[2], Dhieb Nesrine[2], Charfi Hana[2], Frikha Hamdi[2], Fatma Mnif[2], Mouna Mnif[2], Mohamed Abid[2] & Nabila Mejdoub[2]
[1]Chu Hedi Chaker, Endocrinology Sfax, Tunisia; [2]Chu Hedi Chaker, Endocrinology Sfax

Introduction
Pheochromocytoma represents only 5% of adrenal incidentalomas. It is malignant in only 10% of cases. We report a case of pheochrompcytoma with suspucion of double cortico-meullary component or an ectopic secretion of CRH in the context of neurofibromatosis type1
Observation
A26year old woman with a history of unilateral renal lithiasis, colic and breast neoplasia, with no notable personal history, consulted for right lumbar pain. An abdominal CT scan showed a solidocystic right adrenal incidentaloma with a spontaneous density of 40 HU measuring 79$\times$75 mm and a slightly irregular contour. The fleshy portion had an absolute washout of 33%. It displaces the liver above and the upper pole of the kidney below. It displaces the inferior vena cava and the right renal vein medially. The left adrenal gland is unremarkable. Pheochromocytoma was suspected in the presence of paroxysmal malaise with headaches, palpitations, and weight loss. Her BMI was of 25 kg/m^2. ambulatory blood pressure measurement had shown blood pressure paroxysms with concomitant tachycardia In addition, she had café au lait spots, axillary lentigines and cutaneous and subcutaneous neurofibromas. However, she had no signs of hypercorticism or recent virilisation. Hotmonal exploration concluded to a mixed secretion of catecholamin and cortisol. ACTH was 34.8 pg/ml. 17 OH progesterone and SDHEA levels were normal fter confirming the diagnosis of pheochromocytoma, a thoracic-abdominal-pelvic CT scan did not reveal any metastases or secondary locations. Indeed, our patient neurofibromatosis type 1 and Slit lamp examination revealed lish nodules. she had no flush syndrome and Calcitonin was normal. She underwent a right adrenalectomy by right laparotomy The anapatomopathological examination showed a pheochromocytoma of 10 cm with a PASS score of 5 with cystic and haemorrhagic changes without necrosis nor capsule infiltrationThe immunohistochemical study was strongly positive for chromogranin, and negative for ACTH, but not unavailable for CRH. At 2 months postoperatively, normalization of Metanephrine and Normetanephrine levels as well as a positive minute braking were noted. ACTH was normal and The CT scan performed showed postoperative remodelling of the right adrenal gland without signs of recurrence.
Conclusion
Mixed corticomedullary tumour (MCMT) of the adrenal gland is an extremely rare tumour characterised by a mixture of steroidogenic and chromaffin cells in a single tumour mass. It is associated with ectopic adrenocorticotropic hormone in some cases. Current theories regarding the pathogenesis of MCMT should be further investigated by genetic testing
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EP1020

Hypokalemia and neurocognitive impairment in a female patient admitted to the emergency department – case report
Dumitras Teodor[1], Duta-Ion Simona[1], Juganaru Ruxandra[1], Clement Robert[2,3] & Fica Simona[1,2]
[1]Department of Endocrinology, Elias University Emergency Hospital, Bucharest, Romania; [2]'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania; [3]Department of NeuroSurgery, Colentina Clinical Hospital

Introduction
Hypokalemia is a dyselectrolytemia which can cause weakness, paralysis, neurological symptoms, cardiovascular complications and sometimes can be fatal. It can be diagnosed in uncontrolled diabetes mellitus, hyperaldosteronism, gastrointestinal or renal pathologies.
Case report
A 67 year old female was admitted to the emergency department with confusion, cognitive impairment and headaches and no other known medical history. She presented discrete ecchymoses, discrete facial hirsutism, hypertension 170/110 mmHg, obesity with a BMI of 32 kg/m^2. Laboratory exams revealed hypokalemia (2.9 mmol/l: normal range 3.6-5.1), metabolic alkalosis and newly diagnosed diabetes mellitus (glycemia 254 mg/dl and Hba1c 10%). She was also diagnosed with severe cognition impairment and depression. Renin and aldosterone levels were normal, but the basal cortisol value was very high (37.3 mg/dl: normal range $<$20 mg/dl) with high ACTH (108 pg/ml: normal range 7.2-63.3 mg/dl) and also high DHEAS (2 times upper limit of normal value). After the 1mg dexamethasone overnight test the cortisol value was 26.5 mg/dl, after 2$\times$2 dexamethasone test 21.9 mg/dl and after 8$\times$2 high dexamethasone supression test 7.8 mg/dl (supression $>$50%, but still $>$1.8 mg/dl). Thorax, abdominal and pelvis computed tomography performed in the ER showed no other tumors. The cerebral and pituitary MRI revealed left sided pituitary microadenoma 5/5/5 mm and a right cerebellopontine angle tumor (neurinoma) of 20/30 mm. After a multidisciplinary team approach we decided to go for transsphenoidal surgery, and in the weeks before the operation she received medical treatment with spironolactone 100mg/day, mifepristone 200mg/day, potassium oral and IV supplementation, antihipertensive medication, antidepressive medication, oral antidiabetics. She performed the surgery, with the pathological exam confirming the diagnosis of pituitary tumor with basophilic ACTH secreting cells. First day after the operation she presented a cortisol level of 1,1 mg/dl and at one week the patient presented low cortisol (3,15 mg/dl) and low ACTH (12,75 pg/ml) with significant improvement of neurocognitive and depressive status, tension and glycemic control. She was discharged with substitutive corticotherapy for secondary adrenal insufficiency (20mg hydrocortisone equivalent to 5mg prednisone per day).
Conclusions
Cushing disease is a very important endocrinological pathology which can present under multiple clinical presentations. It requires an efficient work-up and diagnosis in order to offer the best medical approach available. What is more, the

postoperative periodic follow-up is mandatory due to the known risk of recurrence.

Keywords: hypokalemia, neurocognitive impairment, cushing disease

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EP1021

Primary pituitary abcess: case report

Aicha Lachkhem[1], Mezaache Ahlam[1], Abdelkader Yahi[1], Lounes Haffaf[1], Bensalah Meriem[1], Abderrahim Derriche[2] & Derradji Hakim[3]

[1]Army Central Hospital, Endocrinology, Algiers, Algeria; [2]Army Central Hospital, Radiology, Algiers, Algeria; [3]Army Central Hospital, Neurosurgery, Algiers, Algeria

Introduction

Pituitary abscess (PA) is a rare accounting for 0,2-1% of all sellar lesions, it is generally classified as primary or secondary according to their etiopathogenesis.

Case

A 20-year-old female with a history of vulvitis a year ago, dental abscesses on multiple dental caries who presented 05 months ago with intracranial hypertension syndrome in a febrile context. One-month later amenorrhea sets in as well as polyuropolydeptic syndrome, hormonal exploration reveals panhypopituitarism and the MRI showed a pituitary abscess measuring 13×14 mm extended to a height of 10 mm presenting in discrete T1 hyposignal, T2 hypersignal and diffusion with clear drop in ADC, enhancing in an annular and peripheral manner after injection of gadolinium salts, the patient was treated with double antibiotics therapy for 21 days without success as well as dental care. The abscess disappears spontaneously after 8 months of evolution.

Discussion

Primary PA represent the most common type, accounting for 67% of all cases so far reported and result from hematogenous bacterial spread to an otherwise normal pituitary gland. On the contrary, secondary PA occur in only 33% of cases and represent a secondary infection of pre-existing sellar lesions. In those cases of secondary PA, factors such as the anatomical distortion and subsequently impaired circulation, as well as the altered immunological status may be considered a pre-existing condition for abscess formation. On the contrary, due to the limited number of cases so far reported and their heterogenous management, little is known about the risk factors and natural history typical of primary PA. PA pathophysiology is still unknown for both primary and secondary PAs, even though several hypotheses have been considered. Atlas *et al*. reported that either primary or secondary PA could be the result of both hematogenous seeding or direct extension from an adjacent infectious process, as in cases of sphenoid sinusitis, meningitis, or contamination from a CSF fistula. Vates *et al*., in their series, reported that 16.7% of patients had a history of sepsis, Charles-Henry Mallereau *et al*. reported only 4 of 84 patients with a medical history of dental granuloma that could potentially be considered as the primary infectious focus. Other risk factors considered included an underlying immune-compromised condition and previous radiotherapy

Conclusion

Despite highly sophisticated clinical and radiological investigations, the preoperative diagnosis of PA remains challenging and recently led to the proposal for a management algorithm for sellar masses suspected for being PA.

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EP1024

Erdheim-chester disease: a case report with pituitary involvement

Tugce Apaydin[1], Shahla Aghamaliyeva[2] & Özlem Üstay[3]

[1]Alanya Alaaddin Keykubat University Training Hospital, Endocrinology and Metabolism, Antalya, Turkey; [2]Marmara University Faculty of Medicine, Internal Medicine, Pendik; [3]Marmara University Faculty of Medicine, Endocrinology and Metabolism, Pendik

Introduction

Erdheim-Chester disease (ECD) is a rare non-Langerhans histiocytic multisystem disorder, which mainly presents with multifocal sclerotic lesions of the long bones, followed less frequently by heart, lung, central nervous system, skin, pituitary, and orbital involvement. Here, we presented a rare case of ECD manifested in a young male subject with pituitary involvement.

Clinical Case

A 19-year-old man was referred to our outpatient clinic with polydipsia and polyuria. He complained of headaches, retro-orbital pain, and swelling in the scalp. Physical examination showed bilateral exophthalmos, and bone swelling on the right frontal and parietal bone. In laboratory examination, urine density, serum sodium, and serum osmolarity were 1005 g/mL, 140 mEq/l, and 285 mOsm/kg; respectively. His FSH, LH, free testosterone, growth hormone, and IGF-1 levels were low, and the remaining anterior pituitary hormones were within normal range. The water deprivation test confirmed the diagnosis of Arginine vasopressin deficiency (AVP-D) and desmopressin nasal spray (10 μg/day) was started. Pituitary magnetic resonance imaging showed 8x6 mm nodular enlargement with diffuse contrast enhancement after intravenous contrast material (IVCM) injection in the middle part of the distal-pituitary gland. Multiple mass developments, enlargement of the diploe distance both in the fronto-occipital and parietal bones were observed after IVCM. A 4×2.5×2.5 cm lesion extending to the cerebellar vermis was observed in the posterior fossa. Radiographic investigation of the long bones determined lytic lesions and positron emission tomography revealed an increased uptake of 18F-FDG in the both proximal humerus, radius, ulna, distal ends of femur, tibiae and all bones in the cranium. Resection of posterior fossa lesion was performed and pathology revealed foamy CD68+, CD163+, S100-, CD1a− histiocytes, sparse giant cells, and fibrosis. This diagnosis of ECD was confirmed both histologically and immunohistochemically. BRAF V600E mutation screening was positive. Vemurafenib 480 mg twice daily was started due to the central nervous system involvement. Bone pain was regressed three months after the treatment, and anterior pituitary hormone deficiency was recovered. However, AVP-D persisted.

Conclusion

Diabetes insipidus is usually the first and most common endocrine manifestation of ECD. Hypopituitarism is rare but in order from most frequent to least; hypogonotrophic hypogonadism, growth hormone deficiency, thyrotropin deficiency, and adrenocorticotropic hormone deficiency can be present. Treatment is warranted for patients with symptoms or those with evidence of central nervous system involvement or organ dysfunction. Pre-existing AVP-D and endocrinopathies typically tend to persist, even after radiographic regression of disease.

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EP1025

A low-grade somatotroph adenoma presenting as a giant pituitary macro-adenoma

Yin Yin[1], Rebecca Evans[1], Cynthia Mohandas[1], Itopa Abedo[1] & Arthur Ogunko[1]

[1]Darent Valley Hospital, Dartford and Gravesham NHS Trust, Endocrine and DM, Dartford, United Kingdom

A 31-year-old lady was referred to the outpatient endocrine clinic for subfertility, intermittent galactorrhoea and amenorrhoea since birth of her son 5 year ago. However, she denied visual disturbances and headache. She was struggling to lose weight but she had no clinical features suggestive of corticosteroid or growth hormone excess apart from an increase in her UK shoe size from 5.5 to 6.5 and family members noted her hands were slightly bigger. She was on an antidepressant, Sertraline, which was withheld for two weeks, so that a repeat pituitary profile can be carried out. It showed hypogonadotropic hypogonadism. The results were as follows: FSH 1.2 IU/l (2.5-10.2), LH <0.2 IU/l (1.9-12.5); oestradiol <55 pmol/l (55 - 422), Prolactin 1200 mIU/l (70 - 566) and IGF11 45 mol/l (10.2 to 40.7). But the Cortisol level, TSH and ACTH were within acceptable range. MRI pituitary demonstrated a pituitary/suprasellar mass with a 45mm craniocaudally dimension, which was displacing the optic chiasm superiorly and compressing on it. Formal visual field testing showed bilateral superior temporal quadrantanopia. She underwent Trans-sphenoidal surgery and was initiated on hydrocortisone replacement post-operatively. There was evidence of residual tumour in postoperative MRI scan and histology showed eosinophilic excess with intranuclear inclusions and immunohistochemistry demonstrated PIT 1 lineage pituitary adenoma, variably intense positivity for TSH predominantly, second most frequent was GH with Ki 67 3 %. Post-surgery, the Pituitary multidisciplinary team meeting (MDT), diagnosis was clinically silent and low-grade somatotroph adenoma biochemically. There was subjective improvement in the vision post operatively with normal VF confrontation and normal prolactin 289 mIU/l but persistently raised IGF153.9 mol/l. MDT noted that good debulking surgery but there was still a residual suprasellar part of tumour. Somatostatin analogue (SSA) therapy was recommended and re-do surgery for residual tumour if SSA therapy failed to achieve the therapeutic goal. The plan is to repeat MRI Pituitary and assess pituitary function with insulin tolerance test in 3 months. Learning points: This case highlights the somatotroph adenoma is presenting with a silent pituitary mass for decades and that diagnosis can be delayed until the clinical or biochemical manifestation of acromegaly. We picked up the diagnosis early by chance simply because she was investigated for subfertility. Surgical debulking surgery is main stay of treatment in somatotroph

adenoma as it can lower GH levels and improve the cure rate with subsequent SSAs.

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EP1027

Cushing's vs pseudo-cushing's: neutrophil-lymphocyte ratio assessment

Ekin Yiğit Köroğlu[1], Didem Özdemir[2], Muhammed Saçıkara[1], Hüsniye Başer[2], Oya Topaloğlu[2], Reyhan Ersoy[2] & Bekir Cakir[2]
[1]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Cankaya; [2]Ankara Yıldırım Beyazıt University Faculty Of Medicine, Endocrinology and Metabolism, Cankaya

Objective
The neutrophil-lymphocyte ratio may increase in Cushing's Syndrome. We aimed to demonstrate the usability of the neutrophil-lymphocyte ratio in the differentiation of Cushing's Syndrome and Pseudo-Cushing's Syndrome, whose differential diagnosis is clinically and laboratory challenging.
Material and Methods
23 patients were included in the study. Patients were divided into Cushing's Syndrome and Pseudo-Cushing's Syndrome groups according to clinical findings and combined Dexamethasone-CRH test results (with cut-offs of 1.4 mg/dl, 3.1 mg/dl, and 3.9 mg/dl). The neutrophil and lymphocyte values and screening tests of Cushing's Syndrome were recorded. The neutrophil-lymphocyte ratio was calculated and compared between Cushing's Syndrome and Pseudo-Cushing's Syndrome groups.
Results
The neutrophil-lymphocyte ratio differed significantly when we grouped patients clinically (2.47 ± 1.38 vs 1.51 ± 0.44, $P=0{,}033$). Since only one patient was evaluated as having Pseudo-Cushing's Syndrome with a cut-off value of 1.4 mg/dl, statistical analysis could not be performed for this value. When grouping was made according to the 3.1 mg/dl cut-off, there was no significant difference in neutrophil-lymphocyte ratio (2.41 ± 1.50 vs 1.63 ± 0.51, $P=0.095$). When patients were grouped according to a cut-off of 3.9 mg/dl, the neutrophil-lymphocyte ratio was significantly higher in those with Cushing's Syndrome (2.68 ± 1.57 vs 1.59 ± 0.49, $P=0{,}021$).
Conclusion
The neutrophil-lymphocyte ratio is significantly higher in Cushing's Syndrome patients than in Pseudo-Cushing's Syndrome patients. However, instead of using this parameter alone for diagnosis, it would be more accurate to use it as a contributor to other tests.

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EP1028

Neurosteroids in human pituitary adenomas

Esra Hatipoglu[1], Ebubekir Akpinar[2], Buruç Erkan[2], Selahattin Yalcinkaya[3], Şeyma Aksoy[4], Sebnem Burhan[1], Omur Gunaldı[2], Osman Tanriverdi[2] & Mutlu Niyazoğlu[1]
[1]University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Division of Endocrinology, Department of Internal Medicine, Istanbul, Turkey; [2]University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Department of Neurosurgery, Istanbul, Turkey; [3]Forensic Medicine Specialist 8 th Specialization Committee, the Council of Forensic Medicine of Turkey, Istanbul, Turkey

Neurosteroids refer to hormones with a steroid structure and, their synthesis pathways are identical to those of traditional steroids. However, neurosteroids are generated denovo in the central and peripheral nervous systems and utilize cell surface receptors. Few animal studies indicated synthesis of NS in pituitary. Presence of neurosteroids in human pituitary adenomas(PAs) has yet to be assessed. This is preliminary data of an ongoing study. Seventyseven specimens from human PAs were included. Blood samples were obtained preoperatively. Samples were analyzed by using mass spectrometry. Table 1 compares tissue availability and levels of NS between

(Abstract EP1028) Table 1.

	NFA ($n=43$)	Somato-tropinoma ($n=20$)	Cortico-tropinoma ($n=9$)	Prolactinoma ($n=5$)	p
PREG					
Availability*	36 (86%)	6 (3%)	4 (44%)	1 (20%)	**0.04**
Level**	104.6[43.7-202]	0.3[0-1.8]	0.7[0-2.8]	21.3	**0.05**
7OHPREG					
Availability*	3 (33%)	16 (80%)	32 (74%)	3 (60%)	0.06
Level**	47.1[18.5-106.3]	36.6 [10.1-25.8]	45.4[32.9-45.4]	41.4[34.6-184.5]	0.9
DHEA					
Availability*	36 (84%)	16 (80%)	6 (67%)	4 (80%)	0.7
Level**	8.1[4.8-20.9]	11.7[7.8-20]	18.1[11.5-50.3]	64.1[30.7-444.2]	**0.04**
DHEAS					
Availability*	43 (100%)	20 (100%)	9 (100%)	5 (100%)	-
Level**	16.4[7.2-46.2]	30.4 [15.6-42.9]	31[16.6-106.7]	55.3[23.5-202.9]	0.06
AE					
Availability*	16 (37%)	10 (50%)	3 (33%)	1 (20%)	0.6
Level**	0.5[0.3-1.5]	0.8[0.4-1.2]	1.7[0.3-3.7]	0.6	0.6
T					
Availability*	27 (63%)	10 (50%)	2 (22%)	1 (20%)	0.06
Level**	0.7[0.5-1.5]	0.8[0.5-0.9]	2.5 [2-2.9]	0.9	0.3
DHT					
Availability*	2 (5%)	1 (5%)	1 (11%)		0.8
Level**	38.1	99.7	3.3		0.4
Androsterone					
Availability*	24 (56%)	11 (55%)	4 (44%)	5 (100%)	0.2
Level**	10.5[1.8-39.2]	17.3[3.7-31.8]	12.4[2.6-390.7]	19.1[3.7-143.7]	0.9
PRG					
Availability*	5 (2%)	1 (5%)	2 (22%)		0.5
Level**	0.9	0.9	2.9		0.9
ALLO					
Availability*	1 (1%)				
Level**	148.5				
DOC					
Availability*	13 (30%)	7 (35%)	2 (22%)		0.5
Level**	0.4	0.7	1.9		0.07
Corticosterone					
Availability*	9 (21%)	6 (3%)	1 (11%)	1 (20%)	0.7
Level**	1.3[0.4-4]	0.9[0.6-3.8]	9.7[1.2-2.7]	0.8	0.4
Aldosterone					
Availability*	2 (5%)				
Level**	0.7[0.39-]				
17OHPRG					
Availability*	7 (16%)	4 (20%)	2 (22%)	2 (40%)	0.6
Level**	0.9	0.7	1.7	2.9	0.8
11 Deoxycortisol					
Availability*	43 (100%)	20 (100%)	9 (100%)	5 (100%)	
Level**	1	1.7	3.1	6	**<0.001**
Cortisol					
Availability*	43 (100%)	19 (95%)	8 (89%)	4 (80%)	0.09
Level**	4.7[1.9-7.9]	6.1[2.9-12.8]	12.1 [7.7-30.1]	10 [2.5-45]	**0.04**
*	n	(%),**	ng/g		

subgroups of cases with PAs.Tissue levels of DHEA,DHEAS,17-Hydroxyprogesterone and cortisol were correlated with their blood levels ($r=+0.3, P=0.04$; $r=+0.6, P<0.001$; $r=+0.7, P=0.005$ and $r=+0.4, P<0.001$,respectively). In conclusion PAs harbor neurosteroids.The tissue type can have an impact on both diversity and levels of neurosteroids.Further investigations can determine whether the pituitary gland is the origin or recipient.

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EP1030

Panhypopituitarism diagnosed in old age: a case report

Kader Ugur[1,2], Melik Genç[1], Mithat Mızrak[1,2] & Süleyman Aydın[3]
[1]Firat University School of Medicine, Department of Internal Medicine, Turkey; [2]Fırat University School of Medicine, Department of Endocrinology and Metabolism, Elazıg, Turkey; [3]Firat University School of Medicine, Department of Endocrinology and Metabolism, Turkey

Introduction
Hypopituitarism is a clinical syndrome that develops as a result of inadequate production and release of one or more pituitary hormones. The prevalence is 45/100,000 and the incidence is 4/100,000 cases/year. Here, we aimed to present a patient with complete pituitary hormone deficiency.
Case
A 75-year-old woman had been followed up with hypertension for 20 years and osteoporosis for 16 years. She underwent surgery 7 years ago for a femur fracture due to a fall. She was admitted to our clinic because of 11 kg weight loss and anemia for the last 6 months. In her anamnesis, we were informed that she had a long history of fatigue, loss of appetite, slowed movements and depressive appearance. She had 6 birth stories and breastfed all her children. She had her last period at the age of 45. We were informed that the patient had a history of 2 head traumas at the age of 15 and 65 years. Basal pituitary hormones and pituitary MRI were requested from the patient with poor general condition. Whole body CT, endoscopy and colonoscopy were requested because of weight loss and anemia. The hormone results were consistent with those of panhypopituitarism (Table 1). The pituitary MRI revealed that pituitary height decreased by 2.5 mm and this result is compatible with partial empty sella. Age-related changes were detected on the whole body CT. Endoscopy and colonoscopy were normal. The DEXA T score was reported as L1-L4: −3, L2-L4: −3.1 and femoral neck: −2.6. Corticosteroids, levothyroxine replacement and bisphosphonate-calcium were initiated. The patient, whose general condition was better, was followed up.
Discussion
Since most of the signs and symptoms seen in pituitary hormone deficiencies in adult patients are non-specific, we suggest that the most important step to avoid a dela, in diagnosis is to carefull, investigate the cause.

Table 1. Laboratory findings of the patient

WBC: 8.61X10E3/μl (3.8-8.6)	IgF-1: <15 ng/dl
Hgb: 11 g/dl (11.1-17.1)	Growth hormone: <0.05 ng/ml (0.06-5)
Hct: 33.2 % (33-57)	FSH: 3.75 mIU/ml (21.7-153)
Plt: 258X10E3/μl (140-360)	LH: 2.14 mIU/ml (11.3-39.8)
Glucose: 77 mg/dl (75-115)	Prolactine: 6.9 mg/dl (3.4-24.1)
AST: 26 U/l (5-40)	Estradiol: <11.8 pg/ml (<30)
ALT: 25 U/l (5-40)	ACTH: 17.3 pg/ml (0-46)
Urea: 75 mg/dl (10-20)	Cortisol: 3 μg/dl
Creatinine: 0.76 mg/dl (0.6-1.2)	TSH: 1.62 IU/ml (0.5-5.5)
Na: 138 mEq/l (135-145)	fT4: 0.79 ng/dl (0.86-1.76)
K: 4.9 mEq/l (3.5-5.5)	fT3: 2.17 pg/ml (1.57-4.71)

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EP1031

Empty sella in a patient with clinical and biochemical diagnosis of acromegaly - a case report

Meryam Alahyane[1], Sana Rafi[1], Sidebatt Ammar[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Mohammed VI University Hospital of Marrakesh, Department of Endocrinology, Diabetes, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Background
Acromegaly is an acquired disorder related to excessive production of growth hormone (GH) and insulin-like growth factor-1 (IGF-1). Empty sella (ES) is an anatomical condition of sella turcica that is partially or completely filled with cerebrospinal fluid mainly due to intrasellar herniation of subarachnoid space. Here, we describe a rare case of a patient who presented with clinical and biochemical features of acromegaly who had an ES on pituitary magnetic resonance imaging (MRI).
Case report
A 51 year old female patient, with a recent prediabetes history, Hypertension well controlled under monotherapy. The patient has no history of pituitary apoplexy and has never noticed morphotype changes. Acromegaly was suspected by an endocrinologist during a consultation for goitre. Serum IGF1=481.4 ng/ml (N: 55-234), An oral glucose tolerance test showed no suppression of GH values. Serum levels of prolactin, cortisol, prolactin, TSH and FT4 were normal. Sella contrast-enhanced MRI was performed for tumor localization: T1 and T2 - weighted images revealed ES with no adenoma. Visual field examination was normal. Due to lack of availability, PET/CT couldn't be performed To rule out an ectopic GH secretion. We have decided to start medical treatment with long-acting Lanreotid 120 mg per 28 days, and reeavaluate clinical, Biological and radiological features in 6 months.
Discussion
Acromegaly stems from GH-secreting pituitary tumors in approximately 95% of all cases, and most tumors are visible on MRI of the sella. In 5% of cases, it is caused by the ectopic secretion of growth hormone-releasing hormone (GHRH), which is responsible for pituitary hyperplasia. Primary ES may occur due to the inherent weakness of the diaphragm sella and/or the increase in intracranial pressure promoting herniation of the arachnoid membrane into the pituitary pit. When ES is seen after surgery, irradiation, or medical treatment of pituitary adenoma, it is defined as secondary. Pituitary hyperfunction is rarely seen in ES and acromegaly is the least common finding. The mechanism underlying the association of acromegaly and ES remains unclear. Apoplexy on existing pituitary adenoma and then formation of necrosis can proceed to ES. Since our patient did not have a history of pituitary apoplexy and we could not find any reason for secondary ES, we considered primary ES.

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EP1032

Diabetes insipidus with dilated cardiomyopathy and premature ventricular contractions: case report

Hemmet Al Haddad[1], Amr El Meligi[1], Merrit Makram[1], Noha Tarek[1], Randa Salam[1], Ahmed Fayed[2], Ahmed Atef[1] & Bishoy Yakoob[3]
[1]Cairo University, Internal medicine, endocrinology, Cairo, Egypt; [2]Cairo University, Internal medicine, nephrology, Cairo, Egypt; [3]Cairo University, Cardiology, Cairo, Egypt

Introduction
Central diabetes insipidus (CDI) results from a deficiency of arginine vasopressin (AVP) secretion. It is treated by replacement therapy with the synthetic AVP analogue desmopressin. With atrial distension there is increased afferent vagal stimulation that decreases renal sympathetic tone and inhibits antidiuretic hormone (ADH) release, which in turn leads to the diuresis response. Additionally, atrial distension leads to atrial natriuretic peptide (ANP) release, which has powerful diuretic and natriuretic properties.
Case presentation
25 year male presenting with polyuria of 5 litres daily for 1.5 years not preceded by head trauma, surgery, convulsions nor drug intake.
Physical examination
BP: 140/90 mmHg, Pulse: 58 b/m with frequent irregular irregularity, BMI: 23.3, normal RR and temperature. Unremarkable abdominal, neurological, chest and cardiological
Investigations
Normal CBC, liver kidney functions., Calcium, potassium, and thyroid function HbA1C: 4.4%, Serum osmolality: 279 mOsm/kg (275 to 295), serum sodium: 144 mmol/l (135-145) Urine specific gravity:1015, urine osmolality: 287 mOsm/kg (500-800), urinary sodium in 24 hours showed heavy saluresis: 593 mmol/day (40-220 mmol/day) According to the results of water deprivation test The patient was diagnosed as partial central diabetes insipidus Urine osmolality 302 mOsm/kg, after desmopressin admistration 699 mOsm/kg The patient started treatment with oral desmopressin 0.2 mg/day
Outcome and follow up
The polyuria did not improve despite increasing doses of desmopressin. Even though the patient did not complain of palpitation, he was referred to cardiac electrophysiological studies for his persistent PVCs. Holter showed episodes of sinus tachycardia, frequent polymorphic PVCs (16%) with numerous couplets and triplets. Echo: dilated right and left ventricular internal dimensions with mildly reduced ejection fraction:41% Cardiac MRI: scattered left ventricular mural myocardial areas of altered bright signals on T2w with delayed myocardial enhancement Suggesting inflammatory myocarditis not ischemic disease. The polyuria improved on anti-arrhythmic drugs (b blockers) in addition to anti-ischemic measures.
Conclusion
Inhibition of ADH occurs in cases of atrial dilatation that leads to the diuresis response. Also, atrial distension leads to ANP release, which has powerful diuretic

and natriuretic properties and usually associated with saluresis and can give false positive results with water deprivation test. We report a case of apparently healthy male presenting with polyuria as sole presentation of dilated cardiomyopathy misdiagnosed as diabetes insipidus (DI) by water deprivation test.

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EP1034

Clinical profile of patients with pituitary tumors in a tertiary endocrine center in Kathmandu, Nepal

Ansumali Joshi[1], Srijana Karmacharya[1], Puspa Dahal[1] & Rama Rana[1]
[1]Kathmandu Diabetes and Thyroid Centre, Endocrine, Lalitpur, Nepal

Pituitary tumors are infrequently seen in an endocrine practice. We collected retrospective data from our clinical records of our patients with pituitary tumors from January 2018 to December 2023. There were a total 31 patients; males 9 (29.03%) and females 22 (70.97%). Mean age was 38.54±12.37 years and average BMI was 26.10±3.91. Headache and visual problem was the most common symptom in 13 (41.9%) patients each followed by menstrual irregularity in 8 (25.80%) patients. Hypertension was seen in 12 (38.70%) patients and diabetes seen in 9 (29.03%) patients. Nonfunctioning pituitary adenoma (NFPA) was seen in 8 (25.80%) patients. Most NFPA were macroadenoma 6 (75%). Functioning pituitary adenoma(FPA) was seen in 23 (74.20%) patients. Somatotroph adenomas were 8 (34.78%), prolactinomas were 7 (30.43%), ACTH secreting tumors were 7 (30.43%), thyrotropinoma was 1(4.35%). Most somatroph adenomas were macroadenomas 6(75%). Most prolactinomas were macroadenomas 4 (57.14%). Most ACTH secreting tumours were microadenomas 6 (85.71%). Optic chiasmal compression was seen among 12 (38.71%) patients and all had macroadenomas and 7(58.33%) had functioning tumors. Cavernous sinus invasion was seen in 12 (38.71%) patients and all had macroadenomas. Treatment of NFPA was surgical in 5 patients (62.5%), conservative in 2 (25%) patients and 1 (12.5%) patient underwent combined procedure (surgery and conventional radiotherapy). Mean follow up period of NFPA who underwent surgery was 29.33 months, and mean decrease in tumor size was 27.26 mm (in greatest dimension). All of the tumor removal was possible in 2(33.33%) patients. Treatment of FPA was surgical in 12 (52.17%)patients. Mean follow-up years of FPAs who underwent surgery was 54.83 months and mean decrease in tumor size was 18.02 mm (in greatest dimension). All of the tumor removal was possible in 4(30.77%) patients. Among 8 patients with acromegaly, 6 patients had surgery, 1 patient had cyberknife surgery and 1 patient lost to follow up. Among 7 patients with prolactinoma, 2 patients had surgery and all patients were treated with cabergoline. One patient with prolactinoma underwent a combined procedure (surgery and radiotherapy). Among 7 patients with ACTH secreting tumors, 4 patients had surgery, 2 had medical treatment with ketoconazole and 1 lost to follow up.

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EP1035

Double pituitary lesions in cushing disease – a case report

Lara Ormanac[1,2], Silvija Canecki-Varžić[1,2], Romana Marušić[2,3], Ema Schonberger[1,2], Kristina Steiner[1] & Ines Bilić-Ćurčić[1,2]
[1]Clinical Medical Center Osijek, Department of Endocrinology, Osijek, Croatia; [2]Medicinski fakultet, Osijek, Croatia; [3]Place of Remembrance - Vukovar Hospital, Vukovar, Croatia

Introduction
Double and multiple pituitary adenomas (PAs) are rare in patients with Cushing's disease. If two PAs are found, MRI cannot assess secretory activity. The claimed diagnostic effectiveness of inferior petrosal sinus sampling (IPSS) ranges from 82 to 100% across various studies. Yet, this procedure has limitations in everyday clinical practice. Thus, more clinical data on these lesions and possible advanced yet simpler diagnostical procedures are needed, as treatment options are dependent on precise clinical diagnoses.
Case report
We present a 27-year-old patient who was referred to the endocrinology clinic for obesity treatment and elevated values of serum cortisol (589 nmol/l (ref. 171-536)) and urine cortisol (687 nmol/dU (ref. 100-379)). He noticed the roundness of his face, an increase in anxiety requiring therapy, purple stretch marks around the navel, and gained about 6-7 kg, despite regular physical activity. Due to excessive body mass (BMI 31.46 kg/m^2), liraglutide was introduced and an endocrinological workup was performed. In the overnight and low-dose dexamethasone suppression test no suppression occurred and ACTH values of 9.8 pmol/l were recorded indicating Cushing disease. The initial MRI of the pituitary gland was performed and showed no abnormalities, as well as the CT of the thorax and pelvis excluding visible ACTH-producing tumors. In addition, mildly increased values of IGF-1 were recorded with no clinical implication since mildly elevated IGF-1 in Cushing's disease does not imply pathological growth hormone (GH) excess. To distinguish between ectopic ACTH and Cushing disease IPSS was performed, revealing the ACTH ratio of the right petrous sinus and periphery significantly greater than 2, while on the left side, it was below 1 confirming the diagnosis of Cushing's disease. To control hypercortisolemia, ketoconazole was introduced into therapy. A control MRI of the pituitary gland was performed after 3 months, now exposing two potential pituitary lesions (in the caudolateral part diameter of 2.5 mm and the posterolateral part a diameter of 3 mm), which could indicate ACTH secreting microadenomas. Therefore; ^{18}F-FET PET is planned to localize corticotroph microadenoma.
Conclusion
The diagnostical challenges in differentiating Cushing syndrome never cease to exist. In this case report we intended to increase awareness of the need to explore the possibility of the presence of two distinct corticotroph tumours. Initial studies using ^{18}F-FET-PET/MR suggest a high predictive value for localizing corticotroph microadenomas posing a promising method in the differentiation of Cushing's disease.

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EP1036

A rare cause of acromegaly due to ectopic secretion of growth hormone

Nassim Ben Hadj Slama[1], Taieb ACH[1], Zeineb Jemni[2], Rihen Meddeb[2], Ghada Saad[1], Kaouthar Chatti[2], Asma Ben Abdelkrim[1], Koussay ACH[1] & Molka Chadli[1]
[1]Farhat Hached University Hospital, Endocrinology Soussa, Tunisia; [2]Sahloul University Hospital, nuclear medicine, Soussa, Tunisia

Introduction
Acromegaly is a rare condition characterized by growth hormone (GH) excess and elevated Insulin-like growth factor 1 (IGF-I) levels attributed in the vast majority of cases to a pituitary adenoma. In rare cases, GH secretion is from an ectopic origin.
Case Presentation
We present the case of a 70-year-old patient complaining of headaches without visual symptoms. The patient had a 15-year history of sleep apnea, hypertension and diabetes. Clinical examination revealed a dysmorphic syndrome characterized by extremity enlargement, prominent forehead wrinkles, widened nasal base, prognathism, and dental arcade enlargement. The rest of the examination was unremarkable. Biochemical investigation showed an elevated IGF-1 level of 757 ng/mL. GH during an oral glucose tolerance test was 3.1 ng/ml, confirming the diagnosis of acromegaly. Pituitary MRI revealed a right temporoparietal expansive process corresponding to a meningioma measuring 28×32×27 mm. The pituitary gland was normal, without a visible adenoma. The GHRH assay returned normal at 40 ng/l. A whole-body CT scan revealed no abnormalities except for a compressive right temporoparietal meningioma. Octreoscan showed intense fixation at the ileo-caecal junction, and the meningioma exhibited moderate fixation. Colonoscopy revealed no abnormalities, and several biopsies of the ileo-caecal junction returned normal. The decision was to put the patient on somatostatin analogs for the treatment of acromegaly and not to operate the meningioma due to the high surgical risk.
Discussion
In cases of biologically confirmed acromegaly where no pituitary adenoma is detected, pituitary MRI is the initial examination. Ectopic acromegaly, comprising less than 1% of cases, typically results from ectopic GHRH secretion. They are often associated with pulmonary or pancreatic neuroendocrine tumors. However, GHRH levels in our patient were normal, indicating a rare case of acromegaly due to ectopic GH secretion, with only 19 cases reported in the literature. Octreoscan identified two fixation sites, with the meningioma's fixation being non-specific due to somatostatin receptors. The second fixation at the ileo-caecal junction suggests ectopic GH secretion by a digestive neuroendocrine tumor. Nevertheless, colonoscopy and biopsy revealed no abnormalities.

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EP1037

Chronic granulomatous mastitis in a patient with microprolactinoma

Mirna Hrabar[1], Anamarija Zrilic Vrkljan[1] & Vlatka Pandzic Jaksic[1]
[1]University Hospital Dubrava, Department of Endocrinology, Diabetes, Metabolism and Clinical Pharmacology, Zagreb, Croatia

Treatment of patients with a microprolactinoma is considered when hypogonadism is present in the form of menstrual cycle dysfunction or infertility. The presence of galactorrhea alone does not require treatment unless it is bothersome to the patient. The exact etiology of granulomatous mastitis is still unclear. Hyperprolactinemia has been identified as a possible factor in the occurrence and development of granulomatous mastitis. A 42-year-old female patient was referred to our clinic because of persistent hyperprolactinemia (3-4 times the upper limit) and MRI finding of a 5 mm microadenoma. This workup had been performed by her gynecologist because of menorrhagia and slightly irregular menstrual cycles. Her gynecological condition was to be treated with a levonorgestrel-releasing intrauterine system. She was not taking any medication. Her medical history was unremarkable, with the exception of a breast abscess that required surgical intervention twice in the last two years. Both times a biopsy of the lesion was performed, which revealed lobulocentric granulomatous inflammation, while the microbiologic analysis was sterile. Autoimmune disorders were excluded. No previous or current galactorrhea was detected. Laboratory tests revealed no other pituitary dysfunction. Only follow-up was recommended. Transient hyperprolactinemia due to recent breast manipulation was considered, but prolactin levels remained consistently elevated. The size of the microadenoma also remained stable. At the age of 44, she developed oligomenorrhea and occasional nipple discharge, that did not correspond to typical galactorrhea. Ultrasonography revealed duct ectasia and an inhomogeneous, hypoechoic, oval lesion in the upper left quadrant of the left breast that probably corresponded to a chronic abscess. FNA of the lesion confirmed persistent inflammation. At this point, we decided to change the approach and introduced a dopamine agonist. This was followed by prolactin level decrease, microadenoma shrinkage, and repeated ultrasound examination confirmed the regression of the long-standing inflammatory breast process. Hyperprolactinemia as a possible etiologic and predisposing factor for the occurrence and development of granulomatous mastitis should not be neglected. It seems that the presence of granulomatous mastitis should be taken into account when deciding on the introduction of a dopamine agonist in a patient with microprolactinoma and no other indication for drug therapy. Further clinical studies are needed to clarify the role of dopamine agonist use in patients with granulomatous mastitis and microprolactinoma.

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EP1042

Predictive factors of a Delayed response during insulin tolerance test

Sahar Abidi[1], Nadia Khessairi[1], Sabrina Ayari[1], Kammoun Elyes[1], Ibtissem Oueslati[1] & Melika Chihaoui[1]
[1]Endocrinology Department, Rabta Hospital, Tunis, Tunisia

Introduction
The insulin tolerance test (ITT) is commonly used for the evaluation of the corticotropic axis. There are different protocols depending on the number and timing of blood samples. The aim of our study was to investigate the predictive factors of a late response during ITT.
Methods
Our study was cross-sectional and descriptive. One hundred patients with suspected adrenal insufficiency (AI) were evaluated. An intravenous rapid insulin bolus of 0.1 to 0.2 units/kg was administrated. Eight blood samples for glucose and cortisol measurements were taken: before the insulin injection, at the time of hypoglycemia and samples every 10 minutes for 60 minutes after hypoglycemia. An adequate response was defined as a serum cortisol level above or equal to 18 µg/dl after a serum glucose level below 40 mg/dl. we considered a late response if it occurred 30 minutes after hypoglycemia.
Results
The mean age was 41.4 ± 15.12 years. The gender ratio (F/H) was 0.2. Forty-two patients (42%) had an adequate response and 58 patients (58%) had an inadequate response. Twenty-six patients (62%) had an early response and 16 patients (38%) had a late response. Mean age was comparable between the two groups (39.5 ± 16.1 years vs 44.8 ± 12.5 years; $P = 0.26$). We didn't find a difference between early and late responders patients regarding weight, BMI, hypoglycemia onset time and fasting blood glucose ($P = 0.48$, $P = 0.60$, $P = 0.24$ and $P = 0.34$ respectively). Basal cortisol level was lower in late responders patients than in early responders patients ($P = 0.001$). A basal cortisol level $\leq$ 11.2 µg/dl had a sensitivity of 62% and a specificity of 82% to predict a late response.
Conclusions
Our study showed that the occurrence of late response is frequent. Therefore, it is necessary to multiply the number of cortisol level samples after hypoglycemia, especially in patients with basal cortisol level below 11.2 µg/dl.

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EP1045

Cabergoline-resistant pituitary prolactin adenoma: a case report

Ghita Khamel[1], Sara Oualhadj[1], Ikram Amira[1], Hind Iraqi[1], Kaoutar Rifai[1] & Mohamed Hassan Gharbi[1]
[1]Chu Ibn Sina, Rabat, Morocco

Introduction
Prolactin adenomas are the most common pituitary tumors. The aim of treatment is to achieve normal prolactin levels in order to reduce tumor mass and restore the gonadotropic axis. Dopaminergic agonists, including cabergoline, are the standard treatment. But some adenomas can be resistant to this treatment and behave like aggressive tumors. We report the case of a macroprolactinoma resistant to cabergoline.
Observation
50-year-old female patient referred from neurosurgery after a surgical management of a 63 mm giant invading macroadenoma complicated by apoplexy, with histological examination of an adenoma expressing prolactin. Postoperative biological workup revealed persistent hyperprolactinemia at 10379/ml, and a pituitary macroadenoma measuring 42 × 35 mm on hypothalamic-pituitary MRI. The visual field revealed a bitemporal hemianopia. The patient was put on cabergoline at a dose of 1 mg per week, gradually increasing to 3 mg per week, with persistent hyperprolactinemia at 6028 ng/ml and a macroadenoma at 38 mm. Transphenoidal revision surgery was indicated, with persistent hyperprolactinemia at 2598 ng/ml at 6 months postoperatively on 4 mg cabergoline.
Discussion
Four histological observations have been made in DARP studies increased angiogenesis, cellular atypia, increased proliferation and invasiveness. Resistance to cabergoline is due to decreased expression of dopamine receptor subtype 2. This resistance could result from the reduced dopaminergic signalling caused by these changes, or may be the result of uncharacterized mutations. As described, invasion of the cavernous sinus is a more frequent finding in DARP management is delicate and requires a multimodal approach, including transphenoidal surgery, alternative medical therapies such as somatostatin analogues and estrogen receptor antagonists.
Conclusion
The notion of resistance to dopaminergic agonists (DAs) remains controversial. Although rare, they constitute pathological entities that require the emergence of new therapies.

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EP1081

Medullary thyroid microcarcinoma revealed by lymph node metastases. about a case

Karimi Meryem[1], Hajar Azagouagh[1], Nawal Moussaid[1], Rifai Kaoutar[1], Iraqi Hind[1] & Mohamed Elhassan Gharbi[1]
[1]Chu Ibn Sina, Endocrinology Rabat, Morocco

Introduction
Micro medullar, thyroid carcinoma is defined as a rare variant of MTC, with a size less than or equal to 1 cm , often incidentall, discovered.
Observation
A 67-year-old patient with no medical history presented with two supraclavicular lymph nodes four years ago. A biopsy revealed metastatic tumor proliferation suggestive of a carcinomatous process. Immunohistochemistry confirmed cervical lymph node metastasis of MTC, and further testing showed a calcitonin level of 10,769 ng/ml. A PET SCAN revealed no anomalies, and a thorough evaluation for multiple endocrine neoplasia (MEN) was normal. Total thyroidectomy with bilateral extensive lymph node dissection was performed, revealing a 5mm intraparenchymal low-grade micro medullary carcinoma.
Discussionl and Conclusion
Contrary to the common perception of micro medullary thyroid carcinoma as having a favorable prognosis, a significant increase in the prevalence of lymph node metastases is observed. Due to the severity of complications associated with recurrences and distant metastases, two approaches are utilized: regular monitoring of serum calcitonin levels, showing a decreasing trend, and genetic screening, particularly in hereditary cases. Biochemical screening programs are crucial for identifying sporadic cases of micro medullary thyroid carcinoma in patients with thyroid nodules.

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EP1112

Acromegaly in humans, cats and dogs: epidemiological, pathophysiological, clinical and management resemblances and differences

Mariana Lopes-Pinto[1], Patrícia Lunet Marques[2,3], Ema Paula Ricca Lacerda Nobre M Caetano[1], Diego Miceli[4], Rodolfo Oliveira Leal[2,3] & Pedro Marques[5,6]
[1]Unidade Local de Saúde de Santa Maria, Hospital de Santa Maria, Endocrinology Department, Lisbon, Portugal; [2]Centre for Interdisciplinary Research in Animal Health, Faculty of Veterinary Medicine, University of Lisbon, Portugal; [3]Associate Laboratory for Animal and Veterinary Sciences (AL4AnimalS); [4]CONICET, Buenos Aires, Argentina, Buenos Aires, Argentina; [5]Pituitary Tumor United, Endocrinology Department, Hospital CUF Descobertas, Lisbon, Portugal; [6]Faculdade de Medicina, Universidade Católica Portuguesa, Lisbon, Portugal

Background
Acromegaly is a rare disorder associated with excessive levels of growth hormone(GH) and insulin-like growth factor-1(IGF-1). GH/IGF-1 excess leads to morphologic craniofacial and acral changes as well as cardiometabolic complications, but the phenotypic changes and presentation differ across species.
Aim
To present the resemblances and distinctive features of acromegaly in humans, cats and dogs.
Methods
A literature review of the epidemiology, pathophysiology, clinical features, diagnosis and management of acromegaly in humans, cats and dogs was performed by doctors and veterinaries specialized in Endocrinology. The key aspects of each species were summarized and compared.
Results and conclusion
Acromegaly is associated with prominent craniofacial changes: frontal bossing, enlarged nose, ears and lips are typical in humans; increased width of the head and skull enlargement are common in cats; dogs may present with exophthalmos. Malocclusion, prognathism, dental diastema and upper airway obstruction may occur in the three species, as well as growth and widening of extremities resulting in osteoarticular compromise. Increase of articular joint cartilage thickness, vertebral fractures and spine malalignment is more evident in humans, while arthropathy and spondylosis deformans may occur in cats. Organomegaly, heart failure, ventricular hypertrophy, and an increased cardiometabolic risk is observed in humans and cats. Diabetes may be present in humans, cats and dogs. In GH-secreting pituitary tumours, local compressive effects and behavioral changes are mostly observed in humans, but may also affect cats. Being particularly rare in dogs, hypersomatotrophism may occur due to GH hypersecretion in mammary glands, primary hypothyroidism or, extremely uncommon in this species, due to a GH-secreting pituitary adenoma. Cutis verticis gyrata and skin tags are exclusively found in humans, palmigrade/plantigrade stance is sometimes observed in acromegalic cats, while dogs can present with excessive skin folds and coat thickening. Serum IGF-1 is used for acromegaly diagnosis in humans, cats and dogs, but oral glucose tolerance test with GH measurement is only useful in humans and dogs. Imaging studies are performed after biochemical diagnosis of acromegaly. Hypophysectomy is the first line treatment in humans and cats, although not always available in veterinary medicine. In dogs, GH-secreting mammary tumours may require surgery, while radiotherapy and pasireotide have been successfully used for pituitary adenomas. In conclusion, GH-secreting pituitary tumours are the main cause of acromegaly in humans and cats, but they rarely occur in dogs. Substantial acromegalic similarities are present across the species, however there are few species-specific features and management particularities can be found.

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EP1113

Acromegaly revealed by unstable diabetes

Karimi Meryem[1], Ali Halouache[2], Isswani Jad[2] & Guerboub Ahmed Anas[2]
[1]Ibn Sina Rabat, Endocrinology Rabat, Morocco; [2]Hôpital Militaire D'Instruction Mohammed V, Endocrinology Rabat, Morocco

Introduction
Acromegaly is a rare condition characterized by the hypersecretion of growth hormone (GH), resulting in morphological anomalies, metabolic disturbances, including overt diabetes, and endocrine abnormalities.
Case Report
We present the case of a 54-year-old patient with a history of cervical lumbar sciatica under treatment. The disease history dates back 3 years with the onset of polyuria-polydipsia syndrome and fatigue. On clinical examination, the patient exhibits acrofacial dysmorphic features. The laboratory findings revealed an HbA1c of 8%, IGF1 level twice the normal range. Hypothalamo-hypophysial MRI reveals a 12 mm pituitary macroadenoma without invasion of the cavernous sinuses. The patient was prescribed oral antidiabetic drugs and subsequently referred to a neurosurgeon for surgical intervention.
Discussion and Conclusion
Acromegaly is an insidious and slowly progressive pathology, often leading to a late diagnosis. This prolonged diagnostic delay is responsible for the onset of complications, including diabetes.

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EP1114

Cushing's syndrome complicated with pulmonary embolism: report of three cases and literature review

Nana Hao[1], Sumita Cholekho[2], Huiwen Tan[2,3], Chun Wang[2], Jianwei Li[3] & Yerong Yu[3]
[1]Sichuan University China; [2]Sichuan University Department of Endocrinology and Metabolism, China; [3]

Objective
To summarise and analyze the pathogenesis, clinical risk assessment, and treatment of venous thromboembolic events (VTE) associated with Cushing syndrome (CS), and to improve clinicians' understanding of this complication.
Methods
The clinical diagnosis and treatment of 3 patients with Cushing disease (CD) combined with pulmonary embolism were reviewed, and relevant literature at home and abroad was reviewed.
Results
Three patients, all female, were diagnosed with CD and underwent resection of the saddle region. Three-dimensional reconstruction of pulmonary arterial vessels on the 6th day after the operation indicated pulmonary embolism, and they were treated with low molecular heparin and rivaroxaban anticoagulant therapy successively, and the CTA of the pulmonary artery was reexamined after 3 months without any abnormality. The keywords "Cushing's disease, Cushing's syndrome" and "pulmonary embolism, venous thromboembolism" were searched. A total of 73 articles were retrieved from the Pubmed database, of which 28 were case reports, 10 were reviews, and 35 were clinical studies. The risk of VTE in CS is more than 10 times higher than that in the general population, and the pathogenesis and clinical risk assessment are complex, while the duration of prophylactic anticoagulation and its protocols have not yet reached a consensus.
Conclusion
CS is associated with multisystem complications. The risk of VTE in CS is significantly higher, with a rapid onset of disease and a high mortality rate. Clinical vigilance, avoidance, and screening of CS-related complications are needed for early diagnosis and treatment.

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EP1115

Severe hyponatremia revealing lymphocytic hypophysitis

Abdelkader Yahi[1], Lachekham Aicha[1], Haffaf Lounes[1], Benabdellatif Katia[1], Longo Redoune[1], Derriche Abderrahim[1], Talbi A[1], Derradji Hakim[1], Ould-Kablia Samia[1] & Bendalah Meriem[1]
[1]El Djazair, Endocrinology Bir Mourad Rais

Background
Hypophysitis is a rare pathology its symptoms and radiological signs are non-specificy making its diagnosis difficult
Case Description
A 62-year-old Women, mother of 5 children, with a History of type 2 diabetes mellitus, hypothyroidism. During a period of fasting, the patient presented with profound asthenia, a tendency to hypotension. A severe hyponatremia at 119 mmol/l was diagnosed. The patient received urgent treatment. The hormonal biological assessment revealed a collapsed cortisol level with a normal ACTH level confirming the corticotrope deficiency. The rest of the assessment is in favor of anterior pituitary insufficiency with gonadotrope, somatotrope and lactotrope deficiency. The hypothalamic-pituitary MRI suggests a partially empty sella turcica and a nodular thickening of the pituitary stalk of 5.5 mmy strongl, enhanced in favor of lymphocytic hypophysitis.
Discussion
Lymphocytic hypophysitis is linked to lymphocytic infiltration of the pituitary gland. Its probably autoimmune pathogenesis remains poorly understood. It can be associated with autoimmune thyroiditis or another autoimmune disease in 20% of cases. There

are asymptomatic forms where the diagnosis can be made several years after the initial event. The diagnosis is sometimes made in the presence of anterior pituitary insufficiency with normal imaging or with an empty sella turcica appearance, especially in a multiparous woman. Corticotropic deficiency is the most common, and makes this disease serious due to the risk of acute adrenal insufficiency.
Conclusion
A number of clinical, biological and neuroradiological arguments may suggest the diagnosis of lymphocytic hypophysitis, but the certainty can only be histological.

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EP1116

Hyponatremia secondary to neurohypophysitis in a patient on nivolumab (immune checkpoint inhibitors): a case report

Macarena Dubert *P*érez[1], Miguel-Angel Ruiz-Gines[1], Marina Fernández-Rufete Lozoya[1], María Zurdo López[1], Laura Morell Jurado[1], Mercedes Agudo Macazaga[1] & Juan-Antonio Ruiz-Ginés[2]
[1]Hospital Universitario de Toledo, Análisis Clínicos, Toledo, Spain; [2]Hospital Clinico Universitario Lozano Blesa, Neurocirugía, Zaragoza, Spain

Introduction
Immune checkpoint inhibitors (ICIs) are a type of immunotherapy approved for the treatment of certain tumors. As the use of ICIs increases, the incidence of rare side effects, called immune-related adverse effects (IRAE), is also increasing, and can affect different systems (gastrointestinal, hepatic, and endocrine among others), with hyponatremia being a possible side effect in patients treated with ICIs. Our objective is to describe one of the few clinical cases published in the scientific literature that induce SIADH, secondary to pituititis, in patients with monotherapeutic treatment with Nivolumab.
Case report
A 69-year-old man diagnosed with stage IV melanoma, undergoing chemotherapy treatment with Nivolumab, was referred to the Emergency Department from outpatient Medical Oncology clinics due to severe hyponatremia of 103 mmol/l in a follow-up test (prior to the chemotherapy cycle). The patient presents a history of several days of evolution of fatigue, anorexia and hypotension (107/64mmHg; 120 bpm). No fever.
Discussion and conclusions
The possible etiology of hyponatremia would be SIADH in an oncological patient undergoing immunotherapy treatment with Nivolumab. This involvement would be considered secondary to ICI-induced hypophysitis (IRAE), a well-known complication of Lipilimumab, having ruled out adrenal insufficiency and hypothyroidism leading to euvolemic hyponatremia. Nivolumab is a monoclonal antibody that binds to the PD-1 receptor and blocks interaction with its ligands (PD-L1 and PD-L2) located on a large number of cancer cells, quickly establishing itself as the standard of care for locally advanced or metastatic melanoma. It is a very attractive treatment because it achieves better response rates and long-term survival, but due to the growing number of indications, the set of toxicities, in clinical practice, is increasing dramatically. These drugs have been shown to cause a unique set of toxicities that most clinicians were unaware. Therefore, due to their relative novelty and rarity, it is of vital importance that clinicians in the different medical services (Medical Oncology, Emergency Department, Intensive Care United, Primary Care, among others) receive training on the recognition and treatment of potential complications. The use of these drugs in the treatment of a wide variety of malignancies is being investigated, and as their use spreads, it is inevitable that the number of patients with endocrine side effects, such as neurohypophysitis, will increase.

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EP1117

The aggressiveness of rarity - a case of neuroendocrine tumor of the colon

Sara Loureiro Melo[1,2], Leandro Augusto Silva[1,2], Gonçalo Varela Cunha[1,2], Benilde Barbosa[2], José Moura[2] & Lèlita Santos[2]
[1]Portuguese Institute of Oncology of Coimbra Francisco Gentil; [2]ULS of Coimbra, Portugal

Introduction
Neuroendocrine Tumors of the Colon are often aggressive and metastatic at diagnosis. The diagnosis is histologicaly obtained through immunohistochemical evaluation of biopsy specimens/metastases, with positive staining for Chromogranin A and Synaptophysin.

Case Report
A 54-year-old independent patient with Type 1 Diabetes, leading to diabetic nephropathy, underwent a renal transplant followed by graft failure and is currently on hemodialysis and systemic corticosteroid therapy. She presented to the Emergency with abdominal pain, described as constant, squeezing, located in the left flank, refractory to analgesia, associated with unintentional weight loss of 1.5 kg , night sweats, and constipation, all during the last month. Imaging studies revealed a lombo-aortic and mesenteric lymph node conglomerate, leading to hospitalization for further evaluation and symptomatic control. During the hospitalization, additional studies showed presence of an ulcerative and vegetative tumor in the descending colon, measuring 3 cm in length. Biopsy results were consistent with poorly differentiated colon carcinoma (CK20+ /CK7/CDX2+), with neuroendocrine differentiation. Additional CT-CTAP imaging revealed the presence of supra and infra-diaphragmatic conglomerates. A diagnosis of metastatic Neuroendocrine Tumor of the Colon was made, and immunotherapy with Ipilimumab and Nivolumab was proposed. The patient is currently awaiting the first cycle of treatment.
Conclusion
This case report aims to demonstrate not only the importance of reviewing rare tumors, particularly neuroendocrine tumors, but also to highlight their nonspecificity and aggressiveness.

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EP1119

Clinical symptoms of pituitary apoplexy are not the diagnosis itself - a case of pituitary chordoma

Igor Kopczyński[1], Sonia Kaniuka-Jakubowska[1], Dominik Stodulski[2], Tomasz Przewoźny[2] & Renata Świątkowska-Stodulska[1]
[1]Medical University of Gdansk, Department of Endocrinology and Internal Medicine, Gdańsk, Poland; [2]Medical University of Gdansk, Department of Otolaryngology, Gdańsk, Poland

Chordomas of the skull base are rare lesions, which account for less than 0.2% of all intracranial tumours. They arise from embryonic remnants of the primitive notochord. They are described as locally aggressive, rarely metastatic tumours with a tendency to frequent relapses. They usually grow slowly with the destruction of the surrounding tissues. The symptoms are very unspecific which is the cause of the delay of the diagnosis. The most common initial symptoms are headaches and neuro-ophthalmological dysfunctions. Involvement of the suprasellar region may lead to partial or complete destruction of the pituitary gland, causing hypopituitarism and diabetes insipidus. Literature data indicates that the treatment of chordomas should be a combination of maximal surgical resection and adjuvant radiotherapy. A 60-year-old man reported impaired movements of the left eye with ptosis and secondary diplopia over two weeks before the admission to the neurology ward. He also suffered from nasal blockage with bloody discharge on the left side. Physical examination revealed a palsy of the 3rd left cranial nerve. He was transferred to our endocrinology department with clinical suggestion of pituitary apoplexy. In the meantime, brain computed tomography and magnetic resonance imaging were performed showing a large mass (78x54x55mm) in the sphenoid bone and clivus, extending to the sella, elevating upward the pituitary and optic chiasm, infiltrating into the nasopharynx, nasal cavities, bilateral cavernous sinuses, surrounding both internal carotid arteries. There was a suspicion of bleeding into the mass and thrombosis of the superior sagittal sinus and confluence of sinuses. The endocrine assessment revealed hypopituitarism with adrenal and thyroid deficiency with mild hyperprolactinemia. The patient underwent transnasal biopsy of the mass. Histopathology examination revealed a chordoma. The patient underwent cytoreductive endoscopic surgery, awaiting for the proton-beam therapy. The presenting case visualizes that the symptoms typical of pituitary adenomas also apply to the rare non-adenomatous sellar region lesions. It emphasizes the need for a multidisciplinary approach, with apart from endocrinologist and neurosurgeon, dedicated neuroradiologist, otorhinolaryngologist and radiation oncologist and confirms the need for pituitary centres of excellence.

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EP1120

Endocrinological features of operated craniopharyngiomas: about 7 cases

Fatimzahra Bentebbaa[1], Imane Ziani[1], Siham Benouda[1], Siham Rouf[1] & Hanane Latrech[1]
[1]Mohamed VI University Hospital center, Oujda, Endocrinology-Diabetology and Nutrition Department, Oujda, Morocco

Introduction
Craniopharyngioma is a rare benign epithelial tumour arising from the pituitary stalk or pituitary gland, developing in the sellar and suprasellar region, it affects both adults and children, The clinical presentation may include endocrine symptoms suggestive of hypopituitarism, ophthalmologic symptoms, signs of intracranial hypertension and focal neurological signs. However, after surgical treatment, hypothalamic-pituitary endocrine damage is common. The aim of our work was to study the pituitary hormone profile of operated craniopharyngiomas.
Material and Methods
Retrospective descriptive study including 7 patients followed at the Endocrinology-Diabetology-Nutrition Department at the Mohammed VI University Hospital of Oujda Morocco, with surgically treated craniopharyngioma, hospitalised in our department for postoperative hormone exploration.
Results
Four women and three men, aged 21.8±12.6 years, referred for endocrine management of a craniopharyngioma, all patients had visual impact, and the craniopharyngioma was intra and suprasellar in all patients, transphenoidal endoscopy was used for 4 patients, frontal approach was used for 3 of our patients. With regard to the postoperative hormonal profile, 6 patients developed a polyuro-polydipsic syndrome (85.7% of cases), 5 patients had a corticotropic deficiency (71.4% of cases), 2 of whom had this deficiency pre-operatively, the thyreotropic deficiency was observed in 3 patients (42,8% of cases), 1 of these patients had this deficiency pre-operatively, gonadotropic deficiency was observed in 6 patients (85.7% of cases), 2 of whom had hypogonadotropic hypogonadism pre-operatively, and finally somatotropic deficiency was present pre-operatively in only 1 patient. For hormone replacement, it involved hydrocortisone supplementation for corticotropic deficiency, levothyroxine for thyroid insufficiency, estrogen and progestin treatment for women with gonadotropic deficiency, and testosterone replacement therapy for men.
Conclusions
Our study confirms that in craniopharyngiomas, antehypophyseal insufficiency and diabetes insipidus are frequent after surgical treatment. Adequate hormone replacement therapy and long-term medical monitoring are therefore necessary.
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EP1148

Case report of a young woman with central diabetes insipidus
Nives Gojo Tomić[1,2] & Mirjana Kardum Pejić[2,3]
[1]Clinical Hospital Dubrava, Endocrinology and Diabetes, Zagreb, Croatia; [2]Clinical Hospital Dubrava, Department of Endocrinology and Diabetes, Zagreb; [3]Clinical Hospital Dubrava, Endocrinology and Diabetes, Zagreb

Arginine vasopressin deficiency (or central diabetes insipidus - CDI) is a rare disorder (1 in 25 000 individuals). It is characterised by decreased release of antidiuretic hormone (ADH) which results in polyuria and polydipsia. Majority of cases are acquired and caused by neurosurgery or head trauma, primary or secondary brain tumours, infiltrative diseases or autoimmune neurohypophysitis. Only about 5% of all reported cases are caused by genetic or congenital disorders. It has been suggested that an autoimmune process is involved in many patients with non-traumatic CDI (30-50%). Antibodies to AVP neurons were found in approximately one-third of the patients with 'idiopathic' CDI. We present a nineteen year old female, previously healthy, who presented in January 2022 with polyuria (10-12L daily), polydipsia (10-15L of water daily), nocturia (4-5 times) and nocturnal thirst during the previous 2-3 months. After excluding diabetes mellitus she was admitted to hospital to exclude possible diabetes insipidus. During the water deprivation test, laboratory tests showed low urine osmolality and mild plasma hyperosmolality. After administration of nasal desmopressin, urinary osmolality increased and the patient's symptoms improved. Water deprivation test was positive for central diabetes insipidus. Magnetic resonance showed medially positioned infundibulum with thickened pituitary stalk (about 3.8 mm). There was no hyperintense signal ('bright spot') in the neurohypophysis. According to the radiologist, differential diagnosis of these changes could include lymphocytic hypophysitis. During hospitalization, extensive laboratory tests and imaging were done. Infiltrative diseases, infections including tuberculosis, and autoimmune diseases including sarcoidosis were excluded. Results of imaging (abdominal ultrasound, chest x-ray) were normal. There were no other pituitary deficits, or other hormonal deficits. The baseline hormone test showed slightly elevated prolactin level. Other laboratory tests showed high thyroid peroxidase antibodies. Ultrasound changes which indicate Hashimoto thyroiditis were found. After starting therapy with intranasal desmopressin, there was significant clinical improvement. Control MR imaging 9 months and 18 months after diagnosis showed no change in comparison with the first one. Desmopressin therapy was continued with excellent clinical and laboratory results.
Conclusion
The aetiologic diagnosis of central diabetes insipidus is difficult. The underlying cause remains unknown in many cases. This case did not show exact aetiology of central diabetes insipidus. We cannot determine vasopressin secretory cells antibodies, so possible autoimmune aetiology could not be confirmed. Although aetiology of the disease was not proved, proper treatment led to symptom control, clinical improvement and normalization of pathologic laboratory tests during 2 years after diagnosis.
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EP1149

Silent mixed growth hormone and prolactin pituitary adenoma, a case report
Zahra Ismail[1], Sidiebatt Amar[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]University Hospital Center Mohamed VI, Departement of Endocrinology, Diabetes and Metabolic Disease, Marrakech, Morocco

Introduction
Silent somatotroph pituitary adenomas are defined as pituitary adenomas with positive immunostaining for GH without signs of clinical or biochemical acromegaly. Silent somatotroph adenomas are rare and diagnosis is made post-operatively. Almost two-thirds are mixed GH-prolactin tumors. We report the case of a non-functioning macroadenoma coexpressing prolactin and GH.
Observation
A 37-year-old man presented with headache and progressive vision loss. Clinical examination revealed no gynecomastia, galactorrhea or signs of acromegaly. A cerebral MRI revealed a heterogeneous tumor in the sellar region invading the ethmoid and sphenoid sinus and containing calcifications, measuring 56×55×54 mm, suggestive of a chondroma sphenoid sinus. The hormonal profile: prolactin=206 ng/ml, thyrotropin and corticotropin deficiency. Visual field was restricted. The patient underwent trans-sphenoid surgery. Pathology and immunohistochemistry showed a mixed pituitary adenoma positive for prolactin and GH antibodies with a Ki67=3%. The IGF1 performed post operatively was normal at 107.6 ng/ml. The follow-up MRI showed tumor residue. We started treatment with dopaminergic agonists (Cabergoline) and proposed radiotherapy and somatostatin analogue (Lanreotide).
Discussion
Somatotroph adenomas are often identified in the setting of acromegaly. Occasional cases of silent adenomas have been described in the literature, mainly in young females. The cause of tumor silence is still unknown. Preoperative biochemical work-up should include an IGF-1 measurement and if clinical suspicion for GH excess, GH measurement. Management of this type of adenomas is initially based on surgery. Because of the potential of phenotype change to clinical acromegaly and recurrence, the need for radiation is higher than other non-functioning tumors and close follow-up is recommended.
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EP1150

Pituitary apoplexy- a case report
Jona Troshani[1], Olta Zeneli[1], Bruno Teme[1], Sindi Bushati[1] & Agron Ylli[1]
[1]Mother Teresa Hospital, Tirana, Endocrinology Tirana, Albania

Background
Pituitary apoplexy is a rare but potentially life-threatening condition in which the pituitary gland undergoes infarction or haemorrhage, most commonly in the setting of an underlying tumour. We report on apoplexy of a diagnosed pituitary adenoma who presented with a sudden onset of headache, vomiting, ophthalmoplegia and vision loss. Neuroimaging revealed hemorrhagic pituitary mass. Trans-sphenoidal surgery was performed, which resulted in moderate neurological recovery.
Case presentation
A 36 years old patient presented in our emergency unit with a sudden onset of headache, vomiting, ophthalmoplegia, visual disturbance –vision loss. Medical history: Patient was diagnosed with pituitary macroadenoma since he was 31-years-old. He was not taking medication for this pathology. In the objective examination the patient was agitated but had a clear consciousness. His skin and mucous membranes were pale. There were no pathological sounds in the auscultation of the heart and lungs. There were not peripheral edema. Laboratory analysis: the most important data is the low value of cortisol - 1.00 mg/dl [2.9-17.3], his thyroid hormone levels, TSH, gonadotropins, prolactin and progesterone

were within range. He had a low testosterone level 0.49 ng/ml [2.4-8.7]. CT Scan revealed a lesion with sellar and suprasellar extension with hyperdensity inside and around, measuring 42x38x47 mm, which modifies the sella turcica, suggestive of macroadenoma. The patient was hospitalized in Neurosurgery where intravenous fluids and hydrocortisone was immediately started. Transsphenoidal surgery was performed the next day which resulted in moderate neurological recovery.
Conclusion
Enlargement of the pituitary gland may precipitate haemorrhage. Pituitary apoplexy has a widely varied symptomatology—it should be considered as a differential diagnosis for headache or visual disturbance. Although the treatment of pituitary apoplexy is still a matter of debate with regard to surgery, the results of early sphenoidal procedure within 1 week after pituitary apoplexy are satisfactory than patients operated later.
Keywords: pituitary apoplexy, transphenoidal surgery, adenoma, infarction
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EP1152

Sarcoidosis presenting as cranial diabetes insipidus- a case report
Ishara Ranathunga[1], Chandima Idampitiya[1] & Fathima Pambinezhut[1]
[1]Cumberland Infirmary United Kingdom

Background
Sarcoidosis is an immune-mediated condition characterized by the presence of non-caseating granulomas, primarily impacting the respiratory system, lymphatic system and heart. The involvement of the central nervous system, especially hypothalamic- pituitary involvement is a rare occurrence. We report a patient initially presenting with Cranial Diabetes Insipidus who was later diagnosed to have sarcoidosis.
Case presentation
A-67-year old male presented with progressive polydipsia, polyuria and nocturia for 7 months duration without any other systemic symptoms. He had no headaches or constitutional symptoms such as poor appetite, weight loss or night sweats. His physical examination had been unremarkable. He was noted to have a high serum osmolality of 307 mmol/kg and a relatively dilute urine osmolality of 143 mmol/kg. His serum co-peptin after an overnight fast came back relatively low at 1.9 pmol/l in the presence of a serum sodium of 148 mmol/l suggestive of Cranial Diabetes Insipidus. The rest of the pituitary hormones were within the normal range and the MRI pituitary showed thickening and enlargement of the pituitary stalk with absent posterior pituitary bright spot. The anterior pituitary appeared normal in size, signal intensity and enhancement pattern. He was successfully treated with Oral Desmopressin 50 mg in the morning and 100 mg at night which completely resolved his symptoms. Fifteen months after developing the initial symptoms of cranial diabetes insipidus, he presented with general lethargy, weight loss, chronic cough and multiple large joint pains. Further investigations revealed a marginally raised ACE level (74 U/l) and CT chest showed irregular septal thickening in left upper and lower lobe, scarring in left apex, multiple mediastinal and hilar nodes, suggestive of sarcoidosis with central nervous system involvement.
Conclusions
The occurrence of central nervous system manifestations in sarcoidosis is rare and individuals might display these symptoms without accompanying systemic manifestations. Recognizing this unusual presentation holds significance in guiding investigations and initiating early treatment to prevent the disease from advancing further.
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EP1153

An incidental pituitary finding on an 18FDG PET scan
Sawsen Nouira[1], Hamza Elfekih[1], Fatma Ben Abdessalem[1], Amel Maaroufi[1], Yosra Hasni[1] & Molka Chaieb[1]
[1]University Hospital Farhat Hached, Endocrinology, Sousse

Introduction
Pituitary adenomas stand as the most prevalent form of tumorous pathology impacting the pituitary gland in adults. Their discovery might arise from either hypersecretion in functional adenomas or the manifestation of compression symptoms on neighboring structures. Detection of a pituitary adenoma can occur incidentally during various imaging modalities, encompassing both structural and functional assessments. This study documents a case involving the incidental detection of a pituitary macroadenoma during a PET-CT scan.
Observation
We report the case of a 61-year-old patient with a history of large B-cell gastric lymphoma evolving over four years, managed with chemotherapy. A post-chemotherapy evaluation was conducted through an 18FDG PET-CT scan. The scan revealed a significantly increased metabolic activity in the sellar region associated with tissue infiltration. A hypothalamic lymphomatous localization was deemed unlikely as there was no pathological metabolic activity observed in lymph nodes or in the gastric region. Clinical examination and laboratory tests showed no signs of hormonal overproduction or pituitary deficiency. An MRI of the pituitary gland confirmed the presence of an expansive intra-sellar process, demonstrating heterogeneous enhancement after gadolinium injection, measuring 17×15×14 mm, exerting a mass effect on the optic chiasm. Visual field examination revealed no abnormalities. The diagnosis of a non-secreting pituitary macroadenoma with suprasellar extension was established. The patient was referred to neurosurgery for further management.
Discussion et conclusion
The discovery of an incidental pituitary adenoma through an 18FDG PET scan is exceedingly rare. This rarity in discovery and the lack of definitive correlation between FDG uptake and functional status raise questions about the metabolic behavior of these tumors. Understanding the mechanism of uptake in non-secreting adenomas could potentially unveil novel insights into their biology and pathogenesis. This aspect of our research highlights the complexity of pituitary adenomas and emphasizes the need for further investigations into their metabolic characteristics to elucidate their clinical significance and management.
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EP1154

The differential diagnosis between cushing's disease and pseudocushing syndrome in a pre-agonic patient
Simone Antonio De Sanctis[1,2], Sabrina Chiloiro[1,2], Eloisa Sofia Tanzarella[3,4], Filippo Bongiovanni[4], Antonella Giampietro[1,2], Gennaro De Pascale[4], Laura De Marinis[1,2], Massimo Antonelli[4], Alfredo Pontecorvi[1,2] & Antonio Bianchi[1,2]
[1]Policlinico Agostino Gemelli, Dipartimento di medicina traslazione, Università Cattolica del Sacro Cuore, Rome, Italy; [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Endocrinologia e Diabetologia, Rome, Italy; [3]Fondazione Policlinico Universitario A. Gemelli IRCCS, Dipartimento di Scienze Biotecnologiche di Base, cliniche intensivologiche e perioperatorie, Rome, Italy; [4]Fondazione Policlinico Universitario A. Gemelli, IRCCS, Dipartimento di Scienze delle emergenze, Anestesiologiche e della rianimazione, Rome, Italy

Introduction
The pseudo-Cushing's encompass several disorders that can occur in high-stress situations, such as the sepsis, and that show biochemical features like those of Cushing's syndrome. We present a case with difficult differential diagnosis, for overlapping laboratory findings.
Case description
A 74-year-old man was admitted to our hospital for worsening dyspnoea since a month, 15 kilograms weight loss in the previous months, asthenia, hypotonia and muscle hypotrophy. In past medical history: glucose intolerance in treatment with metformin, depression in treatment with mirtazapine and vortioxetine and pancreatic intraductal papillary mucinous neoplasm (IPMN). Due to the onset of acute hypoxic-hypercapnic respiratory failure, the patient was treated with not-invasive ventilation and then admitted to the intensive care united, for pneumonia and respiratory failure due to Meticillin-sensitive Staphylococcus aureus (MMSA) and Klebsiella Aerogenes. Antibiotic therapy was started according to the results of the antibiograms and sepsis. The neurological assessment showed a severe strength deficiency of the neck flexors and four limbs and hypophonia, reflexes were not revocable. No abnormalities in ocular motility, palpebral ptosis and muscular or lingual fasciculations were detected. Electromyography of deltoid muscles, brachial biceps and right rectus femur documented a method of recruitment of the myopathic type, suggestive for a sporadic late onset nemaline myopathy (SLONM). During the treatment in ICU, the patient underwent endotracheal intubation for the worsening of respiratory function and inotropic drug therapy was introduced for the development of septic shock. According to patient's clinical condition, hormones were tested showing an ACTH-dependent hypercortisolism. The results of Nugent, Liddle and the dexamethasone suppressed CRH stimulation tests suggested a not-neoplastic ACTH-dependent hypercortisolism. The pituitary contrasted magnetic resonance image showed a gland hypertrophy and the abdominal computed tomography (CT) ruled out adrenal lesions. Unfortunately, the patient developed a multi-organ failure, and at least died. The autopsy finding confirmed the absence of pituitary and other neuroendocrine tumours and showed a bilateral adrenal hypotrophy.

Conclusions
Our clinical case described a patient with pseudo-Cushing's syndrome during sepsis and pre-agonist phase, with difficult differential diagnosis, in which the combination of the low-dose dexamethasone suppression test and the CRH test allowed a conclusive and correct diagnostic orientation.

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EP1155

Rheumatological complications during cushing's disease: about 51 cases

Bassiratou Hamza Maliki[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]CHU Ibn Rochd - Casablanca, Morocco, Endocrinology and Metabolic Disease Service, Casablanca, Morocco

Introduction
Rheumatological manifestations are frequent in Cushing's disease with impact on quality of life.
Objective
The aim of our study is to describe rheumatological manifestations in Cushing's disease
Material and methods
Retrospective study of 51 patients diagnosed for Cushing's disease followed in the Endocrinology of CHU IBN Rochd from Casablanca from 2012 to 2023. Osteo-articular complications were detected either at diagnosis or during monitoring. The statistical analysis was done by the SPSS version 25 software.
Results
We included 51 patients including 45 women and 6 men, the average age of patients was 36.20 years (17-69). The average seniority of the disease was 2.5 years. The average Clu was 657 UG/24 hours (116.8 - 2196). To pituitary MRI: macroadenoma in 27 patients, microadenoma in 21 patients and normal in 5 patients. On the clinical level: gonalgia 49% ($n=25$), lumbar dorso rachialies 58.82% ($n=30$), diffuse arthralgia 11.76% ($n=6$), shoulder arthralgia 7.84% ($n=4$), arthralgia of the elbow 7.84% ($n=4$). Biologically: moderate hypocalcemia in 4 patients, hypophosphoremia in 2 patients, hypovitaminose D in 58.82% ($n=30$). To osteodensitometry: osteopenia of the femur 17.65% ($n=9$), wrist osteopenia 27.45% ($n=14$), osteopenia of spine 11.76% ($n=6$), osteoporosis of the 31.37% ($n=16$), osteoporosis of the femur 7.84% ($n=4$) and normal 27.45% ($n=14$).
Conclusion
Rheumatological complications are frequent in Cushing's disease dominated by lumbar dorso rachialgia, hypovitaminose D and spine osteoporosis.

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EP1156

Hyperprolactinemia: a rare association between primary hypothyroidism and macroprolactinoma

Eya Sassi[1], Sondes Chermiti[2], Bochra Zitoun[2], Hajer Marzouk[2], Issam Kharrat[2], Yosra Hasni[3] & Wided Debbabi[2,2]
[1]Ibn Aljazzar Hospital, Endocrinology, Kairouan, Tunisia; [2]Ibn Aljazzar Hospital, Endocrinology, Kairouan, Tunisia; [3]Farhat Hached Hospital, Sousse, Tunisia

Introduction
Primary hypothyroidism is a common cause of hyperprolactinemia. TSH measurement is part of the first-line investigation of hyperprolactinemia wich usually disappear after L-thyroxine therapy. the presence of pituitary hyperplasia mimicking a pituitary macroadenoma has been reported by several authors, but coexistence oh primary hypothyroidism and prolactinoma is rarely reported.
Case
We report a rare case of hyperprolactinemia revealing the association of primary hypothyroidism with a pituitary microprolactinoma. was 29 years old referred to endocrinology consultation for hyperprolactinemia (Prolactin level: 120 ng/ml) discovered in the context of infertility and secondary amenorrhea. Hyperprolactinemia was confirmed, and the first-line investigation concluded to peripheral hypothyroidism (TSH > 60 mUI/l) secondary to autoimmune thyroiditis (antiTPO antibodies: 453 mUI/l). Management consisted in hormone replacement therapy with thyroxine. Clinical evolution was marked with hormonal normalization 3 months later but persisting amenorrhea and hyperprolactinemia justifying pituitary MRI leading to the diagnosis of macroprolactinoma. Anti-dopaminergic treatment was prescribed with prolactin levels normalization, pituitary microadenoma size reduction and recovery of menstrual cycles.
Conclusion
Hyperprolactinemia is common in primary hypothyroidism, due to compensatory increase in the discharge of central hypothalamic TRH as a result of low thyroxine. Association of primary hypothyroidism and prolactinoma as cause of hyperprolactinemia is a rare condition which requires long-term follow-up to avoid missing the diagnosis and preserve the gonadal function and fertility.

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EP1185

Role of tolvaptan as a cost-cutter in hospitalized SIADH patients

Kirtanya Ramachandran[1,2], Bashir Mahamud[2] & Gideon Mlawa[2]
[1]Redcliffe hospital, Redcliffe, Australia; [2]Queens Hospital, London, United Kingdom

Background
SIADH is a condition characterized by excessive ADH secretion from the posterior pituitary in the absence of triggers like high plasma osmolality and low blood volume or low blood pressure. This leads to excessive and unwanted water retention and increase in the total body water content, though the plasma sodium levels are normal.
Case
An 89 y/o gentleman was admitted after he sustained a fall at his home and was diagnosed with right neck of femur fracture by the orthopaedic team. He had a background of atrial fibrillation, COPD, BPH, HTN, CKD, hypercholesterolemia, GORD for which he was on edoxaban 30mg OD, alfuzosin hydrochloride 10mg OD, atorvastatin 20 mg OD, salbutamol 100 mg, indapamide and omeprazole. He underwent right hip hemiarthoplasty and was making good progress clinically. However his renal functions started deteriorating mild AKI The patient was immediately started on IV fluids for the AKI and it resolved subsequently. However, his bloods showed his sodium levels to be quite low at 122. Therefore, the indapamide he was taking was stopped as well as the omeprazole he was on, was changed to famotidine. He was started on Fluid fluid restriction upto 750 ml. He was started started on oral Tolvaptan as sodium did not improve with fluid restriction. Sodium level improved remarkably to 130 with tolvaptan. His bilateral leg swelling also improved and he was clinically and biochemically stable. He was discharged and followed up a week later in the clinic to ensure his renal function was stable.
Discussion
SIADH alone contributes to nearly one third of the hyponatremia cases seen. Tolvaptan, is most effective treatment in euvolaemic hyponatramia and is given orally given. It is V2 receptor antagonist and leads to aquaresis. One of the remarkable features of this drug is, how quick it is at correcting the hyponatremia as well as the added advantage of not having to keep the patient in fluid restriction.
Conclusion
Hyponatremia when profound, is independently associated with a higher risk of death, with increased length of stay and in turn the cost of care for hospitalized patients. The vaptans represent a revolutionary step forward in the treatment strategy for patients with SIADH. They no longer need fluid restriction, the correction of hyponatremia occurs efficiently and quickly, and duration of hospitalization is shorter than with fluid restriction or demeclocycline.

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EP1186

Ocular manifestations of pituitary adenoma

Rekik Mona[1], Kammoun Sonda[1,2], Jallouli Aida[1,1], Ben Mrad Aymen[1], Nabila Mejdoub[3] & Trigui Amira[1]
[1]Habib Bourguiba Hospital; [2]; [3]Hedi Chaker Hospital

Introduction
Pituitary adenomas are common, and their impact on visual function is often significant, given the intimate relationship between the anterior pituitary and the optic pathways. Ocular symptoms may be indicative. Compressive optic neuropathy and oculomotor paralysis present a diagnostic challenge. This report details four cases where ocular manifestations played an essential role in establishing the diagnosis of pituitary macroadenomas.
Observation
Observation 1: A 63-year-old man with no significant medical history, presented with sudden-onset ptosis and diplopia. Ophthalmological examination revealed a complete paralysis of the third cranial nerve, and cerebral magnetic resonance imaging (MRI) showed a partially hemorrhagic macroadenoma. Observation 2: A 56-year-old man with no significant medical history, presented with complains of

bilateral progressive visual loss. Visual acuity was reduced to 1/20 in the right eye and negative light perceptions in the left eye. The pupillary light reflex in the right eye was normal, but a positive Marcus Gunn sign was observed in the left eye. Fundoscopy revealed bilateral optic atrophy. Brain MRI identified a sellar and suprasellar macroadenoma. Observations 3 and 4: The other two patients were women aged 25 and 33, who presented with complain of persistent headaches and vomiting. Ophthalmological examination indicated preserved visual acuity and bilateral stage II papilledema on fundoscopy. Brain MRI revealed a macroadenoma with a mass effect on the optic chiasm. The endocrine investigations have concluded to a non-secreting pituitary macroadenoma in cases 2,3 and 4.

Conclusion

Pituitary adenomas can manifest as a tumor syndrome, an endocrine syndrome or an acute intrasellar syndrome. The tumor syndrome primarily involves ophthalmological signs related to compressive optic neuropathy. This is most often associated with non-functional pituitary adenomas. Consequently, their discovery is often delayed until the tumor syndrome stage. When the macroadenoma extends supra-sellar with compression of the optic chiasm and/or pituitary stalk, it results in stasis papilledema, most commonly bilateral, causing visual field deficits. It can manifest as oculomotor paralysis, primarily affecting the third cranial nerve. Brain MRI allows for the diagnosis of pituitary macroadenomas and provides a precise assessment of their extension. These clinical cases highlight the diverse clinical manifestations of pituitary macroadenomas, underscoring the importance of brain imaging and ophthalmological evaluation in the diagnosis and management of these conditions.

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EP1187

Insulinoma: diagnostic difficulties of a rare tumor

Marwa El Arem[1], Bilel Ben Amor[2], Ekram Hajji[1], sana abid[1], Ines Bayar[1], Héla Marmouch[1], Hanene Sayadi[1] & Inès Khochteli[1]
[1]Hospital Fatouma Bourguiba, endocrinology; [2]Hospital Fatouma Bourguiba

Introduction

Insulinoma is a rare neuroendocrine tumor. Its diagnosis is clinico-biological. Preoperative topographical diagnosis is necessary to guide the therapeutic procedure.

Observation

We report the case of a 37-year-old patient, without notable pathological history, who was admitted for exploration of severe hypoglycemia, not felt, evolving for 2 years and complicated by convulsive attacks. The initial etiological investigation revealed corticotropic insufficiency and thyrotropic insufficiency. Despite substitution with hydrocortisone and L-thyroxine, hypoglycemia persisted. The dosage of insulinemia and C-peptide, carried out at the time of hypoglycemia, were inappropriate, thus confirming the presence of associated endogenous hyperinsulinism. The concomitant dosage of sulphonylureas was negative. Pancreatic MRI and CT angiography were normal. Likewise, the octreoscanner did not show any pathological uptake in the pancreas. Endoscopy ultrasound showed a small cystic lesion measuring 8x9 mm at the level of the pancreatic uncus. The cytopathological examination after cytopuncture showed an immunocytochemical appearance compatible with a neuroendocrine tumor. A second CT angiography, guided by the endoscopic ultrasound results, confirmed the presence of a cystic tumor at the level of the uncus. The patient underwent enucleation with disappearance of the hypoglycemia.

Conclusion

The cystic form of insulinoma is exceptional. In our case, only endoscopic ultrasound allowed the localization of this particular form.

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EP1188

Isolated ophthalmoplegia should we think about pituitary apoplexy?

Abdelkader Yahi[1], Haffaf Lounes[1], Lachekham Aicha[1], Benabdellatif Katia[1], Longo Redoune[1], Derriche Abderrahim[1], Talbi A[1], Derradji Hakim[1], Ould-Kablia Samia[1] & Bensalah Meriem[1]
[1]Algeria, Endocrinology Bir Mourad Rais

Background

Pituitary apoplexy (PA) is a rare neuroendocrine emergency due to acute ischemic infarction or hemorrhage of the pituitary gland. We report a case of apoplexy manifesting with isolated ophtalmoplégia.

Case description

We report the case of a 48-year-old man with a history of hypertension, type 2 diabetes mellitus, and dyslipidemia. Consult a private ophthalmologist following the sudden appearance of double vision and sagging of the right upper eyelid. The ophthalmological examination revealed paralysis of the right common oculomotor nerve (3rd cranial nerve). The patient was placed on symptomatic treatment. A week later, given the worsening of the ptosis, a brain CT scan was requested, which revealed a tumor process in the sellar region with hemorrhagic changes. Hypothalamic-pituitary MRI revealed a hemorrhagic pituitary macroadenoma measuring 30 mm long axis. The diagnosis of pituitary apoplexy was made. Since the patient was scored 2 according to the Pituitary Apoplexy Score (PAS), he benefited from conservative treatment (corticotherapy) with complete recovery of the visual impairment. The morphological evaluation carried out at 3 months found a clear regression of the tumor volume with the persistence of a remainder of 11 mm.

Discussion

PA is an atypical condition. The incidence ranges from 2 to 10% of all pituitary adenomas (PITNET). Despite the best diagnostic and treatment conditions, morbidity and mortality remain high at 15.3%. Therapeutic management, particularly medical or surgical management, is still debated and remains at the discretion of the practitioner. The interest in the PituitaryApoplexy Score (PAS), rated from 0 to 10, was reported in the 2011 British consensus, without threshold established to guide management.

Conclusion

The study of this observation underlines the variable clinical presentation of pituitary apoplexy whose evolution is conditioned by early diagnosis and treatment making it possible to first preserve the vital prognosis, as well as the visual prognosis and prevent irreversible damage.

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EP1191

Challenges in treatment of cortikotroph pituitary macroadenoma

Tamara Dojcinovic[1], Aleksandra Markovic[2] & Jelena Malinovic Pancic[3]
[1]University Clinic centre of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina; [2]University Clinical Centre of the Republic of Srpska; [3]University Clinical Centre of the Republic of Srpska

Cushing's syndrome is a condition characterized by hypercortisolism (endogenous and exogenous) regardless of its etiology. Hypercortisolism caused by an adrenocorticotropin secreting pituitary adenoma is defined as Cushing's disease. These tumors represent 10-12% of all pituitary adenomas. ACTH-secreting macroadenomas occur in only 4-23% of all patients with Cushing's disease. We present the case of 56-year-old female patient with hypercortisolism and stigmata of Cushing's syndrome. On physical examination we registered "buffalo hump", "facies lunata", hematomas on the skin and central obesity. Laboratory findings verified a disturbed diurnal cortisol rhythm with elevated ACTH values, as well as high cortisol values in low-dose dexamethasone test and partially suppressible values of cortisol in the high-dose dexamethasone test. An NMR of the pituitary gland was performed, verifying a 1.2 cm pituitary macroadenoma. The patient was further referred to a neurosurgeon and neurosurgical treatment was performed (PH: pituitary neuroendocrine tumor PiTNET type of corticotroph tumor, densely granulated subtype). Due to the persistent complaints of the patient, hypokalemia, unregulated hypertension and diabetes, the testing was repeated 3 months following surgery. Along with a disturbed diurnal cortisol rhythm, elevated ACTH values were also maintained. The patient has been referred to a higher reference center and treatment with the steroidogenesis inhibitor metyrapone had been initiated. In the further course, a control pituitary NMR was performed 6 months after the first one, and the rest of the 18 mm adenoma was verified. ACTH values were persistently increasing, and the diurnal rhythm of cortisol was still significantly impaired despite metyrapone therapy. The patient was reoperated on, and immediately postoperatively, elevated ACTH values were registered. The patient was advised to continue therapy with newer generation steroidogenesis inhibitors (osilodrostat), which is not registered in our country, and at this moment she is unable to obtain metyrapone, so cabergoline as only option was introduced. In later course, patient received gamma knife radiosurgery, and reevaluation in order to assess effects will be made. As already stated, Cushing's disease is a rare condition with many challenges in treatment because in a certain number of cases surgical resection does not provide complete remission. Additionally, the treatment of such a patient in our region is hard due to impossibility of obtaining and prescribing steroidogenesis inhibitors, so the only therapeutic option here in case of failure of cabergoline and radiotherapy is ultimately bilateral adrenalectomy.

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EP1193

Pediatric pituitary microadenomas: a case series and review of diagnostic challenges and treatment outcomes

Ashraf Soliman[1], Noor Hamed[1], Nada Alaaraj[1], Fawzia Alyafei[1] & Shayma Ahmed[1]
[1]Hamad Medical Centre, Department of Pediatrics, DOHA, Qatar

Background
Pituitary microadenomas in pediatric populations, though infrequent, present diagnostic and therapeutic challenges.
Methods
We retrospectively reviewed six pediatric cases of pituitary microadenomas diagnosed and treated at our institution. The cases were analyzed for presenting symptoms, hormonal profiles, and treatment responses.
Results
Case 1: A 12-year-old with growth hormone deficiency showed significant height improvement with somatropin treatment, without change in microadenoma size. Case 2: Central hypothyroidism was managed with levothyroxine, resulting in the resolution of headaches and fatigue, though growth deceleration persisted. Case 3: Precocious puberty was treated with a GnRH analogue, with ongoing monitoring. Case 4: The patient awaits further evaluation for recurrent headaches and elevated IGF1. Case 5: Early puberty signs were managed with triptorelin, with ongoing monitoring for microadenoma. Case 6: Treatment for precocious puberty and GH hypersecretion involved a GnRH analogue, with abnormal growth patterns under investigation.
Conclusions
The six cases exhibited a spectrum of growth anomalies ranging from short stature with slow growth velocity to precocious puberty with accelerated growth. Hormonal disturbances included growth hormone deficiency, central hypothyroidism, and central precocious puberty.

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EP1195

Therapeutic challenges in the treatment of acromegaly

Aleksandra Markovic[1,2], Mirjana Bojic[1], Tamara Dojcinovic[1,2], Danijel Djekic[1], Bojana Caric[1,2] & Jelena Malinovic-Pancic[1,2]
[1]University Clinical Centre of the Republic of Srpska, Internal Medicine, Banja Luka, Bosnia and Herzegovina; [2]University of Banja Luka, Faculty of Medicine, Banja Luka, Bosnia and Herzegovina

Introduction
Acromegaly is a chronic disease that occurs as a result of excessive growth hormone secretion, caused by somatotropin-secreting tumors of the pituitary gland in 98% of cases. The first line of treatment for these patients is operative via transsphenoidal approach, however, absolute remission is not achieved in 50% of patients and pharmacological therapy is indicated.
Case report
We will present the case of a 43-year-old patient who was hospitalized at the endocrinology department in 2016 due to enlargement of the hands, feet and nose, galactorrhoea as well as secondary amenorrhea. Elevated basal growth hormone (GH) values were verified: 79.05 ng/ml, there was no suppression in the oral glucose tolerance test, which established the diagnosis of acromegaly. NMR of the pituitary gland was performed, and described a macroadenoma of size 31×31×20 mm (LL×KK×AP) with expansion into the suprasellar cistern and cavernous sinuses on both sides. Operative treatment was indicated by the neurosurgeon, and conducted via transsphenoidal approach. After that, she was examined on several occasions by an endocrinologist from a lower reference center with persistently high IGF1 values but never came to our institution. She came to our centre in 2023 because of headaches, poorly regulated diabetes and hypertension. Again she had elevated basal GH values with the absence of suppression in the oral glucose tolerance test (GH 0 30, 60, 90, 120 min: 210 - 245 - 216 - 193 - 210 ng/ml), as well as high IGF1 443, 9. NMR of the pituitary gland was obtained and it showed deformed sella turcica, with a macroadenoma that spreaded parasellarly on both sides, invading both cavernous sinuses, compressing the optic nerves and the optic chiasm. Octreotide LAR 30 mg was introduced into the therapy immediatelly. A neurosurgeon was consulted again and a reoperation was indicated and performed. Postoperatively, elevated values of IGF1 persisted - 760 ng/ml, and the application of octreotide LAR was continued. Since she continuously had elevated levels of IGF1, we planned on introducing pasireotide or pegvisomant into the therapy, but that was not possible at this moment, given that these drugs are not available in our country.
Conclusion
As already mentioned in the introduction, the treatment of acromegaly is complicated and in most cases requires a combination of therapeutic modalities since transsphenoidal surgery does not lead to complete remission. We will also consider other therapeutic modalities (such as radiation).

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EP1196

Hyponatremia after surgery of subdural hematoma and oxcarbasepine therapy

Mubina Hodzic[1], Davorka Dautbegović- Stevanović[1,2], Alma Badnjević-Cengić[1] & Amila Čerim-Aldobašić[1]
[1]Cantonal hospital, Of Internal diseases, Zenica; [2]

Introduction
Hyponatremia is the most common electrolyte disorder that occurs in 15-30% of hospitalized patients. It is manifested by a wide range of clinical changes, from very mild to life-threatening conditions. Hyponatremia in the elderly is mainly caused by drugs (thiazides and antidepressants), SIADH or endocrinopathies. The paper presents a patient with severe hyponatremia after surgery of subdural hematoma and oxcarbazepine therapy.
Case report
A 77-year-old female was admitted to the Department of internal diseases in 2023, September due to slow speech, disorientation, inability of walking, occasionally abdominal pain. At the end of August 2023. she had a surgery of subdural hematoma due to nausea, headache, walking instability with preoperative normal mineral status. Her cousin denies vomiting, diarrhea, head injuries. The patient was taking enalapril hydrochlorothiazide, rosuvastatin in therapy. She was conscious, oriented, bradipsychic, lightly dehydrated, normotensive on admission but later was hypotensive in Intensive care Unit. Also oxcarbasepine therapy mentioned in a Neurosurgery discharge letter due epilepsy but denied taking it. Low values of sodium were noticed at biochemical findings. Other parameters were normal including glucose, renal, hepatic. Urine culture was positive in Escherichia coli. Serum sodium was corrected with small volume of hyperosmolar sodium chloride at admission due acute hyponatremia and later with isotonic sodium chloride. Due epilepsy attack during hospitalization neurologist consulted and oxcarbasepine started. Sodium diminished and the medication discontinued with the consecutively rising of serum sodium. The patient was conscious, oriented, communicative but not able to walk by herself during the hospitalization.
Conclusion
Evaluation of hyponatremia in the elderly is a challenge for the physician. A female patient had anamnesis and symptoms (hypotension, head surgery, improving with

(Abstract EP1193).

Case	Age at Presentation	Presenting Complaints	Main Findings	Hormonal Abnormalities	Treatment/Follow-up
1	12 years	Short stature	WtSDS = -2.22, HtSDS = -2.6, GV = 4 cm/year, MPHSDS = -1.28, IGF1 SDS = -1.81, GH peak 5.2 mg/l	GH deficiency	Started somatropin, no significant change in microadenoma size
2	12.4 years	Headaches and fatigability	HtSDS = -0.5, MPHSDS = 0, GV = 2.6 cm/year, IGF1 SDS = -1.28, GH peak 6.7 mg/l, low FT4, advanced bone age	Central hypothyroidism, GH deficiency	Started on levothyroxine, slow GV, continued levothyroxine after stopping
3	7 years 10 months	Premature thelarche, accelerated growth, premature pubarche	GV = 12.2 cm/year, HtSDS = +1.72, MPHSDS = -0.82, advanced bone age, high basal LH and FSH	Central precocious puberty	Started on GnRH analogue, will be reevaluated
4	12 years	Recurrent headaches, secondary amenorrhea	BMISDS = 2.5, HtSDS = +0.8, GV = 2.2 cm/year, high morning ACTH, normal cortisol, prolactin, LH and FSH	ACTH hypersecretion, central precocious puberty	Planned for GH suppression test, pelvic US, and salivary cortisol
5	2.8 years	Premature thelarche, family concern about accelerated growth	HtSDS = 2.4, BMISD = 0.44, high basal and stimulated LH and FSH, high estradiol, IGF1SDS = +3.1	Central precocious puberty	Started on triptorelin, will be followed for growth and MRI
6	7 years 5 months	Excessive body hair, symptoms of precocious puberty	Advanced bone age, high IGF1, paradoxical increase in GH during suppression test	Central precocious puberty GH and ACTH hypersecretion	Treatment with GnRH analogue, reassessment indicated abnormal growth

isotonic saline) which could favour a cerebral Salt wasting syndrome. On the other side there are uncertain data on using an oxcarbasepine after head surgery as a cause of SIADH which also developed during second hospitalization. These two entities are overlapping with different treatment options.

Keywords: subdural hematoma, hyponatremia, oxcarbasepine, a cerebral Salt wasting syndrome, SIADH

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EP1197

Challenges in the diagnosis and management of psychogenic polydipsia

Zineb Ait Si Ali[1], Manar Bari[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]

[1]Centre Hospitalo-Universitaire Mohammed VI Marrakech, Department of Endocrinology Diabetology Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction

Psychogenic polydipsia occurs in both psychiatric and somatic contexts. Clinically, it presents with a wide range of symptoms, both neurological and psychiatric, and can evolve into acute somatic complications, of which water intoxication is the most severe, with a high mortality rate.

Case report

A 35 years-old male patient, treated for mental retardation since the age of 9 following a tonsillectomy, the post-op effects of which were marked by a coma lasting one month, also treated for epilepsy since the age of 18 on levetiracetam. The patient had presented 5years ago with behavioral problems such as psychomotor agitation, self-aggressivity and suicide attempts, and was put on amisulpride and risperidone. He was referred to us to investigate a Polyuria-polydipsia syndrome that had been evolving for 4 months, with abundant drinking (7l/pd) and abundant polyuria (5l/pd) with a single nocturnal awakening. Clinical examination revealed a conscious patient; normal blood pressure and cardiac rate, eupneic, moderate obesity BMI 33.2 kg /m^2. Input/output fluide balance was 3.9L/4L per day. Paraclinical tests showed: Natremia 137.93mmol/l, Kalemia 3.96mmol/l, renal function normal, urinary osmolarity: On admission (1pm urine): 225.99mosmol/l, Morning urine (1st micturition): Concentrated appearance, Osmolarity: 378.46mosmol/l. Hypothalamo-pituitary MRI: diffuse supratentorial and subtentorial cortico-subcortical atrophy associated with sequellar gliosis lesions, pituitary gland of normal size and morphology, presence of physiological hypersignal of the postpituitary gland. Water deprivation test was not performed, given the context of epilepsy and the appearance of concentrated urine and urinary osmolarity greater than 300mosmol/l. Psychogenic polydipsia was considered, given the psychiatric involvement, the concentrated appearance of urine, urinary osmolarity $>$300mosmol/l and normal MRI. Polyuria secondary to the use of levetiracetam was discussed, but the patient had been on this treatment for at least 5 years.

Conclusions

Psychogenic polydipsia is characterized by a disturbance in the control of thirst that is not due to a disorder of antidiuretic hormone production. Although most often seen in patients with chronic schizophrenia, psychogenic polydipsia is also associated with other mental illnesses such as affective disorders, childhood-onset psychoses, mental retardation, personality disorders and anxiety. Treatment options are limited, if, for psychiatric reasons, a choice of antipsychotic medication has to be made, preference will be given to risperidone, olanzapine and clozapine. Short-term cognitive-behavioral therapies have produced interesting results, based on self-monitoring of fluid intake, behavioral control of stimuli through the use of reduced-capacity bottles, learning coping strategies and the use of reinforcement and gratification mechanisms.

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EP1198

«Diagnostic difficulties of central insipidus diabetes associated with stalk thickening»

Hassiba Khaldi[1,1]

[1]military central hospital, algies, Algeria

Introduction

CID in children is a rare pathology, the diagnosis is generally easy as it manifestes itself by a polyuro_polydipsic syndrome (PPS) of variable severity secondary to an ADH deficiency. The discovery of a thick pituitary stalk in this context must encourage us to look for the etiology with the fear of tumoral causes

Observation

We report the case of a young patient, of 16 years old, with no particular history, hospitalised for sudden polyuroplydipsic syndrome with no precipitating factors. The clinical examination was normal except for a low BMI of 15 kglm^2 and delayed puberty classified G1P2 TANNER.PPS was about 2,3 liters Biological investigation showed a low urinary density $<$ 1005 and Urinary osmolality of **65** mosm/l. Plasmatic osmolarity was about **298** mosmo/l Anterior pituitary investigation after Desmopressine supplementation showed corticotropin deficiency (cortisol: **117,9** nmol/l, ACTH: 5 pg/ml), the othor anterior pituitary functions were normals Pituitary MIR showed a thick pituitary stalk corresponding to a likely infundibulo-neurohypophysitis after eliminating tumoral, infiltrative and infectious pathologies. The patient was put on replacement therapy (DESMOPRESSINE) and underwent clinical and morphological monitoring every 3 to 6 months.

Conclusion

It is advisable to repeat the etiological investigation several years after the so-called idiopathic forms of CID in search of a tumoral or infiltrative pathology, but also to evaluate the progress of the thickening stalk.

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EP1201

Crooke cell corticotrop adenoma: case series

Ekin Yiğit Köroğlu[1], Çağlar Keskin[1], Servet Güreşçi[2], Denizhan Divanlıoğlu[3], Cevdet Aydın[4], Oya Topaloğlu[4], Reyhan Ersoy[4] & Bekir Çakır[4]

[1]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara; [2]Ankara Bilkent City Hospital, Pathology, Ankara; [3]Ankara Bilkent City Hospital, Neurosurgery, Ankara; [4]Ankara Yıldırım Beyazıt University Faculty Of Medicine, Endocrinology and Metabolism, Ankara

Crooke cell corticotroph adenomas are a rare subtype of corticotroph adenomas. It can be detected in less than 1% of all pituitary adenomas. They are usually noticed as invasive macroadenomas on preoperative imaging. They are expected to have a more aggressive course and more frequent recurrences during their clinical course. We present a case series of 11 patients who were followed up with Cushing's Disease in our clinic and were diagnosed with Crooke cell adenoma after surgery. Nine patients were female(81.8%), and 2(18.2%) were male. The average age of the patients was 41.0(19.0-71.0) years. There were macroadenomas in 6 patients(54.5%) and microadenomas in 5 patients(45.5%). The average largest tumor diameter was 14.00 (4.50-35.00) mm. Pituitary adenoma invaded surrounding tissues in 3 patients(27.3%). Optic chiasm compression was observed in 2 patients(18.2%). Preoperative hypopituitarism was present in 6 patients(54.5%). In this group of patients, macroadenoma was detected in 5 patients, and microadenoma was detected in 1. The patients' preoperative laboratory parameters and clinical findings are given in Table 1 and Table 2, respectively. A 1-milligram dexamethasone suppression test was performed in all patients in the preoperative period, and it was found to be high in all patients. 24-hour urinary cortisol was measured in 8 patients and was high in 5. In the postoperative period, two patients could not be evaluated for remission because they continued their follow-up in another center. Biochemical remission was achieved in 4 of the other nine patients(44.4%), and biochemical remission was not achieved in 5(55.6%). Postoperative follow-up periods of patients in biochemical remission have been 33, 39, 56, and 62 months; no recurrence was observed in any patient during this period.

Table 1. Laboratory parameters of patients with Crooke cell corticotroph adenoma

Test	n	Minimum	Maximum	Mean
ACTH($<$46 pg/ml)	11	13,50	443,00	108,8455
Cortisol(5.2-22.4 μg/dl)	11	11,10	60,00	31,0273
1 mg dexamethasone suppression test($<$1.8 μg/dl)	9	3,90	43,56	21,1956
24-hour urinary cortisol(3.5-45 μg/day)	8	24,66	2279,63	547,9125
Midnight salivary cortisol($<$0.69 μg/dl)	4	,64	2,28	1,6100

Table 2. Clinical findings of patients with Crooke cell corticotroph adenoma

Clinical finding	Present	Absent
Central Obesity	9(81.8%)	2(18.2%)
Proximal myopathy	3(27.3%)	8(72.7%)
Moon face	4(36.4%)	7(63.6%)
Abdominal purple striae	3(27.3%)	8(72.7%)
Buffalo hump	6(54.5%)	5(45.5%)
Hirsutism	5(62.5%)	3(27.3%)
type 2 Diabetes Mellitus	5(45.5%)	6(54.5%)
Hypertension	5(45.5%)	6(54.5%)
Hyperlipidemia	6(54.5%)	5(45.5%)
Osteoporosis	1(9.1%)	10(90.9%)
History of thrombosis	1(9.1%)	10(90.9%)
Hypokalemia	3(27.3%)	8(72.7%)

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EP1217

Evaluation of macroprolactinoma in a cohort of 48 patients

Rahal Amel[1]
[1]Bologhine hospital, endocrinology algiers, Algeria

Introduction
Prolactinoma is the most common pituitary tumour; in the majority of cases it is a microadenoma.
Materials and methods
Through a retrospective study of 46 patients followed for macro prolactin adenomas we evaluate the response to medical treatment of macroprolactinoma. In our series, macroprolactinomas are more frequent in men (59%), more often diagnosed between the ages of 25 and 45. As expected, cranial tumour syndrome remains the main reason for consultation in both sexes in 65%. Biologically, the correlation between tumour volume and prolactin is clear, with levels slightly higher in men. Among the macroprolactinomas we recruit 37% of giant adenomas; more common in men. In terms of treatment, medical treatment is the first choice in 83% of cases. Surgery was used in 33% of cases, most often for compression of the optic tracts. Among our patients, 43% were resistant to medical treatment, more frequently in men.
Discussion
The aim of our work was to evaluate the therapeutic response of prolactin macroadenomas. As expected, our results are consistent with the data in the literature; macroadenomas adenomas are more frequent in men with a more striking clinical, biological and morphological presentation. The therapeutic management of macroprolactinoma also revealed a morphological resistance which is more frequent in men, because of a higher tumour volume. Despite this resistance, two thirds of our patients responded to medical treatment.

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EP1218

Evaluation des pratiques de commande des tests de prolactine

Dhouha Zouari[1], Rim Marrakchi[1], Charfi Ameni[1], Mohamed Ccaher Rabah[1], Mariem Boudaya[1], Kamel Jamoussi[1], Mohamed Abid[2] & Mouna Turki1[2]
[1]Laboratory of Biochemistry, Hédi-Chaker Hospital, Sfax, Tunisia, [2]Endocrinology departement, Hedi Chaker Sfax Tunisie

Introduction
Hyperprolactinaemia can be caused by physiological changes, medications, pathological conditions, or can be idiopathic. The aim of this study was to evaluate clinicians's practice in ordering prolactin (PRL) test.
Methods
A retrospective study concerning 75 prolactin requests data collected by the laboratory computer system (Health Lab) during January 2024. We collected age, sex and ordering's origins. PRL tests were performed based on electro-chemiluminescence immunoassay (eCLIA) by Dxi600Û Beckman Coulter. Hyperprolactinaemia was defined by PRL levels above 25ng/ml and 15ng/ml respectively for women and for men.
Results
The mean age of patients was 37 years, with extremes ranging from 13 to 85 years with a male/female sex ratio of 0.3. The majority of PRL requests were from the endocrinology department (58.7%), followed by the gynecology department (18.7%) and the psychiatry department (13.3%). Reasons for prescription PRL were mainly as follows: 22% for gynecological reasons (primary and secondary amenorrhea, irregular cycle, galactorrhoea, metrorrhagia, spaniomenorrhea, infertility), 19% for suspecting pituitary tumour, 17% for monitoring hyperprolactinemia, 10% for investigating polycystic ovary syndrome, 8% for monitoring subjects receiving neuroleptics. We observed 37.3% of the requests without clinical indications. The mean of PRL levels was 27 ng/ml, with extreme values ranging from 1.8ng/ml to 196.15 ng/ml. Among requests with clinical indications of having hyperprolactinaemia and requests without clinical indications,?only 29.4%, and 28.6% had respectively hyperprolactinaemia.?
Conclusion
There was an over-ordering for prolactin in our hospital practice. Further evaluation is needed to determine strategies that can reduce excessive prolactin testing.

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EP1224

Hypoaccousia revealing acromegaly: a case report

Hajar Azagouagh[1], Karimi Meryem[1], Nawal Moussaid[1], Rifai Kaoutar[1], Iraqi Hind[1], Mohamed Elhassan Gharbi[1]
[1]Chu Ibn Sina, Endocrinology, Rabat

Introduction
Acromegaly is a rare disease defined by the clinical expression of hyperfunction of the somatotropic axis with unchecked secretion of growth hormone. It has many complications, which is why early diagnosis is essential.
Observation
We report the case of a 47-year-old patient , with a history of chronic smoking and renal lithiasis operated on in 2018. His history of illness goes back 3 months to the onset of hypoacusis, which prompted the patient to consult an ENT specialist, He then referred the patient to the endocrinology department, where the diagnosis of acromegaly was made in view of the dysmorphic acrofacial syndrome with elevated IGF1 levels, and we completed it with a hypothalamic-pituitary MRI scan showing a pituitary micro-adenoma measuring 7*8*8 mm. Resection surgery was proposed to our patient.
Discussion and conclusion
Because of its insidious nature, acromegaly is often diagnosed late, exposing the patient to the risk of morbidity and mortality, but it may be preceded by abnormalities such as hypoacusis. Complications account for the full severity of the disease, notably cardiovascular, metabolic and neoplastic complications. Thinking about the secondary origin of hypoacusis could lead to earlier diagnosis and better management of acromegaly.

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EP1225

Microadenoma of prolactin revealed by galactorrhea in a man

Karimi Meryem[1], Hajar Azagouagh[1], Hasna Ouirar[1], Mariam Hmaichat[2], Diehah Isselmou[1], Isswani Jad[2] & Guerboub Ahmed Anas[2]
[1]Chu Ibn Sina, Endocrinology, Rabat, [2]Hopital Militaire Mohamed V Rabat, Endocrinology, Rabat

Introduction
Galactorrhea is defined as the secretion and flow of milk from the mammary gland in a man or a woman who is not breastfeeding. It is generally due to a pituitary adenoma secreting prolactin. The etiological diagnosis is based on prolactin levels and imaging.
Case report
We report the case of a 42-year-old patient with no notable medical history. His symptoms date back 17 years, marked by the onset of bilateral gynecomastia, spontaneous galactorrhea, and decreased libido. Biological assessment reveals hyperprolactinemia more than 20 times the normal level, with a significantly reduced testosterone level. Hypothalamo-hypophysial MRI reveals a 5mm microadenoma lateralized to the left. The patient is treated with dopamine agonists, resulting in good clinical and biological improvement.
Discussion and conclusion
Galactorrhea represents a pathognomonic and rare sign of hyperprolactinemia in men, usually secondary to a prolactin-secreting pituitary adenoma. The frequency of microadenomas is much lower in men, possibly due to later diagnosis in this population.

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Reproductive and Developmental Endocrinology

EP9

Use of selective adrenal and ovarian venous sampling in postmenopausal women with severe hyperandrogenism: Report of 3 cases

Valeria Arsentales Montalva[1], Olga Giménez-Palop[2], Ismael Capel[2], David Subías[2], Ana Romero[1], Alba Hernández[1], Andreea Muntean[1], Judith Jover[1], Laura Costa[3], Juan Perendreu[4], Carlos García[5] & Mercedes Rigla[2]

[1] Endocrinology and Nutrition Department, Parc Taulí University Hospital, Sabadell, Barcelona, Spain; [2]Endocrinology and Nutrition Department, Parc Taulí University Hospital, Autonomous University of Barcelona (UAB), Sabadell, Barcelona, Spain; [3]Obstetrics and Ginecology Department, Parc Taulí University Hospital, Sabadell, Barcelona, Spain; [4]Interventional Radiology Department, Parc Taulí University Hospital, Sabadell, Barcelona, Spain; [5]UDIAT Laboratory Department, Parc Taulí University Hospital, Sabadell, Barcelona, Spain

Background
Although the majority of cases of hyperandrogenism in postmenopausal women are due to functional causes, the sudden appearance of a severe and rapidly progressive condition, especially if associated with signs of virilization and defeminization, requires always ruling out the existence of an androgen-producing tumor at both the adrenal and ovarian levels. Etiological diagnosis can be difficult because ovarian tumors are not easily demonstrable by imaging.
Case Reports
Three postmenopausal women (mean age: 69 years) referred to our center for hirsutism and elevated testosterone levels. As relevant associated diseases: obesity, dyslipidemia and type 2 diabetes. They reported growth of facial hair, upper chest and back for the last 3-4 years, acne, seborrhea, androgenic alopecia and weight gain between 5-8 Kg. Two of them, with a history of oligomenorrhea in the reproductive age. The average Ferriman-Gallwey score was 21, without clitoromegaly. High total testosterone levels stood out in all cases, with an average figure of 1.73 ng/ml (reference value 0.03-0.41 ng/ml) and a mean free testosterone of 3.04 ng/ml (reference value 0-0.1 ng/ml). The determinations of dehydroepiandrosterone sulfate (DHEAS), 17-hydroxyprogesterone, prolactin, thyroid function, 24-hour urinary free cortisol excretion and low-dose dexamethasone suppression test were within normal limits. The transvaginal ultrasound and the pelvic MRI did not show any remarkable findings. A CT Scan of the adrenal glands showed a non-functioning left adrenal nodule (measured 25x22 mm) already known and studied, with normal (DHEAS) levels in one of the three cases, without signs of growth or formation of new lesions in any of the glands. In the absence of conclusive radiological localization of androgen hyperproduction, selective catheterization of ovarian and adrenal veins was performed under stimulation of 250 ug of ACTH. In all cases, the high gradient existing between the ovarian vein/peripheral venous blood, sustained the suspicion of excessive production of androgens of ovarian origin, laparoscopic bilateral oophorectomy being performed in all patients. The pathology showed ovarian stromal hyperplasia with bilateral hyperthecosis, as well as foci of Leydig cell hyperplasia in one case. After the surgery, there was a significant improvement in hirsutism, with normalization of testosterone levels in all cases.
Conclusion
Selective venous catheterization and hormone sampling in postmenopausal women with severe hyperandrogenism could be useful to determine the source of androgenic hyperproduction in the absence of conclusive localization with standard imaging modalities, being bilateral oophorectomy as the standard surgical technique after reproductive age.

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EP49

Endocrine and reproductive consequences of pubertal stress in rats

Oksana Faliush[1], Olga Sachynska[1], Anna Lymareva[1], Inna Perchyk[1] & Alexander Reznikov[1]
[1] VP Komisarenko Institute of Endocrinology and Metabolism, National Academy of Medical Sciences of Ukraine, of Endocrinology of Reproduction and Adaptation, Kyiv, Ukraine

Adolescence is one of the most dynamic periods of development, which is highly sensitive to changes induced by stressors. Disruption in hormonal balance associated with stress have a negative impact on puberty and reproductive function. The aim of the work was to study the long-term endocrine effects of chronic pubertal stress in rats. On the 22 postnatal day (PND), the Wistar rats were separated from their mothers and sorted by sex into individual cages, so that animals from different litters were in both the control and experimental groups. The animals were subjected to stress daily in the morning hours from 30 to 45 PND by placing them in cylinders with a diameter of 4.5 cm and a length of 10 cm, equipped with breathing holes. During the stress period and upon its completion, the onset of sexual maturation was recorded in both the control and experimental animals, while observing somatic development. After the stress period ended, the animals were housed in cages in groups of five individuals each. All investigations were conducted on sexually mature rats at the age of 6 months. The weights of gonads and the adrenal glands, and the morphology of the reproductive organs were studied. The quantitative and qualitative indices of the spermatozoa in epididymal washes were determined. The plasma corticosterone levels were measured both at baseline and after one hour of tight restriction. The pubertal chronic stress significantly delayed the sexual maturation of females and adversely affected weight gain in males. In adult animals, pubertal stress did not change the weight and morphology of the gonads, except for slight vacuolation of the spermatogenic epithelium compared to intact ones. The index of spermatogenesis in the experimental group was significantly lower than in the control, due to a decrease in the number of late spermatids, which indicates inhibition of spermatogenesis. Pubertal stress resulted in a 25.9% decrease in sperm count and a 2.4-fold slowing of oxidative-reductive processes in spermatozoa. These animals showed an increase in the number of pathological forms of spermatozoa. A significant decrease in adrenal weight in females and a tendency to a decrease in males were observed. The basal corticosterone levels reduced by 1.7 times in males. Stress reactivity in females and males did not differ from the control. Thus, chronic pubertal stress, under the selected experimental conditions, resulted in adverse long-term sex-specific effects on the reproductive and adaptive systems of adult animals.

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EP98

Orexin A is a new marker of insulin resistance in polycystic ovary syndrome

Yulia Absatarova[1], Yulia Evseeva[1], Elena Andreeva[1] & Margarita Samsonova[1,2]
[1]Endocrinology Research Centre, Gynecology, Moscow, Russian Federation; [2]

Dysregulation of the neuroendocrine system is a key element in the pathogenesis of polycystic ovary syndrome (PCOS). Orexins (hypocretins) are a new class of hypothalamic neuropeptides that influence sleep-wake rhythms and the state of energy metabolism. In addition, their receptors expresses in peripheral tissues, including the endocrine system. Data have emerged on the role of orexins in the regulation of the reproductive system and, in particular, ovulation, through a direct effect on the hypothalamic-pituitary-ovarian axis, and their stimulating effect on GnRH neurons has been described.
Objective
To study orexin status in women with PCOS and its role in the pathogenesis of the disease.
Methods
The study involved women 18-39 years old: 20 patients with PCOS with a body mass index (BMI) ≥ 25 kg/m^2 (group 1), and 20 women with PCOS and BMI $<$ 25 kg/m^2 (group 2). The diagnosis of PCOS based on the Rotterdam criteria (2003). The control group consisted of 20 healthy women with a regular menstrual cycle and BMI <25 kg/m^2. We determined the levels of orexin A, LH, FSH, testosterone, insulin in the blood serum in all three groups in the 1st phase of the menstrual cycle (3-7 days of cycle) or against the background of a menstruation delay for more than 2 months (in patients with PCOS).
Results
All three groups were age-matched. In group 1, the median BMI was 30.8 kg/m^2 [26.6; 34.6], in group 2 - 21.4 kg/m^2 [19.2; 22.4], in the control group - 20.9 kg/m^2 [20.0; 22.8]. The median level of orexin A was significantly lower in the group of patients with PCOS and BMI ≥ 25 kg/m^2, compared with the group of PCOS with normal BMI and healthy women: 1.32 ng/ml [0.29;3.56], 5.77 ng/ml [3.34;9.87] and 11.06 ng/ml [8.41;17.49], respectively ($P<0.05$). In the overweight PCOS group, insulin level was significantly higher compared to patients with normal weight and healthy participants: 13.7 [8.3; 23.7] mIU/l; 7.2 [5.2; 9.1] mIU/l and 6.2 [5.0; 8.6] mIU/l, respectively ($P<0.05$). We found a negative correlation between the level of orexin A and BMI, orexin A and insulin: the higher was the BMI and the insulin level; the lower was the level of the neuropeptide orexin, respectively.
Conclusion
Orexin A is a potential marker of ovarian hyperandrogenism. It also reflects the severity of insulin resistance, which is one of the main triggers in pathogenesis of PCOS.

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EP109

Sex-specific effects of perinatal exposure to tetrabromobisphenol a, an endocrine disrupting chemical on brain development and behavior in mice

Eui-Bae Jeung[1], YongIn Kim[1], Sun Kim[1] & Inho Hwang[1]
[1]Chungbuk National University, Laboratory of Veterinary Biochemistry and Molecular Biology, College of Veterinary Medicine, Cheongju, Korea, Republic of South

Tetrabromobisphenol A (TBBPA) is a brominated flame retardant and is widely used in electronic goods, plastics, and furniture. TBBPA is frequently detected in water, soil, organisms and even in human breast milk. Though some regulatory agencies have asserted that consumer exposures to TBBPA are unlikely to have adverse implications for human health, the reported evidence of endocrine-disruption of TBBPA has raised concerns regarding its effects on neurodevelopment and behavioral functions. The present study examined the effects of exposure to TBBPA on neurodevelopment. The Developmental Neurotoxicity Test (DNT) was performed to determine whether TBBPA is a developmental neurotoxicant. Additionally, maternal mice were administered 0, 0.24 and 2.4 mg/kg TBBPA. Mice offspring underwent behavioral tests for assessment of locomotor, depressive, cognitive, and social behaviors. Gene expression pattern change at transcriptional level in the brain was investigated with real-time PCR. As a result, TBBPA was classified as a developmental neurotoxicant from the DNT. In addition, the behavioral experiments revealed gender-specific effects. In females, only a deterioration of the motor ability was observed. In contrast, deteriorations in motor function, memory, and social interaction were noted in males. Aberrant expression of several genes, such as Na+/Ca2+ exchanger 2 (NCX2), acetylcholinesterase (AChE) and oxytocin (OXT), were found in the brains of TBBPA-treated mice offspring. To summarize, these findings suggest that perinatal exposure to TBBPA interferes with brain development and behavioral functions in mice. Therefore, it is necessary to pay more attention to the potential effects of TBBPA in the early development of brain.

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EP111

The relevance of endocrine disruptors, obesity, and cytokines for polycystic ovary syndrome

Michaela Duskova[1,2], Jana Vítků[3], Lucie Kolatorova[4], Jana Vrbikova[4], Michala Vosátková[3], Josef Včelák[5] & Markéta Šimková[5]
[1]Institute of Endocrinology, Department of Steroids and Proteofactors, Praha 1, Czech Republic; [2]General Teaching Hospital Prague, 4th department of internal medicine, Praha, Czech Republic; [3]Institute of Endocrinology, Department of Clinical Biochemistry, Praha 1, Czech Republic; [4]Institute of Endocrinology, Department of Clinical Endocrinology, Praha 1, Czech Republic; [5]Institute of Endocrinology, Department of Molecular Endocrinology, Praha 1, Czech Republic

As genetic and environmental components contribute to the PCOS expression, we compared levels of endocrine disruptors, steroid hormones, cytokines, and metabolic parameters in twenty healthy, nine normal-weight PCOS women, and ten obese PCOS women. Steroid hormones, bisphenols (BPA, BPS, BPF, BPAF) and parabens (methyl-, ethyl-, propyl-, butyl-, benzyl-parabens) were measured by liquid chromatography-tandem mass spectrometry. Differences between the groups were assessed using the Mann-Whitney U test. Spearman correlation coefficients were calculated for the individual parameters relationship. Significantly higher levels of BPA, Anti-Müllerain hormone, lutropine, lutropine/folitropine ratio, testosterone, androstenedione, 7β-OH-epiandrosterone, and cytokines (IL-6, VEGF, PDGF-bb), were found in normal-weight PCOS women compared to controls. In PCOS women concerning the weight, there were no differences in hormonal, but in metabolic levels. Obese PCOS women had significantly higher insulin resistance, fatty-liver index, triglycerides, cytokines (IL-2, IL-13, IFN-γ). In healthy, but not in PCOS, women, there was a positive correlation of BPA with testosterone, SHBG with lutropine, and folitropine, while testosterone negatively correlated with SHBG. In obese women with PCOS, insulin resistance negatively correlated with SHBG and estradiol. No differences were observed in the paraben exposure. Levels of BPA were higher in PCOS women, indicating its role in the etiology. Obesity significantly worsens the symptoms.

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EP133

Vitamin D levels in pregnant women, vitd-supplementation and its association with pregnancy outcomes

Dimitra Pappa[1], Eleftheria Barmpa[1], Stefanos Tamouridis[1], Aikaterini Evagelopoulou[2], Alexander Daponte[2] & Alexandra Bargiota[1]
[1]University Hospital of Larissa, Department of Endocrinology and Metabolic Diseases, Larissa, Greece; [2]University Hospital of Larissa, Department of Obstetrics and Gynecology, Larissa, Greece

Introduction
Data on the desirable Vitamin D (VitD) levels and VitD-supplementation during pregnancy are very controversial and thus everyday practice varies a lot. In our study the aim is to record VitD levels, as well as the VitD-supplementation and their association with pregnancy outcomes in women referred to our center in the second and third trimester of pregnancy.
Methods
We studied 193 pregnant women mean age 30.34±7.07 years old. In each patient we measured 25(OH) Vitamin D3 levels at the second and third trimester of pregnancy (reference range for 25(OH) Vitamin D3 is 20-32 ng/ml, and VitD deficiency is <20 ng/ml). We also recorded the VitD-supplementation, gestational age at delivery (GAd), childbirth type and offspring birthweight (ofBW).
Results
Baseline mean gestational age (GA) was 27.18±6.78 weeks and mean 25(OH) Vitamin D3 levels were 20.64±11.80 ng/ml. 133 out of 193 (68.91%) women had normal 25(OH) Vitamin D3 (ND3, mean levels 23.35±13.19 ng/ml), and 60 out of 193 (31.08%) had 25(OH) Vitamin D3 deficiency (DD3, mean levels 14.76±3.79 ng/ml.) ND3 women had mean age 30.24±7.28 years old, mean GA 27.84±6.23 weeks, 34/ND3 (25.56%) were not on VitD-supplementation, 67/ND3 (50.37%) were on 200-800 IU VitD-supplementation daily, 19/ND3 (14.28%) on 1000-1800 IU/daily and 13/ND3 (9.77%) on 2000-4000 IU/daily. 35 of ND3 (26.21%) were on calcium-supplementation (500 mg/daily). In ND3 the mean GAd was 37.98±1.32 weeks, mean ofBW was 3034.34±587.44 gr and 53/ND3 (39.84%) had a caesarean section. DD3 women had mean age 30.56±6.55 years old, mean GA 25.73±7.70 weeks, 6/DD3 (10%) had VitD-supplementation >4000 IU/daily, 21/DD3 (35%) were on 2000-4000 IU/daily, 9/DD3 (15%) on 1000-1800 IU/daily, 18/DD3 (30%) on 200-800 IU/daily and 6/DD3 (10%) were not on VitD-supplementation. 14 of DD3 (23.33%) were on calcium-supplementation (500 mg/daily). In DD3 the mean GAd was 37.57±1.83 weeks, mean ofBW was 3094.76±587.22gr and 25/DD3 (41.66%) had a caesarean section.
Conclusion
VitD-supplementation doses during pregnancy defer - despite the existing guidelines - depending on the Obstetrician. Current recommendation suggest that women with normal VitD levels require VitD-supplementation with 400-600 IU/daily, whereas women with VitD deficiency a higher dose of 1000-4000 IU/daily. In our study pregnant women who referred to us at the second and third trimester with normal VitD levels were on no or on the minimum daily dose of VitD-supplementation (200-800 IU) and those with VitD deficiency were on the maximum daily dose (2000-4000 IU) - more or less complying with the recommendation. No significant differences on pregnancy outcomes were reported between the two groups.

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EP149

Immunological role of progesterone and cortisol during pregnancy

Atsushi Yasuda[1], Toshiro Seki[1], Hirofumi Kashiwagi[1], Natsumi Kitajima[1], Masami Seki[1] & Yoshie Kametani[1]
[1]

During pregnancy, levels of pregnancy-related proteins and hormones such as progesterone (P4), estrogen, and glucocorticoids (GC) increase. Although the regulatory mechanisms of P4 production in the placenta are not completely understood, studies using mouse models have demonstrated that P4 induces immunosuppression using a GC receptor-dependent pathway, suggesting that both it has been suggested that steroid hormones have a similar effect. Understanding the orchestrated role of P4 and cortisol (COR) is important for understanding the mechanisms of immune regulation during human pregnancy. Based on previous experiments showing that P4-treated T and B cells remained in the spleen, we hypothesized that P4-treated cells could produce functional IgG antibodies. Therefore, we immunized humanized mice and examined antigen-specific antibody production. However, the titer of antiserum in humanized mice varied among individuals and was not significantly different, and the percentage of plasmablasts did not differ between mice treated with P4 and COR. For this, we analyzed the production of antigen-specific B cell clones in mice by preparing hybridomas, treating them with P4 and COR, and analyzing cross-reactivity of

whole antibodies to immunizing antigens and third-party antigens. Results showed that spleen cell numbers were lower in COR-treated mice, the entire IgG-secreting clone was maintained in P4-treated mice, and B-cell clones in COR-treated mice were also observed to secrete IgG. In contrast, P4-treated mice produced antigen-specific IgG-secreting clones, slightly fewer than control mice, whereas COR-treated mice did not produce high-titer antigen-specific B cell clones. These results suggest that transient treatment of lymphocytes with high concentrations of P4 preserves the function of humanized murine B cells, whereas treatment of COR significantly reduces function. Few antigen-specific clones per spleen cell were detected in COR-treated mice. The reason may be the low proportion of B cells among CD45+ cells in the spleen. Defects in antigen-specific plasmablast formation may be caused by defects in functional B cell engraftment due to COR pretreatment. Irreversible and systemic humoral immunosuppression has no benefit for immunity during pregnancy. Therefore, to maintain pregnancy, it may be necessary to neutralize the effects of COR with large amounts of P4. Further analysis of the role of P4 and COR during pregnancy would be necessary to understand the immunomodulatory mechanism.

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EP151

Assessment of non-invasive NAFDL indices in patients with PCOS

Valentina Elezovic Kovacevic[1], Sanja Ognjanovic[1], Bojana Popovic[1], Dusan Ilic[1], Milica Opalic Palibrk[1], Lena Radic[1], Katarina Krstic[1], Jelica Bjekic Macut[2], Danijela Vojnovic Milutinovic[3], Olivera Stanojlović[4] & Djuro P. Macut[1]

[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Department for Enocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia; [2]Clinical Hospital Centre Bezanijska Kosa, Belgrade, Serbia; [3]IBISS, University of Belgrade, Belgrade, Serbia, Belgrade, Serbia; [4]Institute of Physiology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Introduction
Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in reproductive-age women. This highly complex reproductive metabolic disorder is independently associated with high prevalence of non-alcoholic fatty liver disease (NAFLD). While the gold standard of NAFLD diagnosis is liver biopsy or MRI, it is costly and hard to perform in large population. Recently, simple and convenient markers, such as liver fat score (LFS), fatty liver index (FLI), and hepatic steatosis index (HSI) have been demonstrated to exhibit comparable coefficient values to standard diagnosis. The aim of this study was to analyse these non-invasive parameters in women with PCOS.
Subjects and Methods
PCOS was diagnosed using ESHRE/ASRM criteria. PCOS group was divided into four phenotypes: PCOS-A (anovulation (ANOV), hyperandrogenism (HA), polycystic ovary morphology (PCOM)), PCOS-B (ANOV, HA), PCOS-C (HA, PCOM) and PCOS-D (ANOV, PCOM). Fatty liver index (FLI), liver fat score (LFS), and hepatic steatosis index (HSI) were used to assess NAFLD. They were calculated according to the previously defined formulas. Values of LFS > -0.640, FLI >60 and HSI >36 was considered as having NAFDL.
Results
We analysed 165 women with PCOS, mean age at diagnosis 25.2 ± 5.1 years and mean BMI 24.1 ± 6.0 kg/m^2. Most of the group were patients with phenotype A (48.5%), phenotype D (20%), then phenotype B (18.2%) and phenotype C was present in 13.3%. The mean FLI was 21.1 ± 29.2, mean LFS -0.504 ± 2.05 and mean HSI 36.2 ± 5.7. The prevalence of NAFLD in PCOS women evaluated by FLI, LFS and HSI were 14.01%, 36.6 % and 46.4%, respectively. Among phenotypes there were differences in FLI (P-0.0001) and HSI (P-0.036), but not in LFS (P-0.051). Phenotype PCOS-A and PCOS-D shown significant difference in both FLI (P-0.001) and HSI (0.043) as well as PCOS-C vs PCOS-D (FSI P-0.0001; HSI P-0.009); phenotype PCOS-B vs PCOS-C shown difference only in FLI (P-0.01).
Conclusion
In our group, the prevalence of NAFLD varied widely depending on the specific index even though our population is younger and non-obese. Further studies are needed to validate the capacity of NAFLD indices to predict NAFLD in different phenotypes of PCOS.

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EP177

Study on quality of life, self-esteem, anxiety and depression among transgender people in a healthcare area

Irene Zayas Aguilar[1], Almudena Lara Barea[1], Laura Larrán Escandón[1], Daniel Medina Rivero[1] & Isabel María Mateo Gavira[1]

[1]Hospital Universitario Puerta del Mar, Endocrinology and Nutrition Department, Cádiz, Spain

Introduction
Transgender people are a population affected by a variety of negative health indicators. Studies report, among other conditions, a high prevalence of mental health problems, however, long-term longitudinal follow-up studies are scarce.
Objective
The aim of this study is to assess the quality of life (WHOWOL-BREF scale), self-esteem (RSES scale), levels of anxiety (GAD-7 scale) and depression (PHQ-9 scale) of transgender people attended at the Provincial Gender Unit of the Hospital Puerta del Mar (Cádiz).
Materials and methods
This is a descriptive cross-sectional study based on the electronic medical records and the answers obtained in the questionnaires administered to the people attended at the Gender Identity Unit of Hospital Puerta del Mar (Cadiz), between October of 2022 and May of 2023.
Results
Of the 150 people included in this study, 62% were transmen and 32.7% transwomen and 4.7% non-binary gender. The mean age was 19.9 ± 4.9 years. The majority of people (58%) had a previous mental health history and 32.7% visited clinical psychologist during the follow-up. 45.6% declared bullying in the social field. The people analyzed had moderate levels of anxiety and depression, with no significant differences found between groups. The mean score in the self-esteem scale was 13.77 ± 3 indicating low self-esteem. Transwomen had better perception of their health ($3,35 \pm 0.9$) than transmen (2.97 ± 0.96), ($P = 0.03$). Transgender people, who visited the unit's psychological consultation, had a lowed score in the physical domain of the WHOQOL-BREF scale (77.48 ± 15.54 vs 85.22 ± 16.54), ($P < 0.01$).
Conclusions
In our cohort, most transgender people have a previous history of mental health and almost half declared bullying in the social field. People who visit clinical psychologist have less physical wellbeing. It is essential that the Gender Identity Unit team has available mental health professionals to provide psychological support.

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EP190

Audit of the clinical utility of androstenedione

Ruth Byrne[1], Rachel Crowley[1,2] & Patrick Twomey[1,2]

[1]St. Vincent's University Hospital, Dublin, Ireland; [2]University College Dublin, Ireland

Introduction
Hyperandrogenism is a diagnostic feature for polycystic ovarian syndrome (PCOS). Androstenedione is a testosterone precursor that has been shown to be useful in diagnosis of PCOS especially in the setting of normal testosterone. During 2022, our laboratory in St Vincent's University Hospital in Dublin, Ireland, changed from using a radioimmunoassay to an electrochemiluminescence immunoassay, which requires a non-gel tube in line with manufacturers requirements. In the endocrinology department we noticed that many samples were not being processed in the lab due to incorrect tube use. We audited the androstenedione levels processed in St. Vincent's University Hospital over a four-month period at the start of 2023 and analysed results in conjunction with the other serum androgens, testosterone and dehydroepiandrosterone sulfate (DHEAS).
Results
145/319 androstenedione samples were analysed. 41/145 samples were above the upper limit of normal (>4.6 nmol/l), all in female patients. 17/41 had normal testosterone levels (0.4-1.7 nmol/l). This is significant as elevated androstenedione confirmed biochemical hyperandrogenism and a diagnosis of PCOS in 8/17 despite normal testosterone.
Conclusion
The findings support the 2023 International Evidence based guideline for PCOS, which recommend doing androstenedione and DHEAS in patients with normal testosterone.
Recommendations
This audit identifies a need to educate users of sample tube requirements and encourages communication with clinical biochemistry; androstenedione remains part of the biochemical workup of PCOS, as it can identify more subtle hyperandrogenism; reflective or reflex laboratory testing could be an option for adding androstenedione levels, in cases with normal testosterone.
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EP216

Low reproducibility of plasma testosterone concentrations in male patients with hypogonadism treated with transdermal testosterone gel

Valeria Lanzi[1,2], Rita Indirli[1,2], Beatrice Mantovani[1], Iulia Petria[1,2], Eriselda Profka[1], Giovanna Mantovani[1,2] & Emanuele Ferrante[1]
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [2]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy

Introduction
Testosterone replacement therapy (TRT) in male hypogonadism aims at restoring physiological plasma testosterone (T) levels. According to current guidelines, gel formulations should resemble better the circadian T secretion and offer physiological and consistent T concentrations. However, only a few real-life studies have assessed intra-individual reproducibility of T levels in patients treated with gel formulations.
Methods
Thirty patients treated with Tostrex gel 2%® were included (group A, mean age 59 [SD 10] years, median dosage 30 [IQR 20-40] mg). As a comparator group, 14 patients treated with Testavan® gel 2% were recruited (group B, age 54 [13] years, $P=0.19$; dosage 34.5 [23-46] mg, $P=0.05$). All patients maintained the prescribed dosage over 3 months prior to the first sampling. Blood samples were drawn at two time points one week apart (T1 and T2), two hours after gel's application on the same site (medial thigh for Tostrex, shoulders for Testavan). T (CLIA, Roche Elecsys), hemoglobin (Hb) and hematocrit (Htc) were assessed.
Results
The lowest and highest T levels between the two samplings were compared in each group. In group A, the median lowest TT concentrations were 3.8 [2.6-5.5] ng/ml, the highest were 4.9 [3.9-7.8] ng/ml (absolute-Δ 1.1 [0.4-1.9] ng/ml, percent-Δ 25%, $P<0.001$). The discrepancy between T1 and T2 was clinically-significant in 9 patients (30%): in 7, T was below normal in one sampling (which would have prompted Tostrex dosage increase), while it was within normal range in the other sampling (leading to no dosage change); in 2, T was above normal in one sampling (which would have prompted dosage reduction), while it was within normal range in the other sampling (leading to no dosage change). In group B, lowest T levels were 3.4 [2.0-4.2] ng/ml and highest were 4.6 [3.4-5.6] ng/ml (absolute-Δ 1.0 [0.4-1.9] ng/ml, percent-Δ 25%, $P<0.001$). T difference was clinically-significant in 5 patients (36%). As expected, Hb and Htc were comparable between T1 and T2 in both groups. Average TT concentrations, Δ TT, Hb, Htc, and the frequency of patients with clinically-significant T1-T2 difference, were comparable in groups A and B. No correlation was observed between TT and Hb or Htc at either time-point.
Conclusion
TRT with gel formulations is affected by intra-individual variability, which makes it difficult to establish the appropriate dosage. Therefore, therapeutic monitoring should rely not solely on plasma T levels but also on symptomatic response, as well as safety data such as haematocrit.

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EP226

Chitosan/Alginate-loaded astragalus hamosus shows ameliorating effects on lipid profile, inflammatory and hormonal parameters, and reduces mirna-222 expression in polycystic ovary syndrome rats

Maryam Parvini Kohnehshahri[1]
[1]Department of Biology, Urmia Branch, Islamic Azad University, Urmia, Iran

Background
Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder in women of childbearing age. This study aimed to investigate the effects of Chitosan/Alginate-loaded *Astragalus hamosus* extract (Chn/Al-AH) on the histology of Ovaries and uterus, miRNA-222, *ESR1*, and *IRS1* genes expression, pro-inflammatory cytokines, lipid profiles, sex hormone levels in rats with PCOS induced by estradiol valerate (EV).
Methods
25 female Wistar rats, with an average weight of 180 g, were divided into control and PCOS groups. The PCOS model was induced by a single intramuscular injection of EV (4 mg/kg). After 28 days of PCOS induction, the rats were orally administered Chn/Al-AH at doses of 5, 10, and 15 mg/kg. Following four weeks of treatment, histological changes in ovaries and uterus, serum sex hormone levels, lipid profile, pro-inflammatory cytokines, body weight, and the expression of miRNA-222, *ESR1*, and *IRS1* genes were evaluated.
Results
Chn/Al-AH hydrogels were successfully synthesized, and physicochemical properties confirmed their properties. Healthy follicles with normal morphologies at different stages of development were observed in the control group. EV-induced PCOS rats exhibited an increase in cystic follicles and endometrial hyperplasia, a decrease in follicular clusters and corpus luteum, a significant increase in body weight, abnormal lipid profiles, elevated pro-inflammatory cytokine levels, altered sex hormone levels, upregulation of miRNA-222 expression, and downregulation of *ESR1* and *IRS1* genes expression. Treatment with Chn/Al-AH at all doses showed a decrease in cystic follicles, LH/FSH ratio, estrogen, testosterone, insulin, TNF-α, IL-6, LDL, VLDL, triglyceride, cholesterol, and *miRNA-222* expression and an increase in corpus luteum, progesterone, HDL, and *ESR1* and *IRS1* expression in comparison with the PCOS group. LH, FSH, and IL-18 levels were not altered significantly after treatment.
Discussion
Applying Chn/Al-AH exhibited ameliorative effects on the PCOS rats, restoring both endocrine and metabolic abnormalities to normal levels and attenuating complications in EV-induced PCOS rats. Notably, it significantly reduced miRNA-222 expression and promoted follicular development at various stages while reducing cystic follicles and increasing corpus luteum formation.
Conclusions
Chn/Al-AH was found to have beneficial effects in attenuating and improving certain complications in the PCOS rat models.

Keywords: Polycystic ovary syndrome, *Astragalus hamosus*, biomedical effects, miRNA 222, Rat,
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EP230

Body composition influences on serum anti-müllerian hormone (AMH) levels in adult males imply hemodilution

Veronika Tandl[1], Christoph Haudum[1], Katharina Eberhard[2], Barbara Hutz[1], Ines Foessl[1], Ewald Kolesnik[3], Andreas Zirlik[3], Dirk von Lewinski[3], Daniel Scherr[3], Nicolas Verheyen[3], Thomas Pieber[1] & Barbara Obermayer-Pietsch[1]
[1]Medical University of Graz, Division of Endocrinology and Diabetology, Department of Internal Medicine, Graz, Austria; [2]Medical University of Graz, Core Facility Computational Bioanalytics, Graz, Austria; [3]Medical University of Graz, Department of Internal Medicine and University Heart Center Graz, Graz, Austria

Background
A negative relationship between body mass index (BMI) and serum Anti-Müllerian hormone (AMH) levels has been previously reported. Whether this is because of an adverse effect of adiposity on AMH production or the hormone's dilution in a higher blood volume that accompanies larger body size ('hemodilution') is not yet clear. Blood volume can be estimated by body weight, body surface area (BSA) or lean mass (LM). Of note, adipose tissue is poorly perfused and adds relatively little to the overall blood volume.
Objectives
To investigate a possible hemodilution effect, we analyzed the relationships between serum AMH levels and different body size and composition parameters in adult males.
Methods
We used data of 382 adult, male participants of the ongoing, prospective BioPersMed study cohort. Body parameters used include height, weight, waist circumference, BMI, waist-to-hip ratio, body surface area (BSA) and estimated lean mass (eLM). Of 278 participants, dual energy X-ray absorptiometry (DXA)-derived body composition data, including fat mass (FM) and LM, were additionally available. We performed univariate and multivariate regression models with potential confounders (age, follicle-stimulating hormone, and estradiol) included as additional predictors.
Results
In the fully adjusted models, weight ($R2=0.201$; $\beta=-0.002$; $P=0.0022$), BSA ($R2=0.206$; $\beta=-0.231$; $P=0.0006$) eLM ($R2=0.206$; $\beta=-0.006$; $P=0.0006$) and LM ($R2=0.197$; $\beta=-0.006$; $P=0.003$) significantly predicted AMH. In an age adjusted model that challenged FM and LM against each other by including them both as predictors, only LM remained significant ($R2=0.061$; $\beta=-0.007$; $P=0.0035$).
Conclusions
In adult males, weight, BSA, eLM and LM (proxies of blood volume) better predicted serum AMH levels than measures of adiposity – suggesting hemodilution is at least partly responsible for the observed inverse relationship between AMH concentrations and BMI. Thus, hemodilution should be considered for normalization in future studies.

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EP238

Unveiling the uncommon nexus: kallmann syndrome and cardiomyopathy - a singular case study

Ahmed Hussien[1] & Maha Nasreldin[2]
[1]University Hospital of Hairmyres, Cardiology, Glasgow, United Kingdom; [2]Egyptian ministry of health, Cairo, Egypt

This case report delves into the intriguing connection between Kallmann syndrome and cardiomyopathy in a 62-year-old male who presented with new atrial fibrillation (AF) with rapid ventricular response and signs of fluid overload. Despite being a known case of Kallmann syndrome, the emergence of severe impaired left ventricular systolic dysfunction (LVSD) added a distinctive layer to the clinical scenario. Cardiomyopathy screenings for common causes like sarcoidosis, amyloidosis, and hemochromatosis proved negative. The patient's management involved a combination of diuretics, direct oral anticoagulants (DOAC), bisoprolol, digoxin, eplerenone, and dapagliflozin. Notably, the rate control of the underlying atrial fibrillation and improvement in overload symptoms paved the way for outpatient direct current cardioversion (DCCV). This case highlights the rarity of the association between Kallmann syndrome and cardiologic diseases, shedding light on the complexity of endocrinological and cardiovascular interplay.

Introduction

Kallmann syndrome with cardiopathy is a rare genetic disorder affecting the reproductive and olfactory systems, characterised by hypogonadotropic hypogonadism associated with gonadotropin-releasing hormone (GnRH) deficiency, anosmia or hyposmia (with hypoplasia or aplasia of the olfactory bulbs) and complex congenital cardiac malformations (double-outlet right ventricle, dilated cardiomyopathy, right aortic arch). It represents a distinct clinical entity from Kallmann syndrome. This case challenges conventional expectations by revealing a noteworthy connection between Kallmann syndrome and severe LVSD.

Clinical Presentation

The patient's presentation included fast AF and signs of fluid overload, necessitating diuretic therapy. Echocardiography unveiled a dilated left ventricle with an alarming ejection fraction (EF) of 25%, signifying severe LVSD.

Investigations

Blood tests were unremarkable. NT-pro BNP was raised. Chest X-ray showed pulmonary congestion. Thorough screening for common etiologies of cardiomyopathy such as sarcoidosis, amyloidosis, and hemochromatosis yielded negative results, emphasizing the atypical nature of this case.

Management

The multidisciplinary approach involved diuretics and the initiation of DOAC, bisoprolol, digoxin, eplerenone, ramipril and dapagliflozin. This regimen not only stabilized the patient's heart rate but also led to a significant improvement in symptoms of fluid overload.

Outcome

With successful medical management, the patient's heart rate was controlled, and symptoms of fluid overload resolved. Plans for outpatient DCCV were made to address the underlying rhythm disturbance.

Conclusion

This case serves as a unique exploration of the intersection between Kallmann syndrome and cardiomyopathy. The absence of common cardiologic culprits underscores the need for heightened awareness and further research into the intricate interplay between endocrinological disorders and cardiovascular manifestations.

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EP253

Characterization of liver abnormalities in a population of adult turner women: results from an observational study

Carolina Cecchetti[1], Laura Rotolo[1], Paola Dionese[1], Elisabetta Belardinelli[1], Beatrice Solmi[1], Amanda Vestito[2], Elton Dajti[2], Antonio Colecchia[3], Uberto Pagotto[1] & Alessandra Gambineri[1]
[1]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum, University of Bologna, Italy, Bologna, Italy; [2]Department of Digestive Diseases, Gastroenterology Unit, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum, University of Bologna, Italy, Bologna, Italy; [3]Gastroenterology Unit University Hospital, Modena, Italy, Baggiovara, Italy

Introduction

Liver function test abnormalities (LFA) are common in patients with Turner syndrome (TS). The etiopathogenesis of this complication remains unclear, probably being multifaceted. Metabolic syndrome, generalized vasculopathy, and autoimmunity have been proposed as possible causal mechanisms.

Objectives

- To describe the prevalence and possible related factors of morpho-functional liver abnormalities in TS adult patients.
- To evaluate the utility of hepatic elastometry in optimizing the diagnostic work-up of TS patients with LFA.

Materials and Methods

98 adult TS patients, regularly followed up at our Unit, underwent liver elastometry (FibroScan: Echosens, Paris, France) and hepato-splenic ultrasound. Blood samples were obtained to analyze liver enzymes and other metabolic parameters. Alanino-aminotransferase(ALT), aspartate-aminotransferase(AST), gamma-glutamyil-transferase(GGT), and alkaline-phosphatase(ALP) were considered abnormal(LFA) when above 1xULN. Data were retrospectively collected regarding metabolic complications, autoimmune diseases, menstrual history, and hormonal replacement therapies (GH and estrogen-progestin therapy). The presence of structural cardiovascular anomalies and the diameter of the first aortic tract were assessed by retrieving the latest cardiac examination (cardiac MRI and/or transthoracic echocardiography).

Results

61 patients (62,2%) had at least one LFA, GGT being the most frequent (60,2%). No cases of cirrhosis were observed; the prevalence of fibrosis was 8,1% ($n=8$). Patients with LFA (LFA-TS) showed significantly higher BMI, waist circumference, and waist-to-height ratio than patients with normal liver enzymes (NLE-TS) ($P=0.042$, $P=0.008$, $P=0.004$ respectively). Liver stiffness measurements (LSM) and liver fibrosis prevalence did not differ between the two groups; steatosis was the only morphological parameter significantly more prevalent in LFA-TS ($P=0.035$). LFA-TS showed significantly higher fasting glucose ($P=0.010$) and HbA1c levels ($P<0.001$) and more frequently had a diagnosis of hypertriglyceridemia ($P=0.041$). In LFA-TS, the diameter of the Valsalva sinuses was significantly wider than in NLE-TS ($P=0.034$), whereas there was a similar tendency in ascending aortic diameter, without reaching significance ($P=0.068$). No significant difference was detected regarding structural cardiovascular abnormalities, autoimmunity, menstrual cycle history, type of EP therapy, estrogen dosage, and history of GH therapy between the two groups.

Conclusions

LFA are highly prevalent in adult TS women; this complication seems particularly related to metabolic abnormalities, making its management pivotal in this rare disease. A relation with aortic dilation seems plausible, in the context of a possible generalized vasculopathy: further studies are needed to investigate this finding. Finally, given the presence of liver fibrosis also in NLE-TS, the sole presence of LFAs is not able to discriminate whether liver elastometry should be performed in TS patients.

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EP293

Impact of drospirenone-only-pill on sexual function: experience of our'pcos and female endocrinology outpatient clinic'

Alessandra Tomaselli[1], Marianna Minnetti[1], Elena Rosato[1], Chiara Tarantino[1], Dario De Alcubierre[1], Davide Ferrari[1], Flavio Rizzo[1], Francesca Sciarra[1], Riccardo Pofi[2], Andrea Isidori[1] & Carlotta Pozza[1]
[1]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy; [2]Oxford Centre for Diabetes, Endocrinology and Metabolism and NIHR Oxford Biomedical Research Centre, Department of Endocrinology, Oxford, United Kingdom

Introduction and Objectives of the Study

Combined oral contraceptives (COCs) are frequently prescribed for fertility control, however sexual dysfunction has been reported as a common side effect. In 2020, a novel progestin-only pill containing Drospirenone (DRSP) was approved as an oral contraceptive. To date, here is a notable dearth of data on the impact of DRSP on sexual function and impact on hormones, particularly regarding steroids. This study aims to investigate the potential effects of DRSP on sexual function and hormonal profiles, with a focus on steroids, in a cohort of women referred to our 'female endocrinology' outpatient clinic.

Subjects and Methods

Prospective evaluations were conducted on women taking DRSP at baseline (T0), and at 3 (T1), 6 (T2), and 12 months of follow-up (T3). Blood samples were collected to obtain a comprehensive hormonal profile, and the Female Sexual Function Index (FSFI) questionnaire was administered to assess sexual function. At each timepoint, Ferriman-Gallwey (FG) and GAGS scores were evaluated along with anthropometrics, vital signs, menstrual patterns, and adverse events.

Results

The study population comprised 26 women taking DRSP, including 12 of them with an active sexual life through all the timepoints. The median age was 24 [IQR 21-26] years. Most women (73%) exhibited clinical and/or biochemical

hyperandrogenism, with a baseline FG mean score of 9.0±7.0 points and a GAGS median score of 3.5 [IQR 0-11]. While no significant changes were observed in FSFI total scores at any timepoint, a noteworthy improvement in the satisfaction domain score was identified at T2 and T3 ($P=0.01$ and $P<0.001$, respectively). Regarding hormonal profile, there was a significant reduction in Δ-4-androstenedione levels at T2 ($P=0.01$), persisting at T3 ($P=0.006$), and a notable decrease in total testosterone levels at T2 ($P<0.001$). Conversely, no significant alterations were found in 17-β-oestradiol, gonadotropins, and SHBG levels during follow-up. Also, no significant alterations were found on hypothalamus-pituitary-adrenal axis hormones, thyroid hormones, and prolactin levels. Clinically, improvements in FG score were recorded at T3 ($P=0.006$) and in the GAGS score at T2 ($P=0.008$). No adverse events were reported, although 5 dropouts occurred due to abnormal menstrual profiles.
Conclusions
Preliminary data indicate that after 12 months of DRSP use, there was no worsening in sexual function, whereas there was a significant enhancement in sexual satisfaction. Furthermore, improvements were observed in clinical and biochemical markers of hyperandrogenism. Further assesments are warranted to validate these preliminary findings.

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EP346

Growing up with an endocrine disease: assessing transitional features in a cohort of young patients moving from pediatric to adult clinic

Valeria Citterio[1], Giulia Rodari[1,2], Alessia Gaglio[2], Valentina Collini[1], Alessandro Risio[1], Eriselda Profka[2], Federico Giacchetti[2], Emanuela Orsi[2], Giovanna Mantovani[1,2] & Claudia Giavoli[1,2]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milano, Italy; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milano, Italy

Introduction
Transition from childhood to adulthood represents a time-period in which adolescents/young adults (AYAs) with chronic illnesses start coping with self-managing their disease, often resulting in poor compliance to follow-up. Indeed, up to 50% of AYAs with common endocrine disorders is lost during the referral to an adult clinic. Transition in Endocrinology is poorly investigated yet, in terms of transition readiness, compliance to therapy, adherence to nutritional advice and quality of life (QoL). According to studies performed in other medical fields, these aspects can represent important determinants of a successful transitional program, thus predicting better disease outcomes.
Methods
In the present cross-sectional study, we consecutively enrolled 37 outpatients referring to a tertiary center with a transition-specific endocrine clinic in the presence of at least one chronic endocrine condition. Epidemiological and clinical data were collected. Moreover, transitional features were investigated through four specific questionnaires analyzing transition readiness (TRAQ), quality of life (KINDL-r), medications' adherence (MARS-5) and diet habits (KIDMED).
Results
Thirty-seven patients (F/M 23/14, 62%) were consecutively enrolled (age 18.4± 2.0 years, min-max 15.3-23.5). Among them, 8/37 were affected by childhood-onset growth hormone deficiency, 3/37 ACTH deficiency, 10/37 hypogonadism, 14/37 hypothyroidism, 28/37 vitamin-D deficiency, 1/37 polycystic ovary syndrome and 1/37 hyperprolactinemia (median disease duration 7 years, IQR 2.7-11). In 19/37 patients was found at least one non-endocrine comorbidity and 4/37 two or more. As far as questionnaires were concerned, median MARS score was 24 (IQR 23-24), KIDMED was 4±3, TRAQ score was 3.7±0.6, and QoL was 0.77±0.15, 0.61±0.15, 0.83±0.13, 0.85 (IQR 0.75-0.95), 0.64±0.11 and 0.85± 0.12 for physical, psychological, self-worth, family, friends, functioning and disease-related aspects, respectively. Transition readiness and physical well-being were positively associated with age ($P=0.003$ and $P=0.031$, respectively). Moreover, physical, psychological and self-worth QoL were positively associated with male gender ($P=0.004$, $P=0.008$ and $P=0.002$, respectively) while disease-related QoL was negatively associated with the number of endocrine consultations ($P=0.012$) and positively with the presence of nutritional follow-up ($P=0.016$).
Conclusions
This represents the first study assessing transition aspects in endocrine conditions. According to our results, transition readiness seems to be age-related. Moreover, males show less concern about the underlying disease, with higher levels of physical and psychosocial well-being and more self-esteem. Attendance at the clinic negatively affects diseases-related QoL, though this could be related to disease severity. Interestingly, nutritional support seems to improve disease burden and perception. Further longitudinal studies are needed in order to identify predictors and determinants of adherence during transition in endocrine diseases.

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EP349

Early embryonic testicular regression syndrome: a rare case of primary amenorrhea

Mădălina Elena Iftimie[1], Ramona Dobre[1,2], Burcea Iulia-Florentina[1,2], Larisa Budulucă[1], Emanuela Braha[1] & Catalina Poiana[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Background
Normal sex development is warranted by a complex and coordinated interaction between mutually antagonistic activating and repressing genetic and hormonal factors that act in a strict spatio-temporal sequence. Deviations from this established pattern can result in heterogenous chromosomal, gonadal or phenotypic congenital abnormalities named disorders of sexual development (DSD). We present a rare case of early testicular regression syndrome.
Case report
A 15 years and 11 months old female adolescent presented in our clinic with primary amenorrhea and delayed puberty. At physical examination she had normal female external genitalia, secondary sex characteristics consistent with the pre-adolescent stage (Tanner B1P2), low stature, dextroscoliosis, subtle cranio-facial dysmorphism and a slight psycho-emotional immaturity. Laboratory studies showed elevated gonadotropins with undetectable levels of estradiol and testosterone and abdominal and pelvic magnetic resonance imaging revealed no uterus or gonads, only the presence of a short lower vaginal tract. Her karyotype was found to be 46, XY and fluorescence *in situ* hybridization confirmed the presence of the SRY gene. Laparoscopic exploration of the abdomen and pelvis discovered 2 oblong pelvic masses consistent with rudimentary fallopian tubes with fibrous scarring and paramesonephric remnants on the pathology report. She was started on a gradual estrogen replacement therapy to simulate puberty along with psychotherapy. She now has normal stature and a significant improvement in secondary sexual characteristics (Tanner B3P3) and socio-psycho-emotional features at the age of 19 years and 10 months old.
Conclusion
The true prevalence of testicular regression syndrome remains unknown as the phenotype is highly variable depending on when gonadal regression occurs in utero. A thorough comprehension of embryonic sexual development and differentiation is key in accurately evaluating and managing these rare cases of XY DSD. Providing psychological support resources for patients and their families is also an essential point.

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EP359

Klinefelter syndrome (KS) prevalence at invasive prenatal diagnosis (ipd) procedures: a systematic review of the literature

Francesco Costantino[1,2], Sara De Vincentis[1,2], Maria Chiara Decaroli[1,2] & Vincenzo Rochira[1,2]
[1]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena (Italy); [2]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena (Italy)

Introduction
KS prevalence is estimated to range from 0.1-0.2 % in men and actually the estimated frequency is of about 1:500 to 1:1000 men[1]. However, the real prevalence remains unknown due also to the fact that the disease is often overlooked and undermanaged[1].
Aim and methods
We performed a systematic literature search including studies published between 1971 and January 2024 to investigate the real prenatal prevalence of KS (including both pure and mosaic karyotypes) among chromosome abnormalities (CAs) and sex CAs (SCAs) diagnosed by different IPDs procedures (i.e. chorionic villus sampling, amniocentesis, and cordocentesis). The primary endpoint was the prevalence of KS. No specific criteria for study populations were provided.
Results
Among the 1826 studies detected by the literature search, 59 matched our inclusion criteria, considering so far 776912 IPD procedures, most of them performed for medical indication (88%). A total of 24094 CAs (3.10%) diagnosis were reported, of which 3729, (15.48%), was due to SCAs (i.e. 45,X0; 47,XXY; 47,XXX; 47,XYY). KS was diagnosed in 1074 out of 776912 fetuses, and as expected was the most prevalent SCA in males (median 0.13%, range 0-9.28%), with 46,XY/47,XXY accounting for 8.41% of all KS. Despite a high heterogeneity between studies, KS was mainly reported when genetic tests were performed in the presence of any gynecological indication (median of 0.13% vs 0.01%) ($P<0.0001$). Moreover, KS cases among CAs were more common

when IPD procedures were performed due to any medical indication than without (3.32% vs 0%). A significant association between KS and mother's age at birth was confirmed, hence the median >35/<35 y/o ratio was 1.07 (range 0-3.07).
Conclusions
This study confirms that around 1.3 of 1000 men (0.65/500) may be affected by KS, which is in line with data suggested by the literature. As the vast majority of KS diagnosis have been done after a gynecological indication, it is possible that this prevalence overestimates the prevalence rate in general population. Further studies are needed to analyze the prevalence of KS in the overall population. To our knowledge this is the widest systematic synthesis and confirms the association reported between KS and CAs' risk factors (e.g. advanced mother age, abnormal US).
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EP363

Beta thalassemia major, hypogonadism and cardiovascular risk

Francesca Allosso[1], Lucia Digitale Selvaggio[1], Martina Errico[1], Graziella Grande[1], Claudia Di Ludovico[1], Raffaele Navarra[1], Maddalena Casale[2], Silverio Perrotta[2] & Daniela Pasquali[1]
[1]University of Campania L. Vanvitelli, Department of Advanced Medical and Surgical Sciences, Naples, Italy; [2]University of Campania L. Vanvitelli, Department of General and Specialized Surgery for Women and Children, Naples, Italy

Beta thalassemia major (betaTM) is an inherited hematological disorder characterized by reduced or absent synthesis of beta-globin chains and anemia. Chronic transfusion treatment is necessary, exposing patients to iron overload comorbidities such as hypogonadism. It is due to iron accumulation in the pituitary gland and, more rarely, in testis and ovaries. HPG axis dysfunction can manifest as low estradiol or testosterone with low to normal serum LH and FSH, as commonly seen in hypogonadotropic hypogonadism (HH). The aim of our study was to verify the prevalence of hypogonadism in beta-TM patients (HH-betaTM), to evaluate the differences compared to a non-thalassemic hypogonadal population (HH), to assess the difference in cardiovascular risk (CVR) between beta-TM patients with and without hypogonadism. 47 patients (30 females, 17 males) with betaTM (22-60 years on average) were studied. Associated endocrinopathies included GH deficiency, thyroid nodules, osteoporosis. The control group consisted of 27 HH-nonthalassemic patients (8 women, 21 men), aged 19-73 years. Levels of testosterone, estradiol, LH and FSH were evaluated in both groups. CVR was assessed in betaTM patients using risk score calculators. In the total of 30 women betaTM patients 15 had HH, only six were receiving replacement therapy, while nine were refusing treatment. In the population of 17 male beta-TM patients, 6 had HH with a mean pre-therapy testosterone level of $204 \pm 22{,}118$ ng/dl, FSH level of $4{,}167 \pm 2{,}073$ IU/l and LH level of $3{,}55 \pm 3.92$ IU/l. All were on replacement therapy with testosterone. In male HH-nonthalassemic controls, mean of FSH was $1{,}428 \pm 1{,}528$ IU/l, of LH was $0.928 \pm 1{,}189$ IU/l and of testosterone was $194 \pm 88{,}427$ ng/dl. The difference between levels of FSH and LH in HH-betaTM and HH controls was significant only in the male population ($P < 0.01$). No differences were found in CVR in 15 females with HH-betaTM compared to 15 female non-hypogonadal betaTM. CVR was significantly different in male with HH-betaTM compared to non-hypogonadal betaTM male (1.467% vs 0.633%)($P < 0.05$). Our data confirm the high incidence of hypogonadism in thalassemia, but in the male betaTM population there are higher gonadotropin levels compared to patients with HH, due to the mixed nature of the systemic damage. This characterizes HH in thalassemia as an intermediate clinical entity that deserves differentiated attention in terms of diagnosis, type of replacement therapy and follow-up. In the thalassemic male population, hypogonadism significantly worsens cardiovascular risk and highlights the importance of replacement therapy.

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EP370

Delayed puberty and ataxia – important clinical manifestations of polr3b-related leukodystrophy

Simon Mifsud[1] & Miguel Debono[1,2]
[1]The University of Sheffield, United Kingdom; [2]Sheffield Teaching Hospitals NHS Foundation Trust, United Kingdom

Background
POLR3-related leukodystrophy is an autosomal recessive hypo-myelinating leukodystrophy characterized by specific features on MRI and varying combinations of four major clinical findings[1]. The latter include neurological dysfunction, abnormal dentition, endocrine dysfunction, and myopia[1]. Endocrine dysfunction in POLR3-related leukodystrophy includes hypogonadotropic-hypogonadism (HH), short stature, growth hormone deficiency, and less commonly thyroid dysfunction.
Case report
A 27-year-old lady recently diagnosed with POLR3B-related leukodystrophy was referred to endocrinology to screen for endocrine dysfunction. She gave a longstanding history of ataxia, myopia, and delayed puberty. During childhood and adolescence, she had a short stature compared to her peers. She had very minimal breast development and never had spontaneous menstrual bleeding. She was reviewed by several healthcare professionals and was prescribed the combined oral contraceptive pill (COCP). This led to a growth spurt but had to be discontinued because of worsening mental state. At the time of review, she had been off the COCP for four years. She complained of frequent episodes of hot flushes and sweating. She also sustained nontraumatic vertebral fractures. She denied hyposmia or anosmia. She had a stable weight and appetite. She denied galactorrhoea and was on no medications. On physical examination, she was at Tanner Stage 2. She had grossly normal visual fields to confrontation. Laboratory investigations revealed FSH of 4.5IU/l and LH of 2.9IU/l with an oestradiol of < 91.8 pmol/l, indicating HH. The rest of her pituitary profile including IGF-1 level was unremarkable. A DEXA scan revealed normal bone density. An MRI head showed atrophic cerebellar hemispheres and a low-volume pituitary gland. Transvaginal ultrasound had previously shown no abnormal anatomic disorders of the genital outflow tract. DNA sequencing performed previously revealed that she is a compound heterozygote for POLR3B mutations, specifically c.1244T>C (p. Met415Thr) and c.1263+2T>C. The patient was prescribed low-dose transdermal oestradiol (escalating dose) and progesterone soon after, to enhance the development of secondary sexual characteristics.
Discussion
The differential diagnosis of patients presenting with a combination of neurodegenerative disorders and HH is extensive. This case highlights the importance of maintaining a high level of clinical suspicion for the diagnosis of POLR3–related leukodystrophy in patients presenting with delayed/arrested puberty, particularly in the presence of concurrent cerebellar manifestations. Early diagnosis and timely management can improve the patient's quality of life and avoid complications of untreated hypogonadism.
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EP388

Steroid secreting ovarian tumour causing extreme hyperandrogenism, virilisation and polycythaemia in a post-menopausal female

Ruth Byrne[1], Carla Moran[1,2,3], Catherine Foley[2], Kamal Fadalla[1], Michael Jeffers[2] & Waseem Kamran[2]
[1]St. Vincent's University Hospital, Ireland; [2]Beacon Hospital, Ireland; [3]University College Dublin, Ireland

Introduction
Hyperandrogenism causing virilisation in postmenopausal females is rare. It is caused by abnormal ovarian or adrenal androgen production, but establishing the source of androgen excess can be challenging. Testosterone levels >5 nmol/l can be associated with virilization (Hirschberg, 2022).
Case
A 75-year-old post-menopausal woman, with a 3-year history of androgenic alopecia (Ludwig scale 3/3) and hirsutism (Ferrimen Gallwey Score 32/36) was investigated. She had known, but previously unexplained, polycythaemia (Hgb 17.6 g/dl). Laboratory testing showed extremely elevated Testosterone (30.6 nmol/l, RR 0.4-1.4), moderately elevated Androstenedione (4.29 nmol/l, RR 0.5-2.8) but normal DHEAS levels (1.1umol/l, RR 0.3-4.2). Estradiol (321 pmol/l), LH and FSH levels (both <1 IU/l, <1 IU/l) were inappropriate for her post-menopausal status. There was no evidence of congenital adrenal hyperplasia (17 OHP 1.36 nmol/l) or Cushing's syndrome (cortisol level post dexamethasone administration 36 nmol/l). MRI revealed bilateral mildly enlarged ovaries with multiple small follicles and a thickened endometrium. Adrenal imaging was normal. GnRH was not administered given already suppressed gonadotropins. Hysterectomy and bilateral salpingo-oophorectomy were performed. The left

ovary contained a well circumscribed, non-capsulated tumour which expressed inhibin, Calretinin and Melan-A, indicating a steroid cell tumour. Two months following surgery, biochemistry showed undetectable Testosterone (<0.4 nmol/l). Estradiol (<92 nmol/l), LH (19 IU/l) and FSH (28 IU/l) were physiological for age and polycythaemia had resolved (Hgb 15.8 g/dl). At 6 months postoperatively, her hirsutism and alopecia were persistent, but improved (Ferrimen Gallwey Score 17/36, Ludwig scale 2/3).

Conclusion

This case offers insight into the workup of post-menopausal virilisation, which is rare and always requires further investigation. This patient presented with extreme biochemical hyperandrogenism and virilisation due to an ovarian tumour, and exhibited resolution of endocrine abnormalities and polycythaemia following successful surgery. Her case also highlights the importance of checking a testosterone level in females with unexplained polycythaemia.

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EP396

Low dose estradiol gender-affirming hormone therapy (GAHT) generates rapid feminizing body changes in transgender women: a dual energy x-ray absorptiometry-based prospective study

Iris Yaish[1], Guy Gindis[1,2], Asaf Buch[1,3], Yael Sofer[1,2], Yona Greenman[1,2], Mira Arbiv[1], Yaffa Moshe[1] & Karen Tordjman[1,2]

[1]Tel Aviv Sourasky Medical Center, Institute of Endocrinology and Metabolism, Institute of Endocrinology, Metabolism and Hypertension, Tel Aviv, Israel; [2]Faculty of Medicine, Tel Aviv University, Internal Medicine, Tel Aviv, Israel; [3]Ariel University, Department of Nutrition Sciences, Ariel

Background and Aim

We previously demonstrated that low-dose estradiol (E2) administered sublingually alone for 6 months in treatment-naïve trans women (TW), suppressed testosterone to the same degree, but generated higher serum E2 levels as the same oral dose combined with cyproterone acetate. We now sought to assess the possible differential impact of these approaches on anthropometric and body composition measurements, sex-dependent indicators with proven metabolic prognostic value.

Methods

22 treatment-naïve TW, 23.2±1.1 y, opted non-randomly, in a 1:1, ratio to receive sublingual E2 (2 mg divided into 4 daily doses), or oral 2 mg E2+10 mg cyproterone acetate for 6 months (6M). Anthropometric, hormonal, and body composition by DXA (Lunar Prodigy-GE) measurements were obtained at baseline, and after 6M of GAHT.

Results

Anthropometric, body composition measurements, and testosterone at baseline and 6M did not differ between the groups. In a first step, all subjects were analyzed together for assessment of the general impact of GAHT. By paired comparisons, neither weight nor BMI had changed at 6M. Hip circumference remained unchanged, however, waist circumference decreased by 2.7±1.19 cm ($P=0.047$), resulting in a significant reduction in waist-to-hip-ratio ($P=0.018$). The total regional fat percentage increased from 23.4±2.3% to 27.8±1.8% ($P<0.001$). This increase was significant for all fat depots (gynecoid, arms, legs, trunk) except for the android area. Total body fat mass increased by 2.6 kg, from 18.4±2.4 to 21.0±2.4 kg ($P=0.008$). In contrast, subjects lost lean mass in all compartments. The whole body lean mass loss was 3.4±0.3 kg (a 21.6% decrease, $P<0.001$), leading to a decrease in the lean/fat mass ratio from 4.7 to 2.9, ($P=0.0002$). Analyzed separately, some changes appeared to be influenced by the treatment route, particularly the increases in fat depots that were significantly milder in the sublingual group. The lean body mass decrease, however, was similar with both treatments. After age-adjustment, none of the variables at 6M correlated with hormone levels. However, decreases in total body, legs, and arms lean mass were inversely correlated with testosterone at 6M ($r=-0.41$, $P=0.045$; $r=-0.476$, $P=0.033$; and $r=-0.563$, $P=0.01$, respectively).

Conclusions

A relatively short GAHT period with a low dose of E2 generated significant body feminization in TW. Subjects in the sublingual group were surprisingly spared from body fat accumulation. The reason for this differential effect of sublingual E2 is still unknown. Sublingual E2 could offer some protection from fat accumulation but not from lean body mass loss in TW.

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EP403

Lipid profile in turnerian patients treated with growth hormone

Khawla Rhouzali[1], Hamdane Chaymae[1], Moussa Baraya[1], Siham Rouf[2] & Hanane Latrech[2]

[1]Department of Endocrinology-Diabetology and nutrition, Mohammed VI University Hospital Center. Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco., Oujda, Morocco; [2]Department of Endocrinology-Diabetology and nutrition, Mohammed VI University Hospital Center. Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco., Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy, Mohammed First University Oujda, Morocco, Oujda, Morocco

Introduction

Turner syndrome (TS) is a rare genetic disorder characterized by an aberration of the X chromosome, most commonly associated with various comorbidities, such as metabolic disorders, particularly dyslipidemias. The aim of this study is to determine the frequency of dyslipidemias associated with TS and to evaluate the impact of growth hormone (GH) treatment on lipid metabolism.

Methods

This is a descriptive and retrospective study of 22 patients diagnosed with Turner syndrome at the Endocrinology-Diabetology and Nutrition Department of the University Hospital of Oujda-Morocco, including 11 patients treated with growth hormone (GH) over a period of 6 years. All patients underwent pre-treatment assessments, including lipid profile during evolution.

Results-Discussion

The mean age of our population was 13.91±6.93 years. Five patients (45.5%) had dyslipidaemia prior to initiation of GH treatment; elevated LDL cholesterol levels was observed in 60% of patients, hypertriglyceridaemia in 20% and mixed dyslipidaemia in 20%. After initiation of GH treatment, the evolution was marked by an improvement in the lipid profile in 60% of cases, while 40% maintained dyslipidaemia for up to one year. In contrast, six patients (55.5%) did not have dyslipidaemia on the initial metabolic test, of whom 66.6% did not develop dyslipidaemia during the GH treatment period, whereas two patients (33.3%) developed dyslipidaemia one year after GH treatment. In our serie, GH treatment significantly confirmed its positive effect on lipid metabolism by reducing serum LDL levels.

Conclusion

GH treatment has a positive effect not only on statural gain but also on the metabolic profile of patients with Turner syndrome, which ties in with the conclusions of the literature on the innocuity of GH treatment of patients with TS.

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EP431

Time-dependent progression of metabolic dysfunction in a mouse model of polycystic ovary syndrome

Jelina Basnet[1], Samar Rezq[1], Alexandra M Huffman[1], Licy L Yanes Cardozo[1] & Damian Romero[1]

[1]University of Mississippi Medical Center, Jackson, United States

Background

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in reproductive-age women. PCOS is associated with metabolic disorders such as obesity, dyslipidemia, systemic insulin resistance (IR), and adipose IR. Hyperandrogenism is prevalent in PCOS and is linked to metabolic dysfunction in multiple tissues, including WAT. However, data on the disease onset and progression of WAT mediated metabolic derangements in PCOS women are lacking. Therefore, we aim to test the hypothesis that the androgen dihydrotestosterone (DHT) induces time-dependent progression of WAT and metabolic dysfunction on both the molecular and functional levels in PCOS. This hypothesis was tested using a well-characterized DHT-induced PCOS mouse model after 2, 4, 8 and 12 wks of DHT administration.

Methods

Three-week old female mice (C57BL/6N) were implanted with Silastic tubes filled with DHT (8 mg, s.c.) or vehicle ($n=6$/grp) for 2, 4, 8 and 12 weeks. Weekly body weight (BW, gravimetry), body composition (EchoMRI), subcutaneous fat (SCF)- a WAT depot mass (gravimetry) were assessed. Serum leptin, adiponectin, and insulin were measured by ELISA, while non-esterified free fatty acid (NEFA) and cholesterol by using a clinical chemistry analyzer. Adipose IR (insulin×NEFA) was calculated. SCF androgen receptor (AR), lipolytic marker adipose triglyceride lipase (ATGL), and adipogenesis marker peroxisome proliferator-activated receptor-γ (PPAR-γ) protein levels were assessed by Western blot.

Results

DHT mice showed significant ($P<0.05$) increases in BW (1.15-fold) and lean mass (1.14-fold) starting 2 weeks following DHT-exposure where higher

cholesterol (1.3-fold), insulin (2.3-fold) and adipose IR (2.5-fold) as well as lower insulin-sensitizing adipokine adiponectin levels (50%) were also observed compared to vehicle. The increases in SCF mass (1.5-fold) and total fat mass (2.2-fold) were only significant starting at 8 weeks. DHT significantly increased NEFA (1.3- and 1.2-fold, 8- and 12-weeks post-DHT, respectively) and leptin (1.5-fold, 12 weeks post-DHT). On the molecular level, DHT mice had an upregulation in SCF AR expression (1.5-fold) at 2 weeks and an upregulation of ATGL and PPARγ expression by 50% and 40% at 4 weeks post-DHT.
Conclusion and significance
Our findings suggest that some of the associated metabolic traits such as serum adiponectin, insulin, cholesterol and adipo-IR, occur very early following the induction of hyperandrogenemia that may be drivers of disease progression. Therefore, actively screening and managing risk factors for metabolic derangements from early on in PCOS is critical for disease management.

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EP436

Variations in the assessment and education of polycystic ovary syndrome (PCOS) during initial consultations across europe: a multinational study

Anisah Ali[1], Harshal Deshmukh[2], Alexander Wilde[3], Ashwin Joshi[3], Elena Armeni[4], Isin Yesilkaya Baylan[5], Erkut Attar[5], Fahrettin Kelestimur[5], Meri Davitadze[6,7], Punith Kempegowda[6] & PCOS SEva Working Group[6]
[1]University of Birmingham Medical School, Birmingham, United Kingdom; [2]Hull University teaching hospital NHS trust, Hull, United Kingdom; [3]South Tyneside and Sunderland NHS Foundation Trust, Sunderland, United Kingdom; [4]Royal Free Hospital London, London, United Kingdom; [5]PCOS and hirsutism clinic, Yeditepe University hospital, Istanbul, Turkey; [6]Institute of Applied Health Research, University of Birmingham, Birmingham, United Kingdom; [7]Clinic NeoLab, Tbilisi, Georgia

Objective
To explore the differences in various assessments recommended by the International PCOS guidelines during the initial consultation for women with PCOS across Europe.
Methods
This retrospective multi-centre study was conducted from June 2023 to January 2024. All women over age 18 who attended their first consultation in a dedicated PCOS clinic from 1st January 2020 to 31st December 2023 in the UK ($n=359$), Turkey ($n=239$), Greece ($n=92$) and Georgia ($n=10$) were included. Those undergoing follow-up or without PCOS were excluded. Data were collected on sociodemographic variables and assessments, including diagnosis based on guidelines, cardiometabolic risk, dermatological assessment, emotional well-being, long-term risk education, lifestyle management, and reproductive screening. Descriptive statistics were analysed using SPSS 28.0.
Results
The most common reasons for referral across all countries were irregular periods (65.7%), excess hair growth (61.1%), and acne (38.9%). Irregular periods were the most common reason for referral in the UK (59.6%), Greece (82.6%), and Georgia (100.0%), followed by excess hair growth (UK: 53.2%, Greece: 65.2%, and Georgia: 90.0%). However, in Turkey, excess hair growth was the most common reason for referral (70.3%), followed by irregular periods (67.0%). The most common co-morbidities across all countries were anxiety (9.7%), hypothyroidism (9.0%), and depression (6.7%). Anxiety was the most common co-morbidity in the UK (14.2%) and Georgia (20.0%), whereas hypothyroidism was most common in Turkey (10.9%) and Greece (10.9%). During consultation, the most common parameters assessed across all countries, as per international PCOS guidelines, were dermatological concerns (92.4%), reproductive screening (83.0%), and lifestyle management (80.4%). Similar trends were found in Turkey, Greece, and Georgia, where dermatological concerns and lifestyle management were assessed in 100.0% of women. In Turkey, diagnosis based on guidelines (99.2%), cardiometabolic risk (99.2%), emotional well-being (99.6%), long-term risk education (99.6%), and reproductive screening (99.6%) were assessed in almost all women and in all women from Greece and Georgia. In the UK, dermatological concerns (85.2%), reproductive screening (67.1%), lifestyle management (61.8%), and cardiometabolic risk (60.0%) were mostly assessed for, whereas emotional well-being (20.3%) and long-term risk education (14.8%) were the least followed recommendations.
Conclusion
The findings highlight a significant difference in the assessment and education provided during PCOS consultations across countries in Europe, specifically in emotional-wellbeing and long-term risk education. Developing new models of care which prioritise emotional well-being screening and long-term risk education is crucial to address these gaps and improve patient outcomes.

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EP437

PCOS-like syndrome in the young woman with cortisone reductase deficiency type 1

Katarina Krstic[1], Sanja Ognjanovic[1], Bojana Popovic[1], Dusan Ilic[1], Valentina Elezovic Kovacevic[1], Jelica Bjekić Macut[1,2], Milica Opalic Palibrk[1], Lena Radic[1], Olivera Stanojlović[3], Aleksandra Rasic Markovic[3], Danijela Vojnovic Milutinovic[4] & Djuro Macut[1]
[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Department for Endocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia; [2]University Medical Centre Bezanijska Kosa, Belgrade, Serbia; [3]Institute of Physiology, Faculty of Medicine, Belgrade, Serbia; [4]IBISS, University of Belgrade, Belgrade, Serbia

Introduction
11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) is a dimeric enzyme that catalyzes the reduction of cortisone to cortisol within the endoplasmic reticulum. Loss of this activity results in a disorder termed cortisone reductase deficiency type 1 (CRD). Only mutations in H6PD gene, which encodes an enzyme supplying cofactor for the reaction, have been identified as the cause of disease. Biochemical features of CRD are increased cortisol clearance and ACTH-mediated androgen excess. There are close phenotypic similarities between CRD and polycystic ovary syndrome (PCOS): hirsutism, oligo-amenorrhea, central fat distribution, infertility. We present the case of a 21-year old woman with mutations in H6PD gene who presented with secondary amenorrhea, hirsutism and obesity.
Case
After menarche at the age of 12, there were no spontaneous periods. A pediatric endocrinologist diagnosed PCOS (Rotterdam phenotype A). Menstrual cycles (MC) were established with a combined oral contraceptive pill with antiandrogen properties. The breaks in taking the medicine was followed by absence of MC. The patient's dominant complaints are hirsutism (mFG score - 10), obesity (BMI 33 kg/m^2) and secondary amenorrhea.
Results
Investigations showed elevated basal values of androgens (testosterone 6.8 and 8.0 nmol/l [1.2-3.8 nmol/l], androstenedione 6.2 and 6.0 ng/ml [0.24-3.44 ng/ml] and 17-OH progesterone 7.2 and 7.1 nmol/l [0.4-5.0nml/l]), FAI 29.8, AMH 9.45 ng/ml; DHEAS, serum cortisol, IGF-1, prolactin and thyroid function were normal. The results obtained in 2h-OGTT indicate insulin resistance (HOMA-IR 10.5). In low-dose dexamethasone tests, including prolonged DEX I, androgen suppression was absent. Androgen suppression was occurred after administration of GnRH agonist (Diphereline 3.75 mg). Congenital adrenal hyperplasia (CAH) was biochemically excluded by the Synachten test (maximal 17-OHP 7.0 nmol/l and cortisol 685.4 nmol/l). Selective ovarian and adrenal venous sampling were inconclusive indicating abnormal androgen production from the left adrenal gland and right ovary. Genetic analyzes confirmed mutations in H6PD gene: c.455A>G (p. Tyr152Cys) and c.1123G>A (p. Glu375Lys). The result of cortisol clearance is pending. The enlarged ovaries (diameter 5 cm, volume 28 ml) with polycystic morphology were confirmed by ultrasound. Adrenal glands are described as normal (MRI).
Conclusion
The genetic analysis on H6PD gene should be done if there are inexplicably high levels of androgens in a woman with PCO-like phenotype. Peculiar functional testing is needed including specific genetic testing for rare adrenal enzymatic deficiencies.

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EP448

Clinical and biological aspects of isolated hypogonadotropic hypogonadism

Hager Khiari[1,2], Imen Rojbi[1], Sawsen Essayeh[1], Sabrine Mekni[1], Bennacef Ibtissem[1], Youssef Lakhoua[1], Nadia Mchirgui[1] & Karima Khiari[1]
[1]Charles nicolle hospital, Endocrinology; [2]Charles nicolle hospital, Endocrinology, Tunis, Tunisia

Introduction
Isolated hypogonadotropic hypogonadism is a heterogeneous group of genetic abnormalities affecting the hypothalamic pituitary gonadal axis. The main mechanism consists of an impairment of the production or the action of gonadotropin releasing hormone (GnRH). While several mutations have been identified, the majority of cases remain without etiology. The objective of our study was to describe the clinical and biological profiles of these diseases.

Methods
This was a retrospective study that included patients followed in our department between 2009 and 2023 for idiopathic hypogonadotropic hypogonadism with normal pituitary imaging. Patients with Kallmann syndrome were not included.
Results
We included 15 patients in our study. Twelve patients were males and three were females with a male/female sex ratio (M/F) of 4. The mean age at the initial diagnosis was 26.5 ± 14.5 years with extremes ranging from 14 to 57 years old. The chief complaint was different depending on gender. For males, delayed puberty was the most common ($n=4$). Three patients complained of gynecomastia, two of micropenis, one patient consulted for infertility and another for adrenal insufficiency. For females, reasons for consultation were primary amenorrhea ($n=1$), secondary amenorrhea ($n=1$) and adrenal insufficiency ($n=1$). All patients reported a history of irregular menses. Most patients did not have a family history of hypogonadism ($n=13$), cryptorchidism and infertility were reported in first-degree relatives in two patients. Only one patient had first-degree parental consanguinity. No patient had a congenital malformation. The mean serum testosterone level was 0.99 ± 0.9 ng/ml for men and the mean serum estradiol level was 9 pg/ml for women. The mean (FSH/lH) ratio was 3.8 ± 3.6. An associated pituitary deficiency was observed in six patients. Corticotropic deficiency was the most frequent ($n=5$). Six patients were married, three of them had offspring: one couple had a spontaneous pregnancy and two couples needed treatment with gonadotropins to have children.
Conclusion
Isolated hypogonadotropic hypogonadism is characterized by heterogeneous genetic, clinical and evolutive aspects. The identification of the mutations involved in its genesis is crucial to improve its management and prognosis.

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EP458

Body composition changes and satisfaction associated with gender-affirming hormone therapy in transgender men

Emilia Gomez Hoyos[1], David Primo Martin[1], Esther Delgado Garcia[1], Lucia Estevez Asensio[1], Ana Ortolá Buigues[1], Juan Jose Lopez Gomez[1], Maria Antonia Maniega Rubio[2], Carmen Rodriguez Fernandez[2], Maria Jose Bartolome Albistegui[3] & Daniel De Luis Roman[1]
[1]Hospital Clínico Valladolid, Endocrinology and Nutrition, Valladolid, Spain; [2]University Clinical Hospital of Valladolid, Mental Health, Valladolid, Spain; [3]University Clinical Hospital of Valladolid, Pediatrics, Valladolid, Spain

Introduction
Gender affirming hormone therapy (GAHT) in transgender men favors their virilization. Aims: To determine its impact on body composition measured by electrical impedance and the satisfaction perceived by the subject (CRES-4 questionnaire).
Material and Methods
Prospective study in transgender men with GAHT (>2 years), attended at the Transgender Medicine Unit of the Hospital Clinico of Valladolid from January 2014 to January 2023. Recording of clinical, analytical, body composition and CRES-4 questionnaire data after giving their consent. Statistical analysis of the data by the SPSS-V17 program.
Results
32 transgender males aged 23 [22-32] years and onset of GAHT at 18 [17-25] years with long-acting testosterone ester 2 (6.3%), short-acting 26 (81.3%) and testosterone gel 4 (12.5%). The initial BMI was 21.9 [19.6-24.7] kg/m^2, fat-free mass (FFM) 43.9 [40.8-47.4] kg, fat mass (FM) 15.6 [10.6-22.9] kg and estimated muscle mass (EMM) 29 [24.7-31.9] kg. At 2 years with testosterone, there was 0.82 [0.1-1.9] kg/m^2 increase in BMI, 3.4[2-5] kg in FFM and 3.8 [1.7-8.1] kg in EMM. FM decreased -1.7[-3.3 to 1] kg. 21/22 subjects were satisfied with GAHT, with 255 [242-265] points on CRES-4. Serum testosterone (near the end of the dose interval) was 391 [264-817] ng/dl with 17 (53%) in the low range (</=400 ng/dl) and 15 (47%) subjects in the mid-high range of normal (>400 ng/dl). In both groups, changes in BMI ($P=0.723$), in FFM ($P=0.288$) and in FM ($P=0.288$) were similar. However, the increase in EMM was 4.9[2.8-10] kg in the low range and 3.3[1.2-7.1] kg in the mid-high range ($P=0.077$). CRES-4 score in the low range was 262 [250-275] and in the mid- high range 255 [242-262] points (p 0.273).
Conclusion
GAHT-induced body composition changes in transgender males were satisfactory. Even with testosterone levels near the end of the dosing interval in the low normal range.

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EP547

Knowledge and practices among georgian physicians regarding diagnosis and management of polycystic ovary syndrome: experiences from a middle-income country

Meri Davitadze[1,2], Giorgi Kanchelashvili[2,3], Ann Kobaidze[4], Nino Tedoradze[4], Nino Chikhladze[1] & Giorgi Chakhunashvili[5]
[1]Tbilisi State University, Tbilisi, Georgia; [2]Clinic NeoLab, Tbilisi, Georgia; [3]Health Research Union, Tbilisi, Georgia; [4]Caucasus Medical Center, Tbilisi, Georgia; [5]Georgian National Center for Disease Control and Public Health, One Health Division, Tbilisi, Georgia

Introduction
Polycystic ovary syndrome (PCOS) affects 10-15% of women worldwide, depending on the population and the diagnostic criteria used. The diagnostic criteria include clinical and/or biochemical hyperandrogenism, oligo/anovulation, and polycystic morphologic appearance of the ovaries. PCOS is associated with high risk of obesity, diabetes, cardiovascular diseases, and a wide spectrum of mental health disorders. Despite international recommendations, there is still lack of awareness regarding the diagnostic and management approaches with studies being reported mostly from high-income countries. Herein, we aimed to investigate healthcare professionals' knowledge and practices regarding PCOS in a middle-income country.
Methods
A survey-based study was conducted among Georgian physicians, namely endocrinologist, gynaecologists, and family doctors, in March 2022. The survey consisted of questions regarding participants' general information and their knowledge and experience regarding various aspects of PCOS. T-test and chi-square test were performed. Statistical significance was set at $P<0.05$.
Results
Out of the 133 physicians, 77 (57.9%) were endocrinologists, 21 (15.8%) gynaecologists, and 35 (26.3%) family doctors. 93.5% ($n=72/77$) of endocrinologists, 70.0% ($n=14/20$) of gynaecologists, and 84.8% ($n=28/33$) of family doctors perceived PCOS as an endocrine condition ($P=0.015$). however, 51.9% ($n=40/77$) of endocrinologists referred patients to gynaecologists, and 33.3% ($n=7/21$) of gynaecologists referred patients to endocrinologists ($P<0.001$). Less than half of both specialists (49.4% [$n=38/77$] of endocrinologists and 47.6% [$n=10/21$] of gynaecologists) used Rotterdam criteria, while 14.3% ($n=11/77$) of endocrinologists and 4.8% ($n=1/21$) of gynaecologists responded with 'don't know' ($P=0.474$). For initial evaluation, more endocrinologists used metabolic parameters, compared with gynaecologists ($P<0.05$). Only 12.0% ($n=9/75$) of endocrinologists and 19.0% ($n=4/21$) of gynaecologists offered lifestyle modifications for PCOS on a regular basis. 5.7% ($n=38/75$) and 36.0% ($n=27/75$) of endocrinologists most frequently offered metformin and oral contraceptives for PCOS, as opposed to 4.8% ($n=1/21$) and 66.7% ($n=14/21$) of gynaecologists for the same treatment options, respectively ($P=0.001$). Lastly, 61.0% ($n=47/77$) of endocrinologists and 85.7% ($n=18/21$) of gynaecologists disagreed with the statement 'name 'polycystic ovary syndrome' is confusing and should be changed' ($P=.034$).
Conclusions
The knowledge and practical approaches with regards to PCOS differ across specialities and are inconsistent with the current international recommendations. Future studies are warranted to propose relevant improvements and evaluate the effectiveness of implemented mechanisms in Georgia to promote better patient care. Further perspective would be to explore the perceptions and attitudes towards PCOS among women with this condition to better understand their needs.

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EP548

Beyond the surface: endocrinological implications of thoracic endometriosis syndrome

Aleksandra Czapla-Iskrzycka[1], Katarzyna Pietrzak[2], Renata Świątkowska-Stodulska[1] & Tomasz Marjański[3]
[1]Medical University of Gdansk, Department of Endocrinology and Internal Diseases, Gdansk, Poland; [2]Medical University of Gdansk, Division of Nursing Management, Gdansk, Poland; [3]Medical University of Gdansk, Department of Thoracic Surgery, Gdansk, Poland

Introduction
Thoracic Endometriosis Syndrome (TES) is characterized by clinical symptoms associated with menstruation (eg, catamenial pneumothorax (CP), chest pain, and others) not obligatorily requiring histological confirmation. The treatment is

burdened with frequent recurrences. This study aimed to characterize the treatment of women with TES and assess the concomitant diseases.
Methods
A developed online survey was published in patients' support group. It consisted of sections regarding demographics, symptoms, various treatment strategies, infertility, vitamin D supplementation and diet.
Results
In this descriptive study 40 women with mean age of 37 (22-44y) were included, 85% had confirmed pelvic endometriosis. Eleven patients were diagnosed pathologically with thoracic endometriosis, while the rest (72.5%) experienced the symptoms of TES. 22.5% had a family history of endometriosis, and 1 of them confirmed that a family member had TES. 34 women (85%) were treated with hormonal therapy. 40% of women had comorbidities – the most prevalent were hypothyroidism (50%), insulin resistance(31.3%), asthma (25%), and nodular goitre (18.3%). Progestogens and combined oral contraceptives were the most commonly used, 74.5% and 35.3% respectively. GnRH agonists and among progestogens – dienogest were the most effective in control of recurrent CP (40% of 5 and 30.8% of 26 women). All hormonal drugs alleviated pain. 62.5% of women supplemented vitamin D, 12 of which had previously confirmed insufficiency. Those with insufficiency understandably had higher mean vitamin D dosage (3273 IU vs 2354 IU). Due to hormonal treatment, it was difficult to determine the independent influence of supplementation on symptoms, however, those without hormonal treatment did not notice any changes. 27 women had been pregnant, 7 of whom had miscarriages, but only 2 had not been able to become pregnant again. 35% of all women had been treated due to infertility. 57.5% changed their diet after the diagnosis – the most common changes were an anti-inflammatory diet, sugar withdrawal, and red meat withdrawal. 6 patients had not used hormonal therapy when they changed their diet – most of them did not notice any changes or symptoms appeared more often.
Conclusions
The most prevalent comorbidity with TES is hypothyroidism. The most effective treatment strategies are GnRH agonists and progestogens. All hormonal drugs alleviate pain in TES. Vitamin D supplementation did not change the course of the disease. Infertility is common among TES patients.

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EP549

Premature ovarian failure after cancer treatment: surveillance and management

Mariana Lopes-Pinto[1], Raquel Calheiros[2], Sara Santos[2], Isabel Inácio[2], Pedro Souteiro[2], Joana Oliveira[2], Ana P Santos[2] & Isabel Torres[2]
[1]Unidade Local de Saúde de Santa Maria, Hospital de Santa Maria, Endocrinology Department, Lisbon, Portugal; [2]Instituto Português de Oncologia do Porto Francisco Gentil, Endocrinology Department, Porto, Portugal

Introduction
Cancer treatment including oophorectomy, radiotherapy and chemotherapy with gonadotoxic agents may induce premature ovarian failure. Early diagnosis and treatment of ovarian failure avoids cardiovascular disorders, osteoporosis and compromised sexual health due to estrogen deficiency and also ensures growth and pubertal development in children.
Aim
Raise awareness for early assessment and management of premature ovarian failure after cancer treatment.
Methods
A retrospective longitudinal study was performed by analysis of medical records of patients with premature ovarian failure due to cancer treatment followed at our centre. Demographics, primary tumour clinicopathological data, cancer treatment details, clinical and biochemical features of hypogonadism, puberty induction requirement and hypogonadism treatment were analysed.
Results
Twenty-one women with previously diagnosed ovarian failure due to cancer treatment were included. Median age at cancer diagnosis was 8 years (minimum: 6 months, maximum: 39 years); at last follow-up median age was 17 years (minimum: 9 years, maximum: 44 years) and one was deceased. Hematological and solid malignancies were documented as primary tumours, the former being more frequent: acute lymphocytic leukemia ($n=6$), acute myeloid leukemia ($n=2$), non-Hodgkin lymphoma ($n=2$) and chronic myeloid lymphoma ($n=2$). All patients underwent chemotherapy, four were also submitted to abdominal or pelvic radiotherapy and one underwent additional unilateral oophorectomy due to small cell carcinoma of the ovary. The mean dose of radiotherapy used was 39.5 Gy $\pm$ 10.3 (SD). Eighteen cases underwent chemotherapy in context of conditioning regimens for hematopoietic stem cell transplant. Gonadotoxic drugs were used in 19 patients, the most common agents were cyclophosphamide ($n=15$), busulfan ($n=13$), cisplatin ($n=3$), melphalan ($n=2$) and carboplatin ($n=2$). Primary or secondary amenorrhea had been described in 11 and 7 cases respectively. Mean FSH at diagnosis of premature ovarian failure after cancer treatment was 74.7 $\pm$ 8.5 (SD) mUI/ml. At last follow-up, 3 patients had completed puberty induction and 5 patients were under therapy for puberty induction with estrogen patch. Vigilance of spontaneous pubertal development was described in 3 girls under 14 years with gonadotrophin levels suggestive of primary ovarian insufficiency. Regarding maintenance hormone therapy, 2 patients were treated with estrogen patch and oral progestin, 2 were treated with oral estradiol/progesterone replacement therapy regimens, and 7 were under oral combined contraceptive pill.
Conclusion
Assessment of ovarian function must be performed after cancer treatments with potential risk of inducing ovarian insufficiency. Sex hormones replacement strategies vary according to pubertal development and prevent estrogen deficiency effects.

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EP551

PCOS phenotypes and their relationship to aldosterone levels

Chiara Sabbadin[1], Luciana Bordin[2], Loris Marin[2], Alessandra Andrisani[2] & Decio Armanini[1]
[1]University Hospital of Padua, Endocrine Unit, Padua, Italy; [2]University Hospital of Padua, Department of Women's and Children's Health, Padua, Italy

Objective
Polycystic ovary syndrome (PCOS) phenotypes, generated by the possible combinations of the three Rotterdam diagnostic criteria, show a different scale of metabolic risk among PCOS women, being greatest in the classic subgroup, followed by the ovulatory and normoandrogenic phenotype. Aldosterone is an important cardiovascular risk factor. Previous studies reported increased levels of aldosterone in PCOS women, suggesting a possible role in the development of some cardiometabolic alterations.
Aim of the study
To evaluate the possible differences of aldosterone levels among the three PCOS phenotypes.
Protocol and Methods
100 women with PCOS meeting Rotterdam criteria underwent the following hormonal and metabolic evaluations in the early follicular phase: FSH, LH, testosterone, androstenedione, DHEAS, orthostatic aldosterone and renin, total cholesterol, high density lipoprotein cholesterol, triglycerides, glucose and insulin response to oral glucose tolerance test. 17 healthy women, matched for age and BMI, were considered as the control group.
Results
Women belonging to the classic phenotype (40%) show the worst clinical-metabolic picture, being more obese, insulin-resistant, and hirsute and presenting dyslipidemia. Patients with the ovulatory phenotype (37%) show metabolic alterations similar to the classic subgroup, but have lower systolic blood pressure, waist circumference, and triglycerides levels. Patients with normoandrogenic phenotype (23%) have a metabolic profile similar to controls. Aldosterone levels follow this trend, being significantly increased only in classic and ovulatory subgroups.
Conclusions
Classic and ovulatory PCOS phenotypes show more metabolic alterations and higher aldosterone levels compared to normoandrogenic phenotype. Aldosterone could play a certain role in the increased cardiometabolic risk associated to these PCOS phenotypes.

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EP571

Short and long-term efficacy of minoxidil on beard growth in a group of assigned female at birth transgender people on gender affirming hormone therapy

Lorenzo Marinelli[1], Andreina Bichiri[1], Ezio Ghigo[1] & Giovanna Motta[1]
[1]University of Turin, Department of Medical Sciences, Turin, Italy

Introduction
Minoxidil is a vasodilator drug used as topical treatment of androgenetic alopecia; however, its efficacy for beard enhancement is reported in cisgender men and in a case-report of a transgender assigned female at birth (t-AFAB) adolescent. This study aims to evaluate the short- and long-term efficacy of topical minoxidil in a group of *t*-AFAB people on gender affirming hormone therapy (GAHT) with testosterone.
Materials and methods
Sixteen *t*-AFAB clients with an uncomplete beard development, on GAHT for at least for 6 months, were enrolled at CIDIGEM gender team, Turin. They used Minoxidil 2% 2 ml/day on the interested facial areas for at least 3 consecutive months. Before starting (T0), after 3 (T3) 6 (T6) and 12 months (T12) we evaluated facial hair growth using Ferriman-Gallwey modified score (FGm). Hair gowth pattern and side effects were subjectively reported.
Results
At T0, recruited clients were 26 (2.7) years old, and they were on GAHT for 18,5 [15-54] months; we observed a FGm of 2 [1-2] at the prolabium and 2 [1-2] at the chin. Compared to T0, we observed a statistically significant difference on the pair matched evaluation at T3 (median prolabium FGm 3 [2.25-4] and chin 3.5 [3-4]; $P < 0.05$) and at T6 (FGm 3.5 [3-4] - prolabium and 4 [3.25-4] - chin; $P \leq 0.002$). No major side effects were reported. At T6 73% of the sample stopped minoxidil. At T12 we observed substantial stability of the obtained results (chin FGm 4 [3.75-4] and prolabium FGm 4 [3-4]; $P > 0.05$), even if 2 people reported a slower hair growth since suspension. The other 27% kept using minoxidil due to unsatisfaction of the results or fear of regression.
Conclusion
The use of Minoxidil 2% in a group of t-AFAB people on GAHT showed at 3 and 6 months of use a significative beard growth enhancement. Stopping the therapy at 6 months seemed to maintain the obtained improvements during the subsequent months even if the beard speed growth may be impaired.

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EP576

Combined klinefelter and down syndrome – challenges of testosterone replacement therapy

Kristina Groti Antonic[1,2], Mojca Jensterle[1,2] & Andrej Janez[1,2]
[1]University Medical Center Ljubljana, Department of Endocrinology, Diabetes and Metabolic Diseases, Ljubljana, Slovenia; [2]Faculty of Medicine, Ljubljana, Slovenia

Introduction
Double aneuploidies are extremely rare. Klinefelter syndrome is a chromosomal disorder characterized by an extra X chromosome in male cells - approximately 80% are 47,XXY; the remaining 20% are mosaic 47,XXY/46,XY. Down syndrome is caused by trisomy of chromosome 21. The prevalence of Klinefelter syndrome is approximately 1 to 2.5 per 1000 boys and men (0.1 to 0.25 percent). The incidence of Down syndrome is approximately 1 in every 990 live births across Europe (10.1 per 10,000 live births). Both chromosomal abnormalities rarely occur together; calculated incidence is 0.4-0.9 per 10000 male newborn. Patients with Down syndrome exhibit characteristic features at birth, while features of Klinefelter syndrome might not be apparent until puberty. Typical Klinefelter syndrome clinical features are tall stature with long extremities, small testes, and learning disabilities. Patients with Klinefelter syndrome have impaired gonadal function resulting in testicular atrophy and hypergonadotropic hypogonadism and azoospermia.
Case presentation
The phenotypic characteristics of a 28-year old man showed the presence of features of Down syndrome. The family had no known history of chromosomal abnormalities or other syndromes. At first visit to pediatrician he presented with midfacial hypoplasia and dermatologic disorders (folliculitis), but without accompanying congenital heart defects, hypothyroidism, diabetes or renal disease. During follow-up, he presented decreased bone mineral density, normal body weight and height, and gastroesophageal reflux disease. He had a global developmental delay, small testes by age 12. At the age of 13 he started testosterone treatment with 1000 mg testosterone undecanoate/3 months and supplementation with vitamin D and calcium. Five years later testosterone dose was decreased to 750 mg/3 months because of the worsening skin inflammation. At the age of 25 he was transitioned to adult endocrinologist. Following the altered behavior as a side effect of testosterone therapy in spite of normal serum testosterone concentrations, his therapy was switched to transdermal testosterone. Examinations within the last 12 months show that the patient has not developed diabetes, cardiovascular or autoimmune complications. Thyroid function is normal, abdominal ultrasoud showed hepatic steatosis, cardiologist reported no abnormalities.
Conclusions
Double aneuploidy with Down-Klinefelter syndrome, as seen in our case, usually presents in the neonatal period with the clinical features of Down syndrome, while features characteristic of Klinefelter syndrome appear later. Both aneuploidies have a potential to weaken or enhance each other. In the presence of typical features of Down syndrome, we highly recommend proceeding with chromosomal analysis.

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EP592

Low dose sublingual estradiol decreases protein s, generating a potentially pro-thrombotic state: interim results of a controlled prospective pilot study of treatment-naïve trans women

Shelly Bar On[1,2], Iris Yaish[1], Merav Barzilai[2,3], Yona Greenman[1,2], Guy Gindis[1,2], Yaffa Moshe[1] & Karen Tordjman[1,2]
[1]Tel Aviv Sourasky Medical Center Institute of Endocrinology and Metabolism, Institute of Endocrinology, Metabolism, and Hypertension, Tel Aviv, Israel; [2]Tel Aviv University, Faculty of Medicine, Internal Medicine, Tel Aviv, Israel; [3]Rabin Medical Center, Campus Beilinson, Institute of Hematology, Petha Tikva, Israel

Background
Sublingual estradiol (E) for gender-affirming hormone therapy (GAHT) of transgender women (TW) might obviate the need for an anti-androgen, and mitigate pro-coagulant changes. We recently showed that 2 mg E, divided into 4 daily SL doses (SLE), offers no clinical advantage over the same dose given orally in combination with cyproterone acetate (CPA). Furthermore, we showed that after each sublingual administration, serum E2 (sE2) peaked to levels, the likes of which are achieved only during induction of ovulation with gonadotrophins.
Hypothesis and Aim
Given the exceedingly high peak sE2 measured under SLE-GAHT, we hypothesized it could lead to partial acquired Protein S deficiency, a recognized pro-thrombotic state and risk factor for venous thromboembolic events (VTE). Our aim was to assess the hemostatic system under SLE in comparison with the standard combined oral (CO) approach.
Design and Methods
In this ongoing open label study, treatment-naïve TW are assigned in a 1:1 ratio (15 in each arm) to either standard CO (2 mg E2 with 10 mg CPA once daily), or to 2 mg sublingual E divided into 4 daily doses for 6 months (6M). An extensive battery of hemostatic biomarkers, including free Protein S antigen (fPS), are assessed at baseline (BL) and at 6M.
Results
We herein report on 27 subjects (15 CO/12 SLE) who initiated treatment, 17 of whom have already completed it. The median age of the cohort is 20 y (IQR 19-27; range 18-42]. There were no BL differences between the groups. At 6M, none of the hemostatic markers differed between the groups except for fPS, which was significantly lower in the SL group $79.7 \pm 11.6\%$ vs $104.6 \pm 5.6\%$, $P = 0.039$. By paired comparisons for the entire group, fPS decreased from $104.2 \pm 5.2\%$ at BL to $95.8 \pm 5.9\%$ at 6M, $P = 0.003$. This was entirely accounted for by the change in the SLE group, in which fPS went down from $95.7 \pm 10.3\%$ to $79.7 \pm 11.6\%$, $P < 0.001$; with some values reaching the fPS deficiency range. In contrast, fPS, remained unchanged under CO $108.9 \pm 5.7\%$ and $104.5 \pm 5.2\%$, at BL and 6M respectively, $P = 0.153$.
Conclusions
The most notable interim finding was a clinically significant decrease in fPS under low dose SLE. Given the extreme peaks of sE2 we previously reported with this protocol, an acquired deficiency of this natural anti-coagulant was expected. These preliminary findings support our hypothesis and raise the concern that GAHT of TW with chronic SLE might carry an increased long-term risk for VTE.

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EP596

Statural and weight delay revealing pituitary stalk interruption syndrome: a study of 6 cases

Nora Boutatss[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy- University Hassan II, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
Pituitary stalk interruption syndrome (PSIS) is a rare disease. It is defined by congenital anomalies of the pituitary leading to isolated or combined anterior pituitary deficiency. Its pathophysiology is unknown. Radiologically, it is characterized by an MRI showing the association of a thin or absent pituitary stalk, ectopic and/or absent posterior pituitary, and hypoplastic anterior pituitary. Symptoms of PSIS during the neonatal and early childhood period are often overlooked, leading to delayed diagnosis.
Objective
To describe the clinical, hormonal, and radiological manifestations of PSIS.
Patients and Methods
A retrospective descriptive study, including 6 patients hospitalized in the Department of Endocrinology and Metabolic Diseases at Ibn Rochd University Hospital in Casablanca for statural and weight delay.
Results
SIX cases of PSIS were collected, consisting of 5 boys and 1 girl. The average age at the first consultation was 14.5 years, ranging from 13 to 16 years. The reason for consultation was statural and weight delay in all patients. Pubertal delay was observed in 3 patients. None of them were born of consanguineous marriage. No history of neonatal incidents, obstetric, or cranial trauma was reported. Physical examination found a micropenis in 2 boys, and bone age was delayed by 2 to 4 years. The hypophyseogram showed isolated growth hormone deficiency (3 cases), combined deficiency (3 cases), and no manifestation of diabetes insipidus. Pituitary MRI revealed a hypoplastic anterior pituitary (4 cases), interrupted pituitary stalk (5 cases), and ectopic posterior pituitary (2 cases). Appropriate hormonal replacement therapy is the only effective means, but the timing of treatment is crucial.
Conclusion
PSIS exhibits significant clinical heterogeneity. The clinical presentation can range from predominantly somatotropic anterior pituitary deficiency to combined deficiencies. Pituitary MRI is crucial for diagnosis. Somatotropic deficiency can be isolated or combined from the outset. Management involves regular monitoring due to the evolving nature of the disease.
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EP598

Association of celiac disease and growth hormone deficiency: a report on 4 cases

Nora Boutatss[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy- University Hassan II, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
Celiac disease and growth hormone deficiency can sometimes coexist, presenting a unique clinical challenge. Celiac disease, an autoimmune condition triggered by gluten consumption in genetically predisposed individuals, can lead to malabsorption and various complications. Growth hormone deficiency (GHD) refers to inadequate production of growth hormone, affecting normal growth and development.
Objective
To explore the association between celiac disease and growth hormone deficiency.
Patients and Methods
This is a retrospective descriptive study based on the records of patients followed in our department for growth retardation (GR), where the diagnoses of growth hormone (GH) deficiency and celiac disease (CD) were established.
Results
Our study focused on 4 patients with an average age of 15.5 years, predominantly male (3 boys and 1 girl). All patients were monitored for celiac disease, with initial positive anti-transglutaminase antibody titers. In the absence of growth despite 3 years of a gluten-free diet, GH deficiency was suspected and confirmed by low IGF-1 levels in all cases. Pituitary MRI was normal in all cases. Management involved initiating substitutive growth hormone therapy, resulting in an average height gain of 1.1 SD±2 SD in the first year.
Conclusion
The coexistence of celiac disease and growth hormone deficiency requires a comprehensive and multidisciplinary approach. Timely diagnosis and appropriate management, including a gluten-free diet and growth hormone replacement therapy, can significantly impact the overall well-being and growth trajectory of affected individuals. Regular monitoring and collaboration between gastroenterologists and endocrinologists are essential for optimal outcomes in such case.
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EP609

Pregnancy planning strategy in a patient with mccune-albright syndrome

Margarita Samsonova[1], Yulia Absatarova[1], Tatiana Kokorina[1] & Natalya Sviridenko[1]
[1]Endocrinology Research Centre, Moskva, Russian Federation

Background
McCune-Albright Syndrome (MAS) is a rare genetic disorder characterized by polyostotic fibrous dysplasia of the skeleton, "café-au-lait" skin hyperpigmentation, and hyperfunction of endocrine glands. A distinctive feature of the syndrome is the autonomous activation of the ovaries leading to the formation of unilateral, recurring estrogen-producing cysts. Hyperestrogenism in turn causes precocious puberty in girls and anovulation in women with MAS. This work describes a clinical case of MAS in a young female patient with a recurring estrogen-producing ovarian cyst who is planning pregnancy, and discusses the possibility of spontaneous conception against the background of ovulation stimulation using clomiphene citrate and hCG.
Case Presentation
A 21-year-old patient diagnosed with MAS at the age of 3 due to hyperestrogenism, a cyst in the right ovary, and signs of bone fibrous dysplasia. Following diagnosis, she underwent regular examinations to assess disease severity and screen for potential syndrome components. At 6, she started fulvestrant therapy, which was discontinued at 10 due to a fracture of the right femoral neck. At 14, didrogesterone therapy was initiated, leading to a regular menstrual cycle. Currently, the patient is planning pregnancy. The last examination in 2021 at 19 years old showed signs of polyostotic fibrous dysplasia, recurring right ovarian cyst, and hyperestrogenism. Hormonal investigation on the 3rd day of the menstrual cycle showed elevated estradiol levels (1401.6 pmol/l) and reduced gonadotropin levels (FSH - 1.39 IU/l, LH - 0.84 IU/l). Progesterone was 5.2 nmol/l, AMH - 3 ng/ml. Pelvic ultrasound confirmed cystic changes in the ovary with increased volume to 118.5 cm^3. During a consultation with a gynecologist, various pregnancy preparation methods were discussed, including the possibility of natural conception. In case of failure, controlled ovulation induction using clomiphene citrate and hCG, or if necessary, IVF or adnexectomy of the affected ovary, was considered.
Conclusion
Currently, adnexectomy of the affected ovary is a well-known and documented method for achieving pregnancy, and there are reports of successful In vitro fertilization in patients with MAS. Given the rarity of the condition, specialists must choose the most appropriate and safe treatment approach in each individual case, sometimes resorting to unconventional methods. For instance, the use of clomiphene citrate followed by hCG as an ovulation trigger could be a potential strategy to overcome anovulation and achieve pregnancy in women with MAS suffering from infertility due to unilateral recurring estrogen-producing cysts.
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EP614

Superman-a case report of hyperandrogenemia

Tereza Grimmichova[1,2]
[1]Institute of Endocrinology, Praha 1; [2]Faculty hospital Kralovske Vinohrady and 3rd Faculty of Mediciny of Charles University, Internal Medicine, Praha 10

Introduction
SARMs (Selective Androgen Receptor Modulators) are non-steroidal anabolics and should improve body strength, muscle building and aid in burning excess fat. There have been ongoing clinical trials regarding positive effects of SARMs in patients with cancer cachexia, hypogonadism, benign prostatic hyperplasia, breast cancer, Alzheimeŕs disease, osteoporosis etc. with conflicting results. Liver injury and cardiovascular disease are possible severe side-effects. For these reasons,

SARMs have not been officially approved. Nevertheless, SARMs can be freely purchased on the market as supplements.
Case report
A 29-year-old male was examined due to gynecomastia, which has persisted since puberty. The patient wished to undergo surgical treatment. Medical history: negative. Occupation: croupier in a casino. No history of smoking, alcohol, or drugs. On physical examination: 179 cm, 89 kg, BMI 27.8 kg/m^2, muscular constitution, gynecomastia negative. Breast ultrasound described chronic signs of gynecomastia. Laboratory results: Cholesterol 2.78 (2.90-5.00 mmol/l), HDL cholesterol 0.46 (1.00-2.10 mmol/l), LDL cholesterol 2.12 (1.20-3.00 mmol/l), triglycerides 0.53 (0.45-1.70 mmol/l). Liver enzymes: Bilirubin total 9.4 (2.5-21.0 µmol/l), ALT 4.55 (0.17-0.83 µkat/l), AST 1.40 (0.17-0.85 µkat/l), GGT 0.24 (0.17-1.19 µkat/l). Hormonal profile: LH $<$0.1 (1.7–8.6 IU/l), FSH 0.1 (1.5–12.4 IU/l), testosterone (TST)$>$ 100.00 (10-34 nmol/l), free TST (calculated using TST, SHBG, albumin) 3507.5 (168-735 pmol/l), Free Androgen Index (FAI) (TST/SHBG) 4347.83 (30-150%), dihydrotestosterone 7.96 (0.90-3.60 nmol/l), estradiol 0.579 (0.0948–0.223 nmol/l), androstendion 87.80 (2.16-10.90 nmol/l), progesterone 0.862 (0.00–0.474 nmol/l), and SHBG 2.3 (7.9-38.2 nmol/l). The patient admitted using SARMs for body-building purposes. Laboratory results after stopping SARMs: normalization of the liver enzymes. Hormonal profile: LH $<$0.1 IU/l, FSH $<$0.1 IU/l, TST 47.04 nmol/l, free TST 1613.7 pmol/l, FAI 855.27%, SHBG 5.5 nmol/l. The patient conceded using also TST i.m. weekly and discontinued his follow-ups.
Conclusion
SARMs should have more selective effects (more anabolic and less androgenic) with less side-effects when compared to testosterone. Clear evidence is lacking, and persons, especially the male population should be advised of the potential for harm.

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EP616

Identification of hCG- and LH-dependent ovarian luteoma resulting in marked androgen production during pregnancy states as well as after menopause: characterization *in vivo* and in a human ex vivo model

Mads Jorsal[1], Sam Kafai Yahyavi[1,2], Christine Hjorth Andreassen[1], Hanne Frederiksen[2,3], Anders Juul[2,3,4] & Martin Blomberg Jensen[1]
[1]Copenhagen University Hospital - Herlev and Gentofte, Division of Translational Endocrinology Department of Endocrinology and Internal Medicine, Herlev, Denmark; [2]Copenhagen University Hospital – Rigshospitalet, Department of Growth and Reproduction, Copenhagen, Denmark; [3]Copenhagen University Hospital – Rigshospitalet, International Centre for Research and Research Training in Endocrine Disruption of Male Reproduction and Child Health (EDMaRC), Copenhagen, Denmark; [4]University of Copenhagen, Copenhagen, Department of Clinical Medicine, Denmark

Context
Steroid hormone-producing tumors account for 0.1% of all primary ovarian tumors. According to the cellular origin they are classified into stromal luteomas, Leydig cell tumors and steroid tumors not otherwise specified. Symptoms and phenotype depend on the specific hormones and concentrations released from the tumor. In this report, we present a postmenopausal woman with virilization during two pregnancies and in menopause caused by an androgen producing ovarian tumor. LH and hCG dependency were demonstrated by treatment with a GnRH agonist prior to surgery and following bilateral salpingo-oophorectomy treatment with FSH, LH and hCG in an ex vivo tissue culture model.
Case description
A 61-year-old postmenopausal woman was referred to our clinic with progression of symptoms including hirsutism, hair loss, deepening of voice, depression, clitoromegaly and android muscle appearance throughout 18-months. Interestingly, during her two successful pregnancies, she developed hirsutism and deepening of the voice. The hirsutism regressed postpartum, while the deepened voice frequency sustained. Blood tests in our clinic revealed normal serum levels of estrogen and gonadotrophins compatible with her postmenopausal status, but elevated serum concentrations of androgens with testosterone levels around 15 nM. A CT scan of thorax and abdomen showed no sign of tumors. However, vaginal ultrasound revealed a process in the right ovary. To further evaluate the tumor, the patient was treated with a GnRH agonist, resulting in androgens being suppressed to levels appropriate for postmenopausal women, thus indicating that the hormone production was dependent on gonadotrophins. To alleviate her condition, she underwent bilateral salpingo-oophorectomy. One tumor was found in each ovary. Histological examination concluded that the most likely diagnosis was stromal luteoma. Tissue cultures from the right ovary showed a several fold increase in testosterone, 17-OHP and androstenedione production upon stimulation with hCG or LH. These findings are consistent with the serum levels and phenotypic changes occurring from elevated hCG levels during pregnancy as well as increased LH levels after menopause. Following the operation, the patient experienced improvements in all prior symptoms consistent with the normalization of androgen serum levels.
Conclusion
Stromal luteomas are a rare finding constituting only 20-25% of steroid cell tumors. Of these, only 12% present with androgenic symptoms making this case a rare finding. Identifying these tumors are difficult since symptoms may only occur in situations where gonadotrophins are elevated i.e., pregnancies and menopause. Our data suggest that androgen producing stromal luteomas can be treated with surgery or GnRH agonist.

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EP626

Is the deficiency in secondary sex characteristics a potential manifestation of SPENCD (Spondyloenchondrodysplasia)?

İrem Yıldız İçli[1], Alperen Onur İşler[2], Nur Evşan Boyraz[1], Deniz Cagdas[3], Levent Kılıç[4] & Alper Gürlek[2]
[1]Hacettepe University School of Medicine, Department of Internal Medicine, Ankara, Turkey; [2]Hacettepe University School of Medicine, Division of Endocrinology and Metabolism, Department of Internal Medicine, Ankara, Turkey; [3]Hacettepe University School of Medicine, Department of Pediatric Immunology, Ankara, Turkey; [4]Hacettepe University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Ankara, Turkey

Background
Spondyloenchondrodysplasia (SPENCD) is a rare autosomal recessive skeletal dysplasia characterized by radiolucent spondylar and metaphyseal lesions, representing the persistence of chondroid tissue islands within the bone. Besides skeletal abnormalities and short stature, autoimmune disorders, including systemic lupus erythematosus, Sjögren's syndrome, hemolytic anemia, thrombocytopenia, hypothyroidism, inflammatory myositis, Raynaud's disease, and vitiligo, have been reported to occur in this disease. In here, we present a patient with insufficient secondary sex characteristics, despite having normal testosterone levels.
Case
A 21-year-old patient, born at term to healthy parents from same town after an uncomplicated pregnancy, presented with complaints of paleness, arthritis in his right first metacarpophalangeal joint, and arthralgia involving his left knee, both ankles, elbows, and neck at the age of 4. Laboratory examination revealed anemia, hypocomplementemia, hematuria, and proteinuria. ANA, anti-dsDNA antibody, and lupus anticoagulant were positive. Renal biopsy confirmed class IV lupus nephritis. The endocrine work-up was normal. Homozygous mutation in the ACP5 gene led to the diagnosis of SPENCD. Treatment with various immunosuppressive protocols, including hydroxychloroquine, methylprednisolone, cyclophosphamide, and mycophenolate mofetil, resulted in improvement over a 17-year follow-up. When the patient presented to our clinic at the age of 21, clinical and laboratory findings were consistent with activation of lupus, prompting renewed immunosuppressive treatment. During hospitalization, clinical examination suggested hypogonadism. The patient reported a history of erectile dysfunction, decreased libido, absence of morning erections, loss of body hair, and reduced shaving frequency. His height was 146 cm, arm span length was 148 cm, apex-pubis length was 65 cm, and pubis-heel length was 81 cm. Testicular volume was 12 ml for both testes, and penile length measured 7.5 cm. Pubic hair was at Tanner stage 4. Laboratory examination showed a testosterone level of 515 ng/dl (197-669), with FSH, LH, IGF-1, and other anterior pituitary hormones within normal range. Short stature was considered a manifestation of the primary disease. TSH and free T4 values were normal, but anti-TPO and anti-TG values were elevated. Thyroid ultrasound revealed findings consistent with thyroiditis.
Conclusion
Despite normal testosterone levels, inadequate development of secondary sex characteristics and sexual dysfunction may be newly identified features of SPENCD syndrome. ACP5 defect may lead to immune dysregulation. As the patient was under immunosuppressive therapy, lymphopenia and hypogammaglobulinemia were attributed to secondary immunodeficiency. Although FSH and LH levels were normal, autoimmune orchitis will be further evaluated. Resistance at the receptor level by receptor specific autoantibodies may contibute to the pathophysiology.

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EP637

Defining the normative cut-off for hirsutism in unselected populations: cluster analysis

Asmamaw Bizuneh[1,2], Anju Joham[1,3], Chau Thien Tay[1,3], Arul Earnest[4], Larisa Suturina[5], Xiaomiao Zhao[6], Alessandra Gambineri[7], Fahimeh Tehrani[8], Bulent Yildiz[9], Jinju Kim[10], Liangzhi Xu[11], Christian Makwe[12,13], Helena Teede[1,3] & Riccardo Azziz[14,15,16]
[1]Monash Centre for Health Research and Implementation, Faculty of Medicine, Nursing and Health Sciences, Monash University, 3168 Victoria, Australia; [2]School of Nursing, College of Health Sciences, Woldia University, 400, Woldia, Ethiopia; [3]Department of Endocrinology and Diabetes, Monash Health, Clayton, Victoria, Australia; [4]School of Public Health and Preventive Medicine, Monash University, 3004 Victoria, Melbourne, Australia; [5]Department of Reproductive Health Protection, Scientific Center for Family Health and Human Reproduction, Irkutsk, 664003, Russian Federation; [6]Department of Reproductive Medicine, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, 106 Zhongshan 2nd Road, Guangzhou, 510080, China; [7]Department of Medical and Surgical Science-DIMEC Endocrinology Unit, University of Bologna - S. Orsola-Mapighi Hospital, Italy; [8]Reproductive Endocrinology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences Tehran, Iran; [9]Division of Endocrinology and Metabolism, Hacettepe University of Medicine in Ankara, Turkey; [10]Division of Reproductive Endocrinology, Department of Obstetrics and Gynecology, Healthcare System Gangnam Center, Seoul National University Hospital, Republic of Korea; [11]Department of Obstetrics and Gynecology West China Second University Hospital Sichuan University, Chengdu 610041, China; [12]Department of Obstetrics and Gynaecology, College of Medicine, University of Lagos, Idi-Araba, Lagos, Nigeria; [13]Department of Obstetrics and Gynaecology, Lagos University Teaching Hospital, Idi-Araba Lagos, Nigeria P.M.B. 12003, Surulere, Lagos, Nigeria; [14]Departments of Obstetrics and Gynaecology, and Medicine, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA; [15]Department. of Healthcare Organization and Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, Alabama, USA 35294; [16]Department of Health Policy, Management, and Behaviour, School of Public Health, University at Albany, SUNY. Rensselaer, New York, USA 12144

Background
Hirsutism, characterized by the male pattern distribution of terminal hair in females due to elevated androgen levels, is a diagnostic feature for polycystic ovary syndrome (PCOS), assessed by the modified Ferriman-Gallwey (mFG) score. The 2023 international PCOS guideline suggests an mFG score of 4-6 for hirsutism detection. However, the lack of universally applicable cut-offs in diverse populations necessitates further research. Therefore, this study aimed to define ethnicity-specific normative cut-offs employing the unsupervised clustering methods (K means clustering) in unselected populations.
Methods
The study utilized data from 12,192 participants aged 12 to 80 years. Data were obtained from community-based studies that were conducted in different countries including China, Iran, Italy, Nigeria, Russia, South Korea, Turkey, and the United States of America. K means cluster analysis ($k=2$) and the receiver operating characteristics curve were used to determine the normative cut-offs for the mFG score. The 75th, 85th, 90th, and 95th percentiles were identified and compared between ethnicities.
Results
The mean ($\pm$SD) age of the total population was 32.7 ± 10.7 years and the mean BMI was 24.1 ± 5.5 kg/m^2. The median (IQR) mFG score of the total population was 1 (0-3). The mFG cut-off scores vary widely across different ethnic groups, ranging from 3 to 9, with the highest scores observed among people of the Persian ethnicity (cut-off = 9), followed by White Italians and Black Africans (cut-off = 7), and Asian Chinese/Han and White Turkish (cut-off = 5). Within the hirsute cluster, the median values for various PCOS-related parameters including mFG score, total testosterone, free testosterone, free androgen index, left ovarian volume, right ovarian volume, and menstrual cycle days (length) were significantly higher compared to the non-hirsute cluster. The finding revealed a highly statistically significant difference ($P<0.001$) when comparing the median mFG score, percentiles (75th, 85th, 90th, and 95th), and the mFG cut-off for each ethnic group.
Conclusions
This finding underscores the notable variation in both the distribution and the normal cut-off values for hirsutism, as determined by the mFG score, across diverse ethnicities. Notably, the highest cut-off values were observed in the Persian population, White Italians and Black Africans. The finding suggested a nuanced picture, urging clinicians to move beyond a similar mFG cut-off point and consider the unique ethnic context for optimal diagnostic accuracy in detecting clinical hyperandrogenism.

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EP643

Impact of polycystic ovary syndrome on health related quality of life in correlation with marital status: a multinational cross-sectional study

Elleuch Mouna[1], Elloumi Yesmine[1], Ben Salah Dhoha[1], Boujelben Khouloud[1], Krichen Zeineb[1], Ellouze Roua[1], Mnif Fatma[1], Mnif Mouna[1], Charfi Nadia[1], Hadj Kacem Faten[1], Abid Mohamed[1] & Mejdoub Nabila[1]
[1]Hospital of Hedi Chaker

Background and Aims
The Rotterdam criteria are the most accepted criteria for the diagnosis of polycystic ovary syndrome (PCOS). The aim of this research work is to study the quality of life of Tunisian and French women with PCOS according to their marital status.
Methods
A cross-sectional study involved 172 women with PCOS. Data collection was based on telephone interviews with tunisian patients who were diagnosed with PCOS based on rotterdam criteria and french patients via Google Forms over an international group specifically for women with PCOS. A quality-of-life questionnaire specific to polycystic ovary syndrome that exists in two forms. PCOSQ-42 for single women and PCOSQ-47 for married women. Both of them have 5 domains. The responses are rank-transformed and presented as scores.
Results
The mean age of tunisian patients was 28 ± 5.9 years while the mean age of french patients was 26.39 ± 4.3 years. 44 tunisian patients were married and 44 french patients were married. The study of HRQoL by domain had shown that the domain of menstrual disorders and fertility was the most affected in single women indicating a low mean score ($2.84\pm0,8$). Whereas the adaptation domain reported the highest mean score (3.38 ± 0.8). Married women's quality of life was more impaired than single women's: 48.31% had marked impairment of HRQoL and 39.33% had marginal or moderate impairment of HRQoL. The lowest mean score was in the psychological and emotional state domain (2.86 ± 0.7). The highest mean score was in the fertility and sex life domain (3.26 ± 0.9). So this was the domain with the least impairment.
Conclusions
PCOS contributes to an overall diminished HRQo. These results may have implications for the clinical practice and suggest the need for specific interventions in women with PCOS.

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EP644

Eating disorders in patients with polycystic ovary syndrome: in correlation with marital status

Elleuch Mouna[1], Yesmine Elloumi[1], Ben Salah Dhoha[1], Boujelben khouloud[1], Krichen Zeineb[1], Ellouze Roua[1], Fatma Mnif[1], Mouna Mnif[1], Faten Haj Kacem Akid[1], Nadia Charfi[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hospital of Hedi Chaker

Background and Aims
Polycystic ovary syndrome (PCOS) may be the most common endocrine disorder in women of reproductive age. Most research findings suggest that PCOS is associated with eating disorders (ED). The aim of this research work is to study the eating disorders in women with PCOS.
Methods
A cross-sectional study involved 172 women, 101 of them are Tunisian and 71 are French. Data collection was based on telephone interviews with Tunisian patients who were diagnosed with PCOS based on Rotterdam criteria and French patients via Google Forms over an international group specifically for women with PCOS. The study was based on a Sick control one stone fat food (SCOFF) questionnaire. It is available in two forms for married and unmarried patients. The responses are rank-transformed and presented as scores. It is based on two parts. The first part consisted of questions on socio-demographic data. The second part consists of a questionnaire for assessing the quality of life of PCOS patients.
Results
The results showed that the average age of the participants was 27.34, with extremes ranging from 14 to 49. More than half were Tunisian (58.72%) and married (51.74%). The majority of women (70.93%) had an eating disorder like anorexia nervosa or bulimia nervosa type. 79.52% of single women had an ED. 62.92% of married women had an ED. ED was more frequent in single women than in married women ($P=0.01$).
Conclusions
This study indicates that the prevalence of eating disorders is increased among women with PCOS compared to healthy women These findings suggest that it should be necessary to pay attention to the screening of eating disorders.

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EP645

Ethnic disparities in PCOS consultations: findings from a multinational study highlighting variances in assessment and education

Raghavendar Palani[1], Anisah Ali[2], Alexander Wilde[3], Lucy Murphy[3], Ashwin Joshi[3], Isin Yesim Yesilkaya Baylan[4], Erkut Attar[4], Fahrettin Kelestimur[4], Meri Davitadze[5,6], Punith Kempegowda[6,7], Eleni Armeni[1] & PCOS Seva Working group[7]
[1]Royal Free Hospital, United Kingdom; [2]University of Birmingham Medical School, United Kingdom; [3]South Tyneside NHS Foundation Trust, United Kingdom; [4]Yeditepe university, Turkey; [5]Clinic NeoLab • კლინიკა ნეოლაბი, T'bilisi, Georgia; [6]Institute of Applied Health Research, United Kingdom; [7]Queen Elizabeth Hospital Birmingham, United Kingdom

Objective
To explore whether assessments recommended by the International PCOS guidelines during the initial consultation for PCOS varied by ethnicity.
Methods
This retrospective multi-centre study was conducted from June 2023 to January 2024. All women aged >18 who attended their first consultation in a dedicated PCOS clinic from January 2020 to December 2023 in the UK ($n=359$), Turkey ($n=239$), Greece ($n=92$), and Georgia ($n=10$) were included. Those undergoing follow-up or without PCOS were excluded. Data was collected on socio-demographic variables including ethnicity, and assessments, including diagnosis based on guidelines, cardiometabolic risk, dermatological assessment, emotional well-being, long-term risk education, lifestyle management, and reproductive screening. Descriptive statistics were analysed using SPSS 28.0.
Results
75.5% were White, 4.3% were Asian, 10.3% were Black, mixed, or other groups, and 9.7% preferred not to disclose their ethnicity. The most common reasons for referral were irregular periods (65.7%), excess hair growth (61.1%), and acne (38.9%). Irregular periods, excess hair growth and acne were all higher in the White group (prevalence rates, 67.9%, 63.6% and 45.7%, respectively) compared to the Asian group (53.3%, 53.3%, and 13.3%, respectively) and the group of Black, mixed or other ethnic background (66.7%, 54.2%, 15.3%; respectively). The most common co-morbidities were anxiety (9.7%), hypothyroidism (9.0%), and depression (6.7%). The prevalence of anxiety was similar across White (9.81%), Asian (10.0%), and Black, mixed and other (6.9%) groups. Depression was higher in the Asian group (13.3%) compared to White (5.5%) and Black, mixed or other (5.6%) groups. Dermatological concerns and reproductive screening were more commonly assessed in the White group (93.8% and 91.3%, respectively) compared to the Asian and Black, mixed or other groups. Screening for emotional well-being was particularly lower in the Asian (30.0%) and Black, mixed or other groups (22.2%), compared to the White group (70.0%). Similar trends were seen with long-term risk education, which was higher in the White group (56.1%) compared to Asian (23.3%) and Black, mixed or other (9.7%) groups.
Conclusion
There is a significant gap in the parameters assessed according to ethnicity, as recommended by international PCOS guidelines. Specifically, emotional well-being screening and long-term risk education are lower in minority ethnic groups, highlighting the need for a standardised approach to the assessment of PCOS to provide equal patient care.

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EP646

An international multi-centre study highlights a significant gap in the assessment and education provided during PCOS consultations

Amynta Arshad[1], Sahrish Khan[2], Harshal Deshmukh[3], Agatha Chu[3], Angharad James[4], Kyranna Lafara[5], Gesthimani Mintziori[5], Dimitrios Goulis[5], Elmira Abdullayeva[6] & PCOS Seva Working Group[7]
[1]University of Birmingham Medical School, Birmingham, United Kingdom; [2]Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom; [3]Hull University Teaching Hospital, NHS Trust, Kingston upon Hull, United Kingdom; [4]South Tyneside and Sunderland NHS Foundation Trust, Sunderland, United Kingdom; [5]Medical School, Aristotle University of Thessaloniki, Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynaecology, Greece; [6]PCOS and Hirsutism Clinic, Yeditepe University Hospital, Istanbul, Turkey; [7]Institute of Applied Health Research, University of Birmingham, Birmingham, United Kingdom

Objective
To explore the trends over time in several assessments recommended by the International PCOS guidelines during the initial consultation for women with PCOS.
Methods
This retrospective multi-centre study was conducted from July 2023 to January 2024. All women over the age of 18 who attended their first consultation in a dedicated PCOS clinic from 1st January 2020 to 31st December 2023 in the UK ($n=359$), Turkey ($n=239$), Greece ($n=92$) and Georgia ($n=10$) were included. Those undergoing follow-up or without PCOS were excluded. Data was collected on sociodemographics and assessments, including diagnosis based on guidelines, cardiometabolic risk, dermatological assessment, emotional well-being, long-term risk education, lifestyle management, and reproductive screening. Patients were categorised into four groups based on their first consultation date: A (January to December 2020), B (January to December 2021), C (January to December 2022) and D (January to December 2023). Descriptive statistics were analysed using SPSS 28.0.
Results
The most common reasons for referral across all years and centres were irregular menses (65.7%), excess hair growth (61.1%) and acne (38.9%). While irregular menses were the most common reason for referral during the pandemic (B(70.0%), C (65.1%)), women were most referred for hirsutism pre and post-pandemic (A (62.73%), D (68.31%)). The most common comorbidities across all years and centres were anxiety (9.7%), hypothyroidism (9.0%) and depression (6.7%). The most common comorbidity pre- and post-pandemic were depression (12.7%) and anxiety (11.3%), respectively. Interestingly, anxiety and depression were not among the common co-morbidities during the pandemic. During the consultation, the most common parameters assessed across all years and centres were dermatological concerns (92.4%), reproductive screening (83.0%) and lifestyle management (80.4%). Similar trends were screened across all years. Long-term risk management was the least performed recommendation per international PCOS guidelines across all years and centres (56.1%), followed by screening for emotional well-being (59.0%). There were no alterations in the trend for these parameters over time (emotional well-being: A-23.6%, B-61.4%, C-60.1%, D-81%, long-term risk management: A-26.4%, B-59.5%, C-56.3%, D-73.9%).
Conclusion
There is a gap in the assessment and education provided during PCOS consultations, specifically in emotional well-being and long-term risk management. The study emphasises the need for a standardised approach to ensure consistent and comprehensive care. Developing new models of care that prioritise emotional well-being screening and long-term risk education is crucial to addressing these gaps and improving patient outcomes.

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EP647

Beyond the chromosomal tale: hyperandrogenism in turner syndrome patients

Ingrid-Ioana Stafie[1,2], Stefana Bilha[1,2], Otilia-Andreea Tarcau[1], Anca Matei[1,2], Letitia Leustean[1,2] & Cristina Preda[1,2]
[1]Saint Spiridon County Hospital, Iasi, Romania; [2]''Grigore T. Popa'' University of Medicine and Pharmacy, Iasi, Romania

Introduction
Turner syndrome (TS) is a chromosomal disorder that arises due to the complete or partial loss of one sex chromosome, impacting approximately 1 in every 2500 to 3000 female births. The phenotype is attributed to haploinsufficiency of genes on the X chromosome, which are resistant to inactivation. Virilizing symptoms appearing in a patient with TS advocates for an endocrine assessment and karyotyping to ascertain the virilization's etiology, enabling prompt intervention and prevention of further manifestations.
Case report
We present the case of a 22-year-old patient, diagnosed with Turner syndrome at the age of 1 (partial monosomoy of the short arm of the X chromosome, caused by the deletion of a Xp fragment, which included the whole SHOX gene) with short stature, cardiac malformations (operated VSD at 8-years-old) and renal abnormalities (left renal hypoplasia, neurogenic bladder, recurrent urinary tract infections). She was lost to follow-up from the age of 13 until 20 years old, when she returned for hirsutism and hyperandrogenism. The patient exhibited significant hirsutism (Ferriman score 17), mild acne, and shortened fourth metacarpal. Menarche occurred at 14 years of age with regular menstrual cycles of 30-40 days. Additionally, an abnormal upper-to-lower body segment ratio and macrocephaly were noted. Hormonal evaluation showed elevated baseline testosterone at 1.88 nmol/l, with a repeated measurement of 1.65 nmol/l, DHEAS of 534.9 μg/dl, and 17OHP at 1.28 ng/ml. The patient had a normal HOMA index of 1.4, euthyroid status, and negative ATPO antibodies.

Dexamethasone suppression resulted in an 87% decrease in testosterone and an 80% reduction in DHEAS, ruling out a tumor. Synacthen test revealed 17OHP of 2.15 ng/ml and cortisol of 24.1 µg/dl at 60 minutes, excluding congenital adrenal hyperplasia as a hyperandrogenism source. The CT scan revealed no expansive pelvic masses, excluding the presence of gonadoblastoma. MLPA technique revealed no Y chromosome fragment, but conducting FISH test is mandatory for confirmation - ongoing.

Discussions

In Turner syndrome patients with hyperandrogenism, comprehensive investigations, including genetic testing, are vital to exclude malignancies like gonadoblastoma. The presence of Y chromosome material necessitates a multidisciplinary approach involving endocrinology, genetics, and oncology for optimal management and long-term patient care.

Keywords: Turner Syndrome, hyperandrogenism, SHOX gene

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EP699

Micropenis diagnosed in adolescence: etiology and treatement

Fatima Zahra Najioui[1], Ossama Achach[1], Hanae Rachedi[1], Boutaybi Latifa[1], Siham Rouf[2] & Hanane Latrech[2]

[1]Department of Endocrinology-Diabetology and Nutrition, Mohammed VI University Hospital Center, Faculty of Medecine and Pharmacy, University of Mohammed 1st, Oujda, Morocco, oujda, Morocco; [2]Department of Endocrinology-Diabetology and Nutrition, Mohammed VI University Hospital Center, Faculty of Medecine and Pharmacy, University of Mohammed 1st, Oujda, Morocco, Laboratory of Epidemiology, Clinical Research and Public Health, Mohammed VI University Hospital Center, Faculty of Medecine and Pharmacy, University of Mohammed 1st, Oujda, Morocco, Oujda, Morocco

Introduction

Micropenis represents a diagnostic and therapeutic challenge. The Diagnosis is based on the measurement of penile length. Defined by normal structure, abnormal size: -2 standard deviation (SD) below of average of age. The aim of our study is to evaluate the etiological profile and therapeutic efficacy.

Patients and methods

It's a retrospective and descriptive study including 55 childrens and adolescents with micropenis, treated with hormonal therapy followed up in the Department of Endocrinology-Diabetology and Nutrition of Mohammed VI University, Hospital Center, Oujda, in Morrocco, between 2014 and 2023. All patients in our series were received a clinical examination including measurement of penis size, biological evaluation and bone age. The statistical analysis was done by SPSS version 21.

Results

The average age of our study group was 13 ± 7 years. Forty-eights percent of the patients were the adolescents. The most frequent reasons for consultation were the Growth retardation (55%) then testicular abnormality (22%). The mean penile size is -2.40 ± 0.41 SD. Nine percent of the patients have penis anomaly and 25% have testicule anomaly. The luteinizing hormone-releasing hormone (LHRH) test was performed in 38% of the patients. The exploration revealed that idiopathic micropenis is the most frequent etiology (29%), followed by growth hormone deficiency (21%). All patients of our group were put on hormonal treatment. The transdermal dihydrotestosterone was administred at 60% of the patients and 40% at the intramuscular injection of testoterone enanthate. The post treatement evaluation revealed that the mean penile size is -1.39 ± 0.75 SD. Therapeutic efficacy was observed in 70% of patients ($P < 0.05$).

Discussion and conclusion

The Early diagnosis of micropenis is based on a thorough clinical examination of all newborns and infants, for early and appropriate management. The most etiology of Micropenis is idiopathic but it is a diagnosis of elimination. The hormonal treatment is not always effective in the puberty, hence the importance of psychological support.

Key words: Micropenis -Growth Hormone- Testosterone Enanthate.

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EP751

The effectiveness of cognitive behavioral therapy on insomnia severity among menopausal women: a scoping review

Anastasia Ntikoudi[1], Dimitra Owens[2], Athanasios Tsartsalis[3], Alketa Spyrou[1], Eleni Evangelou[1], George Mastorakos[2] & Eugenia Vlachou[1]

[1]University of West Attica, Nursing, Athens, Greece; [2]National and Kapodistrian University of Athens, Athens, Greece; [3]University of West Attica, Athens, Greece

Introduction

Sleep disorders, including insomnia disorder, can affect all aspects of personal life and often occur during perimenopause, menopause, and postmenopause. Data on the number of women who suffer from sleep disorders during menopause range from 28% to 63%. Cognitive behavioral therapy for insomnia (CBT-I) is a multicomponent, drug-free treatment approach that targets behavioral and cognitive factors that contribute to chronic sleep disorders. The aim of this scope review was to evaluate the effectiveness of CBT-I on insomnia severity among menopausal women.

Methods

An extensive literature search was conducted of the Pubmed, Scopus, Cinahl and Medline electronic databases. The search yielded 459 studies, of which 8 eventually met the entry requirements for RCTs.

Results

The majority of the studies included in the current review demonstrated the benefits of CBT-I intervention in the amelioration of insomnia in menopausal women. CBT-I intervention was found to be an efficacious option for the treatment of menopausal women with insomnia with its effect to be sustained over time.

Conclusion

Further studies in larger populations are needed to confirm the effectiveness of CBT-I programs for treating menopausal insomnia.

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EP752

Mixed gonadal dysgenesis; about 5 cases

Brahimi Hanane[1], Iabassen Malek[1] & Bensalah Meriem[1]

[1]Central army hospital, Algiers, Algeria

Introduction

Mixed gonadal dysgenesis is an anomaly of sexual development, it is a rare pathology, associated with a numerical anomaly of the sex chromosomes resulting from mosaicism of the Y or X chromosome and leading to abnormal development of the gonads. The most common chromosomal formulas are 45X/46 XX, 45X/46XY, 46XX/47XXX, and 46XY/47XXY. The phenotype is variable, ranging from a completely feminine appearance of the external genitalia to masculine or ambiguous. The diagnosis is made by the study of the karyotype. Management is based on the search for associated anomalies, the evaluation of gonadal function on which the choice of sex is sometimes based. Long-term monitoring is necessary to look for malignant degeneration and replace hormonal deficiencies.

Reported cases

We report 5 cases presenting mosaicism whose clinical, biological and radiological characteristics are described in the table below:

	Age	Phenotype	Karyotype	HCG stimulation test	Assigned sex
Case 1	2 months	Male with ambiguity	46XX/46XY	Negatif	FEMALE
Case 2	14 months	Female with ambiguity	46XX/47XXY	Negatif	FEMALE
Case 3	19 months	Male with ambiguity	46XX/47XXY	Negatif	FEMALE
Case 4	5 years	Female with ambiguity	45X/ 46XY	Negatif	FEMALE
Case 5	2 months	Female with ambiguity	45X/46XX	Negatif	FEMALE

Conclusion

Mixed gonadal dysgenesis is a rare pathology; in our serie, this condition represents 5% of desorders of sex development (DSD). The diagnosis is made during early childhood by the ambiguous appearance of the external genitalia and the small size in Turner syndrome, confirmed by the study of the karyotype. All cases were assigned to the female gender. The search for comorbidities is mandatory, and the risk of degeneration is not negligible, requiring regular monitoring and rigorous monitoring of tumor markers

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EP766

A zebra among horses – testotoxicosis as a rare cause of peripheral precocious puberty

Viviana Popa[1], Alexandru Florescu[1,2], Andra Berigoi[1], Irina Puscasu[1], Mihaela Florea[1], Stefana Bilha[1,2] & Cristina Preda[1,2]
[1]Saint Spiridon County Hospital, Iaşi, Romania; [2]Universitatea de Medicină şi Farmacie 'Grigore T. Popa' din Iaşi, Iaşi, Romania

Introduction
Testotoxicosis, also known as familial male limited precocious puberty, is a rare cause of peripheral precious puberty caused by an activating mutation of the gene encoding for the LH receptor on Leydig cells (LHCGR gene, cr2p21). This causes autonomous testosterone production irrespective of prepubertal LH values. Ultimately, this can cause psychosocial complications; advanced bone age and low adult height; as well as central precocious puberty.
Case report
We present the case of a 5 year, 8 month old boy that was directed to the Endocrinology Clinic because of increased testicular volume, penile enlargement, and the presence of scrotal, pubic and upper lip hair. Family history was negative for precocious puberty. Clinical examination revealead a height of 119 cm (-0.42 SD) and weight of 20 kg, BMI 14.2 kg/m^2 (normal), Tanner stage 2; and wrist X-ray showed a bone age of 5 years and 6 months. Hormonal evaluation revealead a testosterone level more than 10 times the upper limit of normal for age and sex (7.22 nmol/l), with low FSH and LH levels (0.411 mIU/ml and 0.146 mIU/ml, respectively), even after Triptorelin stimulation (2.33 mIU/ml and 2.68 mIU/ml, respectively). Low 17OH-progesterone levels ruled out congenital adrenal hyperplasia. Testicular or adrenal tumors were excluded based on negative tumor markers and imaging studies; while McCune Albright syndrome and iatrogenic PPP were excluded based on history and physical examination. Therefore, testotoxicosis was diagnosed by exclusion, and treatment with aromatase inhibitors (anastrozole, 0.1 mg/day) and bicalutamide (25 mg/day) was initiated. At 3 month follow-up, no side effects were reported except for mild headache occasionally, and there was regression of pubertal signs. Gonadotropin levels remained low, while elevated testosterone persisted; and bone X-ray didn't demonstrate advancement of bone age. At the moment, genetic studies are underway to identify the causing mutation.
Conclusion
Testotoxicosis is a rare form of PPP, and the limited studies available suggest optimal treatment is with a combination of aromatase inhibitors and antiandrogen medications. Testosterone levels shouldn't be used as a marker for treatment efficacy, as elevated levels can persist; but rather focus should be on gonadotropin levels and decreasing the bone age to chronological age ratio, if advanced at diagnosis. Finally, genetic studies of the child and both parents should be carried out whenever possible, as the causing mutation is usually inherited in an autosomal dominant manner, and females can be asymptomatic carries, but de novo mutations can also occur in previously unaffected families.

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EP771

An unusual case of arrested puberty and management of puberty induction in the adult endocrine clinic

Lee Si Min[1], Fernando Loo Jia Jing[2] & Brenda Lim Su Ping[2]
[1]Changi General Hospital, Singapore, Singapore; [2]Tan Tock Seng Hospital, Singapore, Singapore

Introduction
Puberty is the process of transition from childhood to adult reproductive capability, body composition, and adult height. In males, the lack of Tanner stage progression after achieving a testicular size of at least 4 cubic cm (cc) suggests pubertal arrest. While delayed puberty could be a normal variant, arrested puberty is usually pathological, and points towards an acquired pathology rather than a congenital disorder. We describe an unusual case of arrested puberty from subclinical pituitary apoplexy.
Case report
An 18-year-old male was referred to our adult endocrine clinic with arrested puberty. Initial examination revealed short stature (height 163 cm), eunuchoid body habitus, a high-pitched voice and minimal secondary sexual characteristics (Tanner Stage 1 for pubic hair). Bilateral testes were descended with testicular volumes of 8cc (Tanner Stage 2 for external genitalia). Initial investigations revealed central hypothyroidism (FT4 8.0 pmol/l, TSH 1.54 mIU/l), hypogonadotropic hypogonadism (total testosterone <1 nmol/l, FSH 2 IU/l, LH 2 IU/l) and growth hormone deficiency (GHD) (IGF-1 43 mg/l). The bone age was delayed at 15 years old when the patient's chronological age was 18 years old and 9 months. MRI brain showed a 2.6 cm T1- hyperintense sellar-suprasellar mass with chiasmal compression, suggestive of pituitary apoplexy. Endonasal transsphenoidal marsupialisation was performed and histology revealed necrotic tissue. His post-operative course was complicated by pituitary abscess, requiring surgical drainage. He developed panhypopituitarism and central diabetes insipidus and was treated with thyroxine, hydrocortisone and intranasal desmopressin. Glucagon stimulation test confirmed persistent GHD (peak GH 0.06 mg/l). SC somatropin 1.2 mg daily was initiated to optimise adult height. The patient was counselled regarding options for puberty induction including testosterone replacement or gonadotrophin therapy. He opted for testosterone replacement and was initiated on IM testosterone 50 mg every 4 weeks. Whilst on concurrent growth hormone replacement and puberty induction, he grew 8 cm over 11 months with increase in penile length and progression to Tanner stage 2.
Conclusion
Pubertal arrest is usually pathological. In this case, pubertal arrest was an atypical presentation of subclinical pituitary apoplexy. Puberty induction in an adolescent with delayed presentation of pubertal arrest and hypopituitarism is challenging. It requires careful titration of multiple hormonal regimens to optimise the final adult height, secondary sexual characteristics and bone health.

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EP772

Influence of aromatase inhibitors on metabolic parameters in obese male patient

Shota Janjgava[1], Revazi Jamburia[1], Ana Davitashvili[1], Tekle Bakhtadze[1], Medea Zhgenti[1] & Natia Goletiani[1]
[1]National Institute of Endocrinology, Endocrinology, Georgia

Overview
Numerous epidemiological studies have demonstrated that low testosterone levels are linked to poor life quality and sexual quality, and that hypoestrogenic hypogonadism in obese male patients is connected with and predicts the development of metabolic syndrome and type 2 diabetes in the future. The purpose of the study was to demonstrate how aromatase inhibitors affected anthropometric traits, HOMA-IR, blood pressure, glycosylated hemoglobin level, and dyslipidemia in individuals with hyperechogenic and metabolic syndrome.
Resources and Techniques
85 males with a BMI of 35.83 ± 3.65 kg/m^2 and an age of 35 ± 6.74 were randomly selected among 125 male patients with hypoestrogenism and obesity for a placebo-controlled trial. Patients were split up into three groups: 1) The first group received standard treatment. 2) The second group received standard aromatase inhibitor medication. 3) The third placebo group received standard care along with a placebo. We incorporated life style modification to all groups.
Results
We retook the diagnostic evaluations six months after starting treatment; lipid profile and free testosterone levels improved in all groups, but it was statistically significant in group II. All groups saw a drop in HbA1c, although group II saw the greatest improvement. All groups experienced a decrease in blood pressure, with comparable outcomes.
Conclusion
In obese male patients with hypoestrogenic hypogonadism, our study showed that increasing testosterone and adjusted estrogens can manage blood pressure, lipid profile, HbA1c, and HOMA.

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EP873

Complications of hysteroscopic surgery in gynecology: analysis of frequency and risk factors following 2,650 operations at a single institution

Hee Dong Chae[1]
[1]ASAN Medical Center, Department of Obstetrics and Gynecology, Seoul, Korea, Republic of South

Objective
To determine the frequency of complications after hysteroscopic surgery and to analyze the risk factors associated with these complications.
Materials and Methods
We retrospectively analyzed outcomes in 2,650 patients who underwent hysteroscopic surgery at Asan Medical Center between January 1996 and September 2023.

Results
Indications for hysteroscopic surgery included submucosal myoma on ultrasonography in 910 patients, space-occupying lesion in the endometrial cavity on ultrasonography in 1,392, abnormal uterine bleeding in 57, uterine synechiae in 221, uterine septum in 25, and removal of intrauterine device in 30. Mean patient age was 40 years (range, 12-74 years). One hundred forty eight patients had a previous history of uterine surgery (cesarean section in 128 and myomectomy in 20). Operative complications occurred in 80 patients (3.02%), including 30 with uterine perforations, 38 with excessive bleeding, and 12 with postoperative infections. In univariable analysis, age $\geq$40 years ($P=0.002$), nulliparity ($P=0.008$), and body mass index $<$20 kg/m^2, and distension media volume $\geq$2,040 ml ($P=0.008$) were significantly associated with a higher risk of complications, but menopause, previous history of uterine surgery, use of Laminaria or misoprostol, type of distension media, postoperative compression of the endometrial cavity, and operating time were not. In multivariable analysis, body mass index $<$20 kg/m^2 (OR, 2.97; 95% CI, 1.41-6.22; $P=0.004$) and distension media volume $\geq$2,010 ml (OR, 2.56; 95% CI, 1.22-5.36; $P=0.013$) were significantly associated with increased risk of complications. Of several types of surgical procedures, hysteroscopic polypectomy was associated with significantly lower (odds ratio, 0.367; 95% CI, 0.161-0.835; $P=0.017$) and hysteroscopic adhesiolysis with significantly higher (odds ratio, 3.521; 95% CI, 1.525-8.127; $P=0.003$) risks of complications.
Conclusion
Hysteroscopic surgery is a safe procedure, with a very low (3.02%) complication rate. Body mass index $<$20 kg/m^2 and distension media volume $\geq$2,040 ml, and hysteroscopic adhesiolysis were associated with higher risks of complications, but hysteroscopic polypectomy was associated with a lower risk of complications.
Keywords: hysteroscopy; hysteroscopic surgery; complication; frequency; risk factor

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EP874

The effect of hyperprolactinemia on the hormonal profile of women with recurrent miscarriage

Diyora Mukhammedaminova[1], Sevara Sadrieva[1] & Khurshidakhon Nasirova[1]
[1]Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

Introduction
Hyperprolactinemia is characterized by persistently elevated levels of prolactin in the blood serum, with its most common manifestation being a disruption of the reproductive system. Hyperprolactinemia contributes to inadequate endometrial preparation for pregnancy, insufficient implantation of the fertilized egg, and may also exert pathological effects on the production of gonadotropin hormones.
Objective
To investigate the hormonal status of patients with recurrent miscarriage (RM) in the first trimester with hyperprolactinemia.
Materials and methods
A total of 54 women in the first trimester of pregnancy were selected for this study. Among them, 34 pregnant women experienced RM in the first trimester with hyperprolactinemia, while 20 had a normal course of pregnancy. The average age in the hyperprolactinemia group was 30 ($\pm$4.8) years, and in the control group, it was 28 ($\pm$4.1) years. The main diagnostic materials included the concentration of prolactin, inhibin A, FSH, and LH in the blood.
Results
Analysis of hormonal indicators revealed the following: prolactin concentration in the first trimester in women with RM was significantly higher than normal (4075.7$\pm$1103.2 ng/ml), while in patients with a normal course of pregnancy, it was 1015$\pm$332.4 ng/ml. Patients with RM and hyperprolactinemia showed an increase in the concentration of FSH and LH, which was 16.3$\pm$2.1 mIU/ml and 1.14$\pm$0.54 mIU/ml, respectively, compared to the control group with values of 0.19$\pm$0.19 mIU/ml and 0.66$\pm$0.34 mIU/ml. The level of inhibin A decreased almost twofold (133.9$\pm$13.4 pg/ml) in women with RPL, while in the control group, inhibin A concentration remained within the normal range (617.3$\pm$252.8 pg/ml).
Conclusion
1. Hormonal analysis among women with hyperprolactinemia indicates that an increase in prolactin significantly elevates levels of FSH and LH compared to patients with reference values.
2. Our study revealed that a decrease of inhibin A levels is associated with hyperprolactinemia, indicating a risk of pregnancy loss.
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EP875

Prevalence of polycystic ovary syndrome and infertility in hidradenitis suppurativa

Malek Cherif[1], Rim Chaabouni[1], Fatma Hammami[1], Abdel Mouhaymen Missaoui[2], Khadija Sellami[1], Nabila Rekik[2] & Hamida Turki[1]
[1]Hedi Chaker University Hospital, Dermatology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Endocrinology, Sfax, Tunisia

Introduction & Objective
Hidradenitis suppurativa (HS) is an inflammatory skin condition which predominantly affects women of childbearing age. Various metabolic and endocrine comorbidities can be associated with HS. The aim of this study was to evaluate the association of HS with male and female infertility.
Materials and Methods
We conducted a retrospective study between January 2012 and December 2022 enrolling all cases of HS in our dermatology department. The diagnosis of polycystic ovary syndrome (PCOS) was made in accordance with the revised Rotterdam criteria from 2003.
Results
We identified a total of 77 cases, with an average age of 39 years and a male-to-female sex ratio equal to 4,1. Among 15 women, four (26,7%) experienced fertility issues. The average age was 27,5 years (20-45 years), and in three cases (75%), HS occurred at a pediatric age (below 18 years). The diagnosis of PCOS was confirmed in two patients (13,3%) presenting with moderate to severe obesity (average BMI$=$35 kg/m^2). Clinical presentations included irregular menstrual cycles and late-onset acne, indicative of clinical hyperandrogenism. Besides, hirsutism with an elevated blood testosterone level (3,99 nmol/l) was observed in one other young patient. The fertility assessment conducted in a reproductive-aged patient revealed hyperprolactinemia associated with a pituitary adenoma. HS manifested in these patients with either axillo-mammary (LC1) or follicular (LC2) phenotype (50% each), and classified as Hurley I or II. A treatment plan involving metformin and a dietary supplement containing myo-inositol and folic acid was prescribed for a single patient diagnosed with PCOS and prediabetes (fasting blood glucose level of 1.21 g/l). Finally, five married men (8,1%) reported unexplored infertility and/or sexual impotence.
Conclusions
Based on previous data, patients with HS face an elevated risk of infertility, particularly among females and individuals aged 36 to 45. Both HS and PCOS affect similar demographics, may be complicated by obesity and metabolic syndrome, and respond to antiandrogen agents. Our data align with those of other previous studies, such as the one by Garg *et al*., where the prevalence of PCOS in patients with HS was 9%. According to the adjusted analysis, the risk of PCOS would be twice as high in women with HS, independent of the influence of obesity and diabetes. In addition, because HS involves the inframammary folds, groin, genitals, and buttocks, patients with HS may be at risk for sexual dysfunction, including abnormal sexual function, impairment, and distress.
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EP876

Correlating adiposity with metabolic disturbances in PCOS patients: a single-centre retrospective study

Puja Thadani[1], Bianca Leca[1], Uzma Khan[1], Danielle Bate[1], Allan Davasgaium[2,3], Rajan Mattu[1] & Harpal S. Randeva[1]
[1]University Hospitals Coventry and Warwickshire NHS Trust, Diabetes and Endocrinology, Coventry, United Kingdom; [2]University Hospital Coventry & Warwickshire, WISDEM, United Kingdom; [3]University Hospital Coventry & Warwickshire, WISDEM, Coventry, United Kingdom

Introduction
Polycystic Ovary Syndrome (PCOS) affects 5-10% of childbearing females and, up to 20% in specific ethnic populations (i.e. South Asians and Hispanics). It is linked with a higher prevalence of obesity and metabolic dysfunction, resulting in increased risk for dyslipidaemia, impaired glucose tolerance, type 2 diabetes mellitus (T2DM) and cardiovascular diseases.
Methods
This is a retrospective study of patients diagnosed with PCOS ($n=142$) based on the European Society of Human Reproduction and Embryology (ESHRE) criteria. Data was collected from case notes and electronic records for patients diagnosed from January to December 2019. Medical history, anthropometric and bioimpedance data, including fat percentage (fat%), total fat mass and total fat-free mass, were recorded. Biochemical assessments were carried out in the early follicular phase of the menstrual cycle to assess biochemical androgen excess (Free Androgen Index – FAI) and screen for metabolic co-morbidities. Patients were grouped based on phenotype: A - anovulatory cycles (ANOV), clinical

and/or biochemical hyperandrogenism (HA), and polycystic ovarian morphology (PCO), B (ANOV + HA), C (HA + PCO) and D (ANOV + PCO). Statistical analysis was performed using SPSS statistics version 29.0, considering $P < 0.05$ statistically significant.

Results

The mean age was 29.08 ± 5.95 years. Most women had BMI greater than 40 kg/m^2 (40.6%). Hyperandrogenic PCOS phenotypes were most common: Phenotype A in 51.7%, Phenotype B in 25.2% and Phenotype C in 11.9%. The analysis revealed significant correlations for Fat% in PCOS patients. There was a positive correlation between fat% and age ($r = 0.227$, $P < 0.05$), and a strong positive correlation with the Free Androgen Index (FAI) ($r = 0.292$, $P < 0.01$), indicating higher fat mass is associated with older age and increased androgen levels. Additionally, fat% was positively correlated with total cholesterol (TC) ($r = 0.234$, $P < 0.05$), the TC to high-density lipoprotein ratio (TC: Hdl) ($r = 0.379$, $P < 0.001$), triglycerides ($r = 0.327$, $P < 0.01$) and Haemoglobin A1c (HbA1c) ($r = 0.312$, $P < 0.01$). These correlations suggest that higher body fat percentage may be related to a greater risk of dyslipidaemia and impaired glucose metabolism.

Conclusion

This study showed that adiposity is significantly linked to key metabolic markers such as TC, TC:HDL ratio, triglycerides, and HbA1c, all of which are known risk factors for cardiovascular diseases. It highlights that body fat%, as measured by bioimpedance, is an important variable in the metabolic profile of women with PCOS, with implications for cardiovascular risk and impaired glucose metabolism. These results suggest that monitoring and managing adiposity is essential to reduce cardiovascular and metabolic risk in women with PCOS.

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EP901

Successful testicular descent induced by gonadotropin replacement therapy in young men with congenital hypogonadotropic hypogonadism

Du Soon Swee[1] & Jielin Yew[2]
[1]Singapore General Hospital, Endocrinology, Singapore; [2]Changi General Hospital, Endocrinology, Singapore

Congenital hypogonadotropic hypogonadism is a rare reproductive disorder characterised by isolated deficiency in the secretion or action of gonadotropin-releasing hormone (GnRH). Diminished GnRH activity in the immediate postnatal months, a period known as minipuberty, has severe consequences on the ontogenesis of male reproductive tract. Affected infant boys may present with micropenis and cryptorchidism. Rarely, adolescents with CHH present with delayed puberty in association with cryptorchidism. While the use of gonadotropins to treat CHH-associated cryptorchidism in infancy is increasingly recognised as a safe and effective therapy, there is scarce data on its utility in adolescents or young adults. Indeed, if such treatment is shown to be efficacious beyond childhood, patients could potentially be spared from surgical orchidopexy. We report two young men who had successful hormonal induction of testicular descent. The first case was a 19-year-old male referred for pubertal failure. He had childhood history of micropenis as well as surgery for undescended testes at 5 years old. Testes were, however, not palpable during examination. Penile length was 4 cm, and there was no sign of any secondary sexual characteristics. Ultrasound scan demonstrated undescended testes (Right: 0.6×0.7×0.8 cm, Left: 0.7×0.8×1.3 cm) in the inguinal canal bilaterally. Kallmann syndrome was subsequently diagnosed based on anosmia and hypogonadotropic hypogonadism (FSH 0.4 U/l, LH <0.1 U/l, testosterone 0.78 nmol/l). Sequential gonadotropin therapy was started with hMG (75 IU daily for 4 weeks) followed by combined hMG and hCG therapy, which were up-titrated to 150 IU 3×/week and 1,500 IU 3×/week respectively. Ultrasound repeated 12 months later showed descent of testes into scrotum bilaterally (Right: 0.9×1.1×1.7 cm, Left: 1.0×1.4×2.4 cm). The second case was a young man who was referred at age 22 years for undervirilisation. Both testes were non-palpable. Biochemistry showed FSH 2.3 U/l, LH 0.8 U/l and testosterone 1.4 nmol/l. Ultrasound confirmed bilateral undescended testes in the upper part of the groin area, on either side of the base of penis (Right: 1.4×1.0×0.8 cm, Left: 1.5×1.1×0.7 cm). Patient was first given FSH monotherapy (75 IU, 3×/week) for 4 months, after which hCG was added and up-titrated to 1,500 IU 2×/week. Ultrasound was repeated 8 months later to reassess testicular position, which showed that the descent of testes into the mid-scrotum, along with a threefold increase in the testicular volume. In concordance, serum inhibin B level rose from baseline 21 pg/ml to 61 pg/ml.

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EP911

Reference ranges of total testosterone in eastern algerian men

Sara Kendri[1,2], Sarra Zouai[1,2], Anis Amara Korba[1,2] & Farida Djabi[1,2]
[1]Faculty of Medicine, Ferhat Abbas University, Sétif, Algeria; [2]Central Laboratory, University Hospital of Sétif, Sétif, Algeria

Reference ranges are the most common decision support tool used for results interpretation and so a very relevant part of the laboratory report. Their use has become increasingly prevalent in clinical practice. A low serum testosterone (T) level in combination with clinical signs and symptoms are required for hypogonadism diagnosis. The goal of this research was to establish the reference intervals of total testosterone (TT) from healthy adult males. The study sample consisted of 179 adult males aged 18 – 63 years and stratified into three age groups: 18-33, 34-42, and 43-63 years, with measured serum concentrations of TT by electrochemiluminescence immunoassay (Cobas e411®, Roche diagnostics). The 2.5th to 97.5th percentiles of subjects for TT were used as the normative range with parametric method. The mean serum TT level for the three age groups: 18-33, 34-42 and 43-63 years were 419 ± 139, 387 ± 135 and 379 ± 134 ng/dl respectively. We found a statistically significant age-related decrease for serum concentrations of TT ($P < 0.001$). The population mean TT was 394 ± 136 ng/dl. The 95% reference interval (with 90% confidence interval) of serum TT from all participants ranged from 126 (97-155) to 662 (633-691) ng/dl. We generated reference ranges for total testosterone specific for our population using data from apparently healthy men, that could be used for results interpretation in our laboratory because population-specific reference ranges are needed to understand normal vs abnormal TT levels. This study can be helpful in broader research to calculate age-specific reference ranges and cutoffs of TT for the diagnosis of male hypogonadism.

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EP931

Two sides of the same coin: infertile couple

Elena Moravcikova[1], Helena Urbankova[1], Peter Vanuga[1] & Michal Kulich[1]
[1]National endocrinology and diabetology institute, Endocrinology department, Ľubochňa, Slovakia

Introduction

Our case is a young couple, both endocrinologically monitored from childhood. Woman with diagnosis of oligomenorrhea – secondary amenorrhea. Man with delayed puberty. After complex endocrinological screening both diagnoses was changed to: woman diagnosed with prolactinoma and man with isolated idiopathic central hypogonadism (IICH). They were trying to concieve for 10 years with no succes.

Case

Woman: At 17 years of age diagnosed cystic degenerative pituitary adenoma with compression of the optic chiasm, producing prolactin. Surgery was carried out. After surgery hyperprolactinomia persisted. Treatment with dopamine agonists was introduced. Treatment with bromocriptine was not tolerated with gastrointestine tract. Quinagolide and cabergoline produced insufficient decline of prolactine levels even at maximum dosing. Residuum of tumor showed little growth progress. Primary infertility, persisting secondary amenorrhea and growth of tumor residuum led to second surgery at 30 years of age. Before that she underwent several unsucessful IVF treatment rounds. After surgery MRI scan showed that pituitary tumor was resected completely. Levels of prolactine reached normal values and other pituitary hormones remained functional. Normal menstrual cycle was regained with succesful spontaneous gravidity within one month after surgery. After 3 years second spontaneous gravidity followed. *Man:* Diagnosed with IICH. At 16 years of age diagnosed with delayed puberty with genital hypoplasia. Anosmia was not present. MRI of hypothalamo pituitary area showed no deposit. Cythogenethic survey confirmend normal male karyotype. Also oligoteratozoospermia and spermiogram surveys were carried out. Treatment with chorione gonadotropine with slow enhancement of clinical picture. Treatment of central hypogonadism continued also in adult age.

Conclusion

Woman with pituitary adenoma caused hyperprolactinemia underwent repeated change of medical treatment and two surgeries with complete remission. Man diagnosed with IICH, at first treated with chorionic gonadotropin injection. After second succesful gravidity treatment was changed to DEPO testosterone injection. Two sucesfully treated endocriopathies led to spontaneous gravidity.

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EP943

Implications of x-linked adrenoleukodystrophy in different family members

Luciana Tonkic[1], Tanja Miličević Milardović[1] & Anela Novak[1]
[1]University Hospital of Split, Internal Medicine Department, Endocrinology, Diabetology, and Metabolism Division, Split, Croatia

Adrenoleukodystrophy (ALD) is a monogenic, X-linked hereditary disorder. Mutation in the ABCD1 gene results in the adrenoleukodystrophy protein (ALDP) deficiency which is involved in the intracellular transport and metabolism of very long-chain fatty acids (VLCFAs). Consequently, VLCFAs accumulate in the central and peripheral nervous systems and adrenal glands leading to the destruction of affected tissues and specific symptoms and signs. There are four distinct types of ALD with adrenomyeloneuropathy being an adult variant. We present a male patient who was hospitalized at the age of 47 with a clinical picture of adrenal insufficiency and progressive paraparesis that made him reliant on a wheelchair. The adrenomyeloneuropathy was suspected. Laboratory results showed low serum cortisol level and normal levels of renin and potassium. The VLCFAs analysis showed the elevated concentration of cerotic acid (C26:0) as well as the elevation of cerotic and lignoceric (C24:0) to behenic (C22:0) fatty acids ratios which confirmed the clinical diagnosis. Genetic testing revealed the hemizygous variant of uncertain meaning in the ABCD1 gene [c.251C > T (p.Pro84Leu)]. Replacement therapy with hydrocortisone was started and since renin, potassium, and blood pressure values were normal, there was no need for mineralocorticoid substitution. At the very beginning of the treatment, the patient took smaller doses of glucocorticoids, which did not lead to the neurological improvement. Because of the above, the total daily hydrocortisone dose was gradually increased to 40 mg and he was able to walk with the help of a cane. As our patient had two daughters, genetic counselling and testing were arranged. Both daughters were healthy but heterozygous carriers of the ABCD1 gene mutation. For heterozygous female carriers, the probability for transmission of the affected gene is 50% for both sons and daughters. It should be taken into account that all affected sons develop disease while daughters are mostly mutation carriers. Therefore, planned pregnancy with the preimplantation genetic testing (PGT) and gender selection is a valuable option. PGT involves in vitro fertilization (IVF), biopsy of the blastocyst, and the transfer of the selected embryo into the uterus. PGT is an option for couples who want to avoid gender-related disorders in offsprings and is mostly allowed for medical reasons in different European countries. In our case, despite genetic counselling, the older daughter had an unplanned pregnancy and gave birth to a clinically healthy son (results of genetic testing are awaited). The younger daughter is going to Belgium for a planned pregnancy.

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EP964

Unusual PCOS presentation and/or functional amenorrhea

Tea Shehu[1]
[1]Salus Hospital, Endocrinology department, Internal medicine department., Tirane, Albania

Introduction
Polycystic ovary syndrome (PCOS) is a multifaceted endocrine disorder traditionally classified into four phenotypes. A recently proposed hyper-/hypoandrogenic phenotype (HH-PCOS) falling under the D phenotype introduces additional complexity, emphasizing the spectrum of androgenic manifestations within this heterogeneous syndrome. This case report focuses on the complexities associated with PCOS diagnosis, particularly in the context of unconventional presentations especially when androgen levels are low.
Case Presentation
A 24 years old lady, with a history of Hashimoto thyroiditis and positive anti-TPO antibodies, presented with irregular menstrual cycles (five per year), a low BMI, Tanner 2 breast development, and halted puberty breast development. Laboratory findings revealed normal TSH, prolactin, follicular phase estradiol, an LH/FSH ratio of 1.46, elevated anti-Müllerian hormone (AMH), low testosterone, and high sex hormone-binding globulin (SHBG). Imaging showed a polycystic ovary appearance. A progesterone withdrawal test led to withdrawal bleeding, supporting presence of PCOS in contrary to functional component. The patient has a short history of living abroad with higher BMI, which was related to occurrence of acne in her face.
Discussion
While fulfilling Rotterdam criteria for PCOS, the case presented challenges due to conflicting hormonal indicators. Notably, the patient's low testosterone and high SHBG levels deviated from the typical PCOS profile. Features resembling hyper-/hypoandrogenic PCOS (HH-PCOS), such as autoimmune markers and a lean BMI, were present. However, considering the patient's low BMI and age, functional amenorrhea was also considered.
Conclusion
This case underscores the complexity of diagnosing PCOS, particularly in patients with atypical hormonal profiles and low BMI. The coexistence of lean PCOS and functional amenorrhea, or a unique PCOS variant, poses diagnostic challenges. The patient's history of living abroad with a higher BMI and the occurrence of acne further complicate the clinical picture. Clinicians should be aware of nuanced presentations and consider alternative diagnoses when faced with conflicting hormonal evidence, such as low testosterone levels. This case highlights the need for individualized approaches in diagnosing and managing PCOS, especially when fertility is desired.

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EP975

Male hypogonadism: an often overlooked consequence of substance use

Ilona-Beatrice Blesneac[1], Diana Nita[1], Otilia-Andreea Tarcau[1], Robu Larisa[1], Andreea Rosu[1], Anca Matei[1,2], Alexandru Florescu[1,2] & Cristina Preda[1,2]
[1]"Sf. Spiridon" Clinical Emergency County Hospital, Endocrinology, Isai, Romania; [2]Grigore T. Popa' University of Medicine and Pharmacy, Medicine, Isai, Romania

Introduction
Western countries present a gradual decline in male reproductive function. The decline in testosterone levels and sperm production witnessed over the past five decades, has been ascribed to environmental factors and unhealthy behaviors. Substance and drug usage is recognized as a detrimental lifestyle choice, that can interfere with the processes of steroidogenesis and spermatogenesis. Hypogonadism due to substance and drug abuse can be reversible.
Case report
A 40-year-old male patient was admitted to the endocrinology department 7 years ago, for general fatigue, low libido, and erectile dysfunction. He had no known medical history and physical examination revealed no significant findings. The biochemical analysis was normal, and hormonal tests shown hypogonadotropic hypogonadism with slightly low testosterone levels on two measurements, while the other axes - thyroid, somatotropic, corticotropic, lactotropic, and thyroid - were within normal limits. In the first two years after initial presentation, the patient underwent multiple investigations for an organic cause. Hypothalamic-pituitary MRI, testicular ultrasound, and abdominal-pelvic ultrasound were normal. DXA scan reveals decreased bone mineral density with mild vitamin D deficiency, so vitamin D treatment was initiated. During this time, his wife becomes pregnant. Two years after the initial presentation, hormonal evaluation reveals severe hypogonadotropic hypogonadism with very low testosterone, leading to the initiation of injectable testosterone treatment. Two years later, a semen analysis shows azoospermia, and testosterone treatment is discontinued. After stopping testosterone treatment, the patient continues to show hypogonadotropic hypogonadism with slightly low testosterone, and semen analysis reveals asthenozoospermia. His wife becomes pregnant again. Currently, the patient returns to our endocrinology department for reevaluation, where a complete pituitary assessment shows normal results, with no hypogonadotropic hypogonadism, but testosterone levels at the lower limit. In his medical history, the patient admits for the first time to consuming illicit substances (cocaine, codeine, amphetamine, synthetic drugs) and alcohol over the past years, with a reduction in frequency after the onset of the COVID-19 pandemic.
Conclusions
The widespread production and consumption of drugs poses a significant threat to public health. Concurrent abuse of more than one substance can have unpredictable effects, but they are often additive. When assessing a patient for hypogonadism, it is essential to inquire about the use of illegal drugs and other substances like tobacco and alcohol, particularly important in younger men, when no underlying organic causes of hypogonadism can be identified. Substance discontinuation typically results in the resolution of hypogonadism and should be strongly advised.

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EP977

Genetics of the y chromosome in male infertility

Hamdi Frikha[1], Nesrine Dhieb[1], Souhir Maalej[1], Khouloud Boujelben[1], Dhoha Ben Salah[1], Faten Haj Kacem Akid[1], Fatma Mnif[1], Nadia Charfi[1], Mouna Mnif[1], Mouna Elleuch[1], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology, Tunisia

Introduction
Couple's infertility is a major public health problem. Its prevalence is estimated at 15%. In half of the cases, this infertility is of male origin. Different etiologies may

be involved, among which genetic abnormalities of the Y chromosome. In this context, we report the cases of two patients with a structural abnormality of the Y chromosome responsible for the abnormalities of spermatogenesis
Case Description
The first 26-year-old case presents for hyper gonadotropic hypogonadism and short stature with biologically a Testosterone level of 2.83 ng/ml contrasting with an increased level of FSH at 20.6 mIU/ml, and a LH level of 5.17 mIU/ml. The testicular ultrasound showed bilateral testicular hypotrophy with a left testis measuring 4.7 cc and a right testicle measuring 4.8 cc. The spermogram showed a reduced ejaculatory volume to 1.3 ml with azoospermia. The genetic study concluded in an isodicentry of the short arm of the Y chromosome with a marked breakpoint in the Yq11.22 region, found in 85% of cells. This chromosomal abnormality is responsible for a total deletion of the Azoospermia factor b (AZFb) and Azoospermia factor c (AZFC) regions, which could explain azoospermia in our patient. The second cell population is monosomy X. The latter is responsible for a single copy of the SHOX gene, involved in height development. The second 29-year-old case presents for morbid obesity and hypergonadotropic hypogonadism with a biology of testosterone at 1.47 ng/ml, FSH at 16.4 mIU/ml, and LH at 5.17 mIU/ml. The testicular ultrasound showed reduced testicles. The spermogram revealed extreme oligoasthenospermia. The genetic study objected to a deletion in the long arm of the Y chromosome carrying the spermatogenesis regulatory genes, involving the Azoospermia factor (AZF) region
Discussion
The study of structural abnormalities of the Y chromosome has made it possible to assign certain regions of this chromosome a major role in spermatogenesis and whose detailed characterization makes it possible to offer the patient an adapted treatment in terms of genetic counseling, preventive self-preservation, and hope of fatherhood

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EP996

Diagnosis of hyperandrogenism-insulin resistance-acanthosis nigricans syndrome during transition: a case report

Najoua Lassoued[1], Elloumi Yassmine[1], Zantour Baha[1], Alaya Wafa[1] & Sfar Habib[1]
[1]Taher Sfar University Hospital, Endocrinology Department, Mahdia, Tunisia

Background
HAIR-AN, a syndrome of hyperandrogenism (HA), insulin resistance (IR) and acanthosis nigricans (AN), is a specific subphenotype of polycystic ovary syndrome, and it is seen in almost 5% of all women with hyperandrogenism. We report the case of a HAIR-AN which posed a diagnostic challenge in a 16-year-old girl.
Case Presentation
A 16-year-old girl was referred by her pediatrician to the Endocrinology Department for exploration of primary amenorrhea. The patient was followed in pediatrics since the age of 6 for primary hypothyroidism with progressive onset of morbid obesity. On physical examination, the BMI was 30 kg/m^2. She had a Tanner stage 5. She had moderate hirsutism with a Ferriman-Gallwey score of 20. Acne was visible over her face and back. She had severe acanthosis nigricans on both axillae and neck. Lab tests revealed testosterone level at 1.13 ng/ml, SDHEA level at 611 µg/dl and delta 4 androstenedione at 4.1ng/ml with E2 at 52 pmol/l, FSH at 2.04 IU/l and LH at 5.3 IU/l. Fasting insulin levels were elevated at 35 µIU/ml with high HOMA-IR at 6.16. We ruled out the diagnosis of congenital adrenal hyperplasia, hyperprolactinemia, Cushing's Syndrome and virilizing tumor of the adrenals or ovaries. Given the above features, the diagnosis of HAIR-AN syndrome was made. The patient was started in metformin along with lifestyle modifications. Four months later, she reported that a decrease in hirsutism starting the treatment and she lost two pounds.
Conclusions
In the presence of hirsutism and signs of insulin resistance in an adolescent consulting for primary amenorrhea, the diagnosis of HAIR-AN syndrome should be considered. This diagnosis could be difficult in the peripuberty period and the collaboration between pediatrician and endocrinologist is important to eliminate all the other differential diagnoses at this age.

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EP999

Predictors of quality of life according to nationality in patients with polycystic ovary syndrome: a multinational cross-sectional study

Elleuch Mouna[1], Elloumi Yesmine[1], Ben Salah Dhoha[1], Boujelben Khouloud[1], Krichen Zeineb[1], Ellouze Roua[1], Mnif Fatma[1], Mnif Mouna[1], Hadj Kacem Faten[1], Charfi Nadia[1], Abid Mohamed[1] & Rekik Majdoub Nabila[1]
[1]Hospital of Hedi Chaker

Background and Aims
Polycystic ovary syndrome (PCOS) may be the most common endocrine disorder in women of reproductive age. The Rotterdam criteria are the most accepted criteria for its diagnosis. The aim of this study is to study the predictors of quality of life in patients with PCOS according to nationality.
Methods
A cross-sectional study involved 172 women, 101 of them Tunisian and 71 French. Data collection was based on telephone interviews with tunisian subjects who were diagnosed with PCOS based on rotterdam criteria and french patients via Google Forms over an international group specifically for women with PCOS.
Results
The mean age of the patients was 27.34 years, with extremes ranging from 14 to 49 years. More than half of the patients were Tunisian (58.72%) and 51.74% of the patients were married. The comparative study between the two groups of patients showed that the French women were more professionally active ($P=0.05$) and were more frequently married (63.38%) vs (43.56%). However, the level of education was higher among Tunisian women who had more university degrees ($P=0.003$). The statistical study showed that menstrual irregularity was more frequent in French women (84.51%) than in Tunisian women (70.3%). However, hypofertility was more frequently reported by married French women. There was no difference between the two groups in terms of pregnancy. Obesity was reported in 32.6% of Tunisian women. Similarly, fatigue and hirsutism were more frequently observed in French women. Acne, however, was more frequent in Tunisian women. A climatic explanation may be proposed. In terms of treatment, 50.70% of French women had a treatment strategy indicated for them, compared with 25.74% of Tunisian women. Physical activity and diet were also applied in both groups, with no significant difference.
Conclusion
These results may have implications for the clinical practice and suggest the need for specific interventions in women with PCOS.

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EP1000

Impact of PCOS phenotypes on quality of life: insights from a serbian pilot study

Milica Opalic Palibrk[1], Sanja Ognjanovic[1], Bojana Popovic[1], Dusan Ilic[1], Jelica Bjekic Macut[2], Valentina Elezovic Kovacevic[1], Lena Radic[1], Katarina Krstic[1], Sarantis Livadas[3], George Mastorakos[4] & Djuro Macut[1]
[1]University Clinical Centre of Serbia, Clinic of Endocrinology, Diabetes and Metabolic Diseases, Beograd, Serbia; [2]University Hospital Medical Center Bezanijska Kosa, Department for endocrinology, Belgrade, Serbia; [3]Athens Medical Centre, Endocrine Unit, Athens, Greece; [4]Unit of Endocrine Diseases, Aretaieion Hospital, National and Kapodistrian University of Athens, Athens, Greece

Introduction
Polycystic Ovary Syndrome (PCOS) stands out as the most prevalent endocrine disorder affecting women during their reproductive years. Diagnosis typically relies on the ESHRE/ASRM criteria, necessitating the presence of at least two of three criteria: anovulatory dysfunction (ANOV), hyperandrogenism (HA), and morphologically polycystic ovaries visualized through ultrasound (PCOM). Using these criteria, patients can be classified into four phenotypes: PCOS-A (HA + ANOV + PCOM), PCOS-B (HA + ANOV), PCOS-C (HA + PCOM), and PCOS-D (ANOV + PCOM). Our pilot study aimed to evaluate the quality of life in various PCOS phenotypes within the Serbian population, using the Serbian version of the Health-related Quality of Life Questionnaire for Polycystic Ovary Syndrome (PCOSQ-50).
Subjects and methods
We analyzed 46 women with PCOS divided into phenotypes PCOS-A ($n=17$, BMI-26.5 $\pm$ 6.1 kg/m^2), PCOS-B ($n=10$, BMI 28.4 $\pm$ 6.2 kg/m^2), PCOS-C ($n=12$, BMI 23.5 $\pm$ 4.6 kg/m^2), and PCOS-D ($n=7$, BMI 22.2 $\pm$ 2.5 kg/m^2), alongside 31 age-matched healthy controls (BMI 22.6 $\pm$ 3.7 kg/m^2). There was no difference in BMI except between the controls and the PCOS-B group ($P=0.011$).
Results
Compared to healthy controls, PCOS-C exhibited lower scores in coping, obesity and menstrual disorders, and total PCOSQ-50 score (2.99 $\pm$ 0.38 vs 3.56 $\pm$ 0.60, $P=0.043$; 3.00 $\pm$ 0.5 vs 3.78 $\pm$ 0.89, $P=0.004$; 3.60 $\pm$ 0.34 vs 3.92 $\pm$ 0.50, $P=0.003$, respectively). PCOS-D displayed significantly lower scores in sexual

function, obesity and menstrual disorders, and coping scale (3.32±1.02 vs 4.37±0.51, $P=0.006$; 2.79±1.23 vs 3.78±0.89, $P=0.004$; 2.35±0.71 vs 3.56±0.60, $P<0.001$, respectively). PCOS-B exhibited a lower total PCOSQ-50 score compared to controls, indicating a lower quality of life (3.37±0.49 vs 3.92±0.50, $P=0.035$). Within the PCOS groups, our study revealed that PCOS-C had a lower score in the obesity and menstrual disorder scale compared to PCOS-A (3.00±0.53 vs 3.80±0.84, $P=0.015$). PCOS-D had lower scores for sexual function and coping scale compared to PCOS-A (3.32±1.02 vs 4.31±0.49, $P=0.021$; 2.35±0.71 vs 3.55±0.59, $P<0.001$, respectively). Fertility and hirsutism scales showed no significant differences within the groups, and compared to controls. While no intra-group differences were observed in psychosocial and emotional scales, these scores exhibited a negative correlation with BMI in PCOS-B ($r=$-0.647, $P=0.004$) and with Free Androgen Index (FAI) in the PCOS-D group ($r=0.924$, $P=0.023$). Higher BMI correlated with a worse Total PCOSQ-50 score in PCOS-B ($r=$-0.522, $P=0.026$). Age showed a positive correlation with sexual function and coping scale in the PCOS-B group ($r=0.567$, $P=0.009$; $r=0.509$, $P=0.22$). However, as expected, coping worsened with higher FAI ($r=$-0.490, $P=0.033$).

Conclusion

These findings underscore the necessity for a more extensive investigation involving a larger participant cohort.

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EP1002

Lipid profile in women with PCOS and their phenotypes

Lena Radic[1], Sanja Ognjanovic[1], Bojana Popovic[1], Dusan Ilic[1], Jelica Bjekic Macut[2], Valentina Elezovic Kovacevic[1], Milica Opalic Palibrk[1], Katarina Krstic[1], Dragan Hrncic[3], Danijela Vojnovic Milutinovic[4] & Djuro Macut[1]

[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Department for Endocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia; [2]Clinical Hospital Centre Bezanijska Kosa, Belgrade, Serbia; [3]Institute of Physiology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [4]IBISS, University of Belgrade, Belgrade, Serbia, Belgrade, Serbia

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine diseases among women of reproductive age and is associated with many metabolic manifestations, such as obesity, insulin resistance, dyslipidaemia and hyperandrogenism. The aim of the research was to analyse lipid profile in women with PCOS and their phenotypes.

Subjects and methods

We evaluated 159 women with PCOS diagnosed using ESHRE/ASRM criteria (PCOS: age: 25.85±5.14 years, BMI 23.75±5.54 kg/m^2) and 51 BMI-matched healthy women (Controls: age: 28.02±5.35 years, BMI 23.17±4.98 kg/m^2). PCOS group was divided into four phenotypes: A (anovulation (ANOV), hyperandrogenism (HA), polycystic ovary morphology (PCOM)), B (ANOV, HA), C (HA, PCOM), D (ANOV, PCOM). We measured levels of lipid indices, total testosterone, SHBG and androstenedione, while values of free androgen index (FAI) were calculated.

Results

Our analysis showed that there were significantly higher triglyceride levels in PCOS group in comparison to controls (PCOS:Controls: 0.95±0.49 vs 0.812±0.49, $P=0.014$), while the levels of total cholesterol, LDL and HDL cholesterol were similar in both groups ($P>0.05$). There were significantly higher levels of total testosterone, FAI and androstenedione ($P<0.001$), as well as significantly lower levels of SHBG ($P<0.001$) in women with PCOS. Comparison of lipid profile between PCOS phenotypes showed that phenotypes B and C differ in triglyceride levels, which were significantly higher in phenotype B (PCOS B:PCOS C: 1.10±0.51 vs 0.84±0.35, $P=0.049$), while the concentration of other lipid parameters between groups was similar ($P>0.05$ in all comparisons). Triglyceride levels showed positive correlation with FAI in PCOS phenotype B ($r=0.551$, $P=0.018$).

Conclusion

In our study we showed that there is a difference in triglyceride levels between metabolic and reproductive phenotypes of PCOS. Positive correlation between triglycerides and FAI in phenotype B represents a direct influence of the PCOS phenotype on metabolic consequences and relevant cardiometabolic outcomes during life.

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EP1009

Female sexual function in pregnancy: impact of gluco-metabolic profile, vitamin D status and chronotype

Roberta Scairati[1], Renata Simona Auriemma[1], Chiara Graziadio[1], Guendalina Del Vecchio[1], Nunzia Verde[1], Giovanna Muscogiuri[1], Attilio Di Spiezio[2], Annamaria Colao[1,3] & Rosario Pivonello[1,3,4]

[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]Dipartimento di Sanità Pubblica, Unità di Ginecologia, Università Federico II di Napoli, Naples, Italy; [3]UNESCO Chair for Health Education and Sustainable Development, Federico II University, Naples, Italy; [4]Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia ed Andrologia, Unità di Andrologia e Medicina della Riproduzione e della Sessualità Maschile e Femminile (FERTISEXCARES), Università Federico II di Napoli, Naples, Italy

Rationale

The gluco-metabolic changes during pregnancy significantly impact women's sexual behavior. This study aimed to define the relationship between metabolic health and sexual function, along with human circadian rhythms and sleep quality during pregnancy.

Methods

This study included 57 pregnant women (14 evaluated at first trimester, G1; 18 at second trimester, G2, and 25 at third trimester, G3). Among groups, no difference between age, gestational hypertension, number of pregnancies obtained by ART, glucocorticoid treatment and BMI before pregnancy (pre-BMI) was detected. In G2 former smokers ($P<0.001$) and physically active women ($P<0.001$) were lower than G1 and G3. All women exhibited vitamin D insufficiency. The entire cohort completed the following questionnaires: 1) FSFI and FSD, to assess female sexuality; 2) PREDIMED, to test adherence to the Mediterranean diet; 3) Pittsburgh Sleep Quality index (PSQI), to assess quality of sleep; 4) Morningness-eveningness (ME), to determine chronotype.

Results

In G1, HbA1c directly correlated with age ($P=0.019$;$r=$-0.98) and inversely with desire score ($P=0.038$;$r=$-0.96). In G2, 4/18 (22%) were diagnosed with gestational diabetes (GDM). Pre-BMI correlated with higher blood glucose (GL) 60 minutes after the OGTT ($P=0.002$; $r=0.9$), while the lubrication score inversely correlated with fasting GL ($P=0.039$; $r=$-0.6), insulin ($P=0.041$; $r=$-0.59), and HOMA-index ($P=0.037$; $r=$-0.60). HOMA index emerged as the best predictor of lubrication score ($\tau=$-2.4; $P=0.037$). In G3, 11/25 (44%) had well-controlled GDM, and the entire group showed lower GL ($P=0.04$) but higher insulin ($P=0.009$) and HOMA-Index ($P=0.03$) than G2. Prolactin levels were significantly higher than G1 ($P=0.02$) and correlated with insulin levels of third trimester ($P=0.002$;$r=0.9$). Vitamin D significantly correlated with sexual satisfaction score ($P=0.007$;$r=0.81$), also confirmed in pregnancy complicated by GDM ($P=0.02$; $r=0.93$). Low adherence to Mediterranean diet (G1, 21.4%; G2, 16.7%, G3, 30.7%) was more prevalent in G3 than other groups ($P=0.03$). In the entire cohort, PSQI indicated sleep disturbances in 91.2% and the ME questionnaire revealed only intermediate and moderate morning chronotype, the latter being more represented in G3 ($P=0.0013$). FSFI score confirmed sexual dysfunction in 57.1% of patients in G1, in 72.2% of G2, and in 64% of G3, with no difference based on chronotype, or between healthy and diabetic women.

Conclusions

Metabolic parameters negatively influence sexual function during pregnancy. Gluco-insulinemic metabolism predicted a worse lubrication score during the second trimester while the lower Vitamin D levels were, the lower satisfaction score was at third trimester. Chronotype did not interfere with sexual function or with metabolic parameters in pregnancy, suggesting that sexual health during pregnancy is independent of circadian rhythms.

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EP1018

Autoimmune Hashimoto's thyroiditis in polycystic ovary syndrome

Ifigenia Kostoglou-Athanassiou[1], Eleni Ziambara[2] & Charilaos Samaras[2]

[1]Asclepeion Hospital, Voula, Department of Endocrinology, Athens, Greece; [2]Asclepeion Hospital, Voula, 1st Department of Medicine, Athens, Greece

In patients with polycystic ovary syndrome (PCOS) a high prevalence of autoimmune Hashimoto's thyroiditis has been consistently observed. Young

female patients present with menstrual and reproductive disorders as well as weight gain. The aim was to present a cohort of patients with PCOS who underwent thyroid function tests and in some of whom autoimmune Hashimoto's thyroiditis was diagnosed. A cohort of 20 female patients aged 17-34 years is described. Patients presented with menstrual irregularity. They were diagnosed with PCOS. All patients underwent thyroid function tests and a thyroid ultrasonogram. In 12 patients autoimmune Hashimoto's thyroiditis was diagnosed, as anti-Tg antibodies were positive in 8 patients and anti-TPO antibodies were positive in 10 patients. In 2 patients clinical hypothyroidism was diagnosed as high TSH levels and low FT_4 levels were observed. In 5 patients subclinical hypothyroidism was diagnosed as they had high TSH and normal FT_4 levels. In patients with clinical and subclinical hypothyroidism thyroxine was administered. The thyroid ultrasonogram revealed micro nodularity and a nonhomogeneous parenchyma. Autoimmune Hashimoto's thyroiditis may be observed in patients with PCOS. Thyroid autoantibodies are detected in serum and thyroid function may be compromised. Oxidative stress and metabolic dysfunction may lead to immune dysfunction and the appearance of autoimmune Hashimoto's thyroiditis in PCOS. Genetic factors may also play a role, however this role has to be further studied and delineated.

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EP1109

A case of missing testicles in a transgender woman - assessment, diagnostic and treatment opportunities

Ioana Madalina Cristian[1], Bianca Andreea Balint[1], Catalina Petrescu[1] & Adina Mazilu[1]
[1]Central Military Universitary Emergency Hospital "Carol Davila", Endocrinology, Bucureşti, Romania

Introduction
Transgender – a common widely spread term that describes people whose gender identity does not match the sex they were assigned at birth. Transgender subjects may undergo various interventions, such as hormone therapy or gender-affirming surgeries to align their physical appearance with their gender identity.
Case report
A 49 year old biologicaly male who declaratively feels like a woman since childhood, who underwent all mandatory psychological examination to legaly change their sex from male to female comes for endocrinological examination. Patient recieved empirical hormonal terapy in the last two years but the feminizing characters are discordant in relation to the dose of hormone replacement administered. At the clinical exam patient presents with bilateral gynecomastia, higher voice, reduced facial hair, hypoplasic penis (2 cm lenght buried in the suprapubic fat pad), right testicle excision for ectopic testicles in childhood no left testicle palpable in scrotum. We raised the suspicion of ovotestis or ectopic testicle, for which an MRI examination is recommended. MRI - hypoplastic penis, the left testicle located in the pelvic subcutaneous fat, anteriorly, left paramedian, with the outline of the scrotum at this level; right testicle not visible, left kidney not visible (surgically removed in childhood). The patient's karyotype was performed with the result was 46, XY. The good result of the patient's feminization with hormone therapy is also generated by the testicular hypofunction. Although the patient's karyotype is confirmed to be 46, XY, further histopathological evaluation is necessary to exclude other causes of cryptorchidism. A different result of the karyotype would have prevented the continuation of the legal transformation of the sex. In the presented case, the resection of the remaining testicle is necessary not only for the gender affirming surgery reason, but also for the risk of malignancy that the restant testicle carries.

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EP1124

Mental state dynamics during perimenopause in women undergone IVF procedures

Desimira Mironova[1] & Violeta Azis[2]
[1]Lozenetz University Hospital, Sofia, Bulgaria; [2]Sofia University St. Kliment Ohridski, Sofia, Bulgaria

This poster delves into the nuanced realm of mental state dynamics during the perimenopausal phase in women who have undergone In Vitro Fertilization (IVF). Recognizing the perimenopausal period as a time marked by diverse emotional and physiological changes, our study places a primary focus on understanding the psychoemotional experiences in this specific cohort.
Methods
A comprehensive examination of mental state dynamics was conducted, utilizing survey-based assessments. Additionally, we measured Follicle-Stimulating Hormone (FSH) levels in perimenopausal women with a history of IVF, providing an additional layer to explore the correlation between FSH and emotional and physiological mood changes.
Results
Our findings illuminate the multifaceted nature of mental state dynamics during perimenopause, emphasizing the unique experiences of women post-IVF. Subsequent analysis revealed a significant correlation between FSH levels and certain aspects of emotional and physiological mood changes, offering an intriguing dimension to the primary focus.
Conclusion
This research underscores the complexity of mental state dynamics during perimenopause in women with a history of IVF. While the primary focus remains on psychoemotional experiences, the correlation with FSH levels adds a valuable layer to our understanding, opening avenues for future exploration.
Significance
Understanding mental state dynamics during perimenopause is crucial for tailored healthcare strategies. The additional exploration of FSH correlation, supported by survey-based assessments, enriches our perspective, paving the way for more targeted approaches that consider both hormonal and psychological aspects.
Keywords: Perimenopause, Mental Health, In Vitro Fertilization, Emotional Fluctuations, Follicle-Stimulating Hormone (FSH), Women's Health.
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EP1125

Induced lactation in an adoptive mother: a case report

Meriem Adel[1], Marwa Chiboub[1], Bel Hadj Sliman Chayma[1], Hajer Kandara[1], Manel Jemel[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technology, Endocrinology, Tunis

Introduction
Over the last twenty years, infertility has continued to rise. According to the WHO, the global incidence of infertility is 17.5%. Adoption is the legal process of achieving parenthood without birth. Since breastfeeding has many nutritional and psychological benefits, induced lactation, the initiation of lactation in a person who has not given birth, may be of interest to some families. We report a case of nonpuerperal induced lactation in a woman.
Observation
A healthy 33-year-old nulliparous woman consulted the endocrinology department for help in inducing lactation before adopting a child. She was prescribed ethinyl estradiol/Drospirenone 0.03 mg/3 mg daily. After 4 weeks, the patient was matched with a child. Therefore, we have decided to use the accelerated protocol. We continued ethinyl estradiol/ Drospirenone and started taking 20 mg of domperidone four times daily. Domperidone is a dopamine antagonist that stimulates prolactin secretion. After 2 months, significant changes in the breasts, including size and the sensation of being heavy and full, were noted, so the pill was stopped and the 80 mg of domperidone per day was continued. Our patient then started expressing milk with an electric double-pump every 3 hours and at least once a night. The adoptive mother initially expressed 10 ml of milk per day. After increasing water intake and adding galactogenic foods (fenugreek seeds, oat bran, fennel, sesame) she expressed 30 ml/day.
Conclusion
Breastfeeding has immunological, metabolic and psychosocial advantages for both mother and infant. In addition, in Muslim countries, breastfeeding establishes religious milk kinship. Despite the growing interest in induced lactation, many health professionals lack detailed knowledge. Prioritising the provision of adequate support and guidance to all women who wish to breastfeed should be a key focus for health professionals. This approach would improve the overall health of both woman and child and lead to increased rates of breastfeeding.

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EP1126

The effects of supplementing myo-inositol plus α-lactalbumin on reproductive and metabolic abnormalities in PCOS

Zelija Velija Asimi[1,2] & Aida Zujovic Ajanovic[1]
[1]UniMed - Polyclinic of SSST University, Endocrinology, Sarajevo, Bosnia and Herzegovina; [2]Sarajevo School of Science and Technology University, Medical School, Sarajevo, Bosnia and Herzegovina

Objective
The open-label clinical study aimed to evaluate the effects of myo-inositol plus alpha-lactalbumin in PCOS women. Alpha-lactalbumin was used being effective in increasing myo-inositol intestinal absorption. This effect is very useful in greatly reducing the therapeutic failure of myo-inositol in some patients (inositol resistant subjects).
Patients and methods
The study involved 36 normal weight, overweight or obese patients aged 18 to 40 years, with anovulation and infertility >1 year and insulin resistance diagnosed by HOMA-Index. Patients were administered orally with 2 g myo-inositol, 50 mg alpha-lactalbumin, and 200 μg of folic acid twice a day for 6 months. Controls were the same patients at t0 (baseline). The primary outcome was HOMA-index decrease after 3 and 6 months of treatment. Other parameters monitored were BMI, progesterone, LH, FSH, total testosterone, androstenedione, lipids.
Results
Recovery was general. The most important results were obtained with insulin, HOMA-index, LH, and androstenedione. The body weight was significantly reduced, the improvement of hyperandrogenism was prominent, the ovulation rate and the duration of the menstrual cycle were also improved.
Conclusions
The combination of myo-inositol and alpha-lactalbumin improve important parameters in PCOS patients characterized by different metabolic profiles. The benefits of combining myo-inositol and α-lactalbumin clearly make this combination a real advantage in the treatment of PCOS.
Keywords: polycystic ovary syndrome; myo-inositol; α-lactalbumin.
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EP1131

Bardet-Biedl syndrome with hypokalaemia paralysis: case report

Hemmet El Haddad[1], Manal Abou Farha[2], Ihab Sameh[2], Ahmed Fayed[2], Asma Ezzat[1], Randa Salam[1], Alaa Abdalla[2], Sara Ihab[2], Haader Essam[2] & Rodina Khaled[2]
[1]Cairo University, Internal medicine, endocrinology, Cairo, Egypt; [2]Cairo University, Internal medicine, Cairo, Egypt

Introduction
Bardet–Biedl syndrome is a rare autosomal recessive disorder with a wide range of clinical features. The primary clinical features include rod-cone dystrophy, postaxial polydactyly, central obesity, cognitive impairment, male hypogonadism and renal dysfunction.
Case report
22 Year old male, mentaly retarded with Bardet Biedle syndrome presented to our ER with vomiting and generalized weakness for 1 week. There was no history of fever, trauma, sensory disturbances, urinary or stool incontinence, no cranial nerve dysfunction. History of orchiopexy for RT sided undesended testes at the age of 5 years, cataract surgery on left eye at the age of 15 His sister is a known case of bardet biedel syndrome. Physical examination: BP: 110/80., normal temperature and respiratory rate. Weight: 75 kg, Height: 160 cm, BMI: 29 kg/m^2, central obesity, Cataract on Rt eye, Squint, High arched palate, Oral monaliasis Polydactyly in both lower limb and left upper limb, Brachydactyly in both feet. Cardiac and chest examination were normal Fundus examination showed the features of retinitis pigmentosa neurological examination: incomprehensive speech, bilateral Lower and upper limb hypotonia, and hyporeflexia, power, Sensory Coordination and gait: could not be examined Tanner stage 3: Left testis 4 cm, Rt testis 3 cm, Penile length 5 cm, Hypospadias Investigations Normal complete blood picture, urea, creatinine, blood gases Normal bilirubin, albumin, ALT: 27 (16-63 U/l), AST:56 (0-50 U/l) ALP: 240 (35-104 U/l) A1c: 5.8%, Na:140 (136-145 mmol/l), k: 2.3 (3.5-5.1 mmol/l), ca:6.3 (8.6-10.2 mg/dl) phosphrous: 1.6 (2.5-4.5 mg/dl), mg:1.1 (1.7-2.5 mg/dl) PTH:411 (15-65 pg/ml), Vitamin D: <3 (20-40 ng/ml) Normal lipid profile, normal thyroid function Abdominal ultrasonography showed: calcular cholecystitis Lt kidney marked back pressure dilated pelvis with upper 1/3 of the ureter (hydronephrosis), rt 112x 48 lt 102x45mm Tone and power of patient improved after correction of k, mg, ca, ph and vitamin d replacement.
Conclusion
Bardet–Biedl syndrome is worthy of special diagnostic effort for starting timely treatment of the various components and associated complications of the syndrome.
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EP1178

Ovarian hyperthecosis vs androgen producing tumour: A challenging and unusual case

Elaf Al-Samaraaie[1], Navya Basavaraju[1], Cherrylene Mari[1] & Probal Moulik[1]
[1]Royal Shrewsbury Hospital, United Kingdom

Introduction
Nearly 10% of all women have experienced hirsutism with hyperandrogenism at some stage in their life. Endogenous sources of androgen excess include ovarian tumours, ovarian hyperthecosis, and adrenal tumors. We present a case highlighting the work-up of hyperandrogenism.
Case report
A 47-year-old female, with background of type 2 diabetes, hypertension, polycystic ovarian syndrome (PCOS), obesity, was noted to have significant androgenisation incidentally in diabetes foot clinic. She had a long history of hirsutism from her 20's but developed deepening of voice, worsening of hirsutism with whole body shaving on alternate days, and androgenic hair loss for two years. She had menarche at 12 years and became hypomenorrhea from her 20's and amenorrhoea for the last few years. She is sexually active but never had confirmed pregnancy without any contraception. There was no significant family history of hirsutism. On examination, male pattern body habitus and male pattern baldness, BMI 42 kg/m^2, modified Ferriman-Gallwey score was 29/36, and clitoromegaly. She was obese but not Cushingoid. Her regular medications included metformin, insulin, dapagliflozin, dulaglutide, amlodipine, ramipril and aspirin. Blood investigations were done in 12years ago during the diagnosis of PCOS and during this referral and results are as tabulated below. CT adrenals was unremarkable with normal appearance of adrenals. Ultrasound of the ovaries showed normal endometrial thickness, enlarged left ovary but right ovary not visualized. Urgent MRI of pelvis has been organised. She was started on flutamide, non-steroidal anti-androgen, along with desogestrel, contraceptive, as sexually active and tolerated well without any side-effects.
Discussion
High testosterone in women may be due to polycystic ovary syndrome, congenital adrenal hyperplasia, ovarian tumours, ovarian hyperthecosis, and adrenal tumors. Ovarian hyperthecosis is associated with high testosterone levels, affecting less than 1% of women in the child-bearing age. In our case, there was partial suppression after overnight dexamethasone along with reassuring radiology pointing towards ovarian hyperthecosis as underlying etiology as initial significantly high testosterone should make the clinician suspicious towards malignancy.

Test	September 2011	November 2023	Reference range
LH	7.2	8.2	4-14 iu/l
FSH	6.3	3.0	3-13 iu/l
Testosterone	3.4	27.1	0-1.8 nmol/l
Testosterone post ONDST		18	In nmol/l
SHBG		35	28-146 nmol/l
DHEAS	2.7	3.23	1.5-7.7 umol/l
D4-Androstenedione	10	3.8	0.9-7.5 nmol/l
17-hydroxy progesterone	2.4	1.6	<6 nmol/l
Prolactin	86		
TSH	0.99	2.1	0.3-4.2 mu/l
Random cortisol	650	290	nmol/l
Cortisol post ONDST	<14	62	<50 nmol/l
Glycated haemoglobin	102	93	20-41 mmol/mol

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EP1189

Precocious puberty: etiology and treatement

Fatima Zahra Najioui[1], Rami Imane[1], Fatima Zahra Zerrouki[1], Latifa Yagoubi[1], Siham Rouf[2] & Hanane Latrech[2]
[1]Department of Endocrinology-Diabetology and Nutrition, Mohammed VI University Hospital Center, Faculty of Medecine and Pharmacy, University of Mohammed 1st, Oujda, Morocco, oujda, Morocco; [2]Department of Endocrinology-Diabetology and Nutrition, Mohammed VI University Hospital Center, Faculty of Medecine and Pharmacy, University of Mohammed 1st, Oujda, Morocco, Laboratory of Epidemiology, Clinical Research and Public Health, Mohammed VI University Hospital Center, Faculty of Medecine and Pharmacy, University of Mohammed 1st, Oujda, Morocco, Oujda, Morocco

Introduction
Precocious puberty results from the premature activation of the gonadal axis. It mimics physiological pubertal development, although at an inappropriate chronological age (before 8 years in girls and 9 years in boys). It is a serious challenge with repercussions on physical and psychosocial development. We aimed to evaluate the different etiology of Precocious puberty and the effectiveness of the Gonadotropin-releasing hormone (GnRH) agonists.
Patients and methods
This is a retrospective, descriptive study including a total of thirty-four children with precocious puberty follow-up in the Department of Endocrinology-Diabetology and Nutrition, Mohammed VI University Hospital, Oujda, Morocco. A clinical examination, statural evaluatiol and hormonal settings were performed in all cases. Statistical analysis was performed using SPSS version 21.
Results
The average age of our study group in the first consultation was $5,77 \pm 2,28$ years. Thirty one girls and 3 boys. Sixty-five percent of the patients were consulted in the first year of evoluation. The most common consultation reason was breast development (35%), followed by pubic hair develpement (27%). Statural advancement was found in 47%, with a bone age differance more than 2 years in 35%. LHRH testing was carried out in 83% of patients. Central precocious puberty was predominant with 24%. Fourty-four percent of our patients were treated with agonists GnRH. Post-treatment evaluation revealed that 73% of des patients presented stability or regression of signs.
Discussion and conclusion
Early diagnosis of precocius puberty can prevent short stature in adulthood. LHRH testing is the key test to. Treatment by GnRH agonists has demonstrated efficacy in central precocious puberty.
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Thyroid

EP7

Recurrent subacute thyroiditis - a genetic disease or a still not well-undestood one?

Cristina Ene[1]
[1] "Dr. Victor Babes" Foundation, Endocrinology, Bucharest, Romania

Background
Subacute thyroiditis is considered a rare form of inflammatory thyroid disease, triggered by a viral infection. The prevalence is higher in women and in the middle-aged groups. The rate of subacute thyroiditis recurrence is between 1.4% and 20%, with wide discrepancies between different studies; the relapse may occur soon after de treatment or even years after, and recent studies show an HLA-dependence.
Methods
We present a case report of recurrent subacute thyroiditis in a patient with co-presence of 2 high-risk HLA haplotypes.
Case report
The patient, a Caucasian 70-year-old woman, presented in the clinic with symptoms consistent with subacute thyroiditis - neck pain, shivers, mild fever, fatigue, malaise, and insomnia – which occurred 2 weeks after a viral throat infection. She also had gastrointestinal (gastroesophageal reflux disease, gastritis with recurrent helicobacter infection) and cardiovascular complications (high blood pressure, dyslipidemia) that needed to be considered. The thyroid ultrasound sustained the diagnosis: painful goiter with ill-defined heterogeneously hypoechoic areas and diminished vascularity. The lab confirmed the subacute thyroiditis with mild elevated inflammatory markers (ESR, CRP) and subclinical hyperthyroidism with negative autoimmune profile. Considering the mild form of the disease and the associated personal risk factors, the treatment was started with 25 mg oral prednisolone, with gastric protection, tapering the dose to 5 mg every week. The patient had a complete resolution of the thyroiditis after 6 weeks of treatment, however, she had elevated blood pressure requiring higher doses of her antihypertensive drugs, and the gastroesophageal reflux worsened, causing gastric discomfort. Unfortunately, our lady came back with milder symptoms after 2 months, with a similar ultrasound and lab profile. After the steroid treatment with the same doses, she had a recurring complete resolution. The disease relapsed once again after one month. Other immunosuppressive diseases were excluded and a genetic test was performed. The PCR test revealed the presence of HLA-DRB1×01, 14 and HLA-B×35:01. Higher doses of prednisolone and pantoprazole were needed.
Conclusion
The presence of HLA-B*35 is a well-known risk factor for recurrent subacute thyroiditis. Recently it has been demonstrated that other haplotypes (HLA-DRB1*01, HLA-B*18:01, HLA-C*04:01) are independent risk factors. A short period of steroid therapy may result in the recurrence of the disease, but known high-risk HLA haplotypes, as an initial diagnostic tool, could lead to a more effective approach to the case. However, its widespread implementation is limited by its costs. Further research is needed to explore more cost-effective strategies.
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EP40

Long-term observation of nodular goiter in japanese – association with thyroid hormones

Hiroshi Yoshida[1] & Takao Kunori[2]
[1]Iwaki-city Medical Center, Surgery, Iwaki-city, Japan; [2]Iwaki-city Medical Center, Surgery, Iwaki, Japan

Background
Nodular goiter (NOD) is one of the most common disease, which does not always need surgery. Long-term outcomes and relation with thyroid hormones, however, are not clear. We analyzed in Japanese patients who take iodine enriched food.
Patients and methods
3, 781 patients with NOD (solid type 37%, cystic 16%; 2007-2022); mean age, 57 (female, 80%) and 66 (man, 20%) entered in this study. Observation period was 5.1 years (mean; 1-21 years). Single solid nodules ($n=1$, 115; sNOD) were examined at year of 1, 2, 4, and 8 from the first visit. Serology was performed for thyroid peroxidase antibody (TPO), anti-thyroglobulin antibody (TgAb), thyroid stimulating hormone receptor antibody (TSH-RAb) and, in some patients, thyroid stimulating hormone antibody (TSAb). Hormonal assay was performed for free thyroxine (FT4), free triiodo-thyronine (F-T3), thyroid stimulating hormone (TSH) and thyroglobulin (Tg). Nodules were examined by ultrasonogram (US) and aspiration cytology. Enlargement rates (size%) of nodules were calculated by current size/ initial size (diameter in US). Statistical significance was determined by probability ($P<0.05$) in student-t or Kai-2 test.
Results
1. Size%: sNOD with the rates (>110%) increased as observed years, 4%(year zero), 26% (1 year), 35% (2 year), 43%(4 year) and 56% (8 year and more). While sNOD with the rate (<90%) also increased 4% (year zero), 22% (1 year), 23% (2 year), 30% (4 year) and 17% (8 year and more). 26% of sNOD was unchanged after 8 years. 2. Initial size and size% at year 4-6: Size% was highest in small size (<1 mm, median 197%), then 150% (10=<<1 mm), 95% (20=<<1 mm) and 106% (1 mm=<)($P<0.05$). 3. Changes of TSH: Patients with Low TSH (< 0.05μIU/ml) increased as observed years; from 21% to 75%. TSH decreased from 1.30IU/ml (sd=1.67) to 0.79 IU/ml in 10 years ($P<0.05$). TSH decreased from 1.46 IU/ml (mean) to 0.74 IU/ml in 8 years ($P<0.05$). 4. Changes of FT4: Patients with FT4>1.1 ng/dl (normal 0.70-1.48), increased as observed years; from 17% to 49%. FT4 increased from 1.12 ng/dl (sd=0.27) to 1.24 IU/ml(sd=0.24) in 8 years ($P<0.05$). 5. Changes of Tg: Tg increased from 74 ng/dl (median) to 439 ng/dl in 8 years.
Conclusions
2/3 of sNOD remained no growth. sNOD appeared to be associated with TSH and thyroid hormones.
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EP66

Neoadjuvant lenvatinib in invasive differentiated thyroid cancer

Virginia Soria Utrilla[1], Viyey Kishore Doulatram Gamgaram[1], Marta Iturregui Guevara[1] & Stella González Romero[1]
[1]Hospital Regional de Málaga, Endocrinology and Nutrition

We present the case of a 41-year-old man with a history of testicular seminoma treated with surgery and chemotherapy, and post-chemotherapy chronic kidney disease. He was initially referred to Otolaryngology for a 1-month history of neck mass sensation, with associated dysphonia, dysphagia and dyspnea. On examination, thyroid gland was enlarged. Fibroscopy was performed in consultation, revealing paralysis of the left vocal cord. The patient was referred to Endocrinology and Surgery departments. A cervicothoracic CT and ultrasound were requested. The CT showed a thyroid neoformative lesion with decreased tracheal lumen and pathological lymph nodes in levels III, IV, V, and VI bilaterally. The ultrasound showed a TIRADS-5 thyroid nodule in the left lobe, in which fine-needle aspiration (FNA) was performed, being insufficient for diagnosis. FNA was also performed on a pathological lymph node at right level III, with thyroglobulin 4729.62 ng/ml and TTF-1 positive, indicating thyroid origin, but unable to determine whether it was a follicular neoplasm or a follicular variant of papillary neoplasm. Biopsy-assisted guided (BAG) was requested, which could not confirm the diagnosis either. A blood test revealed normal calcitonine (5.23 pg/ml). At the same time, upper gastrointestinal endoscopy (UGE) and bronchoscopy were requested to assess resectability. UGE showed doubtful esophageal infiltration. Bronchoscopy revealed lesions in left tracheal wall, from which biopsies were taken. Histological study revealed positive immunoreactivity for thyroglobulin and TTF-1, confirming thyroid origin, but unable to state whether it was metastasis of thyroid carcinoma or ectopic thyroid tumor. The case was presented to a multidisciplinary committee, and neoadjuvant treatment with Lenvatinib was decided. After 1.5 months, a cervicothoracic CT showed partial response to treatment, so Lenvatinib was continued. After another 1.5 months, a new CT showed no significant changes and a new bronchoscopy continued visualizing neoplastic-appearing tracheal lesions, with a biopsy compatible with papillary neoplasia. Likewise, a new thyroid BAG was performed, also compatible with papillary carcinoma. With all this, surgical treatment was decided, being necessary total thyroidectomy, bilateral central and lateral lymph node dissection, resection of second to fourth tracheal rings with reconstruction, and temporary tracheostomy. This case aims to highlight the importance of individualized management of invasive differentiated thyroid cancer despite the difficulty in reaching an accurate diagnosis. Invasion of surrounding structures can lead to aggressive procedures such as tracheal resection, so there is a potential role for neoadjuvant therapy with tyrosine-kinase inhibitors in these patients, although it does not always avoid these procedures.

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EP78

Dysthyroidism in a hypothyroidism patient due to heterophilic antibody interference

Rossana Manzanares Cordova[1], Rocio Dominguez Rabadan[1] & Pilar Rodriguez[1]
[1]Hospital Juan Ramón Jiménez, Endocrinology, Huelva, Spain

Background
heterophilic antibodies are antibodies in patients' sample that can cause false results by binding to the assay antibodies. Interference due to heterophilic antibodies may lead to falsely low or high analytic concentrations. In some settings, the relationship between TSH and thyroid hormones does not fit with the expected feedback mechanisms. This may be due to a pathophysiological process, laboratory error or assay interference.
Case report
A 37-year-old female patient diagnosed with primary autoimmune hypothyroidism since she was 16 years old, well controlled until 2016 when, in relation to a traffic accident with traumatic brain injury, she began with a discordant thyroid hormonal pattern consisting of high TSH levels with normal FT4 or TSH inadequately normal with high FT4, accompanied by symptoms of hyperthyroidism, especially tachycardia, fatigue and weight loss (Table 1) After several check-ups and verifying an abnormal pattern in thyroid function, requiring multiple changes in dose and presentation of levothyroxine, a study of secondary hyperthyroidism and poor absorption was decided; both results were negative. Given the lack of improvement, analysis without interference from heterophilic antibodies was finally performed in an external laboratory since it was not available in our center, the results demonstrates that presence of heterophilic antibodies, presenting adequate levels of TSH and FT4 after their neutralization (Table 2) Currently, the patient maintains follow-up in our clinic with dose adjustment according to analysis carried out without interference from heterophilic antibodies, presenting a significant symptomatic improvement after stabilization of the levothyroxine dose.

Table 1: Summary of Analytical Results

Hormones	08/25/16	10/05/16	10/30/17	01/03/18	04/09/19
TSH (0.27-4.20 UI/ml)	100	3.16	5.83	39.67	1.90
FT4 (0.93-1.70 ng/dl)	1.18	2.29	1.81	1.37	2.14

Table 2: Analyzes without interference from heterophilic antibodies

Hormones	Baseline analysis	After neutralization of heterophilic Ac
TSH (0.27-4.20 UI/ml)	13.08	12.07
FT4 (0.93-1.70 ng/dl)	1.58	0.47

Conclusions
Interference in immunoassays is an important clinical problem that is underestimated and can have important clinical consequences. It is important to recognize the possibility of such interferences early in the diagnostic process and to implement protocols to identify these whenever possible, in a timely fashion, to prevent untoward consequences.

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EP80

A severe case of ophthalmopathy in a primary hypothyroid patient

Diana Vladica[1], Nicoleta Dumitru[1], Daniela Alexandrescu[1] & Adina Mariana Ghemigian[1]
[1]National Endocrinology Institute "C.I. Parhon", Bucharest, Romania

Introduction
Thyroid-associated ophthalmopathy (TAO) represents a common extrathyroidal manifestation of Graves' disease, however 2-7.5% of primary hypothyroid patients can experience a form of TAO as well. This condition is a rare autoimmune disease, where auto-antibodies (anti-TSH receptor antibodies or TRAb) target antigens shared by the thyroid and the orbit. This results in the inflammation, swelling and bulging of the eyes and surrounding orbital tissues. There are no clear guidelines on how to treat TAO in hypothyroid patients, making it a challenging case to manage. However, based on the current Graves' disease associated ophthalmopathy guidelines, there are several treatments available.
Case presentation
We present a case of a 41 year old female patient, who was admitted to our hospital in March 2023 after experiencing an acute episode of periorbital swelling of both eyes, lagophthalmos, pain, decreased ocular mobility, epiphora and chemosis. The patient, who is also suffering from a severe mental disability and is a non-smoker, was diagnosed with primary hypothyroidism one month prior, and was started on levothyroxine. The patient had no previous hyperthyroid state or radioactive iodine therapy. Laboratory investigations confirmed the primary hypothyroidism with positive thyroid peroxidase antibodies (ATPO) and anti-TSH receptor antibodies (TRAb). The orbital CT scan showed bilateral exophthalmos and some signs of optic nerves degeneration. The examination describes asymmetric involvement (left eye being more affected), chemosis, periorbital edema, exposure keratopathy.
Discussions
The ophthalmologist started the patient on an IV steroid course. After the symptoms have significantly improved, the steroid course was paused, however the condition persists even under euthyroid state. The constant high TRAb values from our patient and a lack of clear guidelines on how to treat TAO in hypothyroid patients, can explain the delay in achieving a remission. Other immunosuppressants such as the addition of oral mycophenolate to the regimen, were not taken into consideration due to the side-effects of the substances and the pre-existing anemia and altered liver function diagnoses our patient had.
Conclusion
TAO in hypothyroid patients is a rare condition, therefore early detection and treatment can help prevent sight-threatening complications. Such cases can be successfully treated with steroids, however in rare cases like this, the addition of other immunomodulatory therapy may be indicated. This step requires a close collaboration between endocrinologists and ophthalmologists.

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EP81

Multiple metastases from follicular thyroid carcinoma initially misdiagnosed as benign lesion: a case report

Ben Fekih Nawres[1], El Ajmi Wassim[2], Sellem Ali[2] & Hammami Hatem[2]

[1]Faculty of Medicine of Monastir, Nuclear Medicine, Tunisia; [2]Military Hospital, Nuclear Medicine, Tunisia

Introduction
Follicular thyroid carcinoma typically spreads through the hematogenous route, causing distant metastases, with bone and lung being the most frequent sites, while metastases to the liver and skin are less common. We report a case of reassessing the diagnosis of follicular thyroid carcinoma due to the identification of flesh-colored skin nodules, later confirmed as cutaneous metastases.
Case presentation
An otherwise healthy 60-year-old man underwent subtotal right thyroidectomy due to clinical suspicion of malignancy in 2016, but the histopathological examination of the resected tissue did not confirm the diagnosis, and the patient chose not to persue follow-ups. Six years later, our patient presented with cutaneous, asymptomatic nodules in the digastric region and in the occipito-parietal and fronto-parietal scalp. Histopathological examination confirmed metastatic follicular thyroid carcinoma. The remaining thyroid tissue was resected, and subsequent histopathological examination revealed no signs of malignancy. A second examination of the previously resected thyroid tissue (in 2016) was conducted, reclassifying the lesion as malignant and confirming it as follicular carcinoma. Further radiological investigations were then performed, detected multiple hepatic, pulmonary, and bone metastases. The patient was then referred to our department for radioactive iodine therapy (RAI), recieved a dose of 100 mCi. A postoperative radionuclide thyroid uptake scan revealed findings consistent with a metastatic lesion in the crane, right scapula, chest, liver, the whole pelvis, both humeri, the proximal-third of the right femur and multiple staged lesions in the bone spine.
Conclusion
This case underscores the diagnostic challenges and harmful consequences of misdiagnosing follicular thyroid carcinoma. It also highlights the well-established role of radioactive iodine therapy in managing high and intermediate recurrence risk FTCs, both therapeutically and diagnostically, as well as the importance of post-thyroidectomy follow-up care.

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EP85

Pediatric thyroid surgery: indications and outcomes through the analysis of 25 cases

Houas Jihene[1], Heyfa Belhadj-Miled[1], Monia Ghammam[1], El Ghali Wassim[2], Malika El Omri[1], Abir Meherzi[1], Mouna Bellakhdhar[1], Yosra Hasni El Abed[3], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT Department, Sousse, Tunisia; [2], Department of Anaesthesia, Sousse, Tunisia; [3], Department of Endocrinology, Sousse, Tunisia

Introduction
Thyroidectomy in the pediatric population is a seldom-performed surgical procedure, primarily associated with thyroid neoplasms. However, certain benign thyroid gland conditions, such as Graves' disease, toxic adenomas, congenital hyperthyroidism, and goiter, also necessitate surgical intervention in children. Performing such surgeries in pediatric patients poses significant challenges for surgeons. This study aims to investigate the epidemiological and clinical characteristics, as well as therapeutic outcomes, of children undergoing thyroid surgery in our institution.
Materials and Methods
A retrospective study was conducted on 25 children who underwent thyroid surgery in our department between 2010 and 2023, including systematic histopathological analysis.
Results
The average age of the patients was 14.6 years, with a notable female predominance (90.5%). Relevant medical histories included Graves' disease in 5 cases (22.7%) and one case of congenital hypothyroidism. The most common presentation was basi-cervical swelling. The surgical indication was established based on compressive thyroid nodules in 17 patients (68%) and in 7 cases (28%) within the context of known Graves' disease. Additionally, one case involved suspicious thyroid nodules with cervical polyadenopathies and chronic cough. Total thyroidectomy was performed in 14 patients (56%), lobo-isthmectomy in 10 patients (40%), and isthmectomy in 1 patient (4%). Bilateral mediastino-recurrent functional lymph node dissection was carried out in one case. The average postoperative hospitalization duration was 3 days (range: 2 to 6 days). Histopathological examination revealed 9 cases of multinodular goiter, 5 cases of Graves' disease, 4 cases of lymphocytic thyroiditis, 5 cases of vesicular adenoma, 1 case of oncocytic adenoma, and 1 case of papillary thyroid carcinoma with lymph node and pulmonary metastases, necessitating IRA therapy. Postoperative complications were reported in 32% of cases, with hypocalcemia being the most common (60%). No recurrent laryngeal nerve paralysis was identified. Favorable outcomes were observed in all patients.
Conclusion
Pediatric thyroid disorders requiring surgical intervention are considerably rarer than in adults. Benign thyroid nodules and Graves' disease are the most common surgical indications. Surgical management in children can be intricate, necessitating careful consideration and expertise.

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EP94

Exploring thyroid effects and gender-specific responses to pseudomonas aeruginosa mannose-sensitive-hemagglutinin (PA-MSHA): a rat model study

Katarina Baralić[1], Dragica Bozic[1], Đurica Marić[1], Jovana Živanović[1], Katarina Živančević[1], Evica Antonijević Miljaković[1], Aleksandra Buha[1], Marijana Ćurčić[1], Zorica Bulat[1], Biljana Antonijević[1] & Danijela Đukić-Ćosić[1]
[1]Department of Toxicology 'Akademik Danilo Soldatović', University of Belgrade — Faculty of Pharmacy, Belgrade, Serbia

Pseudomonas aeruginosa mannose-sensitive-hemagglutinin (PA-MSHA) is a bacteria-mediated cancer therapy showing promise in inhibiting cancer growth by impeding tumor cells and inducing natural cell death. Clinical studies indicate its ability to enhance chemotherapy efficacy and stimulate the immune system against cancer, presenting manageable side effects such as fever and skin irritation. Nevertheless, the safety profile of PA-MSHA requires further exploration, emphasizing the necessity for additional investigation. Hence, the aim of the current study was to investigate the thyroid effects of PA-MSHA in a rat model and elucidate gender-specific differences. Animals were subjected to a 28-day exposure to three increasing doses of PA-MSHA (PA-MSHA 1, PA-MSHA 2, and PA-MSHA 3: 0.09; 0, 18 and 0, 36×10^9, respectively), administered intraperitoneally once a week on the 1st, 7th, 14th, and 21st days. Following the conclusion of the study period, blood samples were obtained through cardiac puncture, and serum was isolated for subsequent hormone analysis. The levels of triiodothyronine (T3), thyroxine (T4), free triiodothyronine (fT3), and free thyroxine (fT4) were quantified, and the T3/T4 ratio was calculated. The results revealed gender-specific hormonal responses to varying doses of PA-MSHA. In females, both PA-MSHA 1 and PA-MSHA 3 significantly elevated T3 levels, with PA-MSHA 3 exhibiting a more pronounced effect, suggesting a potential dose-dependent response. Additionally, both doses induced comparable increases in fT3, indicating a potential threshold effect or saturation point in hormonal response. In males, PA-MSHA 2 led to a decrease in fT3 levels, suggesting a specific response to the intermediate dose, while PA-MSHA 3 showed a dose-dependent increase in fT4 levels, akin to the observed effect on T3 levels in females. However, both in males and in females, the absence of a statistically significant difference in the T3/T4 ratio suggests that the relative balance between T3 and T4 remained relatively constant across the experimental groups and the control, indicating that the overall thyroid hormonal equilibrium may have been maintained. However, these findings collectively suggest differential hormonal responses to varying doses of PA-MSHA in female and male animals, emphasizing the importance of gender-specific considerations in the development and interpretation of therapeutic interventions involving PA-MSHA.

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EP95

Retrospective analysis for the utility of beta-adrenergic blockers in thyroid storm: the double-edged sword

Eman Elmenyar[1]
[1]Bahçeşehir Üniversite Hastanesi Medical Park Göztepe, Turkey

Background
Thyroid storm (TS) is a rare, acute, severe, and potentially fatal complication of untreated or poorly managed hyperthyroidism. In such cases, there is multisystem involvement and an 8-25% risk of mortality; hence, early identification and prompt initiation of vigorous treatment is crucial to reduce mortality. Beta adrenergic receptors blockers (BBs) are commonly used early in the treatment of TS, however the risk of inducing circulatory failure (BBIS) remains a major concern. We aim to explore the BBIS in a large scale-data from different populations worldwide.
Methods
Data were collected between January 2003 and December 2023 from published cases on PUBMED/MEDLINE. We included all age groups, genders who had

been diagnosed with TS based on clinical, laboratory and Burch-Wartofsky Point Scale (BWPS) and received BBs early in the treatment of TS. Patients were subdivided into non-BBIS and BBIS, and data were analyzed and compared using Chi-Square and student t test. Multivariable logistic regression analysis was performed to identify the predictors of mortality.
Results
We analyzed 367 TS cases who fulfilled the eligible criteria (65% female and 35% male) with a mean age of 40 ± 17 and BWPS 62 ± 18. The overall mortality was 11.4% and BBIS occurred in 70 patients (19%). Age, gender, BWPS, BNP and troponin were comparable between the study groups. Patients who developed BBIS had significantly higher rate of atrial fibrillation, heart failure, lower left ventricular ejection fraction, multiorgan failure, cardiac arrest and mortality compared with those without BBIS. The BBIS group received more CCB, amiodarone, TPE, CRRT, and ECMO. Multivariable analysis showed that only BBIS (Odds ratio 3.0) and CRRT (Odds ratio 8.0) were the predictors of mortality after adjusting for age, gender, low ejection fraction, and renal failure and liver failure and the use of CCB, ECMO, and TPE. The mortality is 5 times higher in the BBIS group compared to non-BBIS.
Conclusion
BBIS in the treatment of TS occurs almost in one out of five TS patients treated with BBs. In addition to CRRT, BBIS independently predicts the mortality in TS patients.

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EP107

Ultrasound and cytological characteristics of NIFTP tumors compared to papillary carcinomas

Sofia Ouhessaine[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy, University Hassan II, Casablanca, Morocco

Introduction
Non-invasive follicular neoplasm with nuclear features of papillary carcinoma 'NIFTP', formerly encapsulated non-invasive follicular variant of papillary carcinoma, has been removed from the carcinoma category due to its indolent nature and good prognosis. This change impacts clinical and therapeutic care.
Objective of the work
To identify preoperative ultrasound and cytological differences between NIFTP and papillary carcinoma (PTC).
Material and methods
retrospective study includes 153 patients who underwent total thyroidectomy or lobectomy with a histological diagnosis of papillary carcinoma, NIFTP or invasive follicular variant of papillary carcinoma, between 2019 and 2023. Data from ultrasound and cytology were analyzed and compared between NIFTP and non-NIFTP (papillary carcinoma and invasive follicular variant of papillary carcinoma).
Results
Our study included 45 NIFTP, 108 papillary carcinomas including 47 follicular variants. Compared to papillary carcinomas, the nodules corresponding to NIFTP are more isoechoic (69.2% vs 17.4%, $P = .0007$) and have regular contours (92.3% vs 31.1%, $P = .0001$) and have an EU-TIRADS score 3 or 4. Cytologically, NIFTPs are classified categories III, IV and V of the Bethesda classification, while CPTs are mainly classified in categories V and VI of the Bethesda classification. Bethesda. Only the presence of nuclear pseudo-inclusions isemerged as significantly associated with the non-NIFTP group ($P = 0.0031$).
Conclusion
NIFTPs appear mostly non-suspicious on pre-operative ultrasound with absence of nuclear inclusions on cytopuncture. These differences compared to papillary carcinomas can make it possible to suspect the diagnosis preoperatively and to best adapt surgical management towards more conservative management.

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EP126

Papillary thyroid carcinoma arising from thyroglossal duct cyst: Report of three cases and review of the literature

Rachida Bouattay[1], Nawres Bouaziz[1], Hanen Grisia[1], Mahdi Ferjaoui[1], Amel El Korbi[1], Nawrez Kolsi[1], Khaled Harrathi[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction
The malignant degeneration of thyroglossal duct cyst (TDC) is a very rare phenomenon. It occurs 1% of operated cysts. The incidence appears to be greatest in patients in the fifth decade with a slight preponderance in women. Papillary carcinoma represents the most common histologic type. In this study, we report 3 cases of a papillary carcinoma of thyroid occurring in a TDC in adult population in order to present diagnosis and therapeutic aspects of degenerated thyroglossal duct cyst.
Patients and methods
This is a retrospective study of adult patients who underwent surgery for thyroglossal duct cyst at Fattouma Bourguiba University Hospital between 2006 and 2019, and for whom the pathological study revealed a TDC carcinoma.
Results
Of 61 cases of TDC, 3 (4.9%) were found to have TDC carcinoma. Our study investigated two women and one men. The mean age was 42.3 years. All three patients presented with a painless, slowly growing anterior neck mass of several months duration. They had no past history of irradiation. Physical examination was remarkable for a midline neck mass located above the thyroid gland. The mean diameter of the mass was 4 cm. It was non-mobile with swallowing in 2 cases. In all patients, the thyroid gland examination was normal, as were thyroid function tests. Cervical ultrasound and computed tomography scan were performed. Therefore, a diagnosis of TDC was made, and the patients underwent a Sistrunk operation; the cyst was found to be separate from the thyroid gland, which was itself normal. The frozen section from the mass was done in two cases and confirms the diagnosis of papillary carcinoma. A total thyroidectomy with central neck dissection were performed. The final histologic exam confirmed a thyroglossal duct papillary carcinoma in all patients. Wider resection is so indicated in the third case. A complementary treatment by radioactive iodine 131 and thyroxine suppressive treatment were undertaken. The follow-up was marked by the absence of recurrence in a patient and the death in another patient. The third case was not followed up.
Conclusions
Thyroglossal duct carcinoma, most commonly papillary carcinoma, is a rare condition that should be considered in patients presenting with cystic midline neck masses. Surgery and complete excision is the main treatment and the optimal patient management includes multidisciplinary consultation in order to improve survival. The diagnosis of malignancy is made postoperatively, as in the present cases.

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EP131

Epidemiological, clinicopathological, and evolutionary profile of familial non-medullary thyroid carcinoma (FNMTC) in 3 families

Doaa El Bazi[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital - Casablanca, Morocco Clinical Neuroscience and Mental Health Laboratory Faculty of Medicine and Pharmacy - Hassan II University, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Familial Non-Medullary Thyroid Carcinoma (FNMTC) is defined as the occurrence of thyroid cancer in two or more first-degree relatives, in the absence of predisposing environmental factors.
Objective of The Study
Describe the epidemiological, clinical features and its evolutionary profile.
Materials and Methods
A retrospective study including 3 families (10 patients) with FNMTC, collected at the endocrinology and diabetology department of Ibn Rochd University Hospital in Casablanca.
Results
Two families had parent-child relationship, and one family consisted of 2 sisters and a nephew. The average age was 38 years, with a clear male predominance and a male-female ratio of 2.3. The circumstances of discovery were mainly multiheteronodular goiter. For one family, three members discovered it during screening at an average young age of 21 years. All patients presented with clinical and biological euthyroidism. All patients underwent total thyroidectomy, with histopathological examination revealing papillary carcinoma in 3 patients, papillary with vesicular or trabeculovesicular differentiation in 5 patients, microcarcinoma in 1 patient, and papillary carcinoma with high columnar cells in 1 patient. The latter had retrospinal lymph node metastases. Multifocality was observed in 20% of patients, and bifocality in 60%. All patients received additional iratherapy. No recurrence was noted in our series.
Conclusions
Although FNMTC have a higher recurrence rate, with an earlier age of onset, no patient in our series had a recurrence. Early diagnosis and screening can improve prognosis and treatment.

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EP134

Papillary carcinoma reveled by cystic metastases

Amel Elkorbi[1, 2], Nawres Bouaziz[2], Mahdi Ferjaoui[2], Rachida Bouatay[2], Naourez Kolsi[2], harrathi khaled[2] & Jamel Koubaa[2]
[1,2]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction
Cystic cervical metastases of papillary thyroid carcinoma are rare. They precise incidence remains unknown. They can be indicative of a particularly papillary thyroid cancer. However, there is no negative prognostic character compared to non-cystic lymphadenopathy of thyroid carcinoma of the same histopathological type. We aim through this series of cases to discuss diagnostic and therapeutic features of cystic metastases of papillary thyroid carcinoma.
Materials and methods
This is a retrospective study of eight patients who managed for cervical cystic metastasis related to thyroid cancinoma in our ENT department over a period of 11 years (2010-2023). The following data were studied: age, sex, patients 'plaints, data from the clinical examination and explorations as well as the therapeutic approach.
Results
The patients'mean age was of 45.8 years [26-84 years]. The sex ratio is 0.57 with female predominance. The circumstance of diagnosis was a laterocervical swelling in seven patients and an incidental mass on a cervical ultrasound in one case. The supraclavicular localization was found in three cases and in the jugulo-carotid chain in four cases. All of our patients underwent a cervical ultrasound which showed the presence of a cervical cystic mass in all cases. Cervical CT scan was performed in four cases. Malignancy was suggested in three cases based on the presence of intra-cystic microcalcifications. Suspicious thyroid nodules were found in four patients. A fine needle aspiration were performed in all patients. It concluded to cystic metastasis of papillary thyroid carcinoma in five cases. Total thyroidectomy with bilateral recurrent and functional lymphadenectomy was performed in all patients. The histological examination confirmed the diagnosis of papillary thyroid carcinoma in the thyroid gland with cystic metastases. Iratherapy was performed in all patients. Recurrence occurred in only one patient after an average of eight years of fellow-up.
Discussion/Conclusion
Cystic metastases of papillary thyroid carcinoma is a classical but not common. Even though, there are no differences in therapeutic procedure or prognostic compared to classical metastases, we should think about cystic metastases in cases of cervical cystic mass in adult particularly in women. High resolution cervical ultrasound and fine needle aspiration are good tools to accurate the diagnosis.
Disclosure of interest: none declared

Keywords: cystic metastasis, thyroid cancer, papillary carcinoma, surgery
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EP135

Locally extended thyroid carcinoma: report of a case series

Amel elkorbi[1], Nawres Bouaziz[1], Mahdi Ferjaoui[1], Rachida Bouatay[1], Naourez Kolsi[1]. harrathi khaled[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction
Locally extended thyroid cancer is a rare situation that lead to management discussion. Therapeutic strategy depend on the histological type of the cancer and the extension limits. We through this study to discuss therapeutic strategy and relate the evolution features of such cancers.
Materiel and Methods
We performed a retrospective descriptive study collecting all locally extended thyroid cancer managed in our department over a period of ten years [2009-2023].
Results
They were four women and two men. The mean age was 64 years [49-80 years]. The main complaint was an anterior basicervical mass in all cases. It was associated with laterocervical mass in three cases. Dyspnea was reported in two cases and dysphonia in one case related to a recurrent paralysis. Ultrasound was suggestive of malignancy in all cases. A cervical CT scan, was performed in four cases, showed an invasive heterogeneous goiter extended to the trachea in three cases and the trachea and larynx in the fourth one which required emergency tracheostomy due to severe inspiratory dyspnea. Total thyroidectomy was performed in all cases, it was enlarged to the larynx in one case of medullary carcinoma. A recurrential lymphadenctomy was performed in all cases. Lateral lymphadenctomy was performed in four cases: it was unilateral radical in two cases, unilateral functional in one case and bilateral functional in one case. The definitive histological examination concluded to an invasive papillary carcinoma in three cases, a poorly-diffrentiated carcinoma two cases and medullary carcinoma associated with papillary carcinoma in one case. Distant metastases were noted in the two cases poorly-diffrentiated carcinoma: it was a bone in one case and pulmonary in the other case. Ablative iodine-131 radiotherapy was performed in all cases. It was associated to an external radiotherapy in two cases and radio-chemotherapy for the poorly differentiated carcinoma with lung metastases. The course was marked by loco-regional recurrence in one case, and the appearance of distant metastases in one case. The average follow-up was four years.
Discussion/Conclusion
Locally advanced thyroid cancer is a challenging situation. Surgery is the standard and the efficient treatment, even though it can be mutilating in some cases. External radiotherapy remains a complementary treatment and can be an alternative in non-operable tumors.
Disclosure of interest: none declared

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EP136

Coexistence of thyroid cancer and sarcoidosis Series of cases.

Olga Wajtryt[1], Elwira Bakuła-Zalewska[1], Aleksandra Budrewicz[1], Joanna Długosińska[1], Andrzej Kowalczyk[1] & Marek Dedecjus[1]
[1]Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland.

Sarcoidosis is a systemic inflammatory disease of unknown etiology characterized by the formation of granulomas. It most often involves the lungs, although there are evidences that it can be presented in any organ. Involvement of the thyroid gland is a very rare manifestation, defined as below 1% of cases. Thyroid cancer, on the other hand, is a cancer occurring with a frequency of approximately 1-1, 3% of all cancers, but with an increased incidence associated with growing diagnosis in the era of precision imaging. There is limited information suggesting a potential relationship between thyroid cancer and sarcoidosis. Currently, we have limited data based on the coexistence of diseases. Unfortunately, knowledge is based mainly on case reports and small groups of patients. However, there are several hypotheses linking the pathophysiology of both diseases. The impact of the etiology of autoimmune sarcoidosis and the frequent occurrence of autoimmune thyroid diseases remain unclear. Most often, the diagnosis was based on lymph node monitoring. Sarcoid nodes have been found in patients with thyroid cancer. However, in patients with sarcoidosis, changes in the thyroid gland were observed during imaging diagnostics, suggesting diagnosis of thyroid cancer. In both cases, indication to biopsy and cytology are often a difficult challenge. Moreover, in radioiodine scintigraphic examinations, the presence of pleural effusion or the presence of sarcoid lymph nodes may cause false uptake of radioiodine. Based on case reports of 3 patients from our Department, possible manifestations of sarcoidosis, as well as diagnostic paths to diagnosis, imaging and histopathological documentation, and diagnostic difficulties, were presented, as well as possible manifestations of sarocidosis observed in literature descriptions.

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EP137

Thyroid pathology in patients with MUTYH syndrome

Joaquin de Carlos[1], Lucia Zabalza[1], Ana Irigaray[2], Maria Rosario Aznarez[2], Ander Ernaga[3] & Emma Anda Apiñariz[1]
[1]Hospital Universitario de Navarra, Endocrinology, Pamplona, Spain;
[2]Hospital Universitario de Navarra, Gastroenterology, Pamplona, Spain;
[3]Hospital García Orcoyen, Endocrinology, Estella, Spain

Introduction
MUTYH (MutY homolog Escherichia coli, homolog of MYH, hMYH) is a repair enzyme with a crucial role in the correction of DNA errors, being considered a protective factor of the cell. MUTYH mutations have been linked to MUTYH-associated polyposis syndrome (MAP), an autosomal recessive disorder characterized by multiple colorectal adenomas. Patients with MAP show a much higher lifetime risk of gastrointestinal cancers as an additional role of MUTYH, it appears to contribute in the involvement of pathologies based on oxidative stress damage, as well as in the prevention of inflammatory and degenerative based disorders. Although the development of extraintestinal pathology is not fully defined, it seems to increase the risk of tumors and endocrinological pathology.
Materials and methods
Prospective study, selecting 27 living patients diagnosed and registered with MUTYH syndrome under follow-up from the Digestive Department of the

Hospital Universitario de Navarra (HUN) with current or past follow-up in the Endocrinology Department. Radiological tests, clinical, and analytical variables were analyzed.
Results
The study population included 14 men (51.8%) and 13 women (48.2%), with a mean age of 56 years. The median age at diagnosis of FAP was 48 years, with a mean follow-up time of 8 years. All patients underwent thyroid ultrasound examination and blood tests with the determination of thyroid autoimmunity. The prevalence of nodular pathology was 63% (17/27), of which 9 had single nodules and 8 had multinodular goiters. Patients with nodular pathology, 5 had nodules >1 cm (18.5% of the total sample). Of these, 4 had indications for cytologic study. The result of the cytologic study was Bethesda II in two cases. Bethesda III in two, in one of them ultrasound follow-up was decided and in the other surgical was performed revealing nodular hyperplasia. There was another patient who had undergone total thyroidectomy before the study, with a result of incidental papillary carcinoma of 1 mm.
Conclusions
The prevalence of thyroid nodularity in the sample of patients with MAP is above that described in the general population. Studies with a larger sample size are probably necessary to obtain results with greater statistical significance.

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EP138

Thyroid hormone profiles during pregnancy in women with gestational diabetes mellitus

Sawsen Nouira[1], Taieb ACH[1], Asma Ben Abdelkrim[1], Amel Maaroufi[1], Yosra Hasni[1] & Molka Chaieb[1]
[1]University Hospital Farhat Hached, Endocrinology, Sousse, Tunisia

Introduction
Pregnancy induces significant hormonal alterations, potentially affecting thyroid hormones. Our study aimed to assess the prevalence of thyroid dysfunction in pregnant women diagnosed with gestational diabetes Mellitus (GDM).
Methods
A descriptive study was conducted, including 197 pregnant women diagnosed with GDM, under the care and monitoring at the Diabetology, Endocrinology department in Farhat Hached university Hospital, Sousse Tunisia. Our population underwent an evaluation to assess their thyroid function. Exclusion criteria included individuals with pre-existing thyroid dysfunction before the onset of pregnancy.
Results
The average age was 34 ± 5 years. Pre-gestational body mass index (BMI) averaged at 27 ± 6.02 kg/m^2. No cases of hyperthyroidism were identified. Hypothyroidism was observed in 4% of patients. Among patients diagnosed with hypothyroidism, the average TSH (Thyroid Stimulating Hormone) level measured at 6.1 mU/l. The anti-thyroid peroxidase antibodies (anti TPO Ab) tested positive, in one patient with hypothyroidism. Age exhibited a significant positive correlation with hypothyroidism ($P=0.039$). While there was no statistically significant difference in the average HbA1C ($P=0.488$). Patients with higher pre-gestational BMI displayed an elevated risk of developing hypothyroidism ($P=0.026$).
Conclusion
The prevalence of hypothyroidism among pregnant women diagnosed with GDM underscores the imperative for proactive and comprehensive screening strategies. Early detection and management of hypothyroidism during gestation are paramount in mitigating potential obstetric and fetal complications, prioritizing the optimal health outcomes for both the mother and fetus.

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EP139

A pediatric case of abscessed thyroiditis: unveiling an unexpected etiological discovery

Heyfa Belhadj-Miled[1], Houas Jihene[1], Monia Ghammam[1], Oussama Khalfi[2], Malika El Omri[1], Abir Meherzi[1], Mouna Bellakhdhar[1], El Ghali Wassim[3], Yosra Hasni El Abed[4], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT dapartment, Sousse, Tunisia; [2], department of radiology, Sousse, Tunisia; [3], Department of Anaesthesia, Sousse, Tunisia; [4], Department of Endocrinology, Sousse, Tunisia

Introduction
Thyroid abscess in the pediatric population is an uncommon presentation and the rarest form of thyroiditis. Anomalies of the third and fourth branches account for 2-8% of cases. Through the observation of febrile torticollis secondary to an acute suppurative thyroiditis, we describe our diagnostic and etiological approach and specify its therapeutic management.
Materials and Methods
We present a rare case of an abscessed thyroiditis complicated by febrile torticollis, reported in our ENT Department.
Results
The patient is a 6-year-old with no significant medical history, presenting with febrile torticollis and a left basicervical swelling evolving for ten days. Examination revealed a febrile swelling in the left lateral thyroid compartment, measuring 5 cm in the major axis, firm, painful, with inflammatory signs. The rest of the ENT and general examination showed no anomalies except for a fever of 39°C. Ultrasound demonstrated an irregular oval mass with lobulated contours, measuring 54×1 mm, multilocular, located in the left basicervical region, pushing back the ipsilateral carotid axis and the left lobe of the thyroid. Cervical CT revealed a lobulated and multilocular mass in the left lateral and basicervical region, measuring $54 \times 42 \times 57$ mm. Posteriorly, it extended into the retro-pharyngeal space, causing bulging of the left lateral wall of the hypopharynx and reducing the lumen of the ipsilateral piriform sinus. Esophageal transit revealed the presence of an opacified fistulous tract originating from the left piriform sinus. Hypopharyngoscopy showed a small fistulous opening at the bottom of the left piriform sinus, leading to the diagnosis of a fourth branchial cleft cyst. The initial treatment involved incision and drainage combined with intravenous antibiotic therapy. Subsequently, after resolution of the infectious episode, cyst excision was performed along with left lobo-isthmectomy and cauterization of the fistulous opening with silver nitrate. The patient's evolution was favorable with a one-year follow-up.
Conclusion
Febrile torticollis in children is an infrequent reason for consultation. It can be the revealing pattern of extremely rare ENT pathologies, including congenital cervical anomalies in children.

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EP141

Assessment of quality of life in elderly patients with primary hypothyroidism

Meriem Antit[1], Ibtissem Oueslati[1], Amani Terzi[1], Dorra Khomsi[1], Arige Abid[1], Meriem Mabrouk[1] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
Hypothyroidism is a prevalent endocrine disease among the elderly. The thyroid hormones have a wide range of effects on the body, and hypothyroidism can significantly impact both physical and mental functions. The objectives of this study were to evaluate the quality of life in patients over 65 years old with substituted hypothyroidism and to assess their relationship with Thyroid Stimulating Hormone (TSH) level.
Methods
The study was a cross-sectional assessment of 80 patients over 65 years old who had primary hypothyroidism. They were treated with levothyroxine for at least one year. Clinical data and TSH level were collected from medical files. The SF-36 questionnaire was used to evaluate the quality of life (QoL). QoL was good if the overall SF36 score was above 60, poor if it was below 30 an average if it was between 60 and30.
Results
The mean age of the participants was 69.9 ± 4.6 years (Extremes: 65-82 years). The majority of patients (63%) were adequately controlled. The mean SF36 global score was 52.4 ± 22.5. QoL was good in 38% of cases, average in 41%, and poor in 21%. There was neither relationship between QoL and TSH nor QoL and levothyroxine dose. The percentage of patients who were adequately controlled was 70% in patients with good QoL compared to 58% in patients with average or poor QoL ($P=0.002$).
Conclusions
Decreased QoL was prevalent among elderly patients with hypothyroidism. Good control of the disease was significantly associated with better QoL.

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EP144

Pazopanib-induced hypothyroidism in a patient with metastatic renal carcinoma

Zineb Ait Si Ali[1], Hind Ouakrim[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Centre Hospitalo-Universitaire Mohammed VI Marrakech, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction
Pazopanib is a tyrosine kinase inhibitor (TKI), approved for the treatment of metastatic renal cell carcinoma and could improve progression-free survival and overall survival. The frequency of Pazopanib-induced hypothyroidism was reported to be 10–29%. We aim through this case to highlight the importance of thyroid function monitoring during treatment with TKI.
Case report
Female patiente of 41 years old, followed in oncology departement for clear cell renal carcinoma with hepatic metastasis, treated with pazopanib 1 mg per day for 8 months. During the follow-up the patient was refereed to our department for an elevated TSHus 1 ui/l. She presented an intermittent constipation and frilosity. Clinical examination noted no goiter. Neck-ultrasoud showed a normal thyroid gland volume with heterogenous stucture of thyroiditis aspect. Anti-TPO and anti-TG antibodies were negative. The patient started L-thyroxine 75 mg per day with good evolution and normalisation of TSHus levels. After 5 months the patient stopped Pazopanib for 2 months (availability issu), and presented signs of thyrotoxicosis with suppressed TSHus level 0.1 UI/l, L-thyroxine therapy was discontinued 6 weeks later TSHus remained normal 2.1 UI/l. One month later Pazopanib has been restarted, then the patient, represented once again an elevated TSHus: 8.1 UI/l requiring resumption of L-thyroxine therapy. The clinical evolution was favorable, appropriate follow up is planned.
Conclusions
In patients treated with TKI, the thyroid toxicity is common and pauci-symptomatic at the beginning of their evolution but can lead to prolonged hypothyroidism. Pathophysiological mechanisms linked to hypothyroidism in patients receiving TKI are unclear. Some researchers have hypothesized that the hypothyroidism may be due to the direct toxicity of TKI on the thyroid. Other hypotheses have been suggested; VEGF/R-TKI block thyroid hormone biosynthesis through thyroid peroxidase inhibition, increasing type 3 deiodination... The classic presentation of dysthyroidism associated with TKI is silent thyroiditis, beginning with a phase of thyrotoxicosis secondary to thyroid vesicles destruction releasing the stock of thyroid hormones, it can be treated with non-cardioselective β-blockers or even with cholestyramine. Then the patient may develop hypothyroidism, which is reversible in half of the cases. Thyroid function monitoring is important, it's recommended by the French Society of Endocrinology, to measure the TSH/free T4 levels before starting treatment, and every 3 to 4 weeks during the first 6 months as changes in free T4 levels precede the changes in TSH by 3 to 6 weeks. After this period, TSH measurement alone may be conducted every 2-3 months.

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EP145

Persistent post-procedure hyperthyrotropinemia with an RTH? phenotype: a case report

Radvile Matukaitiene[1,2], Martyna Juskiene[2] & Birute Zilaitiene[1,2]
[1]Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania, [1]Clinic of Endocrinology; Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Kaunas, Lithuania

Resistance to thyroid hormone beta (RTH?) is a rare disorder which poses challenges in both diagnostics and management. The prevalence varies from 1/19,000 to 1/40,000. In 14% of individuals manifesting with RTH? phenotype no THRB mutations were identified.
The management of these patients, especially after total thyroidectomy, in the absence of generalized consensus is complicated. 36-year-old woman was referred to endocrinologist with symptoms of thyrotoxicosis and dissonant thyroid hormone levels (TSH 1.3-2.5 mU/l n0.4-3.6, FT4 22-30 pmol/l n7.87-20.3; FT3 5.5-8 pmol/l n3.34-5.14). Medical history revealed the exclusion of thyrotropinoma, toxic adenoma, autoimmune thyroid diseases. In 2009, she underwent hemithyroidectomy for thyroid nodules, at that time she was experiencing milder thyrotoxicosis symptoms. Post-surgery, she felt well for several years. Center endocrinologists suspected resistance to thyroid hormone, particularly RTH?, beta-blockers were prescribed and patient was referred for genetic testing. Despite that she was doing relatively well on propranolol, genetic results were pending, she declined to wait and insisted on a thyroidectomy (based on her well condition after hemithyroidectomy in 2009 and the presence of several 1-1,5cm diameter nodules near the isthmus). Thyroidectomy took place on 13-04-2023. After surgery, she was prescribed 100 mg of Levothyroxine per day. Approximately 1.5 months post-surgery, hypothyroidism was observed (TSH19.4; FT4 11.34; FT3 3.06), leading to an adjustment in Levothyroxine dosage to 100/125mcg. Genetic testing, at least for now, exluded thyroid pathology. Following the dose increase, she experienced a burning sensation in the chest area, spreading to the shoulders, back, and abdomen. Additionally, there was an increase in resting pulse rate to 120 beats/minute, heart palpitations, and a slight tremor in the legs. Beta-blockers were prescribed for tachycardia. The symptoms resolved after several days of discontinuing thyroxine. Due to possible intolerance, Euthyrox was prescribed, the symptoms worsened (severe headache, dizziness), prompting the patient to revert to L-thyroxine with a lower dose. No adverse symptoms were reported on levothyroxine 50mcg, but laboratory tests indicated hypothyroidism (TSH23.8; FT4 9.24; FT3 2.35). Novothyral was added, resulting in a with tachycardia and profuse sweating (beta-blockers were ineffective), leading to the discontinuation of Novothyral. The levothyroxine dose is currently being increased slowly (25mcg over 1-2 months), now on 100mcg p/d. Hypothyroidism is regressing, albeit slowly. Optimal management of RTH? cases is still not known, it seems that thyroidectomy brings a new challenges in postoperative hypothyroidism treatment. Because this pathology is rare, the best solutions can only come from sharing experiences, creating hope for a consensus soon.

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EP146

Thyroid parameters in healthy pregnant women without autoimmune thyroid disease

Violeta Mladenovic[1, 2], Sanja Medenica[3, 4], Zoran Gluvic[5, 6] & Milena Mitrovic[7, 8]
[1]University Clinical Center Kragujevac, Clinic for Endocrinology, Kragujevac, Serbia; [2]Faculty of Medical Sciences University of Kragujevac, Internal Medicine, Kragujevac, Serbia; [3]Clinical Center of Montenegro, Department of Endocrinology, Internal Medicine Clinic, Clinical Center of Montenegro, Podgorica, Montenegro; [4]University of Montenegro, School of Medicine, Podgorica, Montenegro; [5]Zemun Clinical Hospital Center, Division of Internal Medicine, Deptartment of Endocrinology, Beograd, Serbia; [6]University of Belgrade - Faculty of Medicine, Beograd, Serbia; [7]Clinical Center of Vojvodina, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Novi Sad, Serbia; [8]Medical Faculty in Novi Sad, Novi Sad, Serbia

Introduction
Pregnancy has a significant effect on the thyroid gland and thyroid function. Thyroid hormone regulates metabolism, growth, and development in most tissues of the body, including various physiological processes. Normal thyroid function is important in order to ensure the best outcome.
Aim
The aim of this study is to analyse values of thyroid parameters during pregnancy in healthy population of pregnant woman.
Matherial and methods
The study included 77 pregnant women in the first trimester registered in Clinic for endocrinology UCC Kragujevac that were tested using OGTT, according to ADA criteria: pregestational and gestational diabetic women were excluded, and also determinaning thyroid parameters (fT4, TSH, TPOAb). The sample size included women in each trimester. We analyzed the values of thyroid parameters in 46 healthy pregnant women (without gestational diabetes mellitus and thyroid disorders including autoimmune thyroiditis). The characteristics of the participants were expressed as mean ± standard deviation.
Results
The mean age of 46 healthy pregnant women was 29.4±4.5 years. The results has been shown in the tables.

Table 1. The mean values of thyroid status parameters during pregnancy

X±SD (95%CI)	1. trimester	2. trimester	3. trimester	After delivery
fT3 (pg/ml)	2.67±0.49 (2.53-2.82)	2.13±0.49 (1.99-2.28)	2.15±0.45 (2.02-2.29)	2.44±0.5 (2.29-2.59)
fT4 (pg/ml)	10.68±2.16 (10.04-11.32)	7.58±2.11 (6.96-8.21)	7.18±1.48 (6.75-7.63)	10.48±2.27 (9.81-11.16)
TSH(mIU/l)	2.09±1.11 (1.76-2.42)	2.59±1.47 (2.16-3.03)	2.48±1.18 (2.13-2.83)	1.97±0.89 (1.7-2.24)

Table 2 Range of values in the examined population for the movement of thyroid function parameters during pregnancy

parameter (min-max)	1. trimester	2. trimester	3. trimester	After delivery
fT3 (pg/ml)	1.98-3.16	1.64-2.62	1.7-2.6	1.94-2.94
fT4 (pg/ml)	8.52-12.84	5.47-9.69	5.7-8.66	8.21-13.11
TSH (mIU/l)	0.98-3.2	1.12-4.06	1.3-3.66	1.08-2.86

Conclusion
This study demonstrates that as the pregnancy progresses, the average values of fT3 and fT4 decrease, and TSH increases, only to return to values similar to before pregnancy after delivery.
Keywords: thyroid parameters, pregnancy
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EP147

Euthyroid sick syndrome in severe sars-cov-2 disease
Ifigenia Kostoglou-Athanassiou[1], Lambros Athanassiou[2], Eleni Ziambara[3], Alexandra Konstantinou[3], Sofia Nikolakopoulou[3], Charilaos Samaras[3] & Panagiotis Athanassiou[4]
[1]Asclepeion Hospital, Voula, Department of Endocrinology, Athens, Greece; [2]Asclepeion Hospital, Voula, Department of Rheumatology, Athens, Greece; [3]Asclepeion Hospital, Voula, 1st Department of Medicine, Athens, Greece; [4]St. Paul's Hospital, Department of Rheumatology, Thessaloniki, Greece

Euthyroid sick syndrome also known as nonthyroidal illness syndrome is the reaction of the thyroid gland to severe disease. The SARS-CoV-2 virus affects the thyroid gland and may cause subacute thyroiditis, autoimmune Hashimoto's thyroiditis, Graves' disease, exacerbation of Graves' disease and a form of silent thyroiditis. The aim was to study thyroid hormone levels and identify the presence of euthyroid sick syndrome in the context of severe SARS-CoV-2 disease. A group of 108 patients (68 male and 40 female) who were hospitalized for severe SARS-CoV-2 disease were studied. In these patients the levels of TSH, FT_4 and FT_3 were measured. TSH levels were measured in serum by the ARCHITECT TSH immunoassay (Abbott Park IL, USA). FT4 levels were analyzed in the serum of the patients via the ARCHITECT FT4 microparticle chemiluminescent immunoassay (Abbott Park IL, USA). FT3 was measured in serum using the ARCHITECT FT3 microparticle chemiluminescent immunoassay (Abbott Park IL, USA). TSH levels were 1.25 ± 01.19 μIU/ml (mean $\pm$ SEM), FT_4 levels 9.31 ± 0.5 ng/dl and FT_3 levels 3.5 ± 0.09 pg/ml . In 42 patients the presence of euthyroid sick syndrome was identified. The presence of euthyroid sick syndrome was related to the outcome of SARS-CoV-2 disease. The SARS-CoV-2 virus affects the thyroid gland and may cause autoimmune and autoinflammatory disease such as subacute thyroiditis, autoimmune Hashimoto's thyroiditis, a form of silent thyroiditis and exacerbation of Graves' disease. In patients with severe COVID-19 disease the presence of euthyroid sick syndrome was identified. In other reports the presence and severity of euthyroid sick syndrome was related to disease severity and disease outcome in COVID-19 patients.
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EP148

Therapeutic plasmapheresis for the treatment of thyrotoxicosis: a case series
Zineb Ait Si Ali[1], Ilham Midhat[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Centre Hospitalo-Universitaire Mohammed VI Marrakech, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction
Hyperthyroidism is the excessive secretion of hormones by the thyroid gland. Synthetic antithyroid agents, surgery and radioactive iodine are the main available treatments. Plasmapheresis is a rapid and effective treatment option in cases where euthyroidism must be achieved rapidly because of the complications of thyrotoxicosis and the major adverse effects of antithyroid drugs.
Patients and methods
We report a series of 6 patients who underwent plasmapheresis for the treatment of hyperthyroidism. Our aim is to highlight the crucial role played by plasmapheresis in the treatment of hyperthyroidism, especially when other therapeutic options are contraindicated.
Résultats
The average age of our patients was 40, ranging from 22 to 60 years. The etiologies of hyperthyroidism varied between toxic multinodular goitre (2 cases), grave's disease (3 cases) and Hashitoxicosis (1 case): The indications for plasmapheresis were: Preparation for surgery in 5 cases, with contraindications to antithyroid agents in 4 cases (1 case of pregnancy, 3 cases of hepatic cytolysis) and one case of resistance to antithyroid agents, and severe hashitoxicosis in a 12-day-old pregnancy In our 6 cases, we noted normalization of FT4 levels, and a favorable outcome in 5 patients, with one case of death (hepatic failure).
Discussion and conclusion
In the treatment of hyperthyroidism, synthetic antithyroid drugs, radioactive iodine 1131 and surgery may be options, depending on the etiology. In cases where synthetic antithyroid drugs are insufficient or cannot be prescribed due to major adverse effects, free thyroid hormone levels can be reduced by plasmapheresis prior to radical treatment. Plasmapheresis has been reported in the literature in patients with thyrotoxicosis, and is a reliable and effective therapeutic option. However, it cannot be used on a large scale, as it is costly and invasive. In our study, plasmapheresis proved effective in reducing thyroid hormone levels and preparing patients for appropriate radical treatment.
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EP175

Next generation sequencing study in follicular differentiated thyroid cancer: a prospective indian study
Ramesh Bangaraihgari[1], Ramakanth Bhargav Panchangam[2], Sabaretnam Mayilvaganan[3], Rajesh Bangaraiahgari[1] & Udaya Kumar N[4]
[1]TRR Institute of Medical Sciences, Hyderabad, India; [2]BGH, Endocrine and Metabolic Surgery, Vijayawada, India; [3]Sgpgims, Endocrine Surgery; [4]AIMS, Biochemistry

Background
Follicular differentiated thyroid cancer (FDTC) is the most common endocrine cancer, globally. Next-generation sequencing (NGS) in thyroid cancer allows for high-throughput genetic sequencing with quick turnover. NGS Studies on papillary thyroid cancer are scanty from South East Asia. In this context, we conducted this study of a genetic panel wide somatic mutations in thyroid cancer.
Methods
We selected 21 FDTC cases. All of them underwent total thyroidectomy with neck dissection as needed. Tumour tissue samples extracted and paraffin embedded, were taken from ex-vivo specimens. Sample processing, DNA extraction, cDNA preparation and PCR amplification was performed. Mutation analysis with a thyroid cellular pathway specific 56-gene mutation panel using real-time PCR and ThyroSeq v2 on the Ion Torrent PGM sequencer was employed. Common single nucleotide polymorphisms (SNPs) with a minor allele frequency of >0.05 were excluded. Mutations were also manually checked using the Integrated Genomics Viewer v2.4.10 to filter out false positives.
Results
The analysis found mutations commonly in BRAF (17), CDKN2A (9), NRAS (6), PI3KCA (8), RET (4), RAS (12) and TP53 (3) genes. The common mutations found in the samples was RET (M918T), NRAS (Q61R), BRAF (V600E) and missense mutation in TP53 (c.217 – c.1178). A mutation has also been identified in KMT2D gene in two of the patient samples. BRAF, CDKN2A, PI3KCA were more common in papillary cancer. RAS, NRAS, RET mutations were common in follicular cancer. TP53 and KMT2D were seen only in poorly differentiated cancer.
Conclusions
NGS appears to be helpful in patient management and providing risk. More prospective studies are needed for its routine use at clinical level.
Keywords: Thyroid cancer; Mutation; BRAF gene; RAS gene; Genomics
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EP178

Skin metastasis of papillary thyroid carcinoma as a late complication of subcutaneous hematoma associated with fine needle aspiration
Yotsapon Thewjitcharoen[1, 1], Ekgaluck Wanothayaroj[1], Soontaree Nakasatien[1], Veekij Veerasomboonsin[1] & Thep Himathongkam[1]
[1]Theptarin Hospital, Diabetes and Thyroid center, Bangkok, Thailand

Background
While needle tract seeding has long been recognized as an uncommon complication of the fine needle aspiration (FNA) of the thyroid nodules, seeding

tumor metastasis resulted from subcutaneous hematoma following FNA is extremely rare. Herein, we present a challenging case of skin metastasis of papillary thyroid carcinoma as a late complication of subcutaneous hematoma associated with fine needle aspiration.
Clinical case
A 57-year-old male presented with anterior neck mass for 6 months. Neck ultrasound revealed a huge cystic mass with a hypervascularity exophytic solid nodule, 2.7 cm in diameter at the left thyroid lobe. Approximately 55 ml of hemorrhagic fluid was aspirated and followed by FNA of the solid component with a 23-gauge needle. Two days later, he returned with swollen and ecchymosis of the surrounding neck. The cervical hematoma resolved conservatively and total thyroidectomy was done one month later. Classic variant of papillary thyroid carcinoma (PTC) in the left thyroid gland with lymphatic invasion was found. No metastatic lymph node was detected. Postoperative high-dose radioiodine (RAI) ablation and thyroxine suppressive therapy were given. He was doing well with persistent biochemical incomplete response at one year after treatments and subsequently lost to follow-up. He came back two years later with palpable multiple subcutaneous nodules along the right side of the neck for 3 months. Ultrasound revealed small well-defined nodules (0.3 to 0.7 cm in diameter) located superficially over the right sternomastoid muscle. Further investigations revealed no distant metastases. Neck reoperation confirmed skin metastasis of PTC. The patient was in stable condition with persistent biochemical incomplete response at the last follow-up.
Conclusions
FNA of the thyroid is regarded as a safe procedure. However, physicians should be watchful of hemorrhagic complications in high-risk patients and aware that late complications such as seeding tumors could develop many years after bleeding complications.

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EP180

Autoimmune thyroid disease as a risk factor of atherosclerosis

Tamuna Gvianishvili[1, 2] & Maia Kapanadze[2, 3]
[1]Ivane Javakhishvili Tbilisi State University, Alexandre Natishvili Institute of Morphology, Tbilisi, Georgia; [2]Tbilisi State Medical University, Tbilisi, Georgia; [3]Academician O. Gudushauri National Medical Center, Tbilisi, Georgia

The relationship between subclinical hypothyroidism (SH) and Atherosclerotic (At) cardiovascular diseases (CVD) has been one of the most popular and discussing topics, because the existence of a causal relationship between Hashimoto's thyroiditis (HT), the lipid profile, and the molecular biology of the follicular epithelium has not been conclusively established. We investigated 59 patients (female), which had undergone total thyroidectomy, lobectomy. Patients were divided into 3 groups: group I – HT ($n=22$), group II – HT with At ($n=12$), group III – At ($n=25$). Thyroid function and lipid profile were determined by international guidelines of laboratory tests, coronary and femoral arteries intima-media thickness (IMT) - high-resolution ultrasonography, histological (H&E) and immunohistochemical markers were used: transcriptional protein p63 and neuroectodermal marker protein S100. The obtained results showed that: dyslipidemia and the diastolic hypertension accelerate the hypothyroidism in II group (HT with At) by predisposing carotid and femoral arteries IMT. FT4 is related to clinical features of atherosclerosis, THS and anti-TPO antibody levels are directly linked to the cardiovascular disease complications (myocardial infarction and hypertension). Biomarkers S100 and p63 data revealed a direct negative correlation between hypercholesterolemia and high morphological risks of Hashimoto's parenchyma changes. Namely, the trend of follicular epithelial dysplasia changes in the form of remodeling of parenchyma stem cells was revealed.

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EP181

Predictive biomarkers of thyroid dysfunctions associated with the treatment of tumors with immune checkpoint inhibitors

Ketevan Lomidze[1, 2], Marine Gordeladze[3] & Nino Kikodze[2]
[1]Israeli-Georgian Medical Research Clinic Healthycore, Clinical Trials Department, Tbilisi, Georgia; [2]Tbilisi State Medical University, Immunology, T'bilisi, Georgia; [3]Tbilisi State Medical University, Endocrinology, T'bilisi, Georgia

Background
Treatment with immune checkpoint inhibitors (ICIs) for advanced malignancies has been associated with developing immune-related adverse events (irAEs) severe enough to require the cessation of life-saving tumor immunotherapy.
Objectives
The present study aimed to identify predictive inflammatory markers of the development of immune-related thyroid dysfunctions in patients with cervical cancer (CC) and non–small cell lung cancer (NSCLC) treated by ICIs.
Methods
A retrospective study was conducted on twenty-seven patients with CC and NSCLC treated by ICIs. The data were collected before and 12 weeks after treatment. Complete blood count-derived inflammatory markers: dNLR (derived neutrophil to lymphocyte ratio), NLR (neutrophil to lymphocyte ratio), SSI (systemic inflammation index), PLR (platelet to lymphocyte ratio), WHR (white blood cells to hemoglobin ratio) were calculated. In addition, thyroid functional tests were collected. Data statistical analysis was performed by STATISTICA (Stat soft, Inc, USA).
Results
Five patients out of twenty-seven with CC treated by PD-1 and CTLA-4 inhibitors who developed hypothyroidism showed significantly high baseline PLR and low WHR compared to patients without clinical symptoms of hypothyroidism and reference levels of TSH and FT4. Association between NLR, dNLR, SSI, and thyroid dysfunction was not observed.
Conclusions
Our findings strongly correlate with hypothyroidism and WHR and PLR biomarkers. As a result, using these biomarkers for early identification of hypothyroidism helps treat thyroid dysfunction and improves cancer immunotherapy outcomes.

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EP189

Antithyroid medication (carbimazole and propylthiouracil) induced haemolytic anaemia- a case report

Ishara Ranathunga[1], Chandima Idampitiya[1] & Fathima Pambinezhut[1]
[1]Cumberland Infirmary, United Kingdom

Background
Haematological side effects of Carbimazole such as aplastic anaemia, thrombocytopenia and agranulocytosis are widely reported. However, Carbimazole induced haemolytic anaemia is rare. Proplythiouracil is known to cause leucopenia, agranulocytosis, bone marrow hypoplasia and pancytopenia. Nevertheless, Propylthiouracil associated haemolytic anemia is rarely reported. In such situations, the options for managing Hyperthyroidism are limited, especially in frail elderly individuals. We report a case of Carbimazole and Propylthiouracil induced haemolytic anaemia which resolved following discontinuation of the medication and starting on steroids.
Case presentation
An 83-year-old female presented with tiredness, low mood, indigestion, palpitations and anxiety. She was mildy thyrotoxic with no clinically evident goitre. TSH was suppressed at <0.02 mU/l with a fT4 of 32.1 pmol/l. Her thyroid receptor antibody (TRAb) was negative. Thyroid uptake scan revealed a total uptake of 0.7% with 0.5% left lobe and 0.3% right lobe. Both thyroid lobes appeared large with heterogeneous uptake, but there were no discrete avid nodules. The diagnosis of hyperthyroidism due to thyroid autonomy was made and she was started on Carbimazole 10 mg once daily. After 3 weeks, she presented with jaundice and worsening tiredness. On clinical evaluation she was anaemic with a haemogloblin of 1 g/l. The reticulocyte count of 412×109/l, with polychromasia, spherocytes and positive auto anti-e, pan reactive IAT antibody confirmed the diagnosis of Carbimazole induced haemolytic anaemia. Carbimazole was discontinued and high dose corticosteroid was started which was gradually tapered according to the clinical response. Six months following discontinuing Carbimazole, she presented with a relapse of hyperthyroidism. Her TSH was suppressed (<0.1 mU/l) with raised Free T4 32.1 pmol/l and Free T3 7.1 pmol/l. Due to the frailty, the alternative treatment options were limited. Therefore, she was started on a trial of propylthiouracil 1 mg twice daily with close monitoring. Subsequently, she developed a recurrence of haemolytic anaemia with a haemoglobin of 80 g/l just 1 week following Propylthiouracil initiation. Propylthiouracil was discontinued and she was treated with corticosteroids. Cholestyramine 1 g once daily was started as an adjunctive treatment for hyperthyroidism. She responded well to the medications with improvement in the haemoglobin and remains euthyroid to date.
Conclusions
Antithyroid induced haemolytica anemia is an extremely rare adverse effect of the medication. A patient developing haemolytic anaemia to both Carbimazole and Propylthiouracil has not been documented in the literature. The awareness of rare adverse effects related to antithyroid medication and timely management can improve the patient outcomes.

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EP194

Hydatid cyst disease of the thyroid gland: about five cases

El Omri Malika[1], Jemli S[1], Bellakhdher Mouna[1], Meherzi Abir[1], Houas Jihene[1], Ghammem Monia[1], Ach Taieb[2], Kermani Wassim[1] & Abdelkefi Mohamed[1]
[1]ENT department Farhat Hached Hospital, Sousse, Tunisia; [2]Endocrinology Department Farhat Hached Hospital, Sousse, Tunisia

Introduction
The hydatid cyst location in the thyroid gland is very rarely mentioned with an incidence varying between 0% and 3.4%due to the absence of specific clinical elements and the exceptional nature of this location. The aim of our work to study the epidemiological, clinical and therapeutic aspects of hydatid cyst of the thyroid gland. We report five cases of hydatid cyst of thyroid gland carried out in our ENT department.
Results
The average age of the patients was 40 years old with a range of 26 to 51 years. All patients were living in a rural area. Only one patient had undergone previous surgery for hydatid cyst disease. The patients consulted with firm basicervical swelling in 4 cases and renitent in one case. No sign of compression was associated (no dyspnea or dysphonia if dysphagia). Cervical ultrasound showed a multinodular goiter with multiple cystic nodules in 3 cases and a solitary solidocystic nodule in 2 cases. The treatment was loboisthmectomy in 2 cases and total thyroidectomy in 3 cases. The diagnosis was confirmed post operatively by pathology. There was no recurrence after an average follow-up of 3 years
Conclusion
The location of the hydatid cyst in the thyroid gland is rare, even in countries with high endemicity. The clinical symptoms depend on the location and size of the cyst. Positive diagnosis can be difficult preoperatively. The treatment is exclusively surgical, removing the cyst without breaking it.

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EP198

Gynecomastia as the first manifestation of thyrotoxicosis: an unusual case report

Catarina Cidade-Rodrigues[1], Vania Benido Silva[1], Bruna Silva[1] & Margarida Almeida[1]
[1]Centro Hospitalar do Tamega e Sousa, Endocrinology, Penafiel, Portugal

Introduction
Gynecomastia is a benign excessive proliferation of glandular tissue in the male breast and results from an increased breast estrogen/androgen activity ratio. It may be physiological (infancy, puberty or aging) or pathological. The most common cause is drug-induced. Although hyperthyroidism is a rare cause(1.5%), gynecomastia occurs in up to 25-40% of males with Graves' disease and is often undiagnosed. Its development as the first manifestation of this thyroid disease is quite unusual. We present a case of a young man with gynecomastia as a presenting sign of Graves' disease.
Case report
34-years-old male with chronic kidney disease (reflux nephropathy) since childhood, arterial hypertension and hyperuricemia, treated with lercanidipine, alopurinol and sodium bicarbonate, was referred to Endocrinology appointment due to a nonpainful increase in breast volume, right breast tension for 1 year, mild hyperprolactinemia and a newly diagnosed thyrotoxicosis. Clinically, he referred a recent slight hands' tremor at rest and notion of bilateral periorbital edema for 2 weeks. He denied galactorrhoea, headaches, visual disturbances, symptoms of hypogonadism, drug or steroid consumption as well as other thyroid function disruptors, previous testicular surgery, radiation or trauma. Physical examination: bilateral nonpainful gynecomastia, inversion of left nipple, bilateral exophthalmos, resting tremor, BP 153/1 mmHg, HR 107-117 bpm. Blood workup: TSH < 0.01 uUI/ml (0.38-5.33), FT3 5.91 pg/ml (2.5-4.4), FT4 2.1 ng/dl (0.54-1.24), TRAbs 8.1 UI/l (<2.9), prolactin 36.8 ng/ml (2.6-13.1), LH 9.8 mUI/ml (1.2-8.6), FSH 8mUI/ml (1.3-19.3), total testosterone 5.1 ng/ml (1.98-6.79), estradiol 32 pg/ml (<30), SHBG 73.5 nmol/l (13-71), beta-hCG 0.5 mUI/ml (<2.7), alpha-fetoprotein 1.1 ng/ml (<9). Thyroid ultrasound:normal volume, hypoechogenic heterogenous structure, no nodules. Breast ultrasound:asymmetric gynecomastia (more pronounced on the right) and 1 mm left retroareolar cyst. Scrotal ultrasound:mild asymmetry in testicular dimension, homogenous structure, regular margins, no nodules. Diagnosis:hyperthyroidism due to Graves' disease and hyperprolactinemia likely due to chronic kidney disease. Treatment:methimazole (MMI)1 mg/day. At 2 months follow-up, thyroid function tests were TSH <0.01uUI/ml, FT4 1.1 ng/dl (normal), FT3 3.74 pg/ml (normal), allowing for slow reduction in MMI.
Discussion and Conclusions
In this patient, possible causes of gynecomastia were chronic kidney disease, hyperprolactinemia and hyperthyroidism. However, due to long-standing kidney disease with no documented recent worsening of their baseline function, a very slight elevation of prolactin and recent development of gynecomastia and symptoms of hyperthyroidism, the most likely cause is the latter. Hyperthyroidism induces gynecomastia through a combination of decreased free androgen levels and overproduction of estrogens. It is important that clinicians perform thyroid function tests when evaluating a patient with gynecomastia, even when other possible causes coexist, so that the diagnosis and treatment of hyperthyroidism are not missed.

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EP205

Refractory hypothyroidism: 5-days levothyroxine absorption test to diagnose pseudomalabsorption

Doaa El Bazi[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital - Casablanca, Morocco Clinical Neuroscience and Mental Health Laboratory Faculty of Medicine and Pharmacy - Hassan II University, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Refractory hypothyroidism is defined by clinical or biochemical signs of hypothyroidism (serum TSH level >4.5 mU/l after an interval of six weeks after the last dose increase), despite increasing levothyroxine (LVT) doses beyond 2.5 µg/kg per day.
Observation
A 67-year-old female patient, followed for a 1 mm NIFT-P classified as pT1a, low risk, initially put on LVT 150 mg/day, presented with hypothyroidism, clinically with asthenia, constipation, and biologically with a TSHus of 145 mUI/l, despite titration of LVT up to 1 mg/day (i.e, 4.1 mg/kg/day), liothyronine sodium 0.1 mg/day and dexamethasone 1 mg/day. The patient reports good therapeutic compliance, with good levothyroxine conservation. She does not report signs of malabsorption.
Methods
The patient was hospitalized in the endocrinology and metabolic diseases department for a 5-days levothyroxine absorption test. The principle consists of supervised administration of LVT on an empty stomach with monitoring the patient 1h after the ingestion. TSHus and FT4 blood samples were taken before LVT administration in 1st day of the test and 2h after administration in 5th day of the test.
Results
On the first day, TSHus before LVT administration was 91 mIU/l (0.25-5), with FT4 at 0.3 ng/dl (0.7-1.5). Then, on the 5th day, TSHus 2 hours after administration was 40.27 mIU/l (0.25-5), and FT4 was normal at 20.5 pmol/l (10-28.2). The patient was subsequently, switched to LVT tablets (due to the high cost of liquid LVT). A thyroid function test was repeated after 5 days, showing normalization of TSHus at 1.39 mIU/l (0.25-5), and FT4 at 20.4 pmol/l (10-28.2). In addition, a malabsorption check-up was revealed intestinal amebiasis of the Entamoeba histolytica histolytica, treated with a negative control work-up. Associated with a Helicobacter pylori chronic gastritis under treatment.
Conclusions
The 5-days LVT absorption test allowed the diagnosis of pseudomalabsorption in this patient, given the normalization of the thyroid function test, despite the presence of Helicobacter pylori gastritis.

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EP206

Taking nothing for granted- Levothyroxine formulation

Irene Samperi[1], Chiara Bima[1], Piero Radaelli[1], Mara Steffanini[1] & Maria Chantal Ponziani[1]
[1]SSD of Diabetology and Metabolic Diseases - Azienda Sanitaria Locale Novara, Novara, Italy

Background
levothyroxine is the most common medication for the treatment of hypothyroidism. Usually, it is capable of restoring euthyroidism in most conditions. Absorption can be challenging, therefore different formulations are available (tablet, soft gel, liquid). Rarely it is necessary to use liothyronine to achieve normal TSH values.

Clinical case
a 23 y/o woman was admitted to our outpatient clinic for severe hypothyroidism. She was diagnosed with autoimmune thyroiditis at the age of 10. She also has celiac disease and schizoaffective disorder. She lived in a community and was followed by medical personnel. She was on a gluten-free diet and antipsychotic drugs: Lithium, Duloxetine, Lorazepam, Clozapine and quetiapine. On medical examination, she has obesity with no cushingoid aspect, normal heartbeat and blood pressure. She felt tired and had regular menses. She denied any other specific symptoms. She was on treatment with Levothyroxine tabs 200 mg/day (1.78 mg/kg/day), and her TSH was 386 mU/l with no measurable Ft3 and FT4. We excluded Helicobacter pylori infection and emphasized the need for a gluten-free diet and the correct way of taking medication. We advised a shift to soft gel formulation increasing the dose up to 250 mg/day After two months her TSH was 18.1 mU/l. Four months later her TSH was 1 mU/l, we therefore gradually increased levothyroxine to 1 mg shifting to liquid formulation with no benefit. We then changed the levothyroxine brand. We gradually added liothyronine up to 15 mg 3 times per day. After 2 months she was on levothyroxine 1 mg (3 mg/kg/day) and liothyronine 1 mg per day and her TSH was 1 mU/l. We investigated with caregivers who assured us she took medication correctly and properly followed the diet. She could have severe malabsorption so we undertook the levothyroxine absorption test. While she was having the test we realized that she couldn't empty the bottle. We then explained to her and her caregiver how to take the medication and she restored euthyroidism with levothyroxine 164 mg/day (1.6 mg/kg/day) without the need for liothyronine. Regardless of thyroid hormone values she never complained of any other symptoms, or benefit from the restored euthyroidism.
Conclusion
psychiatric patients can be challenging and symptoms can be underestimated. The new formulation of levothyroxine allows us to tailor approaches. Using the right medication and the right formulation for the right patient is crucial. Levothyroxine absorption test can still be used in specific settings.

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EP212

Thyrotoxicosis in a molar pregnancy

Leah Antonette Tabuyo[1] &Hannah Corpuz[1]
[1]Lorma Medical Center, Internal Medicine, San Fernando City, Philippines

Hydatidiform moles are categorized as either complete or partial and can only be confirmed by karyotyping. Complete moles are more frequently associated with medical complications such as hyperthyroidism. A 46-year-old Filipino female presented with tachycardia, hypertension, b-hCG > 10,000 mIU/ml, suppressed TSH 0.006 mIU/l, high FT3 19.04 pg/ml (NV: 2.02 - 4.43) and FT4 7.77 ng/dL (NV: 0.93 - 1.71). Uterus was enlarged with contractions. Antihypertensives and Propylthiouracil (PTU) were given to facilitate urgent hysterectomy due to profuse bleeding. Post-operatively, FT4 decreased (3.94 ng/dl). Antihypertensives were continued, PTU discontinued and she was discharged stable. On follow-up, hCG decreased to 1021 mIU/ml, and she was euthyroid (FT4 9.27 pmol/L). Mechanisms of molar pregnancy-induced hyperthyroidism:
- structural similarity of hCG and TSH molecules and their receptors provides the basis for the thyrotropic action of hCG
- "spillover effect" which refers to a phenomenon where hormones that are not intended to act on a particular receptor can still bind to it and produce an effect
- the hCG found in hydatidiform moles lack the C- terminus and contain lower sialic acid which cause greater stimulation of the TSH receptor Reports have shown that hyperthyroid symptoms become apparent once ?-hCG levels reach 200,000 m[IU]/ml. It has been estimated that for every 10,000 m[IU]/ml increase in serum hCG, TSH decreases by 0.1 mIU/ml and free T4 increases by 0.1 ng/d
This case highlights an important yet uncommon etiology of thyrotoxicosis. Clinical presentation varies from asymptomatic to life-threatening thyroid storm, hence, early recognition and prompt intervention are essential to prevent disease progression. Molar evacuation is the definitive treatment. B-hCG titers and thyroid hormones are expected to normalize after. Up to date, there are no existing guidelines with regard to the use of anti-thyroid medications prior to or after surgery. Further studies are needed to deepen our understanding of this condition to improve early detection, optimize management, and reduce associated complications.

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EP218

Analysis of clinical and ultrasound results after treatment with percutaneous ethanol injection in benign cystic thyroid nodules

Víctor José Simón Frapolli[1,2,3], Diego Fernández García[1], Ana María Gómez Pérez[1], Isabel Mancha Doblas[1] & Francisco Tinahones Madueño[1,2,3]
[1]Hospital Universitario Virgen de la Victoria, Málaga, Spain; [2]School of Medicine, Málaga, Spain; [3]BIONAND, Málaga, Spain

Introduction
Percutaneous ethanol injection (PEI) or thyroid enolisation is a minimally invasive technique applicable to benign cystic thyroid nodules, not adhered to neighbouring structures, due to local compressive symptoms or aesthetic discomfort. Classically, the treatment of choice for these nodules has been simple aspiration, followed by surgery in refractory cases. Currently, PEI has emerged as an alternative to surgery due to its high efficacy, speed, safety, low rate of serious side effects, outpatient nature and low cost. Although it is a procedure with limited experience, it is safe when performed by experienced professionals.
Method
Prospective observational study including 14 patients undergoing PEI in our Endocrinology Clinical Management Unit between January 2020 and December 2022. Demographic, clinical and ultrasound data were collected prior to the procedure. All patients underwent prior ultrasound-guided fine needle aspiration puncture (FNA) with a cytological diagnosis of benignity, and all had a history of simple evacuation with subsequent recurrence of the nodule. Technique: a single ultrasound-guided puncture was performed, without anaesthesia, following a transisthmic approach; using a double guidewire, the cystic content was emptied almost entirely, immediately followed by the administration of 10cc of 99% ethanol; a 30-minute observation was then maintained for the possible appearance of symptoms and/or immediate complications. Evacuated content was quantified and an ultrasonographically follow-up at 3 and 6 months was performed.
Results
The highest percentage of reduction was observed in men vs women (68.0 ± 23.71 vs 23.10 ± 31.6); in patients over 70 y.o. vs under 50 y.o. and between 50-70 y.o. (35.30 ± 27.54 vs 20.0 ± 39.77 and 29.90 ± 25. 22, respectively); in single nodule vs multinodular goitre (34.4 ± 21.57 vs 20.0 ± 25.60); in TIRADS-2 vs TIRADS-1 and TIRADS-3 (32.6 ± 38.37 vs 25.7 ± 24.84 and 21.4 ± 15.91, respectively) and in older nodules vs those with a shorter time of evolution (37.3 ± 28.05 vs 23.4 ± 33.23).
Conclusions
PEI is an effective treatment for symptomatic cystic thyroid nodules, with a mean reduction in nodule size of 29.7% at 6 months. After a second PEI, performed in 3 patients, the performance of the technique improved with a mean reduction of 35.7% at 12 months follow-up. No serious side effects were reported (transient pain in 53.8% of cases). The highest percentage of reduction is observed in men, older than 70 y.o., with single nodule, TIRADS-2 and > 5 years of evolution. These results are not statistically significant, probably due to the small sample size.

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EP222

Dilated cardiomyopathy as a rare complication of inadequately treated hyperthyroidism – a case report

Ana Majic Tengg[1], Vlatka Pandzic Jaksic[1], Jasmina Catic[2] & tomislav novosel[3]
[1]Clinical Hospital Dubrava, Department of Endocrinology, Diabetes, Metabolic Diseases and Clinical Pharmacology, Zagreb, Croatia; [2]Clinical Hospital Dubrava, Department of Cardiovascular Diseases, Zagreb, Croatia; [3]Clinical Hospital Dubrava, Department of Otorhinolaryngology and Head and Neck Surgery, Zagreb, Croatia

Introduction
Thyrotoxic cardiomyopathy is a rare but potentially fatal form of dilated cardiomyopathy caused by hyperthyroidism not timely diagnosed or inadequately treated. The first-line treatment is a treatment of the underlying thyroid disease as the structural and functional cardiac alterations are potentially reversible after achieving a euthyroid state.
Case presentation
A 41-year-old man was admitted to hospital due to the symptoms of heart failure and tachycardic atrial fibrillation. He complained of dyspnea, peripheral edema, and palpitations. Before admission, he had been treated for thyrotoxicosis caused by Graves' disease in another country for seven months. Initially, he was given tiamazole, but it was replaced by propylthiouracil due to an allergic reaction (skin rash). Additionally, he had undergone electrocardioversion three times in the past six months, including the period of current hospitalization, to treat his tachycardic atrial fibrillation. His blood test results were as follows: TSH < 0.01 mIU/l, FT4 3.71 pmol/l, FT3 – 7.8 pmol/l. His TRAb level was 13.03 IU/l and his NT-proBNP level was 2444 pg/ml . Echocardiography revealed a dilation of the left heart chambers. The global contractile ability of the left ventricle was moderately reduced, with an ejection fraction (Simpson method) of 35%. Additionally, global hypokinesia of all segments, moderately severe mitral regurgitation, and a diastolic dysfunction were observed. As other causes of cardiac dysfunction had been ruled out, his heart condition was concluded to be a consequence of

unsatisfactory treatment of his thyroid disease. Therefore, his thyrostatic therapy was adjusted and the standard-of-care treatment for heart failure was initiated. He was also referred to the Multidisciplinary team for thyroid diseases, and it was decided that he would undergo a total thyroidectomy once his cardiac and thyroid status had stabilized. Four months later, a follow-up echocardiography showed that the global contractile ability of the left ventricle had improved significantly, with an ejection fraction (Simpson method) of 64%. There were no more signs of global hypokinesia. Due to the patient's suppressed TSH levels with normal FT3 and FT4 levels, it was decided to administer Lugol's Iodine solution prior to the total thyroidectomy, to achieve a preoperative euthyroid state. The total thyroidectomy procedure was successfully performed, and the patient was discharged as fully recovered. The patient's follow-up visits with a cardiologist and an endocrinologist are scheduled.

Conclusions

Hyperthyroidism should be considered as an etiological factor for dilated cardiomyopathy in the absence of other causes of structural and functional cardiac alterations.

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EP225

Post-partum thyroiditis with concurrent enlargement of thyroglossal duct cyst due to presumed thyroiditis within the cyst wall- a pathophysiological link or a coincidence?

Fatima Azad[1], Nadia Zarif[1] & Jana Bujanova[1]
[1]Southampton University Hospital NHS Foundation Trust, Department of Diabetes and Endocrinology, Southampton, United Kingdom

Introduction

The thyroglossal duct is an embryonic structure, lined predominantly by respiratory and squamous epithelium and typically involutes by the 10th week of gestation. If the thyroglossal duct does not involute, it can form cysts due to recurrent inflammation or infection, as it is lined by epithelium that is secretory in nature, with or without the presence of ectopic thyroid tissue. Thyroid tissue is present in the wall of the cyst/duct in 30-60% of cases.

Case report

38-year-old female presented five months postpartum with symptoms of heat intolerance, palpitations and weight loss. Her bloods confirmed hyperthyroidism with a FT4 of 31.8 pmol/l (7.7-15), TSH of 0.01 mU/l (0.34-5.6), WBC-4.7x10^9/l (4-11) and CRP- 1 mg/l (0-7.5). This was consistent with transient postpartum thyroiditis, followed by spontaneous recovery without the need for anti-thyroid medications. She had a family history of Grave's disease, but her thyroid stimulating immunoglobulins and anti-TPO antibodies were normal. She also had a background history of a stable small 1 mm thyroglossal duct cyst (TGDC) noted on ultrasound in 2010. On examination she was noted to have nontender, firm upper midline neck swelling at site of the known TGDC, however she reported TGDC size increase corresponding with the onset of hyperthyroid symptoms. Neck ultrasound confirmed a thin wall cyst with viscous fluid content and increase in size from 17x12x1 mm in 2010 to 30x15x1 mm). Her thyroid was of normal size with features of thyroiditis. There was no solid component within the cyst and the enlargement of TGDC was presumed to be related to thyroiditis within the cyst wall. The cyst was managed conservatively as ultrasound did not show any suspicious solid components and there was no evidence of infection.

Discussion

Autoimmune thyroiditis and thyroid cancer (predominantly papillary) have been reported within the ectopic thyroid tissue in the TGDC wall. The prevalence of cancer within the excised TGDS is reported at 0.7-4%, but there is no data on prevalence of thyroiditis in excised TGDCs. Our case illustrates that TGDCs might enlarge significantly as part of the post-partum thyroiditis process. In our case, the main contributor to the enlargement, in the absence of solid component on ultrasound, was accumulation of fluid from the epithelium in response to the presumed inflammation of the thyroid tissue within cyst wall. This might explain, why the TGDC size did not regress to baseline with resolution of thyroiditis (last follow up 9 months post onset).

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EP237

Efficacy of Photobiomodulation as an additional Therapy in Hashimoto Thyroiditis

Venera Berisha-Muharremi[1, 2], Bernard Tahirbegolli[3, 4], Ruth Phypers[5] & Reem Hanna[6, 7, 8]
[1]Faculty of Medicine, University of Prishtina., Prishtina, Kosovo; [2]Poliklinika Endomedica., Prishtina, Kosovo; [3]Heimerer College, Prishtina, Kosovo; [4]National Sports Medicine Centre, Prishtina, Kosovo; [5]Laser Medicine Centre, London, United Kingdom; [6]King's College Hospital NHS Foundation Trust, London, United Kingdom; [7]University of Genoa, Genoa, Italy; [8]UCL-Eastman Dental Institute, Faculty of Medical Sciences, Rockefeller, University College London, London, United Kingdom

Hashimoto thyroiditis (HT) is a thyroid-specific autoimmune disorder, and the most common cause of hypothyroidism in a population with an adequate dietary intake. Despite the current conventional treatment focused on the permanent replacement of levothyroxine (LT4) deficiency, it appears that thyroid autoimmunity remains the cause of persistent symptoms in patients with HT, even when they achieve to be in biochemically euthyroid state. Photobiomodulation (PBM) showed to be an effective additional therapy in treatment of autoimmune diseases, but with limited evidence. Hence, our study was conducted to appraise the efficacy of PBM therapy with supplements in restoring thyroid gland homeostasis in patients with HT compared with supplements alone. Seventy-four female subjects aged between 20 and 50 years old were recruited and divided equally into two groups: PBM+conventional treatment group (group 1); and conventional tretament alone group (group 2). The PBM dosimetry and treatment protocols were as follows: wavelength, 820 nm; power output, 200 mW; continuous emission mode; irradiating time, 20 s per point; fluence, 32 J/cm2 per point; treatment frequency, twice a week (excluding weekends); and treatment duration, three consecutive weeks. Whereas, both groups had the conventional treatment protocol, as follows: An appropriate dose of LT4 determined before their enrolment, subjects with a serum level of vitamin D3 <40 ng/dl, received replacement according to their serum levels, and all the subjects had a daily intake of 100 µg of oral selenium. The biochemical (FT3, FT4, antiTPO and antiTG) and anthropometric measurements were evaluated before, after three-months and after six-months follow-up. Our findings showed significant improvement in group 1 parameters (PBM+ convenentional) compared with group 2 (conventional only) in terms of reduction in the following parameters: TSH, antiTPO, antiTG, treatment dose of LT4, BMI, hip and waist circumference, waist/hip ratio ($p<0.05$). Our results, for the first time, demonstrated an efficacy of PBM delivered at a lower fluence with supplements in restoring thyroid function, anthropometric parameters and lifestyle factors in patients with HT. Hence, extensive studies with a longer follow-up period are warranted.

Keywords: Hashimoto thyroiditis; photobiomodulation; autoimmune thyroiditis; Data from the study are published in August 2023 in Journal of Personalized Medicine: https://www.mdpi.com/2075-4426/13/8/1274

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EP245

Thyroid storm: One major endocrine emergency revealing another !!

Ahmed Boukhalfa[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Mohamed VI University Hospital Center, Marrakech, Morocco, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Introduction

Thyroid storm (TS) is a severe manifestation of thyrotoxicosis, (1). It is most commonly seen in Graves' disease and can occur due to a non-compliance to anti-thyroid medications Management includes both addressing end organ damage and attaining a euthyroid state. We report the case of a patient who presented a thyroid storm complicating a grave's disease and unmasking, during its management, a corticotropic insufficiency.

Clinical Case

Fifty one year-old patient, diagnosed since 10 months with grave's disease under anti-thyroid-drugs (ATD) with non compliance, Admitted to the emergency department for vomiting, abdominal pain and fever. Clinically, we noted blood pressure at 16/10 cmhg, heart rate 146, temperature 38.7°C, widespread abdominal tenderness. Biological tests: TSH us <0.001, fT4 >100 pmol/l, fT3: 38, 25 pmol/l, with hepatic cytolysis, CRP: 127 mg/l, WBC: 14610. Thyroid storm was retained and patient undergone plasmapheresis. After an intensive care stay and challenging surgery preparation following deterioration in clinical condition and of biological parameters, a total thyroidectomy was performed without malignant signs in histological study. In the post-operative period, the patient began to experience arterial hypotension reaching 80/40 mmgh, and started vomiting again. Adrenal crisis suspected and 8 h cortisol was: 9 mg/dl. Treatment of an acute adrenal crisis was started with rehydration and bolus of intravenous HSHC with oral hydrocortisone relay, clinical and biological improvement. During follow-up, the patient revealed that she had been self-medicating with corticosteroid (dexamethasone) to gain weight for several years with a sudden stop.

Discussion
Symptoms that highly correlate with thyroid storm include fever ≥38°C, tachycardia ≥130 beats per minute, central nervous system manifestations, congestive heart failure, and gastrointestinal/ hepatic manifestations. First line therapy is represented by: antithyroid drugs, beta-adrenergic blockers, potassium iodid, glucocorticoids, antipyretics. If severe symptoms persist or no improvement, contrindications or toxicity, plasmapheresis is indicated before radical treatment (2). Our patient has non compliance of ATD and his body probably remained in a state of thyrotoxicosis which, in the presence of unrecognized adrenal insufficiency, led to a thyroid storm. Thyroid storm, initially masked adrenal insufficiency, but after surgery the clinical picture was transformed and corticotropic insufficiency due to prolonged corticosteroides self medication has been unmasked.
Conclusion
Our clinical case illustrates the difficulty of diagnosis in the case of association between thyroid storm and adrenal crisis and emphasizes the importance of questioning and physical examination in therapeutic management.
Keywords: thyroid storm, anti-thyroid drugs, thyroidectomy, adrenal crisis.
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EP250

Importance of timely diagnosis and treatment of graves' orbitopathy in euthyroid patient

Ann Kobaidze[1], Nino Tedoradze[1], Ilona Tserediani[2] & Meri Davitadze[3, 4, 5]
[1]Caucasus Medical Center, Endocrinology, Tbilisi, Georgia; [2]Medical center VIvamedi, Ophtalmology, Tbilisi, Georgia; [3]Clinic NeoLab, Endocrinology, Tbilisi, Georgia; [4]; [5]University of Birmingham, Institute of Applied Health Research, Birmingham, United Kingdom

Background
Graves' orbitopathy (GO) is one of the extrathyroidal manifestations of Graves' disease (GD), an autoimmune condition characterised by increased antibodies against TSH receptors (TRAb). The prevalence of GO among patients with GD is up to 40%. Moderate-to-severe, sight-threatening and sometimes even mild GO have significant negative impact on patient's quality of life (QoL). Various clinical presentations of GD itself, evaluation and timely management of GO can oftentimes become challenging resulting in delayed treatment and worsening of patient's QoL. Here, we describe a case of moderate-to-severe form of GO with delayed treatment.
Case
A 57-year-old woman first noticed right eye bulging about 2.5 years ago which she relates to an emotional stress. She was referred to an endocrinologist. Laboratory investigations revealed: TSH = 0.06 μIU/ml, FT4 = 1.1 ng/dl, FT3 = 3.4 pg/ml, Anti-TPO = 1300 IU/ml, TRAb = 3.47 IU/l. Despite GD, antithyroid drugs were not started. Although no treatment was provided, after 9 months, patient's symptoms resolved spontaneously and the laboratory tests revealed euthyroidism. Another year later, patient again suffered an emotional stress following which she developed unilateral right-sided exophthalmos. Laboratory tests revealed elevated TRAb of 1.78IU/l with euthyroidism (TSH = 1.64 μIU/ml). On thyroid ultrasound total volume of the gland was 5.1 cm^3 with heterogeneous structure and moderately increased vascularity, no nodularity. Orbital MRI showed infiltration of the right eye inferior and medial recti muscles. Activity and severity of GO was assessed with CAS = 5 and NOSPECS. The diagnoses of euthyroid GD and unilateral active moderate-to severe GO were established. However, relevant treatment was not initiated even at this point. 6 months later, she presented at our hospital with right-sided exophthalmos, diplopia, and eye movement restriction with upward and lateral gaze. Currently, thyroid function tests again showed euthyroidism with elevated TRAB (TSH = 1.61 μIU/ml, FT4 = 12.1 ng/dl, FT3 = 5.48 pg/ml, TRAb = 1.43 IU/l). Repeated assessment of GO now revealed inactive moderate-to severe form. At the same time, patient's daily activities are affected and QoL severely reduced. Patient was referred to an ophthalmic surgeon and strabismus surgery is now being considered in order to restore binocular single vision.
Conclusions
As our case demonstrates, it is crucial to recognise and treat active forms of GO independent of the thyroid function. Delayed treatment can result in irreversible changes in the orbits that can only be managed by surgery, simultaneously severely worsening patients' quality of life.
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EP272

Impact of smoking on thyroid gland functioning: a literature review

Houas Jihene[1], Heyfa Belhadj-Miled[1], Monia Ghammam[1], Malika El Omri[1, 2], Abir Meherzi[1], Mouna Bellakhdhar[1], Yosra Hasni El Abed[2], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT department, Sousse, Tunisia; [2], Department of endocrinology, Sousse, Tunisia

Introduction
Smoking is a major public health problem with a role as an endocrine disruptor, particularly on the thyroid. The aim of our study is to assess the effects of tobacco on the thyroid.
Methods
We conducted a systematic literature review from 1984 to 2022. The keywords used for the search included "Tobacco, " "Thyroid, " "Goiter, " "Thyroid nodule, " "Hypothyroidism, " "Hyperthyroidism, " "Thyroid cancer, " and "TSH." Evaluation in different studies focused on thyroid function, TSH levels, FT4 levels, thyroglobulins, anti-TPO and anti-TG antibodies, goitrogenic effect, impact on Graves' disease, Graves' ophthalmopathy, and the effect on thyroid cancer.
Results
Eleven articles were included in this literature review, involving a total of 19, 621 subjects, including 17, 000 smokers. The average age of the patients was 47 years. 43.66% of the subjects were male, and 56.33% were female, with a sex ratio of 0.77. According to the studies reviewed, smoking leads to a decrease in TSH levels, potentially resulting in hyperthyroidism. It has a goitrogenic effect, which can be explained by elevated plasma concentrations of thiocyanates in smokers, with the implicated mechanism being a decrease in iodide uptake. Smoking may also worsen Graves' ophthalmopathy and appears to reduce the effectiveness of treatments. Tobacco has not been implicated in the genesis of thyroid cancers.
Conclusion
Tobacco has a direct and often detrimental effect on neuroendocrine and thyroid function. It promotes hyperthyroidism, has a goitrogenic effect, and exacerbates Graves' ophthalmopathy.
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EP274

An uncommon and distinctive type of goiter to recognize: about 5 cases

Houas Jihene[1], Heyfa Belhadj-Miled[1], Monia Ghammam[1], Oussama Khalfi[2], Malika El Omri[1], Abir Meherzi[1], Mouna Bellakhdhar[1], El Ghali Wassim[3], Yosra Hasni El Abed[4], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT Department, Sousse, Tunisia; [2], Department of radiology, Sousse, Tunisia; [3]Department of Anaesthesia, Sousse, Tunisia; [4]Endocrinology Department, Sousse, Tunisia

Introduction
Dyshormonogenetic goiter is a rare entity that affects 1 in 30, 000 to 50, 000 live births, and it is the second most common cause (10% to 15%) of permanent congenital hypothyroidism. It is morphologically characterized by architectural and cellular pleomorphism that may mimic thyroid malignancy and cause difficulties in differential diagnosis.
Material and Methods
We present five cases of dyshormonogenetic goiter gathered at our service.
Results
The cohort comprised three patients, 2 females, and 3 males, with an average age of 18.6 years (range: 7 to 32 years). All five were offspring of consanguineous marriages and were under observation for congenital hypothyroidism. The chief complaint in all patients was a basal cervical swelling. Clinical examination revealed multinodular goiter in 4 patients and a right lobar nodule in one patient. Delayed growth and psychomotor development were noted in two patients. Cervical ultrasound and thyroid scintigraphy were performed in all cases. Ultrasound demonstrated multinodular goiter in all patients. Scintigraphy revealed overall thyroid hyperfixation in all cases, with a hypofixation zone on the right side in one patient. Thyroid function tests indicated hypothyroidism in all five patients. All patients underwent surgical treatment: total thyroidectomy in four cases and right lobectomy in one case. Histopathological examination confirmed dyshormonogenetic goiter in all five cases. Favorable outcomes were observed in all cases, with no recurrence.
Conclusion
Dyshormonogenetic goiter represents a rare benign condition characterized by architectural and cytological characteristics that, if not well understood, may contribute to the overdiagnosis of malignancy. Recognition of this entity becomes crucial in cases lacking strict histological criteria for malignancy, particularly in individuals with a history of hypothyroidism since infancy. An exact molecular diagnosis allows genetic counseling and the identification of asymptomatic mutation carriers
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EP276

Thyrotropin-receptor antibodies - diagnostic and prognostic significance in graves' disease - a clinical case

Radina Dimitrova[1, 2], Kiril Hristozov[1, 2], Savi Shishkov[1, 2] & Yana Bocheva[3, 4]
[1]Medical University "Prof. Dr. Paraskev Stoyanov ", Second department of internal medicine, Varna, Bulgaria; [2]St. Marina's Hospital, Clinic of Endocrinology and Metabolic Diseases, Varna, Bulgaria; [3]Medical University "Prof. Dr. Paraskev Stoyanov ", Department of General Medicine and Clinical Laboratory, Varna, Bulgaria; [4]St. Marina's Hospital, Clinical Laboratory, Varna, Bulgaria

Introduction
Graves' disease (GD) is unique among autoimmune endocrinopathies because the underlying immune disorder results in thyroid stimulation rather than functional or structural inhibition of the gland. However, thyrotropin-receptor antibodies (TRAbs), a specific and sensitive immunological marker for GD, are heterogeneous both in terms of their molecular structure and their biological activity. Stimulating TRAbs (TSIs) activate the thyrotropin (TSH) receptor. Blocking TRAbs reduce the action of TSH but can also be weak agonists. Neutral TRAbs have no effect on TSH binding. They are probably involved in the generation of oxidative radicals and the induction of apoptosis. Some TRAbs also inhibit agonist-independent ("constitutive") signaling and are called "inverse agonists". In fact, the clinical picture of GD is determined by the balance between the opposing activities of these antibodies, but this balance could change in the course of the disease.
Clinical case
A 67-year-old woman was admitted emergently to a cardiology unit due to acute heart failure based on high-frequency atrial fibrillation. The heart rate reached 167 beats per minute. During digitalization, normofrequency atrial fibrillation was achieved. Due to accompanying complaints of weight reduction, increased sweating and anxiety, thyroid function was also investigated, and thyrotoxicosis was established (TSH <0.004 mIU/ml, FT4 1 pmol/l, FT3 13.1 pmol/l). Based on the ultrasound of the thyroid gland (diffuse inhomogeneity with pseudonodulation and increased blood flow) and the examined immunological markers (thyroperoxidase antibodies (TPO Ab) <10 U/ml; TSI 5.7 IU/l), GD was diagnosed. Treatment with 1 mg propranolol and 1 mg thiamazole daily was initiated. Two months later, according to hormonal parameters (TSH 3.8 mIU/ml, FT4 8.1 pmol/l, FT3 4.1 pmol/l), the dose of thyrostatic was reduced to 1 mg daily. Restoration of sinus rhythm was also recorded. Control hormonal tests on the 4th month after diagnosis revealed severe hypothyroidism (TSH 101.25 mIU/ml, FT4 2.1 pmol/l, FT3 2.1 pmol/l) regardless of the reduced dose of thiamazole (1 mg daily). Analysis of immunological markers revealed high TRAbs titers (>40 IU/l) and reduced levels of stimulating immunoglobulins (TSI 2.11 IU/l). The therapeutic regimen was continued with 10 mg thiamazole in combination with 25 μg levothyroxine daily, but without β-blocker.
Conclusion
Both TRAK and TSI are useful for the diagnosis of GD, but their comparison is more important for treatment monitoring. The marked predominance of TRAbs over TSIs in the presented clinical case may be related to the presence of blocking/neutral TRAbs. This conclusion is supported by the observed clinical course of the disease.

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EP280

Role of ultrasound elastography in improving the correlation between thyroid nodule TIRADS scoring and FNA bethesda categories in solitary thyroid nodules

Nishanth David Thomas[1]
[1]Amrita Institute of Medical Sciences, Endocrinology, Kochi, India

Background
TIRADS scoring is used to assess the thyroid nodules using USG, commonest used is ACR-TIRADS; another is K-TIRADS scoring. Nodule stiffness is assessed by elastography strain Rago scoring & FNA nodule gives lower (benign) or higher Bethesda (possible malignant) category report. The combined use of TIRADS & Rago scorings with Bethesda as final output can assess whether addition of elastography improves the correlation between thyroid nodule TIRADS scoring and FNA Bethesda categories.
Methods
This was a Cross sectional study in Endocrinology Deptarment, AIMS. Patients with STNs were assessed because it would not affect elastography findings. ACR-TIRADS, K-TIRADS & Rago scores were done and based on standard criteria, FNA was done with Bethesda categorisation. Those who have Bethesda category II grouped as one & categories III to VI (possible malignant) grouped as other group (higher Bethesda categories). Pearson's Chi square test used for associations; in both groups, the data of ACR-TIRADS, K-TIRADS & Rago scores each alone; and combination of ACR-TIRADS with Rago & of K-TIRADS with Rago analysed with relation to prediction of higher Bethesda categories in them. ROC curves were plotted based on predicted probability scores and its AUC, sensitivity and specificity estimated.
Results
The AUCs for ACR-TIRADS, K-TIRADS & Rago scoring each alone in predicting higher Bethesda categories were not significant (sensitivity & specificity best for Rago alone); same for combined ACR-TIRADS & Rago scoring, and combined K-TIRADS & Rago scoring were statistically significant. Even though TIRADS scores were higher, the lower the elastography Rago score in nodules, the lower were the prediction probability of higher Bethesda categories in nodules.
Conclusions
This study showed that combination of USG elastography and TIRADS scoring data in cases of STNs, predicted higher Bethesda categories on FNA in them. Also showed that the lower the elastography Rago score in STNs, lower was the prediction probability of higher Bethesda categories, however higher the TIRADS scores were.

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EP283

The relevance of a gluten-free diet in the treatment of patients with hashimoto's thyroiditis without celiac disease

Aline Alcantara[1]
[1]UNINOVE - Campus Vergueiro, Department of Medicine, São Paulo

Hashimoto's thyroiditis is an autoimmune condition characterized by the infiltration of lymphocytes into the thyroid gland, resulting in the subsequent production of antibodies directed against thyroglobulin and thyroid peroxidase. This pathology is the primary etiology of hypothyroidism in developing countries. Recently, researchers have focused on studying the inflammatory potential of gluten, not only in the intestinal context, where it can act as a trigger for dysbiosis but also systemically, with the ability to influence the production of pro-inflammatory cytokines by T cells. However, there is controversy regarding individuals without gluten intolerance or celiac disease concerning the inflammatory potential of gluten and whether there is any benefit in its exclusion from the diet. This article aims to conduct a comprehensive literature review covering the last six years, based on records available on the PubMed platform, to clarify the relevance of implementing a gluten-free diet in patients diagnosed with Hashimoto's thyroiditis who do not have concomitant celiac disease. The keywords "Hashimoto thyroiditis gluten" were used, covering the publication period between 2018 and 2023, identifying 34 scientific articles. Excluded were those not directly related to the research topic or duplicated, resulting in the inclusion of 14 works, comprising literature reviews, meta-analyses, case reports, and original articles. As a conclusion, there was no evidence of symptom improvement or antibody reduction with the introduction of a gluten-free diet in patients without celiac disease or gluten intolerance. However, it is important to note that patients with autoimmune diseases, such as Hashimoto's thyroiditis, are statistically more susceptible to developing food intolerances. Thus, a significant number of patients with Hashimoto's thyroiditis may have undiagnosed celiac disease or gluten intolerance and would benefit from gluten removal from their diet. Nevertheless, gluten withdrawal for the rest of the population without indications tends to result in increased caloric intake, higher consumption of processed foods, reduced fiber intake, and approximately a 30% increase in food expenses. Therefore, it is concluded that the addition of a gluten-free diet is not beneficial for patients without a diagnosis of celiac disease or gluten intolerance. However, in patients with autoimmune diseases, such as Hashimoto's thyroiditis, investigating even asymptomatic food intolerances is essential due to their higher prevalence in this population.

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EP284

Diagnostic difficulties in a patient with thyroid lymphoma

Agnieszka Maksymiuk-Klos[1], Joanna Sobolewska[1], Jerzy Zabłocki[2], Agnieszka Wojciechowska-Luzniak[1] & Przemysław Witek[1]
[1]Medical University of Warsaw, Department of Internal Medicine, Endocrinology and Diabetology; [2]Medical University of Warsaw, Department of General and Vascular Surgery

Primary thyroid lymphoma (PTL) is a rare disorder, representing merely 1-5% of all thyroid malignancies, 1-2% of extranodal lymphomas and 3% of non-Hodgkin's lymphomas. It affects mainly women. PTL incidence is low in individuals younger than 40 years old. The most common clinical presentation of PTL is a palpable mass in the neck. It may be accompanied by other symptoms: dysphagia, dyspnea, and hoarseness. Diffuse B-cell lymphoma (DLBCL), is the most common pathological subtype of PTL. Hashimoto thyroiditis (HT) is essential risk factor of PTL. In clinical practice, a rapidly enlarging neck mass, accompanied by compressive symptoms, in women with HT should prompt the exclusion of PTL. Core-needle biopsy is superior to fine-needle biopsy in this cases. A 40-year-old female patient with AIT, on substitution therapy with L-thyroxine, was admitted to the hospital due to increased dyspnea accompanied by stridor. She presented a history of upper respiratory tract infection symptoms for two weeks, a feeling of mild dyspnea and an enlargement of the neck circumference. On admission to the Emergency Department (ED), the patient was cardiovascularly and respiratorily stable, with neck oedema, palpable thyroid enlargement and an exacerbated alveolar murmur on physical examination. Laboratory tests on admission were as follows: WBC 5.97 10^3 [4.00—10.00], CRP 24.00 mg/l [< 5.00], PCT 0.11 ng/ml [< 0.5], TSH 4.898 uIU/ml [0.350-4.940]. Chest X-ray demonstrated tracheal stenosis. In ED, a patient was treated with improvement with hydrocortisone intravenously. Ultrasound evaluation revealed a markedly enlarged thyroid gland (V = 86, 1 cm^3), with heterogeneous reduced echogenicity with focal/infiltrative changes and markedly enlarged pre-tracheal lymph nodes below the isthmus. In an examination performed five months earlier, the dimension of the thyroid gland was significantly smaller (V = 22, 1 cm^3). The BACC performed at that time resulted in a category II in the Bethesda classification. In the following days, due to a massive goitre with associated increasing compression symptoms, she was qualified for a total thyroidectomy. The conditions of the procedure were challenging - numerous adhesions and problematic infiltration of the thyroid parenchyma with surrounding tissues. Postoperative wound healing was as expected, and ENT evaluation revealed no vocal fold mobility disorders. In the following days, due to a tetanic seizure, patient was treated with calcium chloride intravenously, with clinical improvement. Histopathological evaluation revealed a pattern suggestive of large B-cell lymphoma infiltration. Oncological treatment has been initiated. This case emphasizes the difficulties in the early diagnosis of thyroid lymphoma.

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EP302

Ideas commonly held about the treatment of hypothyroidism during pregnancy

Belhadi Leila[1], Bensbaa Salma[1], Haraj Nassim Essabah[1], El Aziz Siham[1] & Chadli Asma[1]
[1]University Hospital Center Ibn Rochd, Department of Endocrinology and Metabolic Diseases, Casablanca, Morocco

Introduction
The occurrence of pregnancy in patients with hypothyroidism is a common event. Thyroxine requirements increase in nearly 80% of pregnant women. Educating young patients with hypothyroidism about the adaptation of treatment and the need for close biological monitoring helps prevent complications of maternal hypothyroidism in the fetus.
Objective
The objective of our study was to assess the knowledge of patients about the management of levothyroxine during pregnancy and the need for TSH monitoring during pregnancy.
Patients and Methods
A descriptive study included 33 patients followed for hypothyroidism in the pregnancy consultation at the Endocrinology and Metabolic Disease Department at CHU Ibn Rochd. We developed a questionnaire of misconceptions reported by our pregnant women in our context. The analysis was performed using the SPSS software.
Results
The average age of our patients was 32 years (21-49). A low socioeconomic level was observed in 89% of patients. The referring physician was a gynecologist in 76% of cases, a general practitioner in 19% of cases, and an endocrinologist in 5% of cases. Pregnancy was not desired in 17% of cases, and 83.3% of patients had planned their pregnancy. The gestational age at the first consultation with us was on average 20 weeks. The average dose of levothyroxine before pregnancy was 100 µg/day. None of the patients had a pre-conception consultation for TSH measurement and adaptation of levothyroxine dose. None of the patients knew their TSH target. Discontinuation of levothyroxine upon pregnancy diagnosis was adopted by 46.1% of patients, and 53.9% of patients kept the same dose while waiting to see their doctor; however, none of the patients titrated the levothyroxine dose. Regarding complications of hypothyroidism on fetal development, 98.8% had no idea about these consequences. For breastfeeding, 74.3% of pregnant women thought that levothyroxine passes into breast milk but did not know if they should stop it.
Conclusion
Women with hypothyroidism of childbearing age should receive education on the vital necessity of substitute treatment and its adaptation before conception and during pregnancy, as well as the need for biological monitoring, to prevent the consequences of maternal hypothyroidism on fetal brain development.

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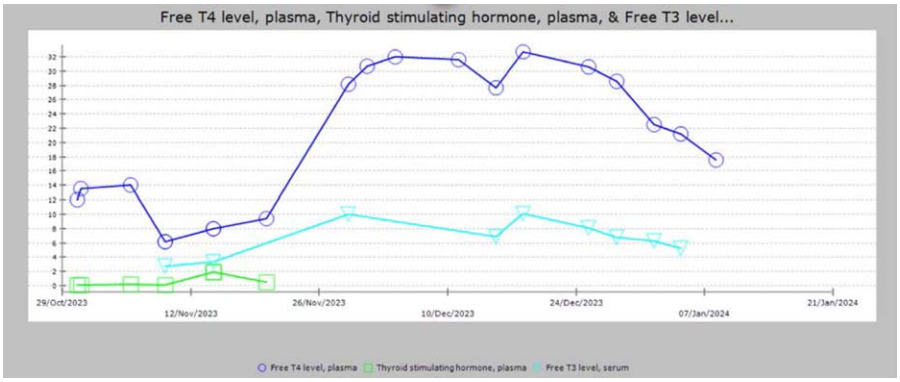
EP310

Propylthiouracil-induced severe hepatotoxicity in grave's disease: a unique case illustrating complex challenges and therapeutic strategies

Sulmaaz Qamar[1], Beenish Masood[1], Raghavendra Palani[1], Nazanin Karimaghaei[1], Ahmed Yousseif[1, 2], Dipesh Patel[1, 2], Bernard Khoo[1, 2], Efthimia Karra[1] & Eleni Armeni[1]
[1]Royal Free Hospital, Endocrinology and Diabetes, London, United Kingdom; [2]University College London, London, United Kingdom

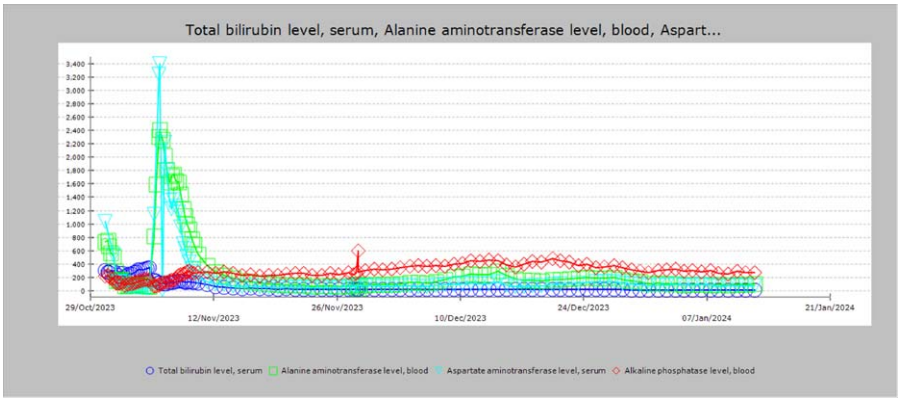
Background
Hyperthyroidism often presents with aberrant liver function. The differential diagnosis of this presentation includes thyrotoxicosis-associated liver dysfunction or antithyroid drug-induced liver dysfunction. We present a case where Propylthiouracil treatment resulted in acute liver failure.
Case Presentation
A female patient diagnosed with Grave's disease in August 2023 initially received carbimazole but discontinued this due to vomiting. Subsequent initiation of PTU in September 2023 resulted in admission with decreased conscious level, jaundice



(Abstract EP310)

TSH remained < 0.01 mIU/l after the 20th November

(Abstract EP310)



and severe acute liver failure after six weeks of starting. Laboratory findings on admission included a bilirubin level of 384, INR of 10.9, ALT of 1200. Propylthiouracil was discontinued.

Intervention and Post-Transplant Course

Urgent liver transplantation was performed in early November 2023, with post-surgical Klebsiella hospital-acquired pneumonia, a prolonged stay in intensive care and a slow wean requiring a tracheostomy. Despite transplantation, she had persistent abnormal liver function. Liver USS and Doppler studies confirmed mild hepatic steatosis with patent vessels. Liver biopsies done at four weeks post-transplant and six weeks revealed severe steatosis and minimal portal inflammation, excluding rejection as a cause. The patient continued azathioprine, tacrolimus, and prednisolone (1 mg daily) for liver function and hyperthyroidism management.

Challenges in Thyroid Management

Efforts to manage hyperthyroidism post-transplant with carbimazole were met with vomiting, which was managed with a dose reduction. She is planned for elective thyroidectomy as of writing.

Importance and Rarity

This case underscores the challenges in navigating severe hepatotoxicity induced by PTU in Grave's disease. Clinicians should be vigilant for this rare but severe complication of PTU treatment.

Conclusion

This distinctive case provides valuable insights into the intricacies of thyroid medication-associated liver failure. It highlights the importance of cautious PTU use, contributing to the growing body of evidence guiding clinicians in managing similar challenging clinical scenarios.

Keywords: Grave's disease, propylthiouracil, hepatotoxicity, liver transplantation, caution. TSH remained <0.01mIU/l after the 20th November

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EP355

Increased psychological distress among patients with two or more endocrinopathies during Covid-19 pandemic: the EPITOME Study

Vasiliki Daraki[1], Theano Roumeliotaki[2], Panagiotis-Nikolaos Tsakalomatis[1], Grigoria Betsi[1], Maria Sfakiotaki[1], Maria Chrysoulaki[1], Eleni-Konstantina Syntzanaki[1], Vasiliki Venetsanaki[1], Rodanthi Vamvoukaki[1], Kalliopi Kontolaimaki[1], Eirini Makraki[1], Ioannis Kopidakis[1], Christos Dimas[1], Stella Lioudaki[3], Christos Ioannou[3], Konstantinos Krasagakis[4], Panagiota Goulia[5] & Paraskevi Xekouki[1]

[1]University General Hospital of Heraklion, Endocrinology and Diabetes Clinic, Crete, Greece; [2]University of Crete, Department of Social Medicine, Heraklion, Crete, Greece; [3]University General Hospital of Heraklion, Department of Vascular Surgery, Crete, Greece; [4]University General Hospital of Heraklion, Department of Dermatology, Crete, Greece; [5]Cambridgeshire & Peterborough NHS Foundation Trust, Cambridge, United Kingdom

Background

Psychological distress is elevated during pandemics such as the COVID-19 outbreak. Patients with diabetes mellitus (DM), are a particularly vulnerable risk group. However, data of the impact of other endocrinopathies on psychological status of patients during pandemics are lacking so far.

Aim

To compare psychological distress about COVID-19 pandemic, between endocrine patients with a variety of endocrinopathies and patients with non-endocrine diseases (controls) seen in the outpatient clinics of the University Hospital, Heraklion, Crete, Greece.

Methods

One hundred and seventy four endocrine patients seen at the outpatient Endocrine clinic and two hundred and four controls without endocrinopathies seen at the Dermatology and Vascular Surgery outpatient clinics completed questionnaires about demographics, need for information, sources of information worries about the COVID-19 pandemic and the Greek version of the DASS-21 for psychological distress questionnaire. The levels and prevalence of stress, anxiety, and depression about the COVID-19 pandemic between the two groups were compared after controlling for age, gender, education, residence, employment status and ever diagnosed with psychiatric disease in multiple logistic regression models. Ethical approval was obtained by Institutional Review Board.

Results

Mean age of endocrine patients was 50.8 years and controls 45.7 years ($P<0.001$); with predominance of women in both groups ($P=0.017$). Among endocrine patients 62.1% suffered from thyroid diseases, 29.9% from DM, 18.9% from gonadal dysfunction and 12.1% from pituitary disorders. Adrenal and calcium disorders were mentioned in less than 10% of patients. The majority of endocrine patients (83.1%) were well-controlled, whereas 28.7% had two or more endocrinopathies. Hypertension and coronary vascular disease were more common in endocrine patients compared to controls (28.7% vs 16.2% and 8.7% vs 3.4% respectively), Mild and moderate stress symptoms were observed in both groups. Patients with two or more endocrinopathies reported significantly increased prevalence of stress symptoms compared to controls (odds ratio (OR): 2, 1; $P=0$, 045). We found no differences in anxiety and depression symptoms between the two groups, which showed low rates of both.

Conclusions

The current study highlights the increased risk of stress symptoms in endocrine patients with two or more endocrinopathies during Covid-19 pandemic. These results are relevant when designing policies on information on pandemics and supportive measures for endocrine patients in General Hospitals.

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EP356

Intrathyroidal dexamethasone therapy in subacute thyroiditis: preliminary findings from the DLISAT Study

Magdalena Stasiak[1, 2], Magdalena Rosińska[2], Zuzanna Berkan[2], Arkadiusz Zygmunt[2, 3] & Andrzej Lewinski[2, 3]

[1,2]Polish Mother's Memorial Hospital - Research Institute, Department of Endocrinology and Metabolic Diseases, Lodz, Poland; [3]Medical University of Lodz, Department of Endocrinology and Metabolic Diseases, Lodz, Poland

Background

Clinically severe or recurrent subacute thyroiditis (SAT) frequently requires treatment with high cumulative doses of systemic steroids. Such therapy is associated with high risk of steroid-related complications. The DLISAT study

aims to evaluate the efficacy and safety of intrathyroidal dexamethasone and lidocaine injections (DLI) in specific patient cohorts compared to standard oral steroid therapy. This report presents preliminary results after the initial six months of the study.
Methods
The study group (SG) comprised five patients, including two patients with treatment-naive SAT and contraindications or lack of consent for systemic therapy, two patients experiencing SAT recurrence soon after completion of oral therapy and one patient with steroid-dependent SAT. The control group (CG) consisted of five consecutive patients treated with oral prednisone. In SG patients, 4 mg of dexamethasone (1 ml of solution), with or without 1 ml of 2% lidocaine, was injected into each thyroid lobe. The injections were ultrasound (US)-guided. On the basis of the obtained results doses were repeated every 2-5 days, as required. Parameters measured before and after injections included pain severity, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), and thyroglobulin (Tg). Ultrasound and shear wave elastography (SWE) results were analyzed before and after each injection.
Results
All SG patients exhibited an excellent rapid and long-term response with no side effects, except for injection-related discomfort. The first injection in SG patients led to significant pain reduction, improved ESR, CRP, thyroid parameters, US and SWE findings. The number of doses required for total recovery were 2-6 and a mean dexamethasone dose for the entire therapy was 32 mg. The longest therapy period was 20 days and no recurrence was observed. Persistent hypothyroidism occurred in one CG patient. In comparison, the mean therapy period in CG was 93 days and a mean dose of oral prednisone was 1580 mg.
Conclusion
The efficacy and safety of DLI in SAT were excellent and the method seemed more beneficial than standard oral steroid therapy, especially in patients with high risk of steroid-related complications.

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EP357

Surgical management of graves' disease: personal experience and literature review

Rachida Bouattay[1], nawres bouaziz[1], Amaidi Rami[1], Mehdi Ferjaoui[1], Elkorbi Amel[1], Naourez Kolsi[1], Harrathi Khaled[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Background
Graves' disease (GD) is a predominantly female autoimmune disorder of the thyroid gland. It is characterized by a diffuse goiter and biological hyperthyroidism. The optimal treatment of GD is still controversial. Surgery is one treatment option along with radioactive iodine (RAI) and antithyroid medication (ATM). The aim of the study is to review our experience in the surgical management in Graves' disease.
Patients and Methods
This is a retrospective study involving patients who underwent surgery for Graves' disease over a twelve-year period from January 2010 to December 2021.
Results
Our series included 51 patients, 38 women (75%) and 13 men (25%) with an average age of 39.41 years and extremes of 14 to 69 years. The mean time between diagnosis and surgical treatment was 18.4 months. At the time of diagnosis, cervical examination revealed a diffuse and homogeneous goiter in 22 cases (43%), nodular goiter in 6 cases (12%) and multi-nodular goiter in 23 patients (45%). Hyperthyroidism was observed in 23 patients (45.1%), and euthyroidism was noted in 28 patients (54.9%). In our series, surgery was indicated in cases of: resistance to medical treatment with an average duration of treatment with ATM of 12 months (84%), poor compliance (8%), associated thyroid carcinoma (6%) and treatment intolerance (2%). All our patients underwent total thyroidectomy with extemporaneous exam in 32 patients (62.7). Intraoperative examination suggested malignancy in 9 cases (17.6%). So, a bilateral central neck dissection was performed in these cases. Postoperative complications included transient hypocalcemia in 21 patients (41.17%), transient dysphonia in 3 patients (5.88%), hematoma in 2 patients (3.92%) and keloid scarring in 1 patient (2%). Histologic exam confirmed the diagnosis of thyroid cancer associated with Graves' disease in 9 patients (17.6%): 8 papillary microcarcinomas and one papillary carcinoma. A radioiodine therapy was indicated in these cases.
Conclusions
If surgery is considered for definitive management, evidence-based criteria support total thyroidectomy as the surgical technique of choice for GD. Available evidence also supports surgery in the presence of severe endocrine Graves' ophthalmopathy. Children with GD should be treated with an ablative strategy. Whether this is achieved by total thyroidectomy or RAI may still be debatable. Data on long-term cancer risk are missing; and until RAI has proven harmless in children, authors continue to recommend surgery in this setting. Postoperative complications are frequent and not negligible, hence the need for preoperative medical preparation.

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EP358

The mutual relationship between trace elements (Ca, Cu, Zn, Fe, Se, I) and thyroid parameters in mothers and neonates

Dorota Filipowicz[1], Ewelina Szczepanek-Parulska[1], Sabrina Asaad[2], Thilo Samson Chillon[2], Aniceta Ada Mikulska[3], Marta Karaźniewicz-Łada[3], Franciszek Główka[3], Lutz Schomburg[2] & Marek Ruchala[1]
[1]Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences; [2]Institute of Experimental Endocrinology, Charité University Medicine; [3]Department of Physical Pharmacy and Pharmacokinetics, Poznan University of Medical Sciences

Introduction
Pregnancy is a challenging time to maintain proper thyroid function in mothers and to provide sufficient thyroid hormones to the developing fetus. Micronutrient deficiencies are very frequent during gestation. So far only a few microelements are recommended as a routine supplementation and there is a gap in understanding the mutual relationship between multiple trace elements. The study aimed to verify the micronutrient status concerning thyroid parameters in the cohort of mothers and newborns.
Materials and methods
Women in the 3rd trimester of pregnancy (114), healthy and with autoimmune thyroiditis (AIT), together with their newborns (93) were recruited in the obstetric department before delivery in the tertiary reference Polish centre. Blood serum and spot urine samples from mothers and additionally neonatal cord blood were analysed. Microelement status was assessed in serum by Total Reflection X-ray Fluorescence analysis (on TXRF spectrometer S4 T-STAR). Additionally, thyroid parameters with antithyroid antibodies were measured in mother-newborn pairs and TSH concentrations from neonatal screening were analysed. The research was funded by the National Science Centre in Poland (2019/33/N/NZ5/02303) as PRELUDIUM-17 grant.
Results
More than half of mothers were poorly supplied in Ca, around 1/4 had Se and Zn shortages and 1/10 were deficient in Cu, where only 2.5% had insufficient Fe concentration. Median ioduria was 101 μg/l, which is below the WHO recommended value. Multinutrient formulas dedicated to pregnancy were taken by 68% of women. Maternal and neonatal micronutrients (Ca, Cu, Zn, Se) were adequately correlated with the strongest relation for Ca ($r=0.5$, $P<0.001$). Multiple correlations were also noticed among various trace elements in mothers and newborns, with the most prominent between Zn and Ca in mothers ($r=0.78$, $P<0.001$) and neonates ($r=0.68$, $P<0.001$). Maternal Ca, Fe and Se were related to ioduria. Additionally, Ca, Cu, Zn in mothers and Fe, Cu, Se in neonates correlated inversely with TSH screening values. Micronutrient supply was not different in AIT vs non-AIT women, although maternal Cu, Ca, Zn and neonatal Se, Fe, Zn correlated negatively with TRAb level.
Conclusions
Many pregnant women are at risk of health-relevant trace element deficiency, despite common supplementation of multinutrient preparations. Maternal supply may affect the newborn microelements status. Trace element screening and supplementation verification in pregnancy would be beneficial to mothers and newborns. Proper nutritional intake may improve thyroid parameters and decrease the concentration of thyroid antibodies. More studies on the mutual interplay between various microelements in pregnancy are warranted.

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EP360

Thyroid and lipid profile values in patients with vs without Graves' ophthalmopathy

Ana-Maria Stancu[1,2], Anastasia Patricia Stanescu-Smocot[3], Daniela Alexandrescu[3], Cristina Stancu[3] & Corin Badiu[2,3]
[1]Mioveni City Hospital, Endocrinology, Mioveni, Romania; [2]University of Medicine and Pharmacy "Carol Davila", Faculty of Medicine, Bucharest, Romania; [3]National Institute of Endocrinology "C.I. Parhon", Endocrinology IV, Bucharest, Romania

Context
Graves' ophthalmopathy (GO) is a debilitating condition that affects 30% patients with Graves' disease (GD). It is the most common extra-thyroidal manifestation of GD, but only 3-5% of GO cases are sight – threatening.
Objective
To compare the thyroid and lipid profile of GD patients who developed GO vs those without GO. The second objective is to analyze the prevalence of smoking status and insufficient 25 (OH) vitamin D levels.
Design
This is an observational, cross-sectional study in a tertiary endocrinology center.
Subjects and Methods
The study includes 151 GD adult patients treated with methimazole (MMI) alone ($n=95$) or MMI with levothyroxine (LT4) ($n=56$), with no history of radioactive iodine therapy or thyroidectomy. Pregnant women were excluded. Patients were divided into two subgroups according to the absence (GO-) or presence (GO+) of GO.
Results
The GO- subgroup included 92 (60.93%) patients aged 46.6±14.5 years and the GO+ subgroup included 59 (39.07%) patients aged 49.7±12.3 years. The proportion of smokers in GO+ subgroup was higher than in the GO- subgroup (*P*-value 0.004). The number of hypothyroid patients (fT4 <8 pmol/l) was higher in the GO+ subgroup than in the GO- subgroup, 4/92 (4.32%) patients vs 8/59 (13.55%) patients (*P*-value 0.04). The mean dose of LT4 was higher in patients on block and replace therapy in the GO+ subgroup than in those in the GO- subgroup, 55.4±21.3 mg/day vs 42±17.9 mg/day (*P*-value 0.01). No differences in mean doses of MMI, treatment regimens and lipid profile were observed between the two subgroups. In patients with mild GO, triglyceride levels were lower than those with moderate-severe and severe GO (90.9±32.6 mg/dl vs 137.3±97 mg/dl, *P*-value 0.012). 25 (OH) vitamin D was measured in 60 patients in subgroup GO- and 42 patients in subgroup GO+. The mean level of 25 (OH) vitamin D was similar between the two subgroups: 26.17±9.74 ng/ml in subgroup GO- vs 23.3±11.8 ng/ml in subgroup GO+, *P*-value 0.2. When 25 (OH) vitamin D <20 ng/ml was selected, 16 (26.67%) of 60 patients in subgroup GO- and 21 (50%) of 42 patients in subgroup GO+ had insufficient vitamin D levels, *P*-value 0.01.
Limitation
The study did not include data on other risk factors for metabolic syndrome.
Conclusion
Identifying and manage GO' risk factors such as smoking, hypothyroidism and high lipid profile may influence the course of GO. Vitamin D cut off below 20 ng/ml could be a risk factor for development of GO.

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EP361

Liothyronine (LT3) prescribing in england – are cost constraints inhibiting guideline implementation?

Adrian Heald[1], Lakdasa Premawardhana[2], John Warner-Levy[1], Peter Taylor[2], Nadia Chaudhury[3], Onyebuchi Okosieme[2], Mike Stedman[4] & Colin Dayan[2]
[1]Salford Royal Hospital, Salford, Department of Endocrinology and Diabetes, Salford, United Kingdom; [2]Thyroid Research Group, Systems Immunity Research Institute, Cardiff University School of Medicine, Cardiff, Wales, Cardiff, United Kingdom; [3]University Hospitals Coventry and Warwickshire, Department of Endocrinology and Diabetes, Coventry, United Kingdom; [4]Res Consortium, Andover, England, Andover, United Kingdom

Introduction
Primary hypothyroidism affects about 3% of the general population in Europe. In most cases, people are treated with Levothyroxine. In relation to the recent British Thyroid Association guidance and the 2020 Competitions and Marketing Authority (CMA) ruling, we examined prescribing data for levothyroxine, NDT and liothyronine by dose, regarding changes from 2016 to 2022.
Design
Monthly primary care prescribing data for each British National Formulary (BNF) code (England Monthly GP Practice thyroid replacement prescribing data. Accessed 17 July 2023). was analysed for Levothyroxine, Liothyronine and NDT
Patient and Measurements
The rolling 12-month total/average was used to identify the moment of change. Results included the number of prescriptions, the actual costs, and the cost/prescription/ mg.
Results
Liothyronine: In 2016 94% of the total 74, 500 prescriptions were in 1 mg dose. In 2020 the % in 1 mg and 1 mg doses started to increase so that in 2022 each reached 27% of total liothyronine. The average Cost/prescription in 2016 of 1 mg was £404/prescription and fell by 80% to £101 in 2022; while the 1 mg cost £348/prescription fell much less by 35% to £255 and 1 mg £355/prescription fell much less by 38% to £242/prescription. Total prescriptions 74, 605 issued in 2016 fell by 30% until 2019 and then started to grow again at 60, 990 15% lower, so total costs have fallen by 70% to £9m/year.

Table 1: Change in the cost between 2016 to 2022 - for LT4, by tablet dose for LT3 and NDT

Drug	Cost per prescription (% change vs 2016)		Total prescriptions (% change vs 2016)		Total cost/year (% change vs 2016)	
	2016	2022	2016	2022	2016	2022
LT4	£2.74	£1.47 (- 48%)	30.8 million	33.4 million (8%)	£90,504, 057	£52,439, 700 (-42%)
Total LT3**	£404 £348	£101 (- 75%)	74, 500	60,999 (- 18%)	£30,034, 992	£ 9,029, 544 (- 70%)
20 mg	£355	£255 (- 27%)				
10 mg 5 mg		£242 (- 32%)				
NDT	£207	£440 (+113%)	4257	2384 (- 44%)	£885s,887	£1,049, 192 (18%)

Conclusions
Liothyronine costs fell after the CMA ruling but remain orders of magnitude higher than levothyroxine so the remaining 0.2% of patients are still absorbing 16% of medication costs. Lower liothyronine doses as recommended by BTA are 240% of the costs of the 1 mg dose, so following the latest BTA guidance incurs substantial additional costs. High drug price continues to impact clinical decisions limiting therapy availability to a considerable number of patients.

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EP362

A case of levothyroxine malabsorption corrected with vitamin c

Yaşar Aydoğmuş[1], Beril Turan Erdoğan[1], Sevgül Fakı[1], Berna Öğmen[1], Cevdet Aydın[1], Oya Topaloğlu[1], Reyhan Ersoy[1] & Bekir Çakır[1]
[1]Ankara Bilkent Şehir Hastanesi, Endokrinoloji, ankara, Turkey

Introduction
Malabsorption of levothyroxine is an important clinical problem. Changes in gastric pH due to various medical conditions might cause challenges in maintaning normal TSH values.
Case
A forty-nine years old female who has been followed up with a diagnosis of primary hypothyroidism for 12 years admitted to our outpatient clinic with a complaint of unachievement of euthyroidism despite increasing the levothyroxine dose up to 200 mg. He did not have any other chronic disease and was not using any other medication. In laboratory examination, free T3 was 1.14 ng/l (2.3 - 4.2), free T4 was 0.32 ng/dl (0.89 – 1.76) and TSH was 129 mU/l (0.55 – 4.78). Thyroid autoantibodies were markedly high (antithyroglobulin >1000 IU/ml and antithyroid peroxidase antibody >13000 U/ml) and thyroglobulin was <0.20 µg/l Tthyroid ultrasonography showed heterogeneous parenchyma with widespread patchy hypoechoic areas and thin-thick fibrous bands. Free T4 was was measured just before and after the administration of oral levothyroxine 200 mg. Basal, first hour and second hour free T4 were 0.23 ng/dl, 0.29 ng/dl and 0.29 ng/dl, respectively. A malabsorption test was performed with 500 mg levothyroxine. Accordingly, free T4 was 0.40 ng/dl at basal state, 0.41 ng/dl in the first hour, 0.50 ng/dl in the second hour and 0.47 ng/dl in the fourth hour. Thus, free T4 level increased by a maximum of 25%. The patient's celiac and anti-pariatel cell antibodies were negative. Helicobacter Pylori antigen tested in the stool was detected positive. The patient's upper gastrointestinal endoscopy revealed antral gastritis and colonoscopy revealed Grade 1 internal hemorrhoids, He was given 1000 mg/day vitamin C. At the third day of vitamin C, serial free T4 levels were measured after ingestion of 250 mg levothyroxine. While basal TSH

was 112 mU/l and free T4 was 0.5 ng/dl, free T4 increased to 0.71 ng/dl at the first, 0.80 ng/dl at the second and 0.80 ng/dl at the fourth hour. A maximum increase of 60% in free T4 value was detected.
Conclusion
There are publications in the literature showing that vitamin C corrects abnormalities in serum free T4, T3 and TSH in patients with hypothyroidism and gastrointestinal pathology. Although the mechanism was not explained clearly, it was suggested that decreasing pH via vitamin C might increase the absorption of the drug. Co-administration of vitamin C with L-T4 may be useful in the treatment of patients with high TSH values despite high doses of L-T4.

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EP364

Management of methimazole allergy with methimazole: about two cases

Oumeyma Trimeche[1], Bilel Ben Amor[1], Ekram Hajji[1], Ines Bayar[1], Sana Abid[1], Héla Marmouch[1], Hanene Sayadi[1] & Inès Khochteli[1]
[1]Fattouma Bourguiba University hospital, Monastir, Tunisia

Introduction
Graves' disease is a frequent endocrine disorder, often treated as first-line therapy with antithyroid drugs. Herin, we report two female patients with Methimazole allergy while detailing its management.
Case Reports
TWO female patients aged respectively 27 and 28 years old were diagnosed with Graves' disease (GD), diagnosed given the association of peripheral hyperthyroidism and elevated anti TSH receptor antibodies. The first developed a generalized dermographism urticaria one week after being put on 10 mg per day of methimazole (MTZ). After being ceased, she was put on 16 mg of Methyprednisone, 25 mg of Hydroxyzine and 10 mg of Cetirizine and careful restart of low dose MTZ. The lesions disappeared after two days and MTZ dose was progressively increased, to an optimal dose of 1 mg per day. Control thyroxine level was normal. The second developed urticaria shortly after MTZ introduction. Thus, she was put on Benzythiouracile (BZT), which was complicated with severe neutropenia. BZT was stopped. A first trial of low dose methimazole, Cetirizine and cholestyramine was carried out but failed since she redeveloped diffuse urticaria. MTZ was ceased and then carefully reintroduced at a dose of 2.5 mg per day associated with Cetirizine, Hydroxyzine and 0.5 mg per kg of prednisone. A significant improvement of her clinical symptomatology was noted few days later. Prednisone was tapered down and parallelly MTZ dose was increased to 40 mg per day. The two patients are actually euthyroid with MTZ and after three months of therapy corticoids were stopped. The first had thyroidectomy and is actually on optimal dose of Levothyroxine and the second had radioactive iodine therapy and was lost to follow up thereafter.
Conclusion
These cases highlight the possible treatment of methimazole allergy with corticoids and anti-histamine drugs and their reintroduction thereafter, while detailing the used protocol.

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EP365

Tocilizumab for the treatment of active steroid-resistant graves' orbitopathy - 2 case reports from a romanian endocrinology department

Aurelian E Ranetti[1], Florentina Smeureanu[1] & Creanga Andreea[1]
[1]Spitalul Universitar de Urgenţă Militar Central 'Dr. Carol Davila', Endocrinology, Bucureşti, Romania

Purpose
To describe pre- to post-treatment changes in clinical activity score (CAS) in patients with Graves orbitopathy treated with tocilizumab (TCZ).
Introduction
Graves' ophthalmopathy (GO) is an autoimmune disorder that affects 30-50% of patients with Graves' disease. The first-line treatment of moderate to severe GO according to EUGOGO is intravenous glucocorticoids, but 20-30% of the cases appear to be corticosteroid refractory. Steroid-resistant GO constitutes a major clinical and therapeutic challenge but promising results have been described with TCZ as a second-line moderate to severe GO treatment. We report a case series of severe GO treated with tocilizumab.
Case report 1
41-year-old man, former smoker who was diagnosed two years ago with hyperthyroidism and GO, presented in our hospital for reevaluation. The patient was in a thyrotoxic state and he was treated with methimazole and with intravenous methylprednisolone (cumulative dose 4.1 gr) with only partial response. He presented with unilateral eyelid swelling, orbital pain, redness and tearing. His CAS was 5 out of 7. A MRI orbits scan showed enlargement of the extraocular muscles, more prominent in the right orbit. The patient rejected radiotherapy. We initiated therapy with TCZ, a monoclonal antibody that inhibits the IL-6 receptor. 'Off-label' authorization for the use of tocilizumab was asked to Pharmacy Committee of our center. After its approbation, he received 4 intravenous doses (8 mg/kg) every 28 days, according to Perez-Moreiras RCT. On follow up, symptoms were improved impressively, and CAS score regressed to 1/7.
Case report 2
52-year-old men diagnosed with Graves' hyperthyroidism and GO one year ago, presented in our hospital for corticosteroid resistant GO. The patient had no general symptoms of thyroid disease. He previously received bolus of methylprednisolone with a weak response. He presented with bilateral eyelid swelling, orbital pain, redness and visual loss on the left side. His CAS was 4 out of 7. Due to the severity and the progression of the disease despite the corticosteroid treatment, we decided to initiate the treatment with TCZ. He received 4 intravenous doses (8 mg/kg) every 28 days. On follow up, symptoms were significantly improved including improved vision in his left eye, and CAS score regressed to 1/7.
Conclusions
We present this cases to raise awareness for the relative efficacy and tolerability profile of intravenous tocilizumab in the management of moderate to severe, corticosteroid resistant or refractory GO, of recent-onset, with lower cost compared to other novel therapies such as teprotumumab.

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EP366

Evaluation of quality of life in pregnant women with dysthyroidism

Meryem Chakir[1], Bensbaa Salma[1], Haraj Nassim Essabah[1], El Aziz Siham[1] & Chadli Asma[1]
[1]Ibn Rochd University Hospital of Casablanca, Morocco Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy-University Hassan II- Casablanca-Morocco, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Physiological changes during pregnancy expose pregnant women to an increased risk of thyroid disorders or decompensation of underlying thyroid conditions, which can impact the quality of life of patients.
Objective
To assess the quality of life of Moroccan pregnant women with thyroid disorders.
Materials and Methods
A case-control study conducted at the Endocrinology-Diabetology Department of Ibn Rochd University Hospital in Casablanca, involving pregnant patients with thyroid disorders. Two groups were included: the first diagnosed during the current pregnancy, and the second followed for thyroid disorders before pregnancy. Patients with other pathologies and thyroid cancers were exclu + ded. Participants completed the ThyPRO questionnaire.
Results
We included 53 patients divided into two groups; 20 were diagnosed with thyroid disorders during the current pregnancy, and 33 had thyroid disorders before pregnancy. The average age was 29.6, with 17.3% having hypothyroidism and 82.7% having hyperthyroidism. 20% reported an unwanted pregnancy. The mean score of thyroid symptoms was higher in the first group, 52 vs 19.3. Patients diagnosed with thyroid disorders during their pregnancy also exhibited more pronounced cognitive problems (33.8 vs 7.6), depression with an average score of 43.03 vs 24.9, and higher anxiety (45 vs 23.3). Additionally, they had a higher average fatigue score, 42.14 vs 32.2. These differences were statistically significant ($P < 0.01$). Maternal-fetal complications affected 74.2% of patients in the first group vs 42% ($P < 0.02$).
Conclusion
Targeted interventions, such as patient education, as well as improvement in the monitoring and management of thyroid disorders during pregnancy, could contribute to improving the quality of life in this population.

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EP367

A case of myasthenia gravis associated with hashimoto's thyroiditis

Raida Ben Salah[1], Siddiqa Soomauroo[2], Faten Hadjkacem[2], Abdelmuhaymen Missaoui[2], Ahmad Ridwaan Auckburally[3], Wiem Feki[3], Mouna Mnif[2], Sameh Marzouk[1], Mohamed Abid[2], Nabila Rekik[2] & Zouheir Bahloul[1]
[1]Hedi Chaker University Hospital, Department of Internal Medicine, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [3]Hedi Chaker University Hospital, Department of Radiology, Sfax, Tunisia

Introduction
Myasthenia gravis (MG) is a chronic neuromuscular condition characterized by weakness in voluntary muscles. It is an autoimmune disorder. The emergence of the condition can be abrupt. As with any autoimmune disease (AID), it may be associated with other AIDs. We report a case of MG associated with Hashimoto's thyroiditis (HT).
Observation
The diagnosis of MG was established in a 58-year-old patient, based on the progressive onset of fatigue, excessive salivation, difficulty in chewing, and ptosis. Electromyography revealed signs indicative of neuromuscular junction involvement. Anti-acetylcholine receptor antibodies were positive. The patient was prescribed Pyridostigmine (Mestinon®) and showed a good response to treatment. The diagnosis of MG was made 3 months before identifying profound hypothyroidism, which was incidentally discovered during the investigation of other autoimmune diseases. The hypothyroidism was attributed to HT, confirmed by positive anti-thyroid peroxidase antibodies and anti-thyroglobulin antibodies. The patient received treatment with L-thyroxine for the thyroid disorder. The clinical and biological outcomes were favorable, achieving euthyroidism.
Discussion/Conclusion
The diagnosis of MG is based on the clinical presentation - often starting with ocular symptoms such as ptosis or diplopia, extending to other muscles in 80% of cases, worsening with exertion, and characterized by episodic progression -, the response to anticholinesterase medications, the detection of anti-acetylcholine receptor antibodies, and the presence of a decrement in electromyography. MG can be associated with numerous autoimmune thyroid diseases (AITDs), especially autoimmune thyroiditis. The underlying pathophysiological basis connecting these conditions is not clearly established, but an immunological cross-reaction between the neuromuscular junction and thyroid components has been identified in both MG and AITD, such as autoimmune thyroiditis. The prevalence of AITD among individuals with MG is generally higher than that in the general population. In fact, 9% of men and 18% of women with MG exhibit autoimmune thyroid diseases. These diseases are predominantly characterized by hyperthyroidism (17.5%), simple goiter (1.7%), or more rarely, hypothyroidism (0.4-0.7%).
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EP368

Adrenal decompensation precipitated by severe graves' thyrotoxicosis

Nauman Jadoon[1]
[1]NHS Greater Glasgow & Clyde, Endocrinology, Glasgow, United Kingdom

Background and Aims
Thyroid hormone can accelerate glucocorticoid turnover and there have been cases of adrenocortical insufficiency reported after radioactive iodine treatment. However, the patient presented here did not have any such precipitant nor any underlying adrenal disease, and her adrenal insufficiency resolved after treatment of thyrotoxicosis.
Methods
A case of a 45-year-old lady with Graves' disease is presented, who developed hypoadrenalism at the time of her diagnosis which settled with the treatment of underlying thyrotoxicosis.
Results
A 45-year-old lady presented with nausea, light-headedness, and sweats which started 3 weeks after her COVID vaccine booster. Her symptoms included syncopal symptoms, muscle weakness, nausea, vague abdominal pain, constipation, dry mouth, intermittent headache, legs feeling shaky, weight loss, and appetite loss. Her blood pressure at the time of presentation was 107/70 with no significant postural drop. She was normoglycemic with no neck lumps and an otherwise normal physical examination. Her initial blood tests showed a free T4 level of 82.9 pmol/l with a TSH of <0.01 mU/l. Her morning cortisol level was 218nmol/l, and short synacthen test showed a rise from 178nmol/l to 371 nmol/l. She was commenced on carbimazole 1 mg daily and hydrocortisone 1 mg BD. Her symptoms improved with treatment and her dose of Carbimazole has gradually been reduced to 1 mg daily over a year. Three months after the initial presentation when her free T4 level dropped to 18.1 pmol/l, she had a repeat short synacthen test which showed a rise of cortisol from 342nmol/l to 546nmol/l. The patient was advised to discontinue hydrocortisone, however, due to her concerns about symptoms it was continued for another 3 months after which a repeat SST was carried out which again showed a satisfactory response, and hydrocortisone was withdrawn. Her adrenal antibodies were checked which were negative while the thyroid receptor antibody was positive at 27U/l.. She remains well on 1 mg of carbimazole a year after her initial presentation and has been off steroids for 6 months.
Conclusions
It is important to be aware of the possibility of adrenal insufficiency in patients with autoimmune hyperthyroidism, which can be a concomitant presentation of autoimmune adrenal insufficiency but in rare cases can be due to increased clearance of cortisol due to an excess of thyroid hormone.
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EP440

Does a dedicated endocrine surgery unit impact treatment decision in patients with thyroid disorders? experiences from an endocrine-surgeon naïve area in southern india

Shreyamsa Manjunath[1] & Praveen Kumar Devarbhavi[2]
[1]Maax Superspecialty Hospitals, Endocrine & Breast Surgery, Shivamogga, India; [2]Maax Superspecialty Hospitals, Endocrinology & Metabolism, Shivamogga, India

Background
Appropriate management of thyroid diseases is crucial, as outcomes directly affect quality-of-life. High-volume thyroid surgeons provide best results, least complications. We aim to assess if a dedicated endocrine-surgery unit influences treatment-decisions(TD) of patients in an endocrine-surgeon naïve area.
Method
Study of 153-patients at Maax Superspecialty Hospitals(Shivamogga, India), from November/2021-October/2023. Previously diagnosed & under treatment elsewhere, referred for or sought expert opinion. These patients had deferred definitive-treatment(fear of complications arising from pre-surgical discussion with physician) or desired radical surgery for low risk lesions where observation was an option("may turn into cancer" as a result of discussion with physician or information obtained from other sources). Multiple consults and difference of opinions also added to this issue. Six questions were asked as a part of self-assessment- Did we add additional information/value with respect to: Q1-Diagnosis? Q2-Overall condition/course-of-disease? Q3-Treatment options? Q4-(a)Why surgery, Q4-(b)why observation? Q5-Advanced procedures? Q6-Complications, how we tackle it? Responses were recorded with a 3-point Likert scale: 1-No useful/convincing additional information 2-New information provided, but not enough to influence TD 3-Meaningful additional information, positive influence on TD.
Results
F:M = 147:6. Sixty-nine had multinodular goitre (14:compressive-symptoms, 9:retro-sternal, 3:toxic-MNG, 4:thyroiditis, 33:high-risk, 9:low-risk), 18-Graves' disease, 12-Diffuse goitre, 51-solitary nodules (25:high-risk, 26:low-risk). On multiple regression analysis, Q1-3 did not significantly influence TD, while Q4, Q5 & Q6 resulted in significant change in TD(p-value: <0.001). Q4, Q5 & Q6

The response and analysis of scores are as follows:

Criteria	Score-1	Score-2	Score-3	No-change in TD	Change in TD	p-value	Multiple-regression analysis
Q1	2	85	66	87	66	0.07	0.512
Q2	6	53	94	59	94	0.02	0.570
Q3	6	69	78	75	78	0.09	0.588
Q4(a) ($n=103$)	2	18	83	20	83	0.001	0.001
Q4(b) ($n=50$)	2	9	39	11	39	0.03	0.001
Q5	1	35	117	36	117	0.001	<0.001
Q6	2	31	120	33	120	0.001	<0.001

strongly correlated with change in TD($\rho = 0.79$, 0.84, 1 respectively).
Conclusions
Dedicated endocrine-surgery unit leads to better acceptance of treatment-plan, reduces fear/anxiety, and unnecessary surgeries. Objective discussion, availability of advanced procedures & reduced fear of complications positively influence TD.

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EP441

Thyroid function in patients with MUTYH syndrome

Joaquin de Carlos[1], Lucia Zabalza[1], Ana Irigaray[1], Maria Rosario Aznarez[2], Susana Oquiñena[2], Javier Pineda Arribas[1] & Emma Anda Apiñariz[1]
[1]Hospital Universitario de Navarra, Endocrinology, Pamplona, Spain; [2]Hospital Universitario de Navarra, Gastroenterology, Pamplona, Spain

Introduction
MUTYH (MutY homolog Escherichia coli, homolog of MYH, hMYH) is a repair enzyme with a crucial role in the correction of DNA errors, being considered a protective factor of the cell. MUTYH mutations have been linked to MUTYH-associated polyposis syndrome (MAP), an autosomal recessive disorder characterized by multiple colorectal adenomas. Patients with MAP show a much higher lifetime risk of gastrointestinal cancers as an additional role of MUTYH, it appears to contribute in the involvement of pathologies based on oxidative stress damage, as well as in the prevention of inflammatory and degenerative based disorders. Although the development of extraintestinal pathology is not fully defined, it seems to increase the risk of tumors and endocrinological pathology.
Materials and methods
Prospective study, selecting 27 living patients diagnosed and registered with MUTYH syndrome under follow-up from the Digestive Department of the Hospital Universitario de Navarra (HUN) with current or past follow-up in the Endocrinology Department. Radiological tests, clinical, and analytical variables were analyzed.
Results
The study population included 14 men (51.8%) and 13 women (48.2%), with a mean age of 56 years. The median age at diagnosis of FAP was 48 years, with a mean follow-up time of 8 years. All patients underwent thyroid ultrasound examination and blood tests with the determination of thyroid autoimmunity. None of them had received radiation therapy treatment in childhood or had been exposed to radioactive sources. 48% (13/27) were diagnosed with this disease in the context of endoscopy by digestive clinic, 37% (10/27) by family screening and 4/27 (15%) in the colorectal cancer screening test. The overall prevalence of autoimmunity is 22.2% (4/18). Measured thyroid autoimmunity was peroxidase antibodies. All of them had normal thyroid function, except for two patients who had undergone total thyroidectomy and were on replacement therapy. These two patients had TSH in the normal range before surgery.
Conclusions
The prevalence of thyroid autoimmunity in the sample of patients with MAP is above that described in the general population. Studies with a larger sample size are probably necessary to obtain results with greater statistical significance.

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EP442

Management of hot thyroid nodules: experience of our department

El Omri Malika[1], Jemli S[1], Lazid Sarra[1], Meherzi Abir[1], Houas Jihene[1], Ghammem Monia[1], Ach Taieb[2], Kermani Wassim[1] & Abdelkefi Mohamed[1]
[1]ENT department Farhat Hached hospital, Sousse, Tunisia; [2]Endocrinology department Farhat Hached hospital, Sousse, Tunisia

Introduction
Hot nodules represent 10% of thyroid nodules. They are defined by scintigraphic examination, which shows areas fixing the radiotracer more intensely than the rest of the gland. The aim of our work is to study the clinical, paraclinical aspects and therapeutic modalities of hot thyroid nodules.
Materials and methods
We report a retrospective study about 45 observations of hot thyroid nodules collected at our department
Results
The average age of our population was 42 years with a sex ratio of 5.4. The nodule was isolated in 28 cases, associated with signs of hyperthyroidism in 17 cases and signs of compression in five cases. The Physical examination revealed a thyroid nodule or isthmolobar located at right in 33 cases and left in 12 cases. The average size of nodule was 3.61 cm. The ultrasound revealed an heterogeneous appearance in 39 cases, homogeneous in six cases, punctiform calcifications in two cases and macrocalcifications in two cases. Thyroid scintigraph showed a completely extinct nodule in 19 cases (42.2%), partially extinguished in six cases (13.3%), not extinguished in 12 cases (26.7%) and necrotic in eight cases (17.8%). Treatment was surgical for 44 patients and radioactive iodine for one patient. Histopathological examination was in favor of benignity in all operated cases.
Conclusions
Hot nodules represent only a small part of hyperthyroidism (2 to 17%). Toxic nodules must be treated because of their cardiac consequences. Surgery is the most cautious in this case, especially in young subjects. The treatment by radioactive iodine is indicated in elderly people or people with a surgical contraindication.

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EP443

Assessment of iodine deficiency among pregnant women in tirana, albania

Ira Xhemollari[1], Dorina Ylli[2] & Agron Ylli[2]
[1]Municipial Hospital, Endocrinology, Kavajë, Albania; [2]Mother Teresa University Hospital Center, Endocrine and Metabolic Diseases Unit, Tirane, Albania

Background
Iodine Deficiency (ID) represent a significant public health problem globally, particularly among pregnant women.
Aim
To estimate the prevalence and predictors of ID among pregnant women residing in Durres Albania
Methods
A survey cross-sectional study conducted on 162 pregnant women, from May to June 2021. Demographic information, iodized salt usage, and other clinical information were collected using a questionnaire cum interview face to face. The presence of iodine deficiency disorders was observed through urinary iodine concentration (UIC). Statistical analysis was done using the methods included in the statistical package of social science SPSS16. A P value <0.05 was considered statistically significant.
Results
Of 162 pregnant women, the higher percentage (48.7%) were in the first trimester. 52.7% of them had 2-3 births, 72% had no history of abortion, 95.6% with no history of premature birth, 95% of them lived in non-coastal areas. The mean age was 28.96 $\pm$ 5.197. UIC median (m UIC) among pregnant women was 114.6 µg/l (7.8-433). mUIC was reduced with increasing gestational age and the lowest value appeared in the third trimester (UIC $<$99.7 µg/l (21.7 -298.5 µg/l) P 0.03). 71.6% of pregnant women had UIC $<$150 µg/l regardless of age, number of births, abortions, premature births and living, reflecting iodine deficiency. Among them, the highest percentage (52.4%) appeared with mild ID, 13% with moderated ID and 6.1% with severe ID. Statistically significant differences were found between trimesters of pregnancy and age groups among women who received supplements of iodine vs those who did not (P 0.01) but there was no statistical difference in m UIC between these two groups. Women who were aware of iodine salt had higher level of m UIC (P 0.01). According to the results models of multi nominal regression the factors of UIC who identified as independent were no history of abort (OR^ 0.45, P 0.048), living in coast areas (OR ^ 0.34, P 0.041), trimesters of pregnancy (OR ^ 0.23 P 0.042) and consumption of fish, meat and fruit.
Konkluzion
Prevalence of ID was high in pregnant women reflecting low iodine intake. UIC reduced with incresing gestational age. Predictors of UIC were no history of abort, living in coast areas, the trimesters of pregnancy and consumption of fish, meat and fruit.

Keywords: UIC, iodine deficiency, pregnant women, supplement of iodine
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EP446

Congenital hypothyroidism presenting as myxedema coma in adulthood treated using oral levothyroxine in a limited setting: a case report

Genwil Agabon[1]
[1]Zamboanga City Medical Center, Internal Medicine, Zamboanga, Philippines

Background
Congenital hypothyroidism is rare and is screened for in the Philippines during the newborn period in order to prevent a treatable cognitive delay. Myxedema coma is a complication due to severe hypothyroidism resulting from failure of homeostatic processes, causing altered mental status, edema, and vital sign abnormalities. It is a rare, life-threatening complication of hypothyroidism, an estimated 0.22 per million new cases of myxedema coma are diagnosed each year.
Case Presentation
A 29-year-old female with a history of untreated hypothyroidism presented to the emergency department after being found on the floor unconscious. In the emergency department, the patient's vital signs were remarkable for a body temperature of 35 C. The patient was also bradycardic to 51 beats per minute with stable blood pressure. On examination, the patient was stuporous, respond to painful stimuli with a GCS of 7 (E1V1M5). Physical examination was remarkable abnormal facies, short stature, and edema of extremities. Based on the history and all findings of clinical signs of hypothyroidism with alteration of consciousness, bradycardia and hypothermia, myxoedema coma was diagnosed and L-thyroxine therapy was promptly initiated. Thyroid function test results showed a free thyroxine (FT4) level of 0.1 ng/dl (0.70-1.48), free triiodothyronine (FT3) level of 1.53 pg/ml (1.71–3.71) and TSH level of >100 uIU/ml (0.35–4.94), and thyroperoxidase antibodies were negative. Thyroid ultrasonography demonstrated Thyroid Hypoplasia which raised suspicion for congenital hypothyroidism. Due to the altered level of consciousness, a nasogastric tube was inserted to allow the administration of oral medications. She was given oral levothyroxine 200 µg every 8 hours, together with intravenous hydrocortisone 100 mg every 8 hours. The patient was admitted to the ICU for close monitoring. Supportive measures were applied, including oxygen support, temperature control, empirical ceftriaxone therapy, and hydration. After 3 days in ICU, the patient was awake and alert. Blood and urine cultures showed no growth. The patient remained comfortable, alert, and oriented with no complaints. She was later discharged with oral 1 mg of levothyroxine daily and outpatient follow up.
Conclusion
Myxedema coma may be rare due to the currently available diagnostic tools and therapies, but it remains a life-threatening condition. In resource-limited settings, oral levothyroxine may be a suitable alternative to the intravenous formulation in the initial treatment of myxedema coma. Early diagnosis, administration of thyroid hormones, and supportive management are vital for a good prognostic outcome.

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EP447

Hypothyroidism and bilateral foot droop

kalyani Nagarajah[1] & Sam Rice[1]
[1]Swansea, Department of Endocrinology and diabetes, Swansea, United Kingdom

Introduction
Hypothyroidism and hyperthyroidism are commonly encountered medical disorders that can be associated with neurologic and neuromuscular dysfunction. Muscle involvement is a common manifestation of both clinical and subclinical hypothyroidism, although this may not always be clinically appreciated. Hypothyroid associated myopathy can cause weakness, cramps, aching and painful muscles, sluggish movements and Severe myopathy secondary to hypothyroidism leading to Rhabdomyolysis and renal failure has also previously been reported.
Case
Here we present a case of a 49 year old male patient with known Type 1 Diabetes and hypothyroidism diagnosed in 2012 with associated raised anti TPO antibody levels of 279 IU/ml (reference range: <34 IU/ml). There was a previous described history of poor compliance with his Levothyroxine. His regular medications were Levothyroxine 150 mg OD, Novorapid and Lantus. He was admitted with 3 days history of bilateral feet swelling and bilateral foot droop. His admission blood tests demonstrated a combination of an acute kidney injury, rhabdomyolysis and severe hypothyroidism. These were his initial admission investigations: TSH >100 mU/l (0.27-4.20 mU/l), Free T4: 0.7 pmol/l (11-25 pmol/l), 9 am Cortisol 490 nmol/l (>420 nmol/l) and Creatine Kinase: 56600 U/l (40-320 U/l). Subsequent test was negative for hepatitis. His MRI spine reported degenerative changes of the L4/l5 intervertebral disc with impingement of L4 nerve root bilaterally. However, there was no evidence of significant cord compression. Vasculitis screening (ANA, ANCA, DsDNA, Anti-GBM) were also negative. Nerve conduction studies indicated peroneal nerve paresis, secondary to anterior compartment syndrome felt to be a results of acute swelling of his lower legs due to severe hypothyroidism which in turn led the development of rhabdomyolysis and renal failure. With Levothyroxine dosed at 200 mg once daily and improved compliance his thyroid function improved rapidly. His TSH was normal within three months, with some improvement of his foot drop. However, his peroneal nerve palsies has not fully resolved.
Conclusion
Anterior compartment syndrome associated with rhabdomyolysis and foot drop is a rare complication of severe hypothyroidism. Anterior compartment syndrome is most commonly unilateral. However, bilateral presentations should trigger the search for metabolic explanations.
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EP451

Thyroxine intolerance: a rare but significant clinical entity

Asif Nawaz[1], David Williams[1], Peter Taylor[2], Thinzar Min[1, 3] & Win Yin[1]
[1]Swansea Bay University Health Board, Endocrinology and Diabetes, Swansea, United Kingdom; [2]Cardiff and Vale University Health Board, Endocrinology, Cardiff, United Kingdom; [3]Diabetes Research Group, Swansea University Medical School, Endocrinology and Diabetes, Swansea, United Kingdom

Introduction
Levothyroxine, the standard therapy for hypothyroidism, is usually well tolerated and very few cases of true allergy to levothyroxine have been reported to date. Here we report two cases of rare occurrence of levothyroxine allergy.
Case 1
A 56-year-old woman with no previous history of allergies started levothyroxine post-thyroidectomy for Graves' disease. She developed facial flushing and urticarial rash within 15 minutes of the first-dose of levothyroxine 1 mg. She was treated with steroids and antihistamine. She developed similar symptoms on the next dose, and tryptase levels confirmed allergy. She was trialed on levothyroxine elixir to exclude excipient-related allergy, but symptoms recurred despite concurrent antihistamine and steroid. Later, she tolerated liothyronine, with no adverse symptoms. Desensitization to levothyroxine was undertaken. A rash appeared at higher doses but settled within 24hours. She currently tolerates 1 mg daily. Given her lack of other allergies and as excipient-related allergy is common in other drugs, we are now investigating an allergy to dextrothyroxine.
Case 2
We report a 56-year-old man with autoimmune hypothyroidism. TSH was 7.1 mU/l when he presented with tiredness, which improved with levothyroxine. Over the last 18 months, his levothyroxine requirement increased to 1 mg daily, with TSH frequently >1 mU/l. Compliance issue and malabsorption disorders were excluded. He gained weight, and developed type 2 diabetes. He developed bilateral foot swelling, and cracking of his feet with facial rash and swelling. He trialed several oral forms (liquid and tablets) of levothyroxine. He was then trialed on Armour Thyroid 1 mg three times daily without adverse effect. His thyroid function improved and he lost weight leading to diabetes remission. Later, due to supply issues he was changed to liothyronine 1 mg twice daily and levothyroxine 1 mg daily with stable thyroid function.
Conclusions
Hypersensitivity to levothyroxine is rare and most patient with reaction to levothyroxine tolerated to alternative thyroxine preparation. It is hypothesized that levothyroxine allergy is likely due to the excipients or fillers rather than the thyroid hormone itself.

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EP452

A rare case of immune thrombocytopenia in a patient with hashimoto's thyroiditis: a case report

Quennie Bien Bien Yu[1], Kurt Bryan Tolentino[1], Sahra Paragas[1], Jasmine Grace Asinas[1] & Fidela Salvador-Badilles[1]
[1]St. Luke's Medical Center, Internal Medicine, Taguig City, Philippines

Background
Immune thrombocytopenia (ITP) is an autoimmune condition where the immune system targets and destroys platelets, resulting in reduced platelet levels. The manifestations of ITP range from cases with no apparent symptoms to severe, spontaneous bleeding that can be life-threatening. ITP is differentiated into primary or secondary categories depending on its correlation with other diseases

or exposure to drugs. Hashimoto's thyroiditis is an autoimmune condition where the immune system attacks and destroys thyroid cells through both cell-mediated and antibody-mediated immune mechanisms. The coexistence of Hashimoto's thyroiditis with immune thrombocytopenia is uncommon. In these instances, ITP may exhibit resistance to conventional first-line and second-line treatments due to a more substantial impairment in immune tolerance. We present a case of a 25-year-old male who was admitted with ITP and was found to have Hashimoto's thyroiditis.

Case Presentation

A 25-year-old Filipino woman with no known comorbidities sought consultation at the ER due to a progressive petechial rash on bilateral lower extremities lasting for 3 days. This was associated with hematoma on the right thigh, dizziness, epistaxis, and spontaneous gum bleeding. The patient denies having colds, cough, fever, or any recent contact with sick individuals. She also denies the intake of any new medications. A complete blood count revealed a platelet count of 8, 000/ul, with a normal white blood cell count (8.6x103/ul) and hemoglobin (11.1 g/dl). Peripheral blood smear (PBS) showed thrombocytopenia with no poikilocytosis, and schistocytes were noted. Common causes of thrombocytopenia were ruled out before diagnosing ITP. The patient received an initial transfusion of 12 units of platelet concentrate, resulting in an initial increase in platelet count to 28, 500/ul. However, the following day, the platelet count decreased again to 18, 000/ul. The patient was then managed as a case of ITP and started on Dexamethasone for 4 days. A workup to rule out secondary causes of ITP was performed, including a hepatitis panel, Dengue virus test, and autoimmune disorder tests, all of which showed unremarkable results. TSH, however, was elevated at 9.844uIU/ml, with a normal fT4 at 1.1 ng/dl. Anti-TPO antibodies were also ordered and showed elevated results at 319.3 IU/ml. The patient was started on Levothyroxine and noted to have improving platelet trends. After 6 days, the patient was discharged with a platelet count of 81, 000 and a home medication of levothyroxine 1 mg. On a follow-up checkup after 1 month, TSH was now normal, and the platelet count was 395, 000.

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EP453

Clinical genetic aspects of CYP17A1 gene polymorphism (RS743572) in the uzbek population

Aziza Nasirova[1] & Dilorom Najmutdinova[1]
[1]Tashkent Medical Academy, Endocrinology, Tashkent

This article discusses the role of gene polymorphisms in the development and clinical progression of autoimmune thyroiditis (AIT) based on our research. By considering the genotypic polymorphism of the studied genes, we aim to develop new effective methods for prognosis, treatment, and prevention in AIT.

Introduction

Autoimmune thyroiditis (AIT) is a significant endocrine problem characterized by autoaggressive lymphoid and plasmacytic infiltration leading to the destruction of the thyroid gland. AIT affects 3-4% of the global population and is more prevalent in women aged 40-50 years. Subclinical hypothyroidism (SH) is a common condition associated with AIT, with a prevalence of 6-17% in the population. The understanding of pathogenetic mechanisms, diagnostic methods, and therapeutic measures for AIT remains insufficient.

Methods

Our study aimed to investigate the role of CyP17a1 gene rs743572 polymorphism in the formation and clinical course of AIT. DNA samples from 113 AIT patients and 94 healthy donors were genotyped using Sintol nPF npF reagent kits. Hormonal and ultrasound studies were conducted to categorize patients into hypothyroidism, euthyroidism, and hyperthyroidism groups.

Results

The study revealed significant differences in the frequency of genotypes and alleles of the CYP17A1 rs743572 SNP among various thyroid status groups. The G197A polymorphism was more prevalent in AIT patients, particularly in the hypothyroidism group, compared to the control group. The IL17A G197A genotypes also exhibited significant differences between AIT patients and the control group, indicating potential associations with thyroid dysfunction.

Conclusion

Our findings suggest a potential association between the G197A polymorphism in the CyP17a1 gene and thyroid dysfunction, especially in patients with hypothyroidism. The study emphasizes the relevance of genetic factors in thyroid diseases and provides insights for further investigations into the molecular mechanisms underlying hypothyroidism. Future research should consider expanding the patient sample and analyzing additional genetic factors for more personalized approaches to diagnosis and treatment. The study establishes a pronounced association of the CyP17a1 gene rs743572 polymorphism with the risk of AIT development in the Uzbek population.

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EP454

Benign thyroid nodules evaluation in lithuania 2018 – 2022. single-centre study

Kamilė Antanavičiūtė[1, 2], Raimonda Klimaite[1, 2], Gabrielė Riškutė[1], Laura Arbatauskaitė[1] & Viktorija Pareikaitė[1]
[1]Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Endocrinology department, Kaunas, Lithuania

Introduction

As our population ages, more people are diagnosed with thyroid nodules (TN). The prevalence of TN varies by country. In this study, we would like to present the evaluation of benign thyroid nodules in Lithuania in 2018 – 2022.

Material and methods

The medical history of 719 patients treated for thyroid nodules (TN) in the Hospital of Lithuanian University of Health Sciences Kaunas Clinics Endocrinology and Surgery departments from 2018 to 2022 were analyzed. The patient's medical history, fine needle aspiration (FNA) of TN cytology results, and histological findings of operative material were interpreted. Calculations were performed using the IBM SPSS Statistics 28.0 package.

Results

The study population comprised 82, 9% women and 17, 1% men with a median age of 54 [10-90] years. We found a slight decrease in cases compared to 2018 (177) and 2022 (123). More than half (53%) of patients' TN were evaluated EU-TIRADS score 3, 18% EU-TIRADS score 4 and 5. Almost half of the patients (52%) had nodules larger than 3 cm. 54% of patients had nodules only in one thyroid gland lobe. There was no statistically significant age difference between genders at the time of the first TN finding ($P = 0, 058$). Women were observed for a statistically longer time before surgery ($P < 0.001$) with a median of 30 [1 - 636)] months. 26% of patients were discussed by a multidisciplinary council before surgery. The most common reason for thyroid surgeries (48%) was shortness of breath or difficulties swallowing. Other reasons: thyrotoxicosis (31%), malignant nodule was suspected (14%), TN were found after parathyroidectomy (4%), cosmetic defect (3%). Due to malignancy being suspected by ultrasound, 33% of patients had a fine needle aspiration biopsy (FNA) before thyroid surgery. Unfortunately, the results of cytology and surgery material's histology differed in 27, 27% of cases, when FNA showed malignancy, but histology showed benign lesions.

Conclusion

The main clinical concern is to exclude malignant nodules and avoid overdiagnosis, because misdiagnosis can decrease the patient's quality of life. Although TN has a low risk of malignancy and patients should continue ongoing surveillance through physical examination and periodic ultrasound evaluations.

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EP455

Immune response mediated by immunoglobulin e in patients with autoimmune thyroiditis: an intricate connection

Sladjana Pejaković[1, 2], Ivana Bajkin[1, 2], Dragana Tomić-Naglić[1, 2], Mia Manojlović[1, 2], Andrijana Milankov[1, 2], Nikolina Vuković[2] & Stefan Janičić[2]
[1]Medical Faculty Novi Sad, University of Novi Sad, Novi Sad, Serbia; [2]Clinic for Endocrinology, Diabetes and Diseases of Metabolism, Novi Sad, Serbia

Introduction

Autoimmune diseases have a high prevalence in the general population, and AITD is one of the most common representatives. Although IgE is the main regulator of allergic reactions, there is evidence to suggest a link between AITD and allergic diseases, demonstrated by the example of chronic spontaneous urticaria (CSU).

Aims

For this research, we have set the following goals: to determine whether there is an association between the serum level of total IgE and the presence of primary hypothyroidism of autoimmune genesis; to determine whether there is a difference in the presence of extrathyroid manifestations of autoimmune thyroid disease in patients with high IgE levels; to determine whether there is a correlation between the severity of the clinical picture of primary hypothyroidism in relation to the height of the IgE and anti-TPO antibody titers.

Materials and Methods
The research was conducted as a prospective study at the Clinic for Endocrinology, Diabetes and Metabolic Diseases as well as at the Clinic for Dermatovenerology, on a sample of 62 patients. All subjects underwent to laboratory tests of interest for the research from a sample of peripheral venous blood, as well as ultrasonography of the thyroid gland. All subjects were divided into two groups based on total serum IgE level (group with elevated total IgE level and group with normal level).
Results
All patients included were diagnosed with AITD, with or without thyroid function disorder. The population in our sample was dominated by females. 19.4% had urticaria. 24.1% of subjects had elevated levels of total serum IgE, and subjects with combined AITD and urticaria had significantly higher values of total serum IgE. Average TSH values were statistically significantly lower in patients with elevated total serum IgE values. The most common ultrasonographic finding was the heterogeneity of the thyroid gland parenchyma. A low moderate, negative correlation was detected regarding the value of total serum IgE and the level of anti-TPO and anti-Tg antibodies.
Conclusion
The results of the conducted research indicate the existence of a statistically significantly higher titer level of the total serum IgE antibodies in the group of subjects with CSU, with statistically significantly lower values of TSH, which implies the possible epipathogenetic effect of an elevated serum level of IgE on the occurrence of the thyroid dysfunction, as well as that a high level of IgE antibodies shows a tendency towards the presence of extrathyroidal manifestations of autoimmunity.

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EP456

Navigating complexities: a case study of mixed hypothyroidism induced by durvalumab in cancer immunotherapy

Carla Ciobanu[1, 2], Carmen Sorina Martin[1, 2], Ahmed Al Jumaili[1] & Simona Fica[1, 2]
[1]Spitalul Universitar de Urgenţă Elias, Endocrinology, Bucureşti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania

Introduction
Immune checkpoint inhibitors targeting cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), programmed cell death ligand 1, and its ligand (PD-1/PD-L1) have become the current standard of care for many cancers. The mechanism of action of these drugs results in some new types of adverse events related to the immune system, most frequently involving the pituitary and thyroid glands.
Case report
We present a case of mixed hypothyroidism (primary and secondary) induced by Durvalumab (PD-L1 inhibitor) that is associated with immune-mediated endocrinopathies. A 64-years female, ex-chronic smoker with a medical history since March 2022 of small cell lung carcinoma of the left superior lobe with secondary cerebral, peritoneal, and lymphatic involvement, has been transferred in October 2023 from the oncology department to the endocrinology ward for facial and bilateral leg edema, fatigue, and shortness of breath. The patient was started on Durvalumab in 04/2022 after chemotherapy and radiation treatment. Physical examination showed facial, bilateral leg edema, hoarse voice, slurred speech, and bradypsyhia. She was afebrile, normotensive, and bradycardic. Laboratory analysis detected mildly elevated TSH = 9.21 uUI/ml with undetectable free T4 levels (0.1 ng/ml-n = 0.8-1.7). Further investigation revealed normal prolactin levels (17.1 ng/ml-n = 4.79-23.3) and normal corticotrope (cortisol = 10.1 ugdl-n = 4.82-19.5; ACTH = 14.16 pg/ml -N:7.2-63.3) and somatotropic axes. The pituitary gonadotropin levels indicated menopause, consistent with age. Ultrasonography showed a hypoechoic shrunken thyroid gland consistent with chronic autoimmune thyroiditis. Thus far, thyroid antibody tests were negative. Based on laboratory tests, thyroid ultrasound findings, and clinical symptoms, the patient was diagnosed with severe hypothyroidism of mixed etiology (primary and secondary) associated with Durvalumab, and treatment with levothyroxine (1 mg) has been initiated. Symptoms worsened after initiating treatment with levothyroxine, leading to suspicion of secondary adrenal insufficiency. We didn't perform stimulated tests for adrenal insufficiency in the acute phase and we preferred to initiate GC therapy replacement, following to be retested after treating thyroid insufficiency. Hydrocortisone hemisuccinate IV was initiated for 2 days with the improvement of symptoms. After two days, HC was switched to prednisone (1 mg/day), and the levothyroxine treatment was gradually increased to 1 mg/day. Follow-up after 2 months was recommended.
Conclusion
The case described the potential complications associated with the PD-L1 inhibitor Durvalumab, in the context of mixed hypothyroidism. Thyroid dysfunction occurs primarily with PD-1/PD-L1 blockade, and the pattern of inflammatory, destructive thyroiditis is observed, which evolves into hypothyroidism. In a minority of cases, central hypothyroidism can develop (TSH deficiency), mostly along with ACTH deficiency which should not be missed. Prompt management is crucial for mitigating adverse events.

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EP457

Cardiovascular manifestations in a complex case of thyroid storm secondary to graves: challenges and therapeutic considerations

Margarida Oliveira[1], Catarina Gama[1], Bruna Pimentel[1], Paula Calvo[1], Carolina Antunes[1], Leonor Lopes[1], Rute Ferreira[1] & João Sequeira Duarte[1]
[1]Centro Hospitalar de Lisboa Ocidental, Endocrinology, Diabetes, and Metabolism Departmen

Introduction
Thyroid storm, a life-threatening manifestation of hyperthyroidism, presents a complex clinical challenge that demands swift and precise intervention. The heart is one of the most important target organs affected by the thyrotoxic state. Thyrotoxicosis may lead to sinus tachycardia, hypertension, tachycardiomyopathy, atrial fibrillation and heart failure.
Case Presentation
A 46-year-old female presented to the emergency department with symptoms of sweating, insomnia, diarrhea and fatigue for three months, and with increasing shortness of breath and palpitations, over the last week. She had a previous history of psoriasis and family history of her father with thyroid malignancy, who underwent thyroidectomy, at the age of 50. At observation, the cardiovascular exam revealed an irregular rhythm, with a heart rate ranging between 105 and 150 beats/min and bilateral edema of the lower limbs. She was afebrile. Thyroid function tests revealed thyroid-stimulating hormone (TSH) 0.008 uIU/ml (0.27- 4.20 uIU/ml), FT3 43.1 pmol/l (3.10-6.80 pmol/l) and FT4 > 100 pmol/l (12.0-22-0 pmol/l) and TRABs 27.3 U/l (< 1.58). The electrocardiogram showed atrial fibrillation. She was diagnosed with a thyroid storm, scoring 55 on the Burch-Wartofsky Point Scale. She started methimazole, hydrocortisone, beta-blocker, anticoagulant and was admitted for further stabilization and treatment. A transthoracic echocardiogram reported a reduced ejection fraction of 34%, moderate biauricular dilation, severe mitral regurgitation, and moderate tricuspid regurgitation. Over a 13-day in-hospital stay, the patient had received increasing doses of methimazole, propranolol, prednisolone, digoxin, and furosemide. However, she remained symptomatic, with frequencies between 100-120 bpm, and high levels of FT3 and FT4. On the 20th day of treatment, she developed a cholestatic pattern secondary to methimazole. The decision to perform a total thyroidectomy, with plasmapheresis before the surgery, was made. After two plasmapheresis sessions, levels of thyroid hormones decreased, and a total thyroidectomy was successfully performed. Maintaining atrial fibrillation, she underwent electric cardioversion and was discharged on the 30th day. One month later, thyroid function normalized with levothyroxine replacement. A holter revealed paroxysmal atrial fibrillation and she remained with anticoagulant and beta-blocker therapy.
Conclusion
Thyroid storm secondary to Graves disease, represents a therapeutic challenge to the clinician, especially when the hyperthyroid state leads to cardiovascular complications. Achieving a euthyroid state may resolve cardiovascular effects, but in this case, prolonged exposure to high levels of circulating thyroid hormone resulted in thyrotoxic cardiomyopathy and atrial fibrillation as sequelae.

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EP461

Thyroid function assessment in individuals previously infected with SARS-CoV-2

Nassim Ben Hadj Slama[1], Taieb ACH[1], Ghada Saad[1], Asma Ben Abdelkrim[1], Molka Chadli[1] & Koussay ACH[1]
[1]Farhat Hached University Hospital, Endocrinology, Soussa, Tunisia

Introduction
COVID-19 is a viral infection that can affect various endocrine tissues, including the thyroid. In some patients, symptoms may persist after the infection, defined as Long COVID. Given the similarity of some of these symptoms to those encountered in thyroid disorders, we have decided to assess thyroid function in patients previously infected with SARS-CoV-2.
Patients & Methods
This was a prospective study conducted from January to December 2022 in the Endocrinology Department of Farhat Hached University Hospital in Sousse,

including patients previously infected with SARS-CoV-2, completely recovered (G1), and patients experiencing Long COVID (G2). A thyroid function assessment was performed by measuring TSH and FT4 levels.
Results
A cohort of 64 patients underwent hormonal evaluation, and the median duration for hormonal exploration was comparable between G1 (fully recovered) and G2 (Long COVID), with respective values of 11.5 months [Q1–Q3]=[9-14] and 11 months [Q1–Q3]=[6-14] ($P=0.498$). Predominant manifestations in the Long COVID group included asthenia and cognitive disturbances, observed in 84.4% and 93.8% of cases, respectively. Mean TSH levels were 5.19 $\pm$ 16.12 mIU/l for G1 and 4.33 $\pm$ 14.38 mIU/l for G2 ($P=0.702$), while mean FT4 concentrations were 9.60 $\pm$ 2.25 pg/ml for G1 and 10.06 $\pm$ 1.93 pg/ml for G2 ($P=0.388$). Within G1, two instances of overt peripheral hypothyroidism were identified, constituting 6.3% of the patients, compared to one case in G2, representing 3.1% of patients. Notably, these cases exhibited positive antithyroid antibodies. No occurrences of central hypothyroidism were observed in the study cohort.
Conclusion
Despite potential symptom overlap between dysthyroid conditions, notably hypothyroidism, and Long COVID, our findings suggest that thyroid dysfunction does not contribute significantly to the pathogenesis of the post-COVID-19 syndrome. Our study aligns with the prevailing evidence from most investigations evaluating thyroid function in the phase following SARS-CoV-2 infection.

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EP484

Unusual distant metastasis of thyroid cancer: about 4 cases

El Omri Malika[1], Jemli S[1], Bellakhdher Mouna[1], Meherzi Abir[1], Houas Jihene[1], Ghammem Monia[1], Ach Taieb[2], Kermani Wassim[1] & Abdelkefi Mohamed[1]
[1]ENT department Farhat Hached Hospital, Sousse, Tunisia; [2]Endocrinology Department Farhat Hached Hospital, Sousse, Tunisia

Introduction
Distant metastases of thyroid tumors are rare. They are mainly localized in the lungs (10-15%), bones (9%) and brain (1%). Metastases to the facial area are exceptional. These metastases are more common with carcinoma of the vesicular (20%) than papillary (3.5%) carcinoma. The aim of our work is to support clinical and radiological aspects as well as therapeutic modalities of these entities.
Observations
Cases 1 and 2: Woman aged 38 and a boy aged 13, admitted for a chronic dry cough. Physical examination found thyroid nodules with lymphadenopathies. Chest x-ray showed a micronodular military. They had a total thyroidectomy with bilateral functional dissection confirming multifocal papillary carcinoma. A supplement with radioactive ablation therapy was associated. Case 3: A 55 years old woman admitted for lumbosciatalgia with a motor deficit. Osteomedullar biopsy revealed a metastasis of a vesicular carcinoma of the thyroid. Additional imaging revealed 2 left thyroid nodules. The patient had a decompressive radiation followed by thyroidectomy associated with bilateral central dissection. Case 4 A 43 year old woman admitted for chronic nasal obstruction. Examination found thyroid nodules. CT showed a mass extended to the right nasal fossa, maxillary sinus, sphenoid sinus, sella turcica and associated with a right lobar thyroid mass. Biopsy was in favor of nasal infiltration by a poorly differentiated carcinoma of the thyroid. The patient had chemotherapy.
Conclusion
Distant metastases of thyroid cancers have no clinical or radiological specificity. These metastases are more frequent with the vesicular histological type and have a more guarded prognosis.

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EP485

Primary thyroid lymphoma: experience of our department

El Omri Malika[1], Jemli S[1], Lazid Sarra[1], Bellakhdher Mouna[1], Meherzi Abir[1], Houas Jihene[1], Ghammem Monia[1], Ach Taieb[2], Kermani Wassim[1] & Abdelkefi Mohamed[1]
[1]ENT department Farhat Hached hospital, Sousse, Tunisia; [2]Endocrinology department Farhat Hached hospital, Sousse, Tunisia

Introduction
Primary thyroid non-Hodgkin's lymphoma, which is defined as a lymphoma occurring in the thyroid gland, is a quite rare pathologic entity, accounting for 1, 3-1, 5 % of thyroid neoplasm, and 0, 5% of lymphoma. The aim of our work is to evaluate the clinicopathological features and treatment outcomes of patients with primary thyroid lymphoma.
Material and methods
We report 8cases of primary thyroid lymphoma collected at our department between 2000 and 2023.
Results
There were 6 women and two men with an average age of 63 years. One patient had a history of neoplasia of the right breast and adenocarcinoma of the colon. The reason for consultation was an anterior basicervical swelling in all patients associated with dysphonia in one patient, dysphagia in one patient, and dyspnea in three patients. The clinical examination revealed a huge painless goiter compressive in one patient, associated with bilateral lymph nodes in two patients, and ipsilateral in a patient. One patient had an emergency tracheotomy. Four patients had biopsy and the other four patients had thyroidectomy. Histological examination concluded to a mantle lymphoma in two cases, a diffuse large B-cell lymphoma in four patients, and a MALT lymphoma in two cases. Only one patient presented an invasion of the medullary bone confirmed by biopsy. All patients underwent chemotherapy. Three patients died and 4 patients presented no recurrence.
Conclusion
Primary thyroid lymphoma is an uncommon pathologic entity. The prognosis is primarily dependent on age, staging, and disease spread, then the histologic subtype.

Keywords: autoimmune thyroiditis, hypothyroidism, euthyroidism, genetic polymorphism.

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EP486

Aggressive papillary microcarcinoma: clinical manifestations and prognostic factors

El Omri Malika[1], Jemli S[1], Kechiche Jaweher[1], Bellakhdher Mouna[1], Meherzi Abir[1], Houas Jihene[1], Ghammem Monia[1], Ach Taieb[2], Kermani Wassim[1] & Abdelkefi Mohamed[1]
[1]ENT Department Farhat Hached Hospital, Sousse, Tunisia; [2]Endocrinology Department Farhat Hached Hospital, Sousse, Tunisia

Introduction
Metastasis in adenopathy accompanying thyroid microcarcinoma (TMC) is a rare clinical situation. We propose to study the risk factors for their occurrence, their clinical characteristics and their therapeutic methods.
Material and methods
A retrospective study of 14 cases of TMC associated with metastatic cervical adenopathy collected in our ENT department, between 1990 and 2023.
Results
The cases studied represented 25% of all TMCs operated on during the same period. The mean age was 47.2 years, with a female predominance. The mean size of the adenopathy was 3 cm. The thyroid gland was clinically anodular in 10 cases. 13 patients had a cervical ultrasound scan showing calcifications within the adenopathy in 4 cases, considered to be a branchial cyst in one case. The thyroid was anodular in 7 cases. A cervical Computed tomography scan was performed in the case of an 8 cm lesion that had fistulated to the skin. It showed the appearance of an 84 mm multiloculated left latero-cervical mass with hypodense necrotic content and heterogeneous calcified peripheral enhancement infiltrating the lateral border of the sternocleidomastoid muscle, and an 8 mm left lobar thyroid nodule. Total thyroidectomy was performed in all our patients, together with a bilateral mediastino-recurrent dissection with unilateral lateral lymph node dissection in 12 cases and bilateral dissection in one case. Adjuvant treatment was performed in 13 patients with Iodine-131.
Conclusion
The presence of adenopathy during TMC is rare. This diagnosis should be considered in young patients. It reflects aggressivity of the tumor.

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EP489

Strange association of graves, hashimoto and papillary thyroid carcinoma

Elena Roxana Novac[1], Velicescu Cristian[2] & Cotirlet Valentin Adrian[3]
[1]Emergency Hospital Moinesti, Bacau, Romania; [2]Universitatea de Medicină şi Farmacie 'Grigore T. Popa' din Iaşi, Med, Iaşi, Romania; [3]Vasile Alecsandri University of Bacău - Mărăşeşti Campus, Bacău, Romania

We present the case of a 32 yeas old male, diagnosed 7 years ago with Basedow disease, with numerous recidives which needed anti-thyroid medication, with poor response (hypo to hyper-thyroid status, with high variations of TSH and FT4) whom after a period of remission (8 months, no treatment) came in for a polymorphic symptomatology sugestive for hyperthyroidism. The hyperthyroid state was confirmed he had high TrAb ()31 UI/ml vs < 1.75 UI/ml)- and we need to mention that on his last check in the detection rate of TrAb was under 0.3. The thyroid ultrasound revels on the left lobe a small mass of 0.8/0.8 cm, with EU-TIRADS score of 4, that was newly diagnosed. At that moment we initiated thyamazole 30 mg/day and non-selective beta-bloker for the four weeks until surgery. Postoperative histopathology revealed papillary microcarcinoma developed on hashitoxicosis-pT1aN0, of 1 mm in the middle of left thyroidian lobe. The particularity of this case consists in a long evolution of Basedow-Graves disease with numerous recalls, the appearance of a thyroid nodule after 7 years in which they identified a papillary microcacinoma associated with Hashimoto thyroiditis and also the postoperative recovery that was slowed by the parathyreoprive tetany.

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EP490

Diagnostic-therapeutic management in patients with non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)

Raúl Rodríguez Juárez[1], Antonia Garcia Martin[1], Mercedes Caba Molina[2] & Pablo J López-Ibarra Lozano[1]
[1]Granada, UCG Endocrinología y Nutrición, Granada, Spain; [2]Granada, Unidad Provincial Intercentros de Anatomía Patológica de Granada, Granada, Spain

Objective
Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) it's a histological entity that describes a low-aggressive neoplasm previously classified as encapsulated follicular variant of papillary thyroid carcinoma and well differentiated tumour of uncertain malignant potential. The preoperative diagnosis it's difficult, and if we suspect it hemithyroidectomy or lobectomy it's the therapeutic management of choice. Therefore, we will evaluate the features and diagnostic-therapeutic management of patients with NIFTP.
Materials and Methods
Retrospective observational study with 23 patients with NIFTP diagnosis in Granada's hospitals between the years 2016 and 2022. Demographic (sex, age), radiological (pre and postoperative ultrasonography), anatomopathological (pre and postoperative sample type, tumoral size) and therapeutic (indication and operation type, postoperative thyroglobulin and treatment and follow-up) variables were collected.
Results
23 patients with NIFTP (73.9% females, 50 ± 13 years). In the preoperative ultrasonography the nodules were classified in TI-RADs 4 and 5 in 47.8% and 8.7% respectively. Fine-needle aspiration (FNA) results were 4.3% for Bethesda I, 34.8% for Bethesda II, 21.7% Bethesda III, 17.4% Bethesda IV, 17.4% Bethesda V and 4.3% Bethesda VI. The surgical indication was PAAF's result in 60.9% of the patients, being total thyroidectomy the technique of choice in 65.2% of patients. The average size of the tumours was 31.8 ± 14.7 mm. After surgery, 65.2% had performed ultrasonography and thyroglobulin levels, and three cases were treated with radioiodine. 87% were followed-up after treatment.
Conclusions
Our study confirms the difficulty in suspecting NIFPT presurgically, that's why total thyroidectomy was performed in more than a half of patients, and follow-up is subsequently performed in the majority of cases.

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EP507

The correlation between the presence of histopathologically different subtypes and aggressive behavior and recurrence in patients with papillary thyroid carcinoma

Müge Keskin[1], Bugra Durmus[1], Gökhan Rıza Baykal[1], Ali Abbas Tam[2], Buket Özdemir[3], Ayca Dilsad Caglayan[4], Oya Topaloglu[2], Reyhan Ersoy[2] & Bekir Cakır[2]
[1]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yildirim Beyazit University Faculty of Medicine, Endocrinology and Metabolism, Ankara, Turkey; [3]Ankara Bilkent City Hospital, Department of General Surgery, Ankara, Turkey; [4]Ankara Etlik City Hospital, Department of Pathology, Ankara, Turkey

Aim
Papillary thyroid cancer (PTC) accounts for 85% of thyroid cancers. Classical PTC has a 10 year survival rate of over 95%. Although the histopathological diagnosis of thyroid tumors, which started in the 1950s, has improved significantly in the last few decades, the effect of aggressive subtypes on survival has not been fully clarified. In our study, we investigated the effect of aggressive cytologic subtypes on behavior and prognosis in patients followed up with a diagnosis of PTC.
Method
Our retrospective study included 484 patients who underwent bilateral total thyroidectomy and were diagnosed with PTC. There were 11 patients with aggressive subtype (columnar cell, tall cell, diffuse sclerosing, solid, hobnail PTC), 382 patients with nonaggressive subtype (papillary, follicular PTC), and 91 patients with mixed subtype. 36 month follow-up results were analyzed. Demographicall findings, imaging and laboratory results, histopathological features (tumor diameter, capsule invasion, vascular invasion, extrathyroidal invasion, lymphatic invasion, distant metastasis), radioactive iodine (RAI) treatment were noted from the records. Dynamic risk scoring (excellent response, biochemical incomplete response, structural incomplete response, indeterminate response) was performed.
Results
The mean age at diagnosis was lower in the aggressive subtypes (44.36 ± 10.63) than in the nonaggressive and mixed subtypes (46.14 ± 12.82 and 47.71 ± 13.24, respectively) ($P = 0.501$). Tumor size was significantly larger in the aggressive subtypes (1.83 ± 2.27 cm) than in the nonaggressive and mixed subtypes (1.21 ± 1.1 cm and 1.60 ± 1.1 cm, respectively) ($P = 0.019$). According to the American Thyroid Association (ATA) risk classification, the proportions of those identified as intermediate and high risk were higher in the aggressive and mixed subtypes (72.7% and 68.1%, respectively) than in the nonaggressive subtypes (23.9%) and the difference was statistically significant ($P < 0.001$). Remission, persistence, recurrence and metastasis rates during follow-up did not differ significantly between groups ($P = 0.926$, $P = 0.903$, $P = 0.776$ and $P = 0.920$, respectively). There was no significant difference in treatment responses according to dynamic risk scoring after initial treatment 6-12 months, 12-18 months, 18-24 months, 24-36 months ($P = 0.931$, $P = 0.961$, $P = 0.892$, $P = 0.698$, respectively).
Conclusion
In our study, we found that tumor size was larger in the aggressive subtype, and those with intermediate and high risk, according to the ATA risk classification, were more common in the aggressive and mixed subtypes. In patients with PTC, aggressive and mixed subtypes in the initial treatment phase may create differences in approach, and further studies are needed.

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EP508

Evaluation of dry eye parameters and vitamin E levels in patients with papillary thyroid carcinoma

Müge Keskin[1, 1], Belma Özlem Tural Balsak[1], Neslihan Bayraktar[2], Keskin Caglar[3], Fatma Dilek Dellal Kahramanca[3], Oya Topaloglu[4], Reyhan Ersoy[5] & Bekir Cakır[4]
[1]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Bilkent City Hospital, Department of Ophthalmology, Ankara, Turkey; [3]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [4]Ankara Yildirim Beyazit University Faculty of Medicine, Endocrinology and Metabolism, Ankara, Turkey; [5]Ankara Yildirim Beyazit University Faculty of Medicine, Endocrinology and Metabolism, Ankara, Turkey

Aim
Dry eye syndrome(DES) is a common finding in patients with thyroid orbitopathy. There are few studies on DES in patients with papillary thyroid cancer (PTC). Retinal pathology may develop in case of vitamin E deficiency, which has antioxidant, anti-inflammatory and anti-apoptotic properties.
Materials and Methods
In our study, 29 patients who received radioactive iodine (RAI) treatment (Group 1) and 22 patients who did not receive RAI treatment (Group 2) with a diagnosis of PTC were included. 26 healthy individuals without PTC were determined as the control group (Group 3). Exclusion criteria were diabetes mellitus, rheumatologic diseases, keratoconus, glaucoma, history of contact lens use, previous eye surgery. Ocular surface disease index, meibomian gland secretion quality, lid margin score, noninvasive tear breakup time were evauated with sirius device and meibomagraphy in all patients. Thyrotropin (TSH), free thyroxine, free triiodothyronine, and vitamin E levels were measured.
Results
TSH levels were significantly lower in Group 1 and 2 compared to Group 3 ($P < 0.001$, $P < 0.001$, respectively). There was no significant difference between

the groups in terms of vitamin E levels ($P=0.599$). The proportion of those with normal noninvasive tear breakup time (>17) was similar in Group 1, Group 2 and Group 3 (30.8%, 27.3%, and 44.6%, respectively, $P=0.145$). The proportion of those with an upper lid margin score of ≥1 was significantly higher in Group 1 and Group 2 than in the control group (64.9%, 56.8% and 17.9%; respectively, $P=0.025$). Lower meibomian gland expressivity was >1 in 34.5% of the patients in Group 1, 22.7% in Group 2, and 7.1% in Group 3 ($P=0.002$). The proportion of patients with lower meibomiagraphy values of ≥1 was significantly higher in Group 1 and Group 2 compared to the control group (61.1%, 52.5%, and 29.5%, respectively, $P=0.007$). There was no significant difference between the groups in terms of lower lid margin score, Oxford values, upper meibomian gland expressibility, and upper meibomiagraphy grades ($P=0.485$, $P=0.064$, $P=0.256$ and $P=0.069$, respectively). OSDI (survey questioning eye-related irritation symptoms) values were 6.25 in Group 1 and 8.12 in Group 2 and were significantly higher than the control group (2.27) ($P=0.034$).

Conclusion

Meibomian gland dysfunction is observed in patients with PTC who received and did not receive RAI. This may be related to TSH suppression. It is important to question these patients for a dry eye because it might affect their daily living activities.

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EP513

Challenges and pitfalls in the management of medullary thyroid cancer – Real-life data from a tertiary center in Romania

Stanescu Laura-Semonia[1, 2], Andrei Muresan[3], Dumitru Ioachim[4], Sofia-Maria Lider-Burciulescu[2, 5], Mara Băetu[2] & Corin Badiu[2, 3]
[1]"C.I. Parhon" National Institute of Endocrinology, Bucharest, Romania; [2]"Carol Davila" University of Medicine and Pharmacy, Bucure?ti, Romania; [3]"C.I. Parhon" National Institute of Endocrinology, Genetics, Bucharest, Romania; [4]"C.I. Parhon" National Institute of Endocrinology, Pathology, Bucharest, Romania; [5]"Ana Aslan" National Institute of Grontology and Geriatrics, Endocrinology, Bucharest

Introduction

Medullary thyroid cancer (MTC) is a thyroid neuroendocrine tumor with a genetic basis and average biological aggressiveness, with a 5-year survival rate of around 90%. However, the presence of calcitonin (CT) biomarker along with genetic beckground could further improve these data, by earlier diagnosis and proper surgical management of genetically predisposed patients.

Patients and Methods

To set specific thresholds for basal CT and calcium-stimulated CT for predicting thyroid malignancy, we included two groups: 74 women with elevated basal CT (>9.82 pg/ml) and 31 women with normal basal CT. After the calcium test, the histopathology of those submitted to surgery was correlated with basal and stimulated calcitonin. The best cut-offs for distinguishing female patients with medullary thyroid carcinoma or C-Cell-hyperplasia from other thyroid disorders are: 12.9 pg/ml, respectively 285.25 pg/ml . For the genetic approach, RET testing for germline mutations was performed in 74 subjects, (58 complete gene analyses and 16 targeted analyses), 72 of whom were diagnosed with MTC. Among all subjects submitted to germline RET analysis, 16/74 (21.6%) were clinically affected by a hereditary disease at diagnosis and 58/74 (78.3%) were presumed to have sporadic MTC. We identified a germline RET variant in a total of 24/74 (32.4%) cases; from these, 16/16 (100%) had a positive family history, while only 8/58(13.8%) were initially considered sporadic cases. We identified five different RET pathogenic variants. When classified in ATA risk categories, two mutations were of high-risk level (12/24, 50% cases) and three mutations of moderate risk level (12/24, 50% cases). The most common RET proto-oncogene alteration was Cys634 in 11/24 (45.8%) cases. All known pathology results of patients with a positive germline mutation and 5/37 with known wild-type RET patients had multifocal disease. Out of 50 cases tested negative for germline RET mutation, eight cases with advanced, metastatic MTC underwent RET somatic testing. From 6/8(75%) cases, a somatic RET mutation was found, 5/6 (83.3%) having Met918Thr mutation, and one case with Cys634Arg mutation. Among patients with known cancer staging, 7/24(29.1%) of those with a germline RET mutation and 20/50 (40%) of wild-type RET patients had locally advanced disease (T>1). We observed a more aggressive disease in patients with a somatic RET mutation, with metastatic disease, requiring systemic treatment with tyrosine kinase inhibitors, vandetanib, or cabozantinib.

Conclusions

Mutational screening is mandatory in all patients with MTC and crucial in selecting targeted treatment with TKI inhibitors and predicting responsiveness to therapy.

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EP525

The epidemiological, clinical, and pathological characteristics of differentiated thyroid cancer in children and adolescents

Hana Charfi[1], Issam Jardak[2], Fatma Hamza[2], Mohamed Maaloul[2], Wissam Amouri[2], S Charfeddine[2], Fadhel Guermazi[2], Khalil Chtourou[2], Mohamed Abid[1] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker Hospital, Endocrinology-Diabetology Departement, Sfax, Tunisia; [2]مستشفى الحبيب بورقيبة بصفاقس,Nuclear Medecine Departement, Sfax, Tunisia

Introduction

Differentiated thyroid cancer (DTC) in children is rare, accounting for 1.5 to 3% of all pediatric cancers. Its clinical presentation differs from that in adults. The aim of our study is to investigate the epidemiological, clinical, and anatomopathological characteristics of DTC in children and adolescents.

Patients and Methods

A descriptive retrospective study was conducted at the Nuclear Medicine Department of Habib Bourguiba University Hospital in Sfax over a 21-year period (January 1996-December 2017), including 20 patients, children, and adolescents, followed for DTC.

Results

The average age of our patients was 14.9 years, with a female-to-male ratio of 1.5. Seventy percent of our patients presented with a thyroid nodule, associated with cervical lymphadenopathy in 10% of cases. One patient had a history of radiation exposure, and another had thyroid dysfunction. Family history of thyroid cancer was present in 3 patients, and thyroid dysfunction in 3 others. All patients underwent total thyroidectomy, with 90% undergoing lymph node dissection. The diagnosis of DTC was based on the histopathological examination of the surgical specimen, revealing papillary carcinoma in 80% of cases and follicular carcinoma in 20%. Pulmonary metastasis was observed in 15% of cases. All patients received thyroid hormone therapy. Complete remission was achieved in 65% of cases.

Conclusion

DTC in children and adolescents is a rare but aggressive entity. Its treatment is based on surgery and radioiodine therapy, resulting in an excellent prognosis.

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EP530

The profile of the patients associating differentiated thyroid cancer and autoimmune thyroiditis – a single center experience

Lazarescu Monica Valentina[1], Andrei Goldstein[2] & Mirela Gherghe[3]
[1]Oncologic Center Sanador, Romania; [2]Oncologic Center Sanador, Bucureşti, Romania; [3]Nuclear Medicine Department, University of Medicine and Pharmacy 'Carol Davila', Bucharest

Background

Differentiated thyroid cancer is the most prevalent thyroid cancer subtype, accounting for more than 95% of cases. Autoimmune thyroiditis, a frequent autoimmune disease, is reported in 25-30% patients with nodular goiter, according to the literatures. Differentiated thyroid cancer is associated with less aggressive disease and better outcome in patients with coexisting thyroid autoimmunity, but the studies already published revelead discordant data.

Aim

To observe the characteristics of patients diagnosed with differentiated thyroid carcinoma associated with autoimmune thyroiditis admitted to the Nuclear Medicine Department.

Methods

We present a retrospective analysis of our patients with differentiated thyroid cancer with coexisting thyroid autoimmunity who were evaluated from January1 to December 31, 2023 in a tertiary Nuclear Medicine Department - Oncologic Center Sanador, Bucharest. The pre- and post-operative thyroid function tests, ultrasound, histological exams as well as clinical history and examination were evaluated.

Results

30 out of 103 patients hospitalized in our department with indication for radioactive iodine therapy had an association of autoimmune thyroiditis with differentiated thyroid cancer. Only two patients (ages 37 and 68) were males, whereas the remaining 28 were women (26 to 71 years). Preoperative the majority of patients (26 out of 30) were euthyroid, 3 had hypothyroidism, and one had autoimmune thyroiditis with the onset of hyperthyroidism. We registered one case of follicular carcinoma and 29 cases of papillary thyroid carcinoma, associated with autoimmune thyroiditis. Multifocality was observed in 40% of cases. 11 patients had lymph node metastases, with N stage: pN1a -5 patients and pN1b – 6 patients. According to ATA guidelines, our patients were divided as follows: 11 low-risk, 12 intermediate-risk, and 7 high-risk. At the moment of the admission in

our Departement the Anti-thyroglobuline antibodies (Tg- Ab) remained elevated in 19 individuals (63.3%), with average values of 677 Ui/ml (35.7 to 3014 UI/ml). Despite being in the high-risk category with nodal involvement, the patients with very high values of Anti-thyroglobulin antibodies (>1000 UI/ml) had a stimulated thyroglobulin level below 1 ng/ml.
Conclusion
The association of autoimmune thyroiditis and differentiated thyroid cancer had lead to better prognostic. Most of our patients were low- and intermediate-risk, necessitating low doses of iodine therapy. More extensive studies are needed to establish a guideline for this subgroup of patients.

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EP531

Differentiated thyroid carcinoma in graves disease

Ruxandra Paula Ristea[1], Teodora Puşcaş[1], Claudiu Zaharia[1], Serghei Tutovan[1] & Mihaela Stanciu[1, 2]
[1]County Clinical Emergency Hospital of Sibiu, Endocrinology, Sibiu, Romania; [2]'Lucian Blaga' University of Sibiu, Faculty of Medicine, Endocrinology, Sibiu, Romania

Introduction
Recent studies have revealed that thyroid autoimmunity and thyroid cancer may coexist, although a pathogenic relationship has not been clearly established. Graves' disease (GD) is an autoimmune thyroid disease and is considered the most common cause of hyperthyroidism. Thyroid cancer is the most common malignancy of the endocrine system and represents the eighth most diagnosed cancer worldwide. Although in patients with GD, the presence of thyroid nodules is not uncommon, thyroid cancer is a very rare occurrence.
Case report
We report the case of a 46-year-old male patient, diagnosed with Graves disease, Graves orbitopathy, and a micronodular goiter in 2018, with two hypoechoic nodules in the right lobe, with a maximum of 0.92/0.67/0.90 cm, and another in the left lobe, measuring 0.45/0.50/56 cm. Thyroid function was effectively controlled with thiamazole, and the morphology was evaluated through periodical cervical ultrasound (US). At the last follow-up in November 2023, the US showed the rapid enlargement of the nodules, with more than 1 cm since the last follow-up in 2022, with hypoechogenicity, microcalcifications, poorly defined margins, and irregular appearance, associated with bilateral lymphadenopathy. Elastography displayed an Asteria score of 3 in strain elastography, indicating a high level of suspicion. A decision was made for the patient to undergo a total thyroidectomy with lymph node dissection. The pathological evaluation following the procedure described multifocal classical papillary carcinoma in both thyroid lobes with lymph node metastasis (pT1b(m)N1aL/V0Pn0Ro). Following surgery, the patient is due to receive radioactive iodine therapy and thyroid-stimulating hormone suppression therapy with levothyroxine.
Conclusion
The case reported highlights the fact that, although rare, the risk of thyroid cancer in patients with both GD and thyroid nodules exists. Further studies are needed to assess if there could be a causal relationship between these entities and the prevalence of thyroid cancer among patients with GD. Clinicians should consider careful evaluation, including ultrasound, nuclear imaging, and fine needle aspiration, when appropriate, in patients with GD and thyroid nodules, as there is no consensus or recommended protocol for the detection of thyroid cancer in these patients.

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EP535

Occult thyroid papillary carcinoma lymph node metastasis discovered on lymphadenectomy specimen of laryngeal cancer

Amel Elkorbi[1], Nawres Bouaziz[1], Mahdi Ferjaoui[1], Rachida Bouatay[1], Nawrez Kolsi[1], Harrathi Khaled[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction
Occult or subclinical thyroid carcinomas are not uncommon. Metastases of thyroid cancers may be discovered incidentally during cervical dissection for squamous cell carcinoma of the upper aero digestive tract. The prevalence of these thyroid metastases is estimated to be between 0.3 and 1.6%. The therapeutic impact is poorly codified, partly related to the frequently severe prognosis of those cancer. We aim through this case to discuss the therapeutic consequences of such metastases.
Case report
This is a 46-year-old smoker patient, presented with chronic dysphonia progressing evolving over eight months with intermittent inspiratory dyspnea. Panendoscopy under general anesthesia showed a voluminous left hemilaryngeal tumor extended to the Morgani's ventricle and the subglottic region. Biopsy confirmed the diagnosis of well-differentiated keratinizing squamous cell carcinoma. The tumor was classified T4AN0M0 according to the UICC/AJCC of 2017. The patient underwent a total laryngectomy with recurrential and functional bilateral lymphadenectomy and total thyroidectomy. The final histopathological examination concluded to a laryngeal squamous cell carcinoma with the presence of lymph node metastasis from papillary thyroid carcinoma. The thyroid gland showed no histological lesions. Iratherapy with cervicofacial external radiotherapy were performed. The patient is currently without evidence of recurrence after 24 months of follow-up.
Discussion/Conclusion
In our case, there was no discussion after the definitive histological findings, as we already performed a total thyroidectomy justified by the subglottic tumor extension. Otherwise, in other cases, incidental histological thyroid metastases should be discussed based on the results of thyroid ultrasound during follow-up and the discovery of a thyroid nodule justifies thyroidectomy for diagnosis confirmation.
Disclosure of interest: none declared

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EP538

Insular carcinomas of the thyroid: diagnostic and prognostic evaluation: a study of 13 cases

Neni Dezoumbe[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital, Endocrinology, Diabetology, Metabolic Diseases, and Nutrition, Casablanca

Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department Ibn Rochd University Hospital of Casablanca, Morocco
Neurosciences and Mental Health Laboratory Faculty of Medicine and Pharmacy-University Hassan II- Casablanca-Morocco

Introduction
Insular carcinoma of the thyroid is an extremely rare tumor, accounting for 4% of cases, with a poor prognosis and malignancy intermediate between differentiated and anaplastic cancers. The objective of this study is to specify the characteristics of this cancer by examining its diagnostic and prognostic aspects.
Patients and Methods
A retrospective study was conducted in the endocrinology and diabetology department, including 13 patients followed for insular thyroid cancer between 1986-2023, among all thyroid carcinomas (1005 patients).
Results
The prevalence was 1.3%. The average age was 56 years. Eight patients presented with multi-heteronodular goiter, and four with an isolated nodule, including one toxic nodule. All patients underwent total thyroidectomy with lymph node dissection. Radioiodine therapy (100 mCi) was administered to all patients. Insular carcinoma represented the entire tumor in 4 cases or was associated with awell-differentiated follicular (2 cases) or papillary (6 cases) component. The average tumor size was 4 cm (2–8 cm). Histological stages (pTNM): T2 (6 cases); T3 (4 cases); T4 (3 cases); N0 (10 cases); N1 (3 cases). Recurrence was observed in 3 patients (locoregional recurrence and bone metastasis) after an average period of 28 months. Predictors of poor prognosis included age, large size, multifocality, and capsule invasion.
Conclusion
Our results emphasize the rarity of insular carcinoma with potential severity (pTNM stage, recurrence frequency).

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EP539

Hyperthyroidism induced by metastatic distant thyroid carcinoma

Dorina Ylli[1, 2], Violeta Hoxha[2], Klodiana Poshi[1, 2], Marjeta Kermaj[2] & Agron Ylli[1, 2]
[1]University of Medicine Tirana, Tirana, Albania; [2]Mother Teresa University Hospital Center, Tirana, Albania

Background
We present a rare case of a 64-year-old patient diagnosed with longstanding untreated Graves' disease and co-occurrence of metastatic thyroid cancer. Very

few cases are reported in literature where the thyrotoxicosis in due to the distant metastasis and optimal treatment remains challenging.
Case Presentation
The patient came to the endocrine unit for thyrotoxicosis treatment. He was diagnosed with Graves' disease and following treatment initiation and hormone normalization, he underwent total thyroidectomy. The histological evaluation revealed a follicular variant of papillary thyroid cancer with capsular invasion (T3aNxMx). Post-surgery, aberrations in thyroid function parameters persisted, marked by suppressed thyroid-stimulating hormone (TSH), elevated free thyroxine (FT4), positive anti-thyroglobulin antibodies, and remarkably elevated thyroglobulin levels (50, 000 ng/ml). Levothyroxine was initially tapered down and later suspended due to persistent hyperthyroidism. However, two months after suspention TSH remained suppressed (0.01 mUI/ml) and FT4 elevated (22 pg/ml). Iodine-131 therapy (100 mCi) was scheduled it was discussed whether the therapy should be postponed since the TSH target was not met. However, Given the high levels of anti-TSH receptor antibodies (40 UI/ml), the decision to proceed with I131 treatment was made, revealing multiple lung and bone metastases on post-I131 imaging. Two months post-I131, symptomatic hyperthyroidism prompted the initiation of a low dose of methimazole, effectively normalizing thyroid function. At 6 months post-I131, thyroglobulin levels decreased to 19, 753 ng/ml with a TSH of 0.5 mUI/ml showing good biochemical response to therapy. However dispite improving Tg remains very high and close follow-up is fondamental and posing a challenge in determining the optimal approach for pre-I131 treatment, especially in countries were where recombinant TSH is not availability
Discussion
This case underscores the intricate balance required in addressing both cancer and hyperthyroidism. Despite the convention of advocating a lower TSH in metastatic thyroid cancer, the persistence of elevated TSH receptor antibodies suggests continued stimulation of residual thyroid cancer cells.
Conclusion
Given the scarcity of such cases, further exploration through additional cases and an extensive literature review is crucial for refining optimal management strategies.

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EP550

Clinical case of a combination of giant prolactinoma and medullary thyroid cancer

Margarita Perepelova[1], Elena Przhiyalkovskaya[1], Ekaterina Pigarova[1], Petr Nikiforovich[1], Lilia Selivanova[1], Anna Roslyakova[1], Aleksandra Shutova[1] & Larisa Dzeranova[1]
[1]Endocrinology Research Centre

Background
The combination of various endocrine tumours is presented both as hereditary syndromes and sporadic forms. Medullary thyroid cancer and prolactinoma are neuroendocrine tumours, the presence of these two pathologies simultaneously has not been previously described in the literature.
Objective
To present a clinical case of a patient with giant prolactinoma and medullary thyroid cancer.
Materials and Methods
To describe the clinical case of a 67-year old patient with giant prolactinoma and medullary thyroid cancer.
Case presentation
The results of magnetic resonance imaging of the cervical spine dated in 2022 revealed an endo-infra-ante-latero(D)sellar pituitary adenoma with the size of $43\times22\times31$ mm. Laboratory tests were as follows: prolactin 94340 mEd/l (60-355), bioactive prolactin 90360 mEd/l (50-300), calcitonin 1340 pg/ml (0-11.8). The patient was initiated on cabergoline therapy. Calcium, parathormone and parathyroid glands - without pathology. US examination of the thyroid gland showed nodules: in the right lobe a moderately reduced echogenicity mass with single fluid inclusions, with clear contours, $p.2.1\times1.9\times1.1$ cm (EU-TIRADS 4), and isoechogenic mass with fluid zones d 0.1 cm (EU-TIRADS 2). Cytogram corresponded a C-cell carcinoma, based on the criteria of the classification system of Bethesda V. A flush from the puncture needle for calcitonin showed concentration of 2000 pg/ml on the right and 705 pg/ml on the left, and a calcium gluconate test was performed. At the 3rd and 5th minute, the calcitonin level was >2000 pg/ml, which indicates a high risk of medullary cancer. The results of computed tomography of the chest revealed a peripheral mass in S8 of the right lung and single small foci in the lungs that require dynamic monitoring. Computed tomography of abdominal organs did not reveal any masses. A right-sided hemithyroidectomy was performed, and the results of the morphological examination showed medullary cancer in the right lobe of the thyroid gland, classified as pT1bN1aMx R0 Pn0 LV0. Family history was negative for diseases of the pituitary gland, thyroid gland, oncopathology and other endocrine diseases.
Conclusions
The occurrence of pituitary tumor in combination with thyroid cancer is rare. According to a literature search, this is the first described clinical case of a prolactinoma and a medullary thyroid cancer. It is necessary to expand the spectrum of possible combinations of different neuroendocrine tumours and to perform additional screening.

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EP572

Effectiveness of radioactive iodine (RAI) therapy and its associations with different factors in people presenting with hyperthyroidism; an analysis from Karachi-Pakistan

Sarwat Anjum[1]
[1]Asian Institute of Medical sciences, Medicine, Hyderabad Sindh Pakistan, Pakistan

Back ground
Hyperthyroidism is a common disorder with multiple etiologies and radioactive iodine (RAI) is the important modality to treat it. Successful treatment is determined by development of euthyroidism and / or Hypothyroidism within 6 months of radioactive iodine treatment. The aim of this study was to find out the outcome of RAI treatment and its association with factors like age, gender various etiologies of hyperthyroidism and baseline TSH, FT4 in our population.
Methods
This retrospective case series study was conducted at Karachi institute of Radiotherapy and Nuclear Medicine' (KIRAN) from January 2018 to June 2020. A total of 199 participants with complete data were recruited in study after IRB approval. Demographic details, age, gender, underlying cause of hyperthyroidism (graves disease, toxic multinodular goitre, solitary toxic nodule etc,) were obtained from medical records along with baseline FT4 & TSH. A fixed dose of 15mci of radioactive iodine was given to all patients and TSH and FT4 were measured at 6 weeks 3, 6, and 12 months to evaluate the outcome of RAI treatment. Data was analyzed by SPSS version 20 to compute mean standard deviation and percentages.
Results
In our study 77.9% were females, 22.1% males, mean age was 41.32 ± 0.99 years. 74.4% participants had Graves' disease, 15% had solitary toxic nodule or toxic multinodular goiter. Post RAI TSH target was achieved earlier compared to FT4. Outcome of RAI treatment in patients with Graves' disease and toxic nodule revealed statistically significant and early result. Females revealed significant improvement in both biochemical markers i-e TSH and FT4 compared to males. Successful treatment was noticed in 35%, 56%, 75.6%, at 6 weeks, 3, 6, 12 months respectively.

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EP573

Asymptomatic subacute thyroiditis presenting as bilateral thyroid nodules and pyrexia of unknown origin

Eirini Kaliakatsou[1], Athanasios Fountas[1], Labrini Papanastasiou[1], Vasiliki Pikou[2], Dimitra Koutete[2], Christos Mpaltas[3] & Athina Markou[1]
[1]'G. Gennimatas' General Hospital of Athens, Athens, Greece, Unit of Endocrinology and Diabetes Center, Athens, Greece; [2]'G. Gennimatas' General Hospital of Athens, Athens, Greece, 3rd Department of Internal Medicine, Athens, Greece; [3]'G. Gennimatas' General Hospital of Athens, Athens, Greece, Radiology Imaging Department, Athens, Greece

Introduction
Subacute thyroiditis (SAT) is an acute inflammatory disorder which can rarely present as pyrexia of unknown origin without other symptoms. Diffuse thyroid heterogeneity, focal hypoechoic areas and decreased/normal gland vascularity are the most common ultrasound findings of SAT. We report a case of asymptomatic SAT presenting as bilateral thyroid nodules and pyrexia of unknown origin.
Case Presentation
A 72-year-old male with a history of tachycardia/bradycardia syndrome (with pacemaker implantation) and thyroid nodule of the left lobe (Bethesda II) was referred to emergency department due to a 2-week history of fever. He complained of a 5 kg weight loss in last 3 months, with no other symptoms. Clinical examination was unremarkable, apart from patient being febrile. Blood tests revealed anemia, leukocytosis, increased inflammation markers and

thyrotoxicosis (TSH 0.01 µIU/l, fT4 31.13 pmol/l, NR: 9-19) with negative anti-TPO, anti-TG and TRAb antibodies. Further investigations were negative for infections and autoimmune diseases, while bone marrow aspiration biopsy was normal. Whole body CT scan showed hypoechogenic lesions in both thyroid lobes but no other findings. Due to exposure to intravenous iodine contrast, thyroid scintigraphy was not performed. Thyroid ultrasound revealed a 4.4×2.3 cm well marginated isoechoic nodule in the right lobe with regular shape, cystic degeneration and hypoechoic halo sign with peripheral/central vascularity (EU-TIRADS 3) and two other nodules in the left lobe, 3.6×2.5 cm and 1.2×2.2 cm, (EU-TIRADS 3) with similar features to the right lobe nodule. Cytology of the two larger nodules revealed atypia of undetermined significance (Bethesda III). Treatment with naproxen 500 mg twice daily for the pyrexia and thiamazole 10 mg daily for the thyrotoxicosis was initiated. One-week later, patient was afebrile, improved thyroid function and decreased inflammation markers were noted; naproxen was continued, while thiamazole was stopped due to borderline fT4 levels. After one month of treatment, naproxen was finally discontinued due to normal inflammation markers and thyroid function. The patient was reviewed three months later and remained asymptomatic and euthyroid without treatment. Repeat thyroid ultrasound revealed complete remission of the 4.4 cm and 3.6 cm nodules and presence of the, already known, 1.5 cm nodule in the left lobe.

Conclusion

This very rare case demonstrates the importance of SAT to be included in the differential diagnosis of fever of unknown origin, even in asymptomatic patients. Furthermore, clinicians should be aware that, in some cases, SAT-associated thyroid lesions may mimic thyroid nodules.

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EP574

Harmony and complexity: unveiling the multifaceted nature of multiple autoimmune syndrome

Raida Ben Salah[1], Siddiqa Soomauroo[2], Faten Hadjkacem[2], Abdelmuhaymen Missaoui[2], Ahmad Ridwaan Auckburally[3], Wiem Feki[3], Mouna Mnif[2], Sameh Marzouk[1], Mohamed Abid[2], Nabila Rekik[2] & Zouheir Bahloul[1]

[1]Hedi Chaker University Hospital, Department of Internal Medicine, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [3]Hedi Chaker University Hospital, Department of Radiology, Sfax, Tunisia

Introduction

Despite being organ-specific autoimmune diseases (AID), autoimmune thyroid diseases (AITD) may be associated with other AIDs either specific to other organs or systemic. These associations are not uncommon. They may be grouped in the form of an autoimmune polyendocrinopathy or multiple autoimmune syndrome (MAS). MAS is defined by the presence in the same person of at least three AIDs.

Patients and Methods

It is a retrospective study over a period of 18 years of patients with AITD associated with another type of AID. The aim of this study was to describe the characteristics of MAS in this population.

Results

one hundred and thirteen cases were collected. A female predominance was observed with a sex ratio (F/M) of 3.52. The average age at the diagnosis of thyroid dysfunction was 38.22 years. The etiology of the AITD was predominantly Hashimoto's thyroiditis (69 patients), followed by Graves' disease (19 patients). In each patient with thyroid disorder, one or more AID were found: 17 types of AIDs distributed into 10 organ-specific AID and 7 systemic AID. The AITD was the primary presenting condition in 35 cases (26.51%), diagnosed concomitantly with another AID in 40 cases (30.3%), and preceded by an AID in 54 cases (40.92%). In our study, we collected 11 patients who presented with a MAS. They were all female. Two of them presented with a MAS type 2 and the 9 others were of type 3. A Hashimotos' thyroiditis was diagnosed in all the cases.

Conclusion

This syndrome was described by Humbert and Dupond[1] in 1988 as the association of at least three AIDs in the same patient. There are 3 types depending on associated pathologies. Family history, genetic, infectious, immunological and psychological factors have been implicated in the development of MAS. Generally, one of the autoimmune disease associated in the MAS, is a skin disease, such as psoriasis or vitiligo. According to the literature, vitiligo is the first AID to be diagnosed during the course of MAS associated with an autoimmune thyroid disease in the majority of cases.

Reference

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EP575

Hypothyroidism: what do our patients know?(about 140 cases)

El Jadi Hamza[1] & Moustaghit Imane[2]

[1]Oued Eddahab Military Hospital, Endocrinology, Agadir, Morocco; [2]Oued Eddahab Military Hospital, Endocrinology, Agadir, Morocco

Summary

Hypothyroidism is a frequent and generally chronic pathology. Hypothyroid patients, particularly women of childbearing age, the elderly and/or cardiac patients, need to have a minimum level of knowledge of their pathology. The aim of our study was to assess the level of knowledge of a group of hypothyroid patients. The study involved 140 hypothyroid patients over a period of 06 months. The evaluation was carried out using a questionnaire, and the responses were recorded and analyzed using Excel software. 88.7% of patients knew that they had a hypo functioning thyroid gland, with 84% identifying the cause of hypothyroidism. 85% knew how to take L-Thyroxine, 22% had an idea of the notion of drug interactions, 2% knew the signs of overdosage and only 3% knew the signs of underdosage. In the case of 52 patients of childbearing age, 92% are unaware that pre-conceptional balancing is compulsory, compared with 8% who are already aware of it. Hypothyroidism is a frequent pathology, predominantly female. It corresponds to a thyroid hormone deficiency, either due to primary thyroid gland or hypothalamo-hypophyseal axis disease. It's often requiring lifelong treatment. If left untreated or inadequately treated, hypothyroidism can have harmful consequences. It can lead to myxedematous coma, cardiovascular complications such as coronary insufficiency, heart failure and conduction disorders, and sleep apnea syndrome. On the other hand, if over-treated, it can lead to osteoporosis and/or atrial fibrillation, as well as impaired quality of life secondary to signs of thyrotoxicosis. Hypothyroid patients must have a minimum of knowledge about how to take L-Thyorxine, the duration of treatment, the risk of drug interactions and the signs and complications of over- and under-dosing. Women of childbearing age must be informed about the obligation of preconception balance. They also need to know how to increase their doses if a pregnancy occurs without being scheduled, while waiting to see their treating physicians. This underlines the major importance of therapeutic education in avoiding the complications mentioned below. Our present survey reveals a significant lack of knowledge among hypothyroid patients, and has enabled us to re-educate this group of patients. Medical prescription must be backed up by proper therapeutic education, which remains a cornerstone of chronic disease management.

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EP577

Prevalence of side effects of synthetic antithyroid drugs

Deus Niyongabo[1], Nassim Essabah Haraj[1], Siham El aziz[1] & Asma Chadli[1]

[1]Ibn Rochd University Hospital of Casablanca, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction

Hyperthyroidism is characterized by an overproduction of thyroid hormones. Synthetic antithyroid drugs are essential to reduce these hormones before definitive treatment, but they can lead to side effects. This study aims to assess the frequency of these effects and their management.

Patients and Methods

A retrospective descriptive study over 5 years (2018-2023) involving 79 patients treated for hyperthyroidism who experienced side effects of synthetic antithyroid drugs.

Results

The mean age of the patients was 38 years, with a female predominance. The most common etiologies were Graves' disease (54.4%), toxic nodular goiter (32.9%), and toxic nodule (7.5%). Approximately 96.2% received initial treatment with synthetic antithyroid drugs (47.3% Neomercazole, 36.8% Thiamazole, 15.7% PTU). 23.6% of patients experienced side effects: agranulocytosis (2.6%), neutropenia (3.9%), hepatic cytolysis (6.5%), and skin rash (10.5%). No cases of acute pancreatitis or vasculitis were recorded. These effects primarily occurred within the first three months of treatment. Management varied from prescribing antihistamines for skin rashes to temporary discontinuation followed by reintroduction of antithyroid drugs after the disappearance of adverse effects, or definitive discontinuation of treatment with rapid medical preparation for definitive therapy. The outcome was favorable in 98.7% of cases, except for one patient who died due to agranulocytosis.

Conclusion

Synthetic antithyroid drugs are associated with potentially serious side effects that need to be clearly explained to patients. Clinical and laboratory monitoring is crucial, especially during the first three months of treatment.

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EP578

An uncommun cause for thyroid cysts: about 5 cases and review of litterature

Houas Jihene[1], Heyfa Belhadj-Miled[1], Monia Ghammam[1], El Ghali Wassim[2], Malika El Omri[1], Abir Meherzi[1], Mouna Bellakhdhar[1], Yosra Hasni El Abed[3], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT Department, Sousse, Tunisia; [2], Department of Anaesthesia, Sousse, Tunisia; [3], Department Of Endocrinology, Sousse, Tunisia

Introduction
While hydatid cysts can manifest in various organs, reports on their occurrence in the thyroid gland are limited in the literature. This report aims to present five cases of thyroid hydatid disease along with a comprehensive literature review.
Materials and Methods
A retrospective analysis was conducted on 5 patients who underwent surgical intervention for thyroid hydatid cysts between 1982 and 2023.
Results
The average age of the patients was 55.8 years, ranging from 31 to 79 years, and none had a significant pathological history. Consultation was sought due to anterior basicervical swelling, raising suspicion of a thyroid nodule. Thyroid ultrasound revealed a multivesicular fluid formation with a regular, thin wall in 4 cases and calcification in one case. Thyroid scintigraphy, performed in 4 patients, indicated a cold nodule. All patients exhibited normal thyroid function. Three patients also presented with hydatid cysts in other organs. Surgical treatment was individualized for each cyst, guided by intraoperative macroscopic observations and histopathological findings.
Conclusion
Although rare, hydatid disease affecting the thyroid gland should be considered in the differential diagnosis of cystic lesions in patients with hydatid cysts in other organs or those hailing from endemic regions. Treatment exclusively involves surgical intervention to excise the cyst without rupture. The prognosis is excellent in cases where total cyst removal is achieved without rupture.

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EP579

On the issue of functional changes in the thyroid gland in patients with breast cancer

Makhbuba Azimova[1, 1] & Khurshidakhon Nasirova[1]
[1]Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

The endocrine and reproductive systems of women work in close relationship and moderates the functional state of visceral systems. In patients with concomitant diseases and breast cancer (BC), some hypofunction of the thyroid gland (TG) was revealed and there is a direct dependence of the decrease in functional activity on the progression and luminal forms of pathological changes in the mammary gland. However, the effect of antitumor methods of treatment in BC on the clinical and morphological structure and function of the TG has not been practically studied.
Purpose
to determine the methods of correcting functional changes in the TG in BC patients by retrospective analysis.
Material and methods
The following gradations of the functional state of the TG in BC were the subject of the study: volume and size, parenchyma structure, hormonal status indicators, local cytomorphological structure of the parenchyma. The object of the study were 38 patients with verified BC: II - and III - stages. The age of patients ranged from 34 to 68 years. Patients received antitumor therapy in accordance with the standards: polychemotherapy - 31, hormone therapy-5 and immuno-chemotherapy-2. Ultrasound, MSCT, the study of biochemical parameters and thyroid hormones, cytomorphology of fine-needle biopsy of the thyroid parenchyma were used to study the studied gradations.
Results
There was a change in the average volume and flatness of the contours depending on the stage of breast cancer, histological type and differentiation of the tumor process. At the same time, a statistically significant decrease in the functional (based on the study of hormones) thyroid activity from 23 to 35% was established against the background of the appearance of new heterogeneous areas in the thyroid parenchyma. Most often, these changes were characteristic of patients aged >50 years and receiving polychemotherapy ($+$immunotherapy). In contrast, in patients with a hormone-dependent form of BC, functional changes in the TG turned out to be insignificant on the background of specific therapy and did not require special correction. The cytomorphological picture of local changes in the study of fine-needle biopsy specimens in 17 patients showed the absence of polymorphism and atypical changes. In 8 patients with breast cancer, there was a parallel development of nodular goiter during polychemotherapy. Thus, the analysis of the obtained results showed the presence and correlation dependence of local changes in the thyroid gland on the stage of BC and the type of therapy.

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EP581

Late relapse of severe graves' ophthalmopathy: a case report

Hamdi Frikha[1], Mona Rekik[2], Sonda Kammoun[2], Yoldez Ben Jemaa[2], Khouloud Boujelben[1], Dhoha Ben Salah[1], Fatma Mnif[1], Mouna Mnif[1], Mohamed Abid[1], Amira Trigui[2] & Nabila Rekik Majdoub[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology, Tunisia; [2]Habib Bourguiba University Hospital, Department of Ophtalmology, Tunisia

Introduction
Graves' disease (GD) is an autoimmune disorder characterized by hyperthyroidism, and it often involves the development of Graves' ophthalmopathy (GO). The latter occurs in a significant percentage (25-50%) of Graves' disease cases. Active and severe ophthalmopathy can lead to a worsened prognosis and, in extreme cases, result in blindness. Reports about late ocular manifestation of GD have become scarce due to improved management.
Case Report
A 68-year-old woman with a 25-year history of Graves' disease presented a unique case of late relapse of GO. Remission had initially been achieved using thyroid synthesis blockers. However, sudden hypothyroid state due to overdose of treatment led to the development of severe active ophthalmopathy, with an activity score of 6 and significant sight impairment. Concomitant Thyrotropin Receptor Antibody (TRAK) levels were remarkably high at 43 UI. The patient underwent methylprednisolone boluses followed by a course of mycophenolate mofetil, resulting in a partial remission of inflammatory phenomena. Decompressive surgery was subsequently performed, leading to partial improvement in sight.
Discussion
This case highlights the challenges associated with late relapses of Graves' ophthalmopathy, even after an extended period of disease management. The importance of caution in thyroid-blocking treatments is underscored, as treatment overdose in this case contributed to the severe manifestation of ophthalmopathy. TRAK play a significant role in the assessment and management of the patient as they correlate with the severity of ophthalmopathy and could therefore guide the use of immunosuppressive therapies like methylprednisolone and mycophenolate mofetil. The successful outcome following decompressive surgery suggests its potential role in ameliorating sight impairment in severe cases of Graves' ophthalmopathy. In conclusion, this case emphasizes the importance of vigilant management in Graves' disease, considering the potential for late relapses of ophthalmopathy. Clinicians should exercise caution in thyroid-blocking therapies to prevent exacerbation of ophthalmic complications. Regular monitoring, prompt intervention, and a multidisciplinary approach are essential in optimizing outcomes for patients with Graves' ophthalmopathy.

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EP583

Hypothyroidism and high CK an association or a coincidence?

Lubna Etbinah[1, 2], Rabia Mahmoud[1], Mustafa alsinan[1], Agne Jovaisate[1], Godwin Simon[1], Lina El-tayeb[1], Bashir Mahmoud[1], Ayan Mohammed[1], Edel Casey[1], Audrey Limbe[1], Belayet Hossain[1], Ali Akram[1], Mariana Dram[1], Furhana Hussain[1], Cathriene Cheung[1] & Gideon Mlawa[1]
[1]Queen's Hospital, Acute Medicine, Romford, United Kingdom; [2]Queen's Hospital, Acute Medicine, Romford, United Kingdom

Introduction
Hypothyroidism presentation can be variable. Some patients are asymptomatic whilst other present with general lethargy and cold intolerance. Depending on the degree of hormone deficiency, patient can also present with by skeletal muscle involvement characterized by muscle aches and weakness (proximal myopathy). In some cases, patients with hypothyroidism will have elevated CK but this usually less that 5000
Cases
1. 46 years old was referred under the medical team directly from GP with a history of 6-8 months history of muscle aches. He also reported feeling cold and lethargic with weight gain. He was found to be severely hypothyroid with high CK. He was cycling to work daily and that might have contributed to high CK. Elevated TSH 57.4, FT4 0.5, FT3 0.6, Cortisol 332, with High CPK levels. CK 8723, Creatinine, He was started on levothyroxine and discharged home. He

improved clinically and after 4 weeks blood test showed CK 1043, FT10.4, TSH 22, FT3 3.8 2. 33 year old male presented with few months' history of tiredness, muscle weakness, weight gain, and being sleepy most of the time. His blood test showed evidence of severe hypothyroidism and high CK4157, cortisol 135, FT4 0.5, TSH > 100, and creatine 130. He was treated with IV fluids and started on Levothyroxine 1 mg once daily. The short synacthen test was normal.

Discussion

Hypothyroidism is a common endocrine disorder which is encountered in non-acute settings. It can be associated with tiredness, weight gain, and cold intolerance as well as proximal muscle weakness (myopathy). Elevated CK (rhabdomyolysis) may be associated with severe hypothyroidism. Heavy exercise, statins, or excessive alcohol intake are some of the factors which may contribute to elevated CK in patients with hypothyroidism. The cause of CK elevation in hyporthyroid patients remains unknown, but is thought to be due to interference or defective mitochondrial oxidative metabolism, insulin resistance. Thyroxine plays a key role in the energy metabolism. Thyroid hormone deficiency leads to impaired metabolism of glycogen (glycogenolysis), triglyceride turnover, and mitochondrial oxidative metabolism which in turn impair muscle function.

Conclusion

Severe hypothyroidism can be associated with high CK (rhabdomyolysis), proximal myopathy and muscle aches. Blood tests including CK and cortisol should be checked in patients with new diagnosis of hypothyroidism. Patients with elevated CK and hypothyroidism should be advised to avoid any precipitating factors rhabdomyolysis such heavy exercise, statins and alcohol.

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EP585

Are thyroid function test ordering practices appropriated?

Dhouha Zouari[1], Rim Marrakchi[1], Mohamed Chaher Rabah[1], Mariem Boudaya[1], Kamel Jamoussi[1], Mohamed Abid[2] & Mouna Turki[1]
[1]Laboratory of Biochemistry, Hédi-Chaker Hospital, Sfax, Tunisia; [2]Endocrinology departement, Hedi Chaker Hospital, Sfax, Tunisie

Introduction

Inappropriate laboratory test utilization can result in unnecessary patient testing and increased healthcare costs. Thyroid-stimulating hormone (TSH) is recommended as the first-line test for investigating and monitoring thyroid dysfunction. We evaluate Thyroid function tests (TFTs) ordering in our hospital practice.

Methods

A retrospective descriptive study included 400 TFTs requests. TFTs of interest were: TSH and FT4. These tests request were classified according to the reasons and origins of ordering. Frequencies of each testing pattern were calculated. Demographic data (sexe, age) are determinate. Thyroid stimulating hormone (TSH), free thyroxine (FT4) were performed based on electrochemiluminescence immunoassay (eCLIA) by Dxi600® Beckman Coulter.

Results

The mean age of patients was 46.7 years, with extremes ranging from 1 month to 86 years with a male/female sex ratio of 0.49. The majority of TFTs requests were from the endocrinology department (43.3%), followed by the cardiology department (12.8%) and the paediatrics department (11.9%). Reasons for prescription were dysthyroid follow-up in 37.3% of cases, suspicion of dysthyroidism in 37% of cases, dysthyroid screening in 23.7% and the presence of thyroid nodules in 2%. TFTs's ordering were for TSH alone in 78.5% of cases, and a TSH + FT4 in 21, 5% of cases. Among subjects suspected of having dysthyroidism and subjects having thyroid nodule only 40% had dysthyroidism (35% had hypothyroid and 5% had hyperthyroid) and only % had dysthyroidism (% had hypothyroid and % had hyperthyroid) respectively. Among subjects who underwent a thyroid check for dysthyroidism, 65% returned normal, 17% with hypothyroidism and 2% with hyperthyroidism. Among subjects with a thyroid nodule or goitre, only 28.6% had hypothyroidism, the rest returned normal.

Conclusion

There was an over-ordering for thyroid tests in our hospital practice. This suggests that this request should be more rational in order to limit costs and invasiveness.

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EP586

An unusual hyperthyroidism presentation

Megi Lekbello[1], Eni Celo[2] & Dorina Ylli[1]
[1]Mother Teresa Hospital, Endocrinology, Tiranë, Albania; [2]Trauma University Hospital, Intern Medicine, Tiranë, Albania

We would like to report the case of a 45-year-old woman who came to our emergency department two months ago complaining of exhaustion, vomiting, and stomach pain. In the last three weeks, she had three admissions to the ER due to vomiting. She did not have any chronic illnesses, and her only medication for the vomiting was oral electrolytes. In the last two months, she claims to have lost four to five kilograms. The physical examination showed tachycardia (135 beats per minute), hypotension (90/60 mmHg), and subfebrile temperature (37.5 °C). The results of the laboratory test revealed mildly increased bilirubin and transaminases along with pancytopenia. For further testing, she was admitted to the gastrohepatology department. Her minor gastritis following fibrogastroscopy does not account for her vomiting. The following were the outcomes of the laboratory findings in the gastrohepatology report: WBC 2.33×10^3/mm^3 (4.0-10), RBC 3.4×10^6/mm^3 (3.8-5.20), HGB 9.75 g/dl (12.0-15.0), HCT 28.1% (35-45), MCV 82.56 μm^3 (80-87), MCH 28.65 pg (27-32), PLT 95×10^3/mm^3 (150-440), AST 53 U/l (8-45), ALT 59 U/l (7-55), Total protein 5.1 g/dl (6.6-8.3), Na 136 mmol/l (138-146), K 2.98 mmol/l (3.5-5.5), TSH < 0.005 mIU/ml (0.27-4.2), FT4 > 100 pg/ml (12-22), FT3 30.44 pmol/l (3.1-30.44), Anti-R-TSH 17 IU/l (< 1.5). Ultrasounds of the abdomen and heart were normal. The first courses of treatment included methimazole 5 mg (4 pills daily) and propranolol 40 mg (1 tablet, twice daily). Within a week of the treatment beginning, the symptoms improved. Leucopenia and thrombocytopenia were completely resolved following discharge: RBC 3.5×10^6/mm^3, MCV 88 μm^3, MCH 28.8 pg, PLT 177×10^3/mm^3, WBC 4.7×10^3/mm^3, HGB 9.9 g/dl, HCT 29.9%. The atypical clinical presentation with vomiting in thyrotoxicosis delayed the diagnosis, resulting in overt hyperthyroidism. Anemia is the most typical symptom of thyroid hormone's effects on the hematopoietic system, but it can also impact other cell lineages. Pancytopenia, in rare cases, is associated with thyrotoxicosis, and the relationship between thyrotoxicosis and pancytopenia is rarely discussed in the literature; typically, hematologic values are corrected once the treatment is initiated, and the thyrotoxicosis is addressed.

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EP587

Lipid profile in patients with peripheral hypothyroidism

Latifa Boutaybi[1], Fatima Zahra Najioui[1], Hajar Charif[1], Zerrouki Fatim Zahra[1], Siham Rouf[2] & Hanane Latrech[2]
[1]Department of Endocrinology-Diabetology and Nutrition CHU Mohammed-VI Oujda, Faculty of Medicine and Pharmacy, Mohammed Premier University Oujda, Morocco, oujda, Morocco; [2]Department of Endocrinology-Diabetology and Nutrition CHU Mohammed-VI Oujda, Faculty of Medicine and Pharmacy, Mohammed Premier University Oujda, Morocco, [2] Laboratory of Epidemiology, Clinical Research and Public Health, Oujda Faculty of Medicine and Pharmacy, Mohammed Premier University Oujda, Morocco, Oujda, Morocco

Introduction

Hypothyroidism is a state of hypometabolism at the origin of numerous metabolic disturbances, including dyslipidemia, which may increase cardiovascular risk in these patients. The aim of our study is to assess the lipid profile in patients with peripheral hypothyroidism.

Materials and methods

Retrospective descriptive study including 130 patients, followed at the Endocrinology-Diabetology and Nutrition Department of the University Hospital of Oujda for peripheral hypothyroidism. Statistical analysis was performed using SPSS version 21 software.

Results

The mean age was 46.15 ± 18.6 years, with an F/M sex ratio of 2.9, the mean TSH value at discovery was 21.84 mu/ml, Hashimoto's thyroiditis was the most frequent cause 63.2%.33% of patients had hypothyroidism of frust origin Dyslipidemia was noted in 44.6% of our patients, represented essentially by hypertriglyceridemia in 55.6%, hypercholesterolemia in 39.2%, hypoHDLemia in 31.8%, hyperLDLemia the least frequent abnormality (24%). Dyslipidemia was noted in 54.6% of patients with Hashimoto's thyroiditis and in 34% of patients with hypothyroidism of frust origin.

Discussion-Conclusion

Hypothyroidism is often associated with dyslipidemia, this atherogenic lipid profile must be systematically detected when this pathology is diagnosed, and reassessed after treatment to prevent cardiovascular complications.

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EP588

Thyroid ectopia: a report on 3 cases

Neni Dezoumbe[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital, Endocrinology, Diabetology, Metabolic Diseases, and Nutrition, Casablanca

Introduction
Thyroid ectopia is a rare condition resulting from an anomaly in the development or migration of the gland. We present two cases of thyroid ectopia.
Case Reports
Case 1: A 44-year-old woman underwent orbital CT scan due to chronic right eye tearing, revealing a lesion at the base of the tongue. Thyroid palpation was negative, and oropharynx examination was unremarkable. Tongue MRI showed a 43 × 37 mm lesion at the base with heterogeneous enhancement after gadolinium injection and global thyroid atrophy. Scintigraphy revealed sublingual ectopic thyroid. Hormonal exploration was normal, and due to its asymptomatic and uncomplicated nature, surveillance was recommended. Case 2: A 40-year-old patient presented with dysphonia and a non-palpable thyroid. Nasofibroscopy revealed a tongue base mass compressing the vocal cords, leading to acute respiratory distress during the procedure, requiring emergency tracheotomy. Surgical excision of the mass was performed, and histopathological examination revealed thyroid parenchyma within fibromuscular tissue, including a focus of thyroid vesicular carcinoma. Case 3: A 61-year-old patient complained of neck discomfort with a grade 1 goiter on clinical examination. Cervicothoracic CT scan showed a heterogeneous goiter extending to the anterior mediastinum, along with an anterior mediastinal mass suggestive of thyroid heterotopia. The patient underwent total thyroidectomy and resection of the mediastinal mass. Histopathological examination revealed a dystrophic thyroid nodule within the anterior mediastinal mass.
Discussion
Thyroid ectopia may be asymptomatic or present with hypothyroidism or compression symptoms. Malignancy risk is rare. In asymptomatic cases, biological and morphological surveillance is recommended, while surgery is indicated for compression or suspected malignancy.

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EP602

Marine-lenhart syndrome: a rare cause of hyperthyroidism

Mohamed Khairi Arous[1], Houcem Elomma Mrabet[1], Fadia Boubaker[1], Mariem Souissi[1], Baha Zantour[1], Wafa Alaya[1] & Mohamed Habib Sfar[1]
[1]University Hospital Taher Sfar, Endocrinology and Internal medicine Department, Mahdia, Tunisia

Background
Marine-Lenhart syndrome (MLS) is defined by the coexistence of Graves' disease and a hyperactive nodule or multinodular goiter. Although rare, its diagnosis by functional imaging coupled with ultrasound is necessary in order to propose a radical treatment. We report the case of a patient followed for hyperthyroidism related to a SML.
Case presentation
A 52-year-old patient consulted for a picture of thyrotoxicosis associating tremor, weight loss, polyphagia, irritability and thermophobia. Physical examination revealed a small goiter with a right lobar nodule and bilateral exophtalmia. Hormonal assessment showed a TSH at 0.002 mIU/l and FT4 at 47.1 pmol/l confirming peripheral hyperthyroidism. Anti-TSH receptor antibodies were positive at 40. The Graves' disease was diagnosed confronted to the proptosis and the positivity of the antibodies. Neck ultrasound showed a hypervascularized goiter and two right lobar nodules classified EU-TIRADS III measuring 7.1 mm and 2.3 mm respectively. Scintigraphy showed an increased diffuse iodine uptake of the thyroid gland along with a partially extinctive thyroid nodule. The patient was put on 20 mg/d of thiamazol in preparation for a radical treatment by total thyroidectomy
Conclusions
The diagnosis of MLS is present in 2-4% of patients with MB; hence the inecessity of a neck ultrasound even in the presence of clinically or biologically obvious Graves' disease, especially in the presence of a thyroid nodule. Scintigraphy is also required to characterize the nodule. The treatment of MLS is surgical, since resistance to synthetic antithyroid drugs is noted in these cases.

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EP603

Symptomatic multinodular goitre with compressive symptoms complicated by obstructive sleep apnoea and hypoxaemia

Rachel Cronin[1], Ali Al-Ashbal[1], Julen Borlle[1], Justin Hintze[2], Paul Lennon[2] & Ma Pyeh Kyithar[1]
[1]Midland Regional Hospital Portlaoise, Portlaoise, Ireland; [2]St James's Hospital, Ireland

Introduction
Most goitres are asymptomatic and do not require surgical intervention. Surgical management is recommended for goitres with compressive symptoms, suspected malignancy, drug-resistant hyperthyroidism, or retrosternal extension.
Case
63-year-old female with a background history of hypertension, type 2 diabetes, obesity (BMI 43 kg/m^2) and possible obstructive sleep apnoea (OSA), presented to Emergency Department following a one-minute episode of apnoea during sleep resulting in peripheral cyanosis, episodes of dyspnoea and stridor. She also had history of partial thyroidectomy in 1993, however no history of thyroid cancer or radiation exposure. CT scan two years prior to admission, showed a multinodular goitre and she was treated with carbimazole for subclinical hyperthyroidism for two years. Clinical examination demonstrated a very large multinodular goitre that was firm in consistency, moving with deglutition. Arterial blood gas on admission showed PO_2 10 kPa, PCO_2 5.61 kPa, bicarbonate 30.1 mmol/l, pH 7.48. During the first night of admission, the patient's SpO_2 level decreased to 60% on room air whilst sleeping. The patient desaturated further to 60% on 4L O_2 on lying down and oxygen saturation improved to 95% on sitting up, and she was subsequently transferred to the intensive care unit for airway monitoring. CT neck and thorax demonstrated a large bilateral multinodular goitre (11x6x1 cm) extending from the neck to thoracic level with predominantly left sided compression of trachea, and the upper neck vascular structures appeared displaced because of the large goitre. Thyroid profile showed free T4 12.1 pmol/l, free T3 5.1 pmol/l TSH 1.37 mIU/l, thereby euthyroid state. The patient was transferred for an urgent Ear/Nose/Throat team review given the significant risk of airway compromise. She subsequently underwent total thyroidectomy without complications. She desaturated on post-op day 1, possibly due to mucous plugging, an element of tracheomalacia, or pre-existing OSA, and was re-intubated for one day. She was then extubated to non-invasive ventilation and the overnight oximetry demonstrated 240 events of desaturation, likely in keeping with OSA. She was discharged on post-op day 9. Her histopathology of thyroidectomy revealed an incidental multifocal papillary thyroid cancer on a background of significant follicular nodular disease and will require ongoing clinical follow-up.
Conclusion
Significant thyroid enlargement, including multinodular goitre, may occasionally cause the upper airway compression, leading to respiratory compromise. Surgical treatment is the management of choice in patients that are surgically fit. Careful post-operative management is important in cases such as this, where a co-existing pathology such as OSA may complicate the clinical picture.

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EP605

A case report of anaplastic thyroid carcinoma

Raimonda Klimaite[1, 2, 3], Ugne Janonyte[3] & Gintaras Kuprionis[4]
[1]Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Hospital of Lithuanian University of Health Sciences, Kauno Klinikos, Department of Endocrinology, Kaunas, Lithuania; [3]Lithuanian University of Health Sciences, Kaunas, Lithuania; [4]Hospital of Lithuanian University of Health Sciences, Kauno Klinikos, Kaunas, Lithuania

Introduction
Anaplastic thyroid cancer (ATC) is a highly aggressive endocrine tumor formed of undifferentiated follicular thyroid cells. ATC accounts for only 1-4% of all thyroid cancers. The therapeutic approach is typically multimodal, combining surgery, radiation and chemotherapy. However, ATC is often resistant to treatment. Hence, the reported median overall survival of ATC patients is ~3 months, with nearly 100% disease-specific mortality.
Case
A 65-year-old man presented to our outpatient endocrinology department with complaints of generalized weakness, sore throat, neck pain and fever. These symptoms lasted about four weeks. Upon examination, a solid ~3 cm nodule at the front of the neck was palpated. A full diagnostic work-up was performed.
Diagnostic tests: Laboratory tests: TSH 2.30 (0.4-3.6) mU/l, FT4 21.63 (7.87-20.3) pmol/l, FT3 4.29 (3.34-5.1) pmol/l, ATPO 3.00 (0-3.2) kIU/l, Anti-Tg 466.5 (0-13.6) kU/l, calcitonin 12.8 (normal range 0.56-2.81) pmol/l.

Thyroid ultrasound
A ~4.4x6.3 cm heterogeneous mass with calcifications in the right lobe of the thyroid gland and enlarged lymph nodes on the right side of the neck were detected.
Microscopic examination
A core needle biopsy (CNB) of the left thyroid lobe identified a stromal tumor, formed by atypical cells with large, polymorphic nuclei and background necrosis. An elevated mitotic rate and multinucleated giant cells resembling osteoclasts were also detected. Immunohistochemically, tumor cells were positive with PAX-8, vimentin, CK7 and focally positive with TTF-1 staining. Immunohistochemical staining with calcitonin and thyroglobulin - negative. CNB of an enlarged lymph node on the right side of the neck was not informative, with no apparent neoplastic changes.
Chest and neck CT
Imaging revealed a $\sim 4.7 \times 4.3 \times 7.5$ cm non-homogeneous nodular right thyroid lobe with calcifications. The mass descends retrosternally to the middle mediastinum, displacing the trachea and esophagus, infiltrating surrounding tissues. Paratracheal lymphadenopathy and an enlarged lymph node near the root of the right lung were visualized.
Treatment
A chemotherapy course with paclitaxel (135–175 mg/m^2) and carboplatin (AUC 5–6) once every three weeks was initiated. The patient has undergone the third cycle of chemotherapy, reporting an overall sense of well-being and a notable reduction in discomfort in the cervical region. As for now, the regiment is continued. If chemotherapy proves effective, surgery will be scheduled.
Conclusion
ATC is a rare and highly aggressive type of thyroid cancer, characterized by uncontrolled and rapid growth. Thus, a prompt and comprehensive differential diagnosis and treatment plan are needed.

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EP606

A transiently toxic solitary thyroid nodule in the context of amiodarone therapy

Denise Sant[1], Simon Mifsud[1], Sarah Craus[1], Arlène Gatt[1], Ebony Sciberras Giusti[1] & Sandro Vella[1]
[1]Mater Dei Hospital, L-Imsida, Malta

Background
Thyrotoxicosis is a well-known complication of amiodarone therapy. Three types of amiodarone-induced thyrotoxicosis (AIT) are recognized; type 1 AIT, type 2 AIT, and mixed/indefinite forms of AIT. Type 1 AIT is an iodine-induced hyperthyroidism that usually occurs in patients with pre-existing nodular goitre or latent Graves' disease[1]. We present a case of type 1 AIT associated with a transiently toxic solitary thyroid nodule, with hyperthyroidism resolving once amiodarone therapy was stopped.
Case Presentation
A 74-year-old lady with paroxysmal atrial fibrillation receiving long-term amiodarone therapy was referred because of biochemical thyrotoxicosis (free thyroxine: 30.1 pmol/l [reference range: 11.9-1 pmol/l], free triiodothyronine: 6.1 pmol/l [reference range: 3.5-6.1 pmol/l], and thyroid-stimulating hormone: 0.018 micIU/ml [reference range: 0.3-3.0 micIU/ml]). She complained of occasional episodes of palpitations and heat intolerance but was otherwise asymptomatic. Physical examination revealed a heart rate of 92 beats per minute with a blood pressure of 130/1 mmHg. There were no signs of thyroid eye disease, and no palpable thyroid nodules or goitre were appreciated. Investigations revealed a negative TSH-receptor antibody status, whilst a neck ultrasound showed a 1.1×0.1 cm hypoechoic nodule on the left thyroid lobe. Thyroid scintigraphy revealed a single focus of increased tracer uptake in the left thyroid lobe with no uptake in the rest of the thyroid gland suggesting a solitary toxic nodule. After consulting with the patient's cardiologist, amiodarone was stopped, and carvedilol was prescribed instead. She was also commenced on carbimazole for type 1 AIT secondary to a solitary toxic thyroid nodule. The patient was reviewed at outpatients regularly and her carbimazole dose was titrated against her thyroid function. Follow-up neck ultrasound studies revealed stable findings. After twenty months, treatment with carbimazole was stopped. Six months following the cessation of carbimazole, she remained clinically and biochemically euthyroid.
Conclusions
This case is noteworthy for two main reasons; (i) the association between AIT and a solitary toxic thyroid nodule is rare[1], and (ii) following the cessation of amiodarone, the patient was eventually able to come off thionamide therapy as her hyperthyroidism resolved, highlighting the transient nature of this toxic thyroid nodule in the context of amiodarone use. Whilst mild AIT may subside in 20% of cases[1], usually patients with type 1 AIT end up requiring definitive treatment because of the underlying thyroid disorder.

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EP607

Central hypothyroidism induced by bexarotene preceding graves' disease after interferon therapy for cutaneous t-cell lymphoma

Mafalda Martins Ferreira[1], Sofia Lopes[1], Tânia Carvalho[1], Patrícia Oliveira[1] & Isabel Paiva[1]
[1]Centro Hospitalar e Universitário de Coimbra, Portugal, Endocrinology, Diabetes and Metabolism, Coimbra, Portugal

Introduction
The simultaneous occurrence of two drug-induced thyroid dysfunctions is rare. We present a case of central hypothyroidism due to bexarotene (BXC), followed by Interferon-α (IFNα)-induced Graves' disease (GD) thyrotoxicosis after 2 years.
Case Report
A 56-year-old man with no prior thyroid disease was diagnosed with cutaneous T-cell lymphoma and commenced treatment with BXC 600 mg/day and IFNα 90 mg/week concurrently. After two weeks, TSH was <0.004 uUI/ml (0.4-4.0) and FT4 was <0.49 ng/dl (0.7-1.5). MRI revealed no selar or parasellar lesions. Central hypothyroidism due to BXC was diagnosed and levothyroxine (L-T4) was initiated at 50 mg/day, gradually reaching 88 mg/day (1.4 mg/kg/day). BXC dose was reduced to 300 mg/day due to severe hypertriglyceridemia and the therapy with IFNα was maintained. After 25 months, TSH remained <0.004 uUI/ml and FT4 was 2.04 ng/dl under L-T4 88 mg/day, which was reduced to 75 mg/day. Four months later, the patient exhibited weight loss, tremors, palpitations, and abnormal thyroid levels (TSH <0.004 uUI/ml, FT4 4.60 ng/dl, FT3 >20 pg/ml (1.8-4.2); anti-TPO antibodies 342 UI/ml (<5.6), TRAbs 30 U/l (<2). IFNα-induced GD was diagnosed. L-T4 was ceased and methimazole (MMI) 15 mg/day initiated. One week later his thyroid function was: TSH <0.004 uUI/ml, FT4 0.79 ng/dl (0.7-1.5), FT3 3.1 pg/ml (1.8-4.2). Recently the patient was under IFNα 90 mg/week and BXC 150 mg/day, maintaining unmeasurable TSH, a FT4 of 1.5 ng/dl and FT3 of 5.3 pg/ml on MMI 12.5 mg/day (increased to 15 mg/day). Unfortunately, the patient deceased at 58 years old due to the progression of the cutaneous T-cell lymphoma with neurolymphomatous involvement.
Conclusions
BXC leads to central hypothyroidism in 30% cases by decreasing TSH secretion and increasing peripheral thyroid hormone metabolism. L-T4 can be initiated with or after confirming reduced FT4 levels, with doses up to 3 mg/kg/day. IFNα can induce autoimmune (Hashimoto's thyroiditis (HT) and GD) and non-autoimmune (non-autoimmune hypothyroidism and destructive thyroiditis) thyroid diseases via immune dysregulation, T cell activation, and direct follicular cell toxicity. IFNα-induced GD is less common than HT and destructive thyroiditis, often irreversible with dose reduction or cessation. In this case, diagnosing GD was delayed as TSH suppression was inherent to central hypothyroidism from BXC and since the initial FT4 elevation was interpreted as excessive L-T4 dosage. The gradual BXC dose reduction led to increased MMI dosage due to predominant IFNα-induced hyperthyroidism. Vigilant thyroid function monitoring during concurrent medication therapies causing thyroid dysfunction is crucial.

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EP608

Distant metastasis at the time of diagnosis in a young male patient with classical subtype of papillary thyroid carcinoma and graves' disease

Sofia Chatzi[1], Gerasimos Tsourouflis[2], Eleni Koukoulioti[1] & Georgios Boutzios[1]
[1]National and Kapodistrian University of Athens, Department of Pathophysiology, Medical School, Athens, Greece; [2]National and Kapodistrian University of Athens, Second Department of Propaedeutic Surgery, Medical School, Athens, Greece

Introduction
Patients with Graves' disease (GD) and thyroid nodules have an elevated risk of developing papillary thyroid carcinoma (PTC). Distant metastasis observed in 1-9% of patients with PTC. The classical subtype usually demonstrates favorable prognosis compared to other more aggressive PTC subtypes, for which an increased risk of extranodal metastases is observed.

Aim of the Study
We present an unusual case of a young male diagnosed with classical subtype PTC and Graves' disease, metastasized to the lungs, at the time of diagnosis.
Case Presentation
A 36-year-old male patient presented with suppressed TSH levels (TSH = 0, 01 mIU/l) and multinodular goiter in thyroid ultrasound. Laboratory tests showed elevated T3 = 2, 19 nmol/l, FT4 = 20, 1 pmol/l and TSI = 114 IU/l (nv: < 1, 0 IU/l). Thus, diagnosis of GD was established. Thyroid ultrasound revealed two large hypoechoic nodules, 1 mm and 1 mm respectively, with micro-calcifications (TIRADS 5), and suspicious deep cervical lymph nodes at compartment II. Fine needle aspiration biopsy for both nodules and lymph nodes with cytological findings were consistent with malignancy. Patient underwent total thyroidectomy with central and left lateral compartment lymph node dissection. The histological examination revealed multifocal PTC of classical subtype without thyroid capsule invasion and metastatic infiltration of lymph nodes (7/33), (pT2N1bMxR0). Subsequently, he received 120 mCi RAI. In the whole-body scan multiple foci of abnormal uptake concentration in lung parenchyma were observed. We performed a chest computed tomography confirming multiple nodular lesions, highly suggestive for metastatic infiltration. Noteworthy, as an incidental finding a solid renal mass 5, 4 cm in the upper pole of the right kidney, suspicious for malignancy, was noticed. Subsequently, patient underwent partial right nephrectomy and histological examination revealed a clear cell renal carcinoma Grade 2 (ISUP/ WHO 2022). Six months later, an additional RAI ablation treatment with 160 mCi, for the PTC derived lung metastases, was performed. Due to the unusual presentation of distant metastases from a classical subtype PTC and the presence of a second primary malignancy, genetic testing was performed for VHL and BRAF V600E/K gene mutation with no pathologic findings.
Conclusions
These findings suggest that prompt and meticulous evaluation of nodules in any patient with GD associated with nodular alterations must be considered. Autoimmunity seems to play a crucial role in tumor behavior since distant metastases from a PTC of classical subtype is an unusual finding.

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EP610

Combination of primary and secondary myopathy in a patient with severe hypothyroidism

Margarita Perepelova[1], Valeria Slokva[1], Ekaterina Pigarova[1], Aleksandra Shutova[1], Anna Kolodkina[1] & Larisa Dzeranova[1]
[1]Endocrinology Research Centre

Background
One of the complications of hypothyroidism is the disorder of the neuromuscular system. Myopathic changes often accompany hypothyroidism and are observed in 30-80% of patients. A distinctive feature of hypothyroid myopathies is the reversibility of clinical manifestations and significant improvement of well-being after levothyroxine compensation of the disease. However, the absence of a vivid clinical picture of hypothyroidism, combined with its rare occurrence, complicates early diagnosis and often requires differential diagnosis with other types of myopathies.
Case presentation
Patient T. was complained on progressive pain and muscle weaknessin the lower limbs, impaired coordination. At the time of admission he moved only with support of relatives. From the anamnesis vitae it is known that the patient is the first of 4 children from a close cousin-sister marriage. Primary hypothyroidism was detected at the age of 17, but he did not receive therapy. Physical examination showed pseudohypertrophy of the upper and lower limb girdle muscles, muscle strength was diffusely reduced to 4 points, tone was symmetrically increased, tendon-periosteal reflexes were high, with expansion of reflexogenic zones. Movements in large joints are limited due to muscle contractures. Hormonal blood analysis revealed a significant increase in the level of TSH - more than 500 mIU/l (0.25-3.5), at dilution - 836 mIU/l, of which bioactive TSH - 174 mIU/l; free T4 - 5.15 pmol/l (9-19), free T3 - 2.3 pmol/l (2.6-5.7). Genetic study revealed homozygous mutations in *MICU1* gene previously described in myopathy with extrapyramidal symptoms (OMIM: 615673) with autosomal recessive type of inheritance and in *IGSF1* gene (NM 001555.5) in exon 8 a variant in hemizygous state leading to amino acid substitution of p.(Lys420Thr), not previously described in the literature. After 2 months from the beginning of therapy with levothyroxine - medically compensated primary hypothyroidism: TSH 1.134 mIU/l (0.4-4.0), T4 free 12.95 pmol/l (7.0-17.6). The patient noted improvement of general well-being, regression of hypothyroidism symptoms, but still had complaints of pain and weakness of lower limb muscles, difficulties with independent movement.
Conclusions
Hypothyroid myopathy usually manifest by nonspecific symptoms in the form of myalgia, muscle cramps, especially increasing with exercise. The severity of myopathy correlates with the duration and degree of thyroid hormone deficiency, which should be taken into account to determine the management of patients with this pathology. An atypical severe course or lack of correction during treatment with levothyroxine should initiate an additional diagnostic search to exclude other forms of myopathy.

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EP612

A perplexing clinical challenge in the follow-up of papillary thyroid cancer: sarcoidosis

Hayri Bostan[1], Gokhan Colpan[2], Ceren Tufan[3] & Ersen Karakilic[3]
[1]Canakkale Mehmet Akif Ersoy State Hospital, Endocrinology and Metabolism, Turkey; [2]Ezine State Hospital, Internal Medicine, Turkey; [3]Canakkale Onsekiz Mart University, Faculty of Medicine, Endocrinology and Metabolism, Turkey

Background
Neck ultrasonography (USG) is an important imaging tool in the postoperative follow-up of papillary thyroid carcinoma (PTC). Sarcoidosis is an inflammatory disease characterized by non-caseating granulomas with involvement in various organs and lymph nodes. Herein, a case with atypical lymph nodes detected on neck USG during routine follow-up for PTC and diagnosed with sarcoidosis will be presented.
Case presentation
A 52-year-old female patient, diagnosed with PTC 7 years ago, applied to our clinic for follow-up. The pathology after total thyroidectomy was compatible with classical-type PTC which was multicentric, bilateral, and had the largest diameter of 22 mm. No residual focus or metastatic lymphadenopathy (LAP) was detected in the patient's 1-year follow-up whole-body iodine scan, who received postoperative 100 millicuries of radioactive iodine therapy. The patient, who has not had regular follow-up for the last 2 years, had TSH: 0.21 uIU/ml (reference range (RR):0.35-4.94), thyroglobulin (Tg): < 0.01 ng/ml (RR:3.68-64.15) and anti-thyroglobulin (a-Tg): 1.14 IU/ml (RR < 4.11) under 125 mg levothyroxine replacement. On neck USG, conglomerate, hypoechoic lymphadenopathies with no echogenic hilum were observed at bilateral cervical levels 3 and 4, the largest of which had a longitudinal dimension of 23 mm. Leukopenia (WBC: 2.92 10^3/ul (RR:4.0-10.5), neutrophil: 1.65 10^3/ul (RR:1.5-6.6), lymphocyte: 0.92 10^3/ul (RR:1.5-3.5)) and hypercalcemia (Ca: 10.8 mg/dl (RR:8.5-10.4)) were also detected in her laboratory tests. Considering hematological malignancies, thoracoabdominal computed tomography (CT) examination was performed. Multiple conglomerated LAPs, the largest of which was paratracheal, measuring 27x25 mm, were observed in the mediastinum, and multiple paraaortic and intraaortocaval LAPs were observed in the retroperitoneal area in thoracoabdominal CT. Her right supraclavicular lymph node was excised and histopathological examination revealed non-caseating granulomas that tended to coalesce. The patient was diagnosed with sarcoidosis, as her serum angiotensin-converting enzyme (ACE) level was found to be high along with the present histopathological findings. The patient, who was in remission in terms of PTC, was planned to continue follow-up by reducing the levothyroxine dose replacement to 100 mg.
Conclusions
The coexistence of PTC and sarcoidosis has been reported as rare case reports. Sarcoid lesions can easily be confused with PTC metastases due to their involvement in both neck lymph nodes and lungs. The current case highlights that granulomatous diseases such as sarcoidosis should also be included in the differential diagnosis if pathological LAP with an advanced hypoechoic, conglomerate appearance is detected in a PTC follow-up patient with no increase in Tg levels.

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EP613

Severe hypothyroidism due to thyroxine malabsorption in a patient with non-celiac gluten sensitivity after thyroidectomy; a rare case report

Vasiliki Daraki[1], Panagiotis-Nikolaos Tsakalomatis[1], Eleni-Konstantina Syntzanaki[1], Rodoula Vamvoukaki[1], Vasiliki Venetsanaki[1], Katerina Augoustaki[2], Maria Sfakiotaki[1], Grigoria Betsi[1] & Paraskevi Xekouki[1]

[1]University General Hospital of Heraklion, Department of Endocrinology Diabetes and Metabolic Diseases, Crete, Greece; [2]University General Hospital of Heraklion, Department of Gastroenterology, Crete, Greece

Introduction
Non-celiac gluten sensitivity (NCGS) belongs to gluten-related disorders. Patients with NCGS develop a variety of intestinal and/or extraintestinal symptoms such as abdominal pain, bloating, bowel habit abnormalities, nausea, gastroesophageal reflux disease and aphthous stomatitis, that improve when gluten is removed from the diet. The diagnosis is made after exclusion of coeliac disease and wheat allergy. Although thyroxine malabsorption has been described in patients with coeliac disease, data on thyroxine absorption in patients with NCGS is lacking so far.
Case-report
A 41-year-old female, with a history of thyroidectomy 2 years ago, presented at the outpatient clinic with chronic hypothyroidism despite progressively increasing doses of levothyroxine (400 μg oral L-thyroxine tablets, plus 100 μg triiodothyronine tablets daily). She stated that she had been experiencing persistent tiredness, general weakness, menorrhagia and severe anemia due to iron deficiency. She had also been suffering from abdominal pain and bloating, and was diagnosed with reflux esophagitis a year ago. Clinical evaluation confirmed severe hypothyroidism with periorbital edema, swelling of the face and lips, dry skin, muscle weakness and bradycardia. Laboratory tests revealed elevated TSH levels (72, 2 mIU/l) with remarkably low FT3 ($<$0, 1 ng/dl) and FT4 ($<$0.42 ng/dl). The patient did not tolerate iv thyroxine; thus she switched on 150 μg/d oral L-thyroxine in liquid form, which was increased progressively to 200 μg/d. Laboratory workup for a possible malabsorptive etiology was negative for coeliac disease or intrinsic anemia as tissue transglutaminase antibodies type IgG and IgA, anti-gliadin IgG antibodies, anti-endomysial antibodies and antiparietal cell antibodies were undetectable. Additionally, endoscopic control revealed the histological picture of mild esophagitis and chronic duodenitis with lymph follicle hyperplasia. However no mucosal changes typical for coeliac disease were identified. The patient was started on pantoprazole 40 mg once daily but 2 months later gastroenteric symptoms persisted and TSH level was still elevated to 25 mIU/l. NCGS was suspected and the patient was advised to follow a gluten-free diet. Subsequently she had normal thyroid function values, with remarkable improvement of her clinical symptoms. Currently, she is on treatment with 200 μg/d oral L-thyroxine in liquid form and remains euthyroid with normal hematological and biochemical laboratory tests.
Conclusion
Data on thyroxine malabsorption associated with NCGS are scarce. Our case highlights that unknown mechanisms associated with gluten sensitivity may be involved in the malabsorption of oral L-thyroxine in solid tablets format. An empirical switch to liquid formulation concomitantly with a free-gluten diet may resolve this therapy refractory issue.

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EP621

Lichenoid dermatitis secondary to a thiamazole-induced toxidermia: a case report

Fatma Ben Zaied[1], Elyes Kamoun[1], Nadia Khessairi[1], Ibtissem Oueslati[1], Fatma Chaker[1], Meriem Yazidi[1] & Melika Chihaoui[1]
[1]Hospital La Rabta Tunisia, endocrinology, Tunis, Tunisia

Introduction
Antithyroid drugs are the firstline medical treatment for hyperthyroidism in addition to symptomatic treatment (rest, beta-blockers). The most widely used in Tunisia is Thiamazole. They are generally well tolerated, but side effects have been reported. The most serious ones are agranulocytosis and liver damage. Allergic skin reactions (pruritus, urticaria) are the most common. We herein report a case of a lichenoid dermatitis bullous toxidermia induced by Thiamazole.
Case report
A 35-year-old female patient was referred to the endocrinology department of Rabta Hospital for the management of a hyperthyroidism. She presented with tachycardia, hand tremor and a weight loss, with TSH = 0.05 mUI/l and FT4 at 3 times the normal range, confirming the diagnosis of hyperthyroidism. Graves disease diagnosis was established based on the positivity of TSH receptor antibodies. Management of our patient relied on beta-blockers and Thiamazole 1 mg/day for 3 months, followed by a dose reduction to 1 mg/day with FT4 level of 21.1 pmol/l (n= 8.9 - 21.6) and TSH level of 0.11 mUI/l. After 5 months of treatment, the patient developed diffuse pruritic erythematous-papular lesions. Other drug intake was ruled out during the interview. A skin biopsy was inconclusive, showing histological features consistent with either bullous toxiderma or bullous pemphigoid. Direct immunofluorescence was performed, revealing a lichenoid dermatosis with IgM vasculitis, and a dermo-epidermal detachment supporting the diagnosis of bullous toxiderma. The decision was made to discontinue Thiamazole and initiate radioactive iodine therapy. The patient's condition improved with a reduction in lesions and disappearance of pruritus, confirming the association with Thiamazole.
Conclusion
This case illustrates the importance of meticulous clinico-biological monitoring after administration of Thiamazole, even several months after the start of treatment, as toxidermia is a potentially serious adverse drug reaction especially when associated with fever, polyadenopathy and multivisceral involvement (DRESS Syndrome), which can be life-threatening. In such rare cases, it is necessary to discontinue the ATS and switch to radical treatment.

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EP623

A case of graves with recurrence after mepolizumab treatment

Ekin Yiğit Köroğlu[1], Güler İnönü[1], Nagihan Beştepe[1], Hüsniye Başer[2], Ahmet Dirikoç[2], Oya Topaloğlu[2], Reyhan Ersoy[2] & Bekir Çakır[2]
[1]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara; [2]Ankara Yıldırım Beyazıt University Faculty Of Medicine, Endocrinology and Metabolism, Ankara

Introduction
Targeted therapies and monoclonal antibodies are known to trigger thyroid autoimmunity. No case of autoimmune thyroid disease with mepolizumab, an anti-IL-5 monoclonal antibody, is reported in the literature. In this case report, we present a case of Graves' disease that recurred after Mepolizumab treatment.
Case
A 74-year-old male patient was referred to the endocrinology outpatient clinic upon detection of hyperthyroidism on 11/2021. The patient, who had known aortic valve replacement, allergic asthma, and benign prostatic hyperplasia, was using warfarin 1×5 mg, atorvastatin 1×20 mg, inhaler salmeterol, 1×5 mg levocetirizine and 1×8 mg silodesin. In the patient's examinations, TSH $<$0.008 mU/l, free T4:3.94 ng/dl, free T3:11.99 ng/l, anti-tg:2.4 IU/ml, and TSH receptor antibody (TRAB):6.77 IU/l ($<$1.5 IU). /l) was seen. On electrocardiography, his pulse was 98 beats/minute, and his rhythm was normal sinus rhythm. While no nodule was detected in the patient's thyroid ultrasonography, bilateral parenchymal heterogeneous and sparse patchy hypoechoic areas were observed. Color flow doppler pattern was observed as 2 in thyroid doppler. The patient, who had no history of recent contrast exposure or amiodarone use, was evaluated as having Graves' disease, and methimazole 3x5 mg and propranolol 2x20 mg were started. No signs of ophthalmopathy were detected in the eye examination performed at the time of diagnosis. After one month, propranolol was discontinued, and methimazole dosage was adjusted, and periodic checks were scheduled. On 05/2023, in the 19th month of treatment, while receiving methimazole 1×2.5 mg treatment, TSH was measured:2.4 mU/l, free T4:1.04 ng/dl, free T3:3.62 ng/l, thyroid stimulating immunoglobulin was 0.52 IU/l (0.1-0.55 IU/l). The treatment was discontinued at this point. In the follow-ups performed one month and two months later, it was observed that the patient was euthyroid. On 07/2023, as the patient's complaints about allergic asthma increased, the pulmonologist started Mepolizumab to be administered 100 mg subcutaneously once a month. On 09/2023, after the patient received two doses of mepolizumab, TSH:0.02 mU/l, free T4:1.86, and free T3:4.68 ng/l were observed in the controls performed in our outpatient clinic, and the patient was started on methimazole 1×5 mg again. The patient, who was evaluated as having a relapse of Graves disease, was assessed in a multidisciplinary council, and radioactive iodine treatment was planned.
Conclusion
Thyroid autoimmunity may be triggered after Mepolizumab, an anti-IL-5 monoclonal antibody. Patients receiving this treatment should also be followed in this respect.

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EP624

Amiodarone-induced hypothyroidism: from myxedema coma to euthyroidism

Daniela Soares[1] & Lia Ferreira[1]
[1]Unidade Local de Saúde de Santo António, Endocrinology, Porto, Portugal

Introduction
Myxedema coma is the most serious manifestation of hypothyroidism and, although rare, it is associated with high mortality. Amiodarone therapy can lead to

thyroid dysfunction, either hyperthyroidism or hypothyroidism; however, in this context, myxedema coma is rare. Amiodarone discontinuance is not recommended in hypothyroidism's treatment, but may lead to its resolution if there is no pre-existing thyroid pathology. We present a clinical case of amiodarone-induced hypothyroidism meeting myxedema coma criteria, reverted to euthyroidism after drug suspension.
Clinical Case
Female, 76 years-old, history of valvular heart disease and atrial fibrillation (AF) treated with amiodarone since 2012. Admitted to the emergency department on 02/2021 presenting with lethargy, dyspnea, orthopnea and peripheral edema. Physical examination revealed hypothermia (34°C), bradycardia (45 bpm), hypotension (88/58 mmHg) and anasarca. Additionally, the presence of type 2 respiratory failure, acute kidney injury (creatinine 3.17 mg/dl), hyponatremia (127 mmol/l), hyperkalaemia (5.74 mmol/l) and AF with slow ventricular response was documented. Under the suspicion of myxedema coma (Popoveniuc score 90 points) thyroid function was assessed, which confirmed the presence of hypothyroidism: TSH 71 uUI/ml (0.30-3.94), T4L 0.42 ng/dl (0.95-1.57) and T3L 1.10 ng/ml (0.78-1.90), with negative thyroid autoimmunity. The patient was diagnosed with severe hypothyroidism meeting myxedema coma criteria, associated with neurological, cardiovascular, respiratory and renal dysfunctions. Levothyroxine therapy was iniciated (200 µg loading dose, followed by IV 100 µg/daily), associated with IV hydrocortisone 100 mg (until adrenal insufficiency was excluded), furosemide and non-invasive ventilation. The patient presented favorable evolution with resolution of all dysfunctions, being discharged under 150 µg levothyroxine and bisoprolol 1.25 mg instead of amiodarone, according to Cardiology recommendations. In outpatient consultations, thyroid ultrasound was performed revealing no changes, supporting amiodarone-induced hypothyroidism. Subsequent assessments documented progressively lower levothyroxine needs leading to its discontinuance on 04/2022, with the patient presenting clinically and analytically euthyroid since then.
Discussion
Amiodarone-induced hypothyroidism can occur in up to 30% of patients undergoing this therapy, which can lead to the development of myxedema coma in extreme situations, especially when its diagnosis is not carried out in a timely manner. Discontinuation of amiodarone in cases of hypothyroidism is not indicated; however, if performed, it may induce hypothyroidism's resolution.

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EP627

Graves' disease resistant to carbimazole, rai and lugol's solution

Hadjer Zeguir[1], Amel Mokrane[1], Safia Achir[1] & Leila Oucherif[1]
[1]CHU Isaad Hassani de Beni Messous hôpital, endocrinology, Alger, Algeria

Introduction
Graves' disease (GD) is the most common cause of primary hyperthyroidism. The standard approach to managing GD involves the use of antithyroid drugs (ATD), radioactive iodine (RAI), and surgery. Additional supportive treatments include beta-blockers (Bb), corticosteroids (CTC), Lugol's solution. In exceptional cases, some patients may exhibit resistance to these conventional methods, necessitating additional forms of management. We report a case of Graves' Disease where ATD, Lugol's solution and RAI failed to produce the expected response.
Case presentation
A 38 years old female, with personal history of gestational diabetes and familial autoimmunity field, referred with symptoms of clinical and biochemical thyrotoxicosis, which were not improving on Carbimazole 80 mg daily and propranolol 1 mg daily, despite of good compliance for 10 months. TRAb was strongly positive confirming diagnosis of Graves' Disease. There was no evidence of malabsorption and a negative serology for Coeliac disease. She was then given methylprednisolone with Lugol's Iodine for 13 days to make her euthyroid before thyroidectomy. However, she remained symptomatic with no improvement in her thyroid functions' tests. Two doses of RAI were then administered 6 months apart. Unfortunately, she did not achieve remission after the 2nd RAI therapy, neither ATD dose reduction.
Conclusion
This case underscores the various management options available for patients with resistant GD. In challenging cases, radioactive iodine and surgery emerge as definitive modes of treatment, with steroids and/or Lugol's solution playing a crucial role in preparing patients for those definitive interventions. The presented case involves a rare scenario where GD exhibited resistance to high-dose of ATD, Lugol's solution and RAI.

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EP678

Twenty years of experience in the use of medial thyroidectomy

Pamputis Sergey[1], Yuriy Aleksandrov[1] & Artem Dyakiv[1]
[1]Yaroslavl State Medicfl University, surgery, Yaroslavl, Russian Federation

Twenty years of experience (4, 573 operations) of performing medial access and thyroid mobilization according to the Nikolaev's method is presented. The operation is preceded by an ultrasound performed by a surgeon. Changes have been made to the primary technique: subcutaneous veins and short neck muscles do not intersect. The secretion of the thyroid gland begins from the trachea with traction of the thyroid gland to the lateral side. Ligation of large vessels begins at the lower pole, while the parathyroid glands are visualized and separated. With subsequent cranial traction of the thyroid gland, it is possible to move away from the esophagus (left) and recurrent nerves with a visual assessment. Vascular ligation at the upper pole is performed last after visualization of the upper parathyroid glands. Twenty years of experience in using this technique (medial thyroidectomy) suggests that it is effective and radical (for thyroid tumors). At the same time, it is possible to preserve thyroid tissue in the upper pole during a benign process. Complications (1.2%) arising during surgery are associated with an incorrect choice of access (including size), excessive traction of the thyroid lobe during its mobilization, and irrational use of electrocoagulation. The technique of the operation allows the use of neuromonitoring, however, the visualization of the nerve by the surgeon is performed at the second stage (cranial traction), in which the nerve should be maximally removed from the manipulation zone, which is achieved due to surgical technique. The technique of medial access has proven itself positively in giant goiter (up to 2000 grams) and large toxic goiter (more than 200 grams). The frequency of complications after surgery: dysphonia–2.1%, bleeding in the early postoperative period–0.3%, hypocalcemia–2.2%. In 93% of patients, dysphonia and hypocalcemia were transient (stopped within 6-12 months)

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EP680

Comparative assessment of hematological, autoimmune and hormonal status of patients with autoimmune thyroiditis

Farida Saidova[1], Jale Aslanova[1], Oruc Shahsuvarov[1] & Nizami Muradov[2]
[1]Scientific Center of Surgery after M.A. Topchubashov, endocrine surgery, Baku; [2]Scientific Center of Surgery after M.A. Topchubashov, anaesthetiology and reanimatology, Baku

The purpose of the study is a comparative assessment of the hematological, autoimmune and hormonal status of patients with autoimmune thyroiditis (AİT).
Material and methods
45 patients with AIT aged from 25 to 76 years were examined (average age 44.3±1.5). 39 of them women (86.7%), 6 men (13.3%). Two groups were determined: 1st group - patients with AIT with anemia - 36 people (average age 44.1±1.7); 2nd group - patients with AIT without anemia - 9 people (average age 45.4±3.8). Mild anemia was observed in 34 (94.4%), moderate anemia - in 2 (5.6%) patients. HGB, HCT, RBC, MCV, MCH, MCHC, serum Fe and ferritin were determined. Immune status was assessed by the level of CD3+, CD4+, CD8+, CD19+, CD4+/CD8+, CİC, Ef, ATPO, hormonal status – according to the level of TSH, T4 free.
Results
İn 1st group by the erythrocyte volume 23 patients (63.9%) were identified with microcytic anemia, 13 patients (36.1%) had normocytic anemia. According to the morphological indicator of anemia MCH-25 (63.9%) patients had a hypochromic type of anemia, 11 (30.5%) patients - normochromic. İn 1st group 23 (63.9%) patients had microcytic-hypochromic anemia, which characteristic for iron deficiency anemia, and 11 (30.5%) patients - normocytic-normochromic anemia, characteristic for anemia of chronic diseases. A comparative assessment of the level of HGB and indicators of iron metabolism in patients with AIT with anemia revealed a decrease in HGB by 21.4%, serum Fe by 33.7%, ferritin by 39.5% in comparison with the corresponding control indicators. To a greater extent, the depletion of iron stores (ferritin) is due to the fact that the development of anemia is preceded by 'latent iron deficiency, ' an indicator of which is ferritin.
Conclusion
AIT is characterized by a high incidence of anemia, often mild (94.4%), microcytic-hypochromic (63.9%), which characteristic for iron deficiency anemia. Severe hematological disorders identified in patients with AIT with anemia are accompanied by profound autoimmune changes and, in 25% of cases with subclinical hypothyroidism.

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EP682

The onset of thyroid eye disease in hyperthyroidism after covid-19 infection: a case report

Hager Khiari[1], Sabrine Mekni[1, 2], Sawsen Essayeh[1], Imen Rojbi[1], Bennacef Ibtissem[1], Youssef Lakhoua[1], Nadia Mchirgui[1] & Karima Khiari[1]
[1]Charles Nicolle Hospital, Endocrinology, Tunis, Tunisia; [2]Charles Nicolle Hospital, Endocrinology

Introduction
Thyroid eye disease (TED) is an autoimmune inflammatory disorder affecting the orbital tissues. It occurs with thyroid dysfunction notably Graves' disease. TED exhibits different severity patterns and has a lot of risk factors. We, herein, report a rare case of a severe TED developing after COVID-19 infection in a patient initially treated for hyperthyroidism without ocular manifestations.
Observation
A 48-year-old female with a history of hyperthyroidism and toxic nodule treated by radioiodine therapy in 2017 was addressed to the endocrinology department for TED symptoms with inflammatory features. In 2017, at the initial diagnosis of thyrotoxicosis, the patient had a toxic thyroid nodule diagnosed by thyroid ultrasound and scintigraphy. Thyroid peroxidase antibodies (TPOAb) and thyroid stimulating hormone (TSH) receptor antibodies (TRAb) were both negatives. She was treated with Benzyl thiouracil then radioactive iodine (RAI) therapy. After developing hypothyroidism post-RAI, she was on 100 mg of levothyroxine daily. In 2021, she was diagnosed with COVID-19 infection and ten days later, she developed eye redness, eye fullness and diplopia. On physical examination, she had active TED with clinical activity score (CAS) of 4/7 points, asymmetric exophthalmia and a restrictive ocular dysmotility. Ocular computed tomography (CT) confirmed the diagnosis of a severe Graves' orbitopathy (GO). Laboratory tests showed elevated TRAb 2.5 mIU/l (<2) and TSH 8.17 mIU/l (0.4-4). The patient was treated with 1 mg of levothyroxine daily and received intravenous methylprednisolone (1 g/day for 3 days) then oral prednisone during three months. Though inflammatory symptoms improved, diplopia worsened and heavily impacted the patient's quality of life. A decompressive eye surgery then a strabismus surgery were ultimately performed. No complications occurred after surgery and the symptoms improved significantly.
Conclusion
In conclusion, we reported a very uncommon case of a TED presenting after COVID-19 infection. It was also a severe case of a restrictive dysmotility caused by Graves's orbitopathy that was treated by surgery. It reinforces the eventual link between COVID-19 and autoimmunity.

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EP684

Propylthiouracil-induced ANCA associated vasculitis: a diagnostic and therapeutic challenge

May Myat Mon[1], Win Lei Yin[1] & Thinzar Min[1, 2]
[1]Swansea Bay University Health Board, Diabetes and Endocrinology, Skewen, United Kingdom; [2]Swansea University, Sketty, United Kingdom

Introduction
Graves' disease, a common cause of hyperthyroidism, occasionally poses therapeutic challenges. This case report highlights complexities of Graves' disease management, particularly an unusual complication: Propylthiouracil (PTU) - induced ANCA vasculitis.
Case report
A 51-year-old lady with Graves' disease diagnosed in 2008, achieved remission with 18 month course of Carbimazole. She experienced a relapse in February 2021 and Carbimazole proved to be ineffective leading to a switch to PTU in May 2022. Twelve months after PTU, she developed recurrent joint pain and intermittent non-blanching vasculitic rash on knees and ankles associated with a rapid decline in renal function and positive ANCA (P+C ANCA), anti-MPO and anti-PR3 antibodies. She had no other features of autoimmune connective tissue disease. Renal biopsy confirmed absence of classical renal vasculitis. Due to her spectrum of presentations, various speciality were involved. A diagnosis of PTU-induced vasculitis was made. Following the replacement of PTU with Carbimazole and immunosuppressant therapy (prednisolone and methotrexate), joint pain and rashes resolved, renal function improved dramatically, and thyroid function improved. Since the complete withdrawal of immunosuppression in October 2023, symptoms of thyrotoxicosis returned with TSH <0.01 mU/l and FT4 >100 pmol/l. Carbimazole dose was up-titrated along with glucocorticoid therapy. She is due to have follow-up in 4 weeks. Total thyroidectomy is considered as a definite therapy once her thyroid function improves.
Discussion
PTU-induced vasculitis is rare and requires a high index of clinical suspicion. Prompt discontinuation of PTU would be sufficient for most case but severe cases might require immunosuppressant therapy.

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EP685

Early approach in a patient with an incipient thyrotoxic crisis

Ignacio Jiménez Hernando[1], Mónica Gómez-Gordo Hernanz[1] & Laura González Fernández[1]
[1]Gregorio Marañón General University Hospital, Endocrinology and Nutrition, Madrid, Spain

Introduction
Thyroid storm or thyrotoxic crisis is a severe manifestation of thyrotoxicosis. Mortality rate is 20-30%. The most common trigger is hyperthyroidism due to Graves-Basedow Disease. There are two validated scales for diagnosis: the Burch Wartofsky scale (BWPS) and the Japanese Thyroid Association scale (JTA). These scales are based on cardiovascular, neurological, digestive, and thermoregulatory clinical manifestations. If clinical suspicion is high, treatment should not be delayed in order to identify and treat precipitating factors, achieve euthyroid state, and address multiorgan damage.
Presentation of the case
A 37-year-old woman with Graves-Basedow Disease without treatment presented to the Emergency Department with symptoms of dyspnea, edema, fever, cough, vomiting, diarrhea, nervousness, and palpitations. On arrival, she had a fever of 38.5ºC, diffuse grade III goiter with a murmur and thrill, and fine distal tremor. Laboratory tests showed hepatic profile alteration and elevated levels of Nt-proBNP and acute phase reactants. Electrocardiogram revealed sinus tachycardia at 137 bpm; bilateral pleural effusion and left bronchopneumonia were observed on chest X-ray. Due to an elevated D-dimer, thrombosis was ruled out with Doppler ultrasound and CT angiography. Echocardiogram showed no structural heart disease. Microbiological isolates were negative. Thyroid profile tests showed suppressed TSH, free T4 at 3.2 ng/dl, and free T3 at 4.78 pg/ml. Suspecting an incipient thyrotoxic crisis, high-dose antithyroid drugs, beta-blockers, steroids, diuretics, and antibiotics were initiated. The ICU was consulted and decided not to admit the patient due to stability and prompt initiation of treatment. The patient was diagnosed with left basal pneumonia that triggered a thyrotoxic crisis with multiorgan dysfunction (BWPS 75). At the first follow-up visit two weeks after discharge, she showed favorable progress, leading to consensus on I131 treatment.
Conclusions
Thyrotoxic crisis is a potentially life-threatening condition that can cause multiorgan dysfunction. Therefore, clinical suspicion and early initiation of treatment are important.

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EP686

Clinical aspects of the schmidt's syndrome: a retrospective monocentric study

Oumayma Zarrouk[1], Taieb Ach[1], Rihab Khochtali[1], Ghada Saad[1], Asma Ben Abddelkrim[1], Molka Chadli Chaieb[1] & Koussay Ach[1]
[1]University Hospital of Farhat Hached, Endocrinology Departement, Sousse, Tunisia

Introduction
Schmidt's syndrome also known as autoimmune polyglandular syndrome type 2 (APS type 2) is a rare endocrine disorder defined by the combined occurrence of Addison disease with autoimmune thyroid disease. The rarity of the condition and the atypical presentation of adrenal insufficiency and hypothyroidism often lead to misdiagnosis with life-threatening consequences for the patient. In this study we report an exhaustive monocentric analysis of 22 patients diagnosed with a Schmidt's Syndrome.
Patients and Methods
We carried out a retrospective study of all the patients diagnosed of a Schmidt syndrome or APS type 2 in the Department of Endocrinology and Diabetology of University Hospital Farhat Hached of Sousse, over a period from 1999 to 2013. Adrenal insufficiency was diagnosed with a basal cortisol level <40 ng/ml or peak <180 ng/ml after Synacthen. Autoimmune Hypothyroidism was diagnosed with a T4<7 pg/ml and TSH>10 mUI/l associated with the positivity of anti-Peroxydase antibodies. We analyzed clinical and biological aspects of these patients with SPSS ver. 23.0 software.

Results
We reported 22 cases, with a mean age of 31.77 ± 11.26 yo, with 36.3% between 20 and 39 yo ($P = 0.02$) and a predominance for female sex with a sex ratio = 0.22 ($P < 10^{-3}$). The mean age of discovery of Addison's disease was 32.5 ± 9.2 with extremes ranging from 12 to 58 years. According to the age of discovery compared to hypothyroidism, Addison disease was diagnosed significantly before the diagnosis of Hashimoto's disease in 59% ($P = 0.03$), concomitant in 27.2% and posterior in 13.6%. Clinical symptoms made of melanodermia and hypoglycaemia suggested the diagnosis in 47% of all patients. An acute adrenal insufficiency was triggered by the hormonal thyroxin substitution in one case. Other autoimmune diseases were found in 27.2%, as a celiac disease (8%), type 1 diabetes (8%), Biermer anemia (7%) and autoimmune ovaritis in 4.2%.
Conclusion
Schmidt's Syndrome is more likely to be associated with the female sex and young age. In our study, Hashimoto's hypothyroidism was the first autoimmune disease discovered. The presence of at least one component of the APS type 2 must lead to the autoimmune screening of the other diseases. This screening could avoid the triggering of an adrenal insufficiency in thyroid hormonal substitution.
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EP697

Lack of thyroid-stimulating hormone receptor expression on natural killer t cells: implications for the immune-endocrine interaction
Magdalena Stasiak[1], Emilia Adamska[1], Przemysław Śliwka[1], Arkadiusz Zygmunt[1, 2] & Andrzej Lewinski[1, 2]
[1]Polish Mother's Memorial Hospital - Research Institute, Department of Endocrinology and Metabolic Diseases, Lodz, Poland; [2]Medical University of Lodz, Department of Endocrinology and Metabolic Diseases, Lodz, Poland

Introduction
The functional interaction between the immune and endocrine systems remains intricate, and the relationships among various cell types and humoral mediators are not fully elucidated. Natural killer T (NKT) cells, being a heterogeneous T cell subpopulation, express markers specific for both natural killer (NK) cells (NK1.1, CD56) and T cells (TCR - T cell receptor). Thyroid-stimulating hormone (TSH) influences the immune system, and TSH receptors (TSHR) have been identified in various immune cell types. Although the impact of TSH levels on the quantity of NKT cells in peripheral blood has been postulated, no reported studies have explored the expression of TSHR on NKT cells. This study aimed to assess the expression of TSHR on NKT cells, with analyses conducted on NKT cells isolated from the peripheral blood of individuals with and without autoimmune thyroid disease (AITD).
Methods
NKT cells were isolated from peripheral blood mononuclear cells (PBMC) using a magnetic beads cell separator. Fluorescence-activated cell sorting (FACS) was employed to analyze TSHR expression on the surface of NKT cells. TSHR gene expression was assessed using the RT-PCR method on total RNA isolated from both PBMC and NKT cells. Blood samples were collected from 81 individuals, including 16 AITD patients and 65 persons without AITD.
Results
Neither FACS analysis nor RT-PCR gene assays revealed the expression of TSHR on the surface of NKT cells. These findings were consistent in both AITD and non-AITD patient groups.
Conclusion
Our results suggest the absence of direct TSH-mediated effects on NKT cells via TSHR. Further investigations are warranted to elucidate potential indirect mechanisms underlying the influence of TSH on NKT cells.
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EP700

Thyrogastric syndrome: a case report
Jaddi Oussama[1], Manar Bari[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Mohammed VI university hospital of Marrakesh, Department of Endocrinology, Diabetes, Metabolic diseases and Nutrition, Marrakesh, Morocco

Introduction
Thyroid-gastric autoimmune syndrome (TGS), described in the 1960s, is the autoimmune association of thyroid disease (Hashimoto's or Graves' disease) and gastric mucosal disease (Biermer's disease) in the same patient. Although this association is part of the autoimmune polyendocrinopathies, its prevalence is largely underestimated in the literature. We report the case of a 56-year-old female patient with TGS.
Observation
Patient aged 56; followed for mitral stenosis on VKA, followed for Biermer's disease discovered during an etiological workup of macrocytic anemia with positive anti-parietal cell and anti-FI Ac levels, the patient was put on Hydroxocobalamin. The patient consulted for asthenia and recent weight gain considered moderate, a TSH us requested returned at 22.4 mUI/l, thyroid ultrasound objective an aspect of thyroiditis, anti TPO Ac returned positive confirming the diagnosis of Hashimoto's thyroiditis. The patient was put on a progressive dose of Levothyroxine in view of the atrial fibrillation she presented on ECG.
Discussion
Biermer disease (BD) is an autoimmune atrophic gastritis causing vitamin B12 deficiency, frequently associated with other autoimmune diseases, notably endocrinopathies. Autoimmune thyroid disease generally has a favorable course, but when associated with autoimmune gastritis, there is a risk of developing gastric tumors. Digestive malabsorption also affects medications (levothyroxine), making it difficult to substitute for hypothyroidism. The prevalence of BD is around 10-15% in prospective series of autoimmune thyroiditis. The search for this association is important because of its frequency and its therapeutic and prognostic implications.
Conclusion
Systematic thyroid assessment during BD is necessary to detect and treat these thyroid disorders, which are sometimes in the sub-clinical stage.
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EP762

Treatment of pediatric grave's disease: a single-center experience
Telma Moreno[1, 2], Joana Filipe Ribeiro[3], Sofia Ferreira[2, 4], Carla Costa[2, 4], Rita Santos Silva[2, 4] & Cíntia Castro-Correia[2, 4]
[1]Centro Hospitalar Universitário de São João, Endocrinology, Porto, Portugal; [2]Universidade do Porto, Faculty of Medicine, Porto, Portugal; [3]Hospital Sousa Martins, Pediatrics, Guarda, Portugal; [4]Centro Hospitalar Universitário de São João, Pediatrics, Porto, Portugal

Introduction
Grave's disease is a rare disease in children. Treatment options are the same as in adults but remission rate with antithyroid drugs (ATD) appears to be lower in children and more prolonged courses of ATD are recommended. We aimed to evaluate the outcome of ATD treatment and to identify factors associated with remission.
Methods
Retrospective study of 36 pediatric patients diagnosed with Grave's disease at the Pediatric Department of a tertiary hospital in Portugal between 2002 and 2023. Remission was defined as euthyroidism for more than 12 months after stopping ATD treatment. Patients who achieved remission were compared to those treated for more than 2 years with ATD without remission. Statistic results are expressed as median (interquartile range) or frequency (percentage).
Results
Twenty-eight patients (77.8%) were female and median age at diagnosis was 14 (5.50) years. Twenty-four patients were sypmtomatic at diagnosis, mostly presenting with tachycardia (35.3%) and unintentional weight loss (26.5%). The median thyroid-stimulating hormone (TSH), free T4 (fT4), free T3 (fT3) and TSH-receptor antibodies (TRAbs) at diagnosis were 0.002 (0.01) µUI/ml, 2.49 (1.57) ng/dl, 8.76 (11.62) ng/dl and 14.35 (36.90) U/l, respectively. All patients started methimazole with a median initial dose of 10 (5) mg/day and a median treatment duration of 24 (28.50) months. Mild side effects were reported for only one patient. During follow-up, 9 patients achieved remission, 2 patients experienced relapse after discontinuation of ATD and 13 patients were treated for more than 2 years with ATD without remission. The ATD course duration for both patients who had a relapse was less than 2 years. In patients who achieved remission, the fT4 at diagnosis [1.80 (0.72) vs 2.91 (1.66) ng/dl, $P = 0.020$], the time for fT4 normalization [24.5 (13.5) vs 49.0 (107.5) days, $P = 0.010$], the time for TSH normalization [4.5 (6.8) vs 12.9 (11.0) months, $P = 0.010$] and TRAbs levels at diagnosis [3.30 (12.65) vs 40.00 (25.35) U/l, $P = 0.002$] were significantly lower than the non-remission group.
Conclusion
The overall remission rate after ATD treatment in our cohort was 25%, which is in accordance with previously reported rates. Lower fT4 and TRAbs levels at diagnosis and lower time for fT4 and TSH normalization were associated with higher chances of remission.
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EP774

Thyroid carcinoma in a 7 year old child: a case report

Redhouane Longo[1], Mourad Benrabah[2], Abdelkader Yahi[3], Benabdelatif Katia[3] & Ould Kablia Samia[3]
[1]Endocrinology department, Regional University Military Hospital of Oran, Algeria; [2]Nuclear medicine department, Regional University Military Hospital of Oran, Algeria; [3]Endocrinology department, Central Military Hospital, Algiers, Algeria

Introduction
Thyroid nodules are much less common in children and adolescents than in adults. However, thyroid nodules in children are more likely to be malignant. Most thyroid cancers in children are differentiated thyroid cancers, which arise from the follicular cells of the thyroid gland. Although extremely rare (1.5% of all tumours before the age of 15), there are two types of differentiated thyroid cancer in children: papillary and follicular. Around 90% of paediatric thyroid cancers are papillary thyroid cancers. Despite the higher tendency to spread in children compared with adults, differentiated thyroid cancer has an excellent outcome, with a survival rate of over 95%.
Observation
Child aged 07, with no particular history, consults following the appearance of a basal cervical mass. It is a hard, painless mass, roughly oval in shape, approximately 03 cm long, mobile axis with swallowing movements, non-compressive, without inflammatory signs, and in clinical euthyroidism. Cervical ultrasound reveals a solid isthemic nodular formation, with presence of micro calcifications measuring 23x1 mm, classified EU-TIRADS V, associated with multiple bilateral cervical lymphadenopathy. TSH and thyrocalcitonin levels returned to normal. Patient underwent a total thyroidectomy with lymph node dissection and was placed on levothyroxine 100 $\mu g/m^2$/day. Anatomopathological study concluded that there was a 4 cm non-encapsulated intrathyroidal papillary carcinoma with 4 recurrent lymph node metastases, classified pT2N1bMx.
Discussion-Conclusion
Accounting for around 90% of paediatric thyroid carcinomas, papillary thyroid cancer is the most common type of thyroid cancer in children and adolescents. The second most common type of thyroid cancer is follicular thyroid cancer, and both types can usually be treated similarly.

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EP787

Injury to the mandibular branch of the facial nerve after thyroid surgery. a not so uncommon case

María Isabel Gutiérrez[1], Angel Luis Sanchez Alvarez[1], Raquel Sanchez Gutierrez[2] & Jorge Loro Perez[1]
[1]Complejo Hospitalario Universitario Insular Materno Infantil, Cirugia General Y Aparato Digestivo, Las Palmas De Gran Canaria, Spain; [2]Complejo Hospitalario Universitario Insular Materno Infantil, Logopedia, Las Palmas De Gran Canaria, Spain

The most feared nerve injury when treating thyroid cancer is that of the recurrent laryngeal nerve. However, there are other nerve complications, underestimated and underpublished, such as the lesion of the mandibular branch of the facial nerve, which requires a multiprofessional approach to recover functionality and esthetics, both affected.
Clinical Case
A 44 year old woman, under study for anemia, underwent a cervical ultrasound that showed in the left thyroid lobe a nodule with lobulated edges and poorly defined, iso-hypoechoic, with micro and macrocalcifications inside and peripheral vascularization of 21 mm and an adjacent adenopathy to the ipsilateral submandibular gland (level II), with microcalcifications and minimal vascularization of 16 mm. The FNA of the thyroid nodule was category VI of the Bethesda Classification and the thyroglobulin in aspirate of the adenopathy was 34.65 ng/ml. With these findings, total thyroidectomy + bilateral central lymphadenectomy and functional left lateral cervical lymphadenectomy of compartments II, III, IV and V were performed. Intraoperative neuromonitoring of both vagus and recurrent laryngeal nerves showed a superimposable signal pre and post-surgery and intraoperative PTH determination showed a decrease of 77.87% with a final PTH of 15.2 pg/ml, so that, according to our protocol, calcium and vitamin D supplementation was not required. In the post-anesthetic recovery room, facial asymmetry was observed with deviation and descent of the left labial commissure, which persisted 24 hours later, when she was discharged. The patient was referred to the speech therapist for assessment and myofunctional rehabilitative treatment.
Discussion
Injury to the mandibular branch of the facial nerve in lateral lymphadenectomy occurs when compartment II of the neck is approached. The lesion can be produced by different mechanisms: mechanical (the most frequent), thermal or chemical. To try to avoid injuring this nerve branch, it is recommended to be careful in the traction and compression with the retractors when approaching the lympho-fatty tissue of compartment II. Although it is a less described complication than spinal nerve injury, it significantly affects esthetics and oral functionality and interferes with the patients' quality of life. For this reason, in the patient's informed consent process for a lateral lymphadenectomy, it should be mentioned as a possible complication that, although it is generally transitory, can affect the patient's social and working life.

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EP789

Management of poorly differentiated follicular-derived thyroid carcinoma in an adolescent: a case report

Eva Rimkute[1], Aiste Kondratiene[1, 2] & Ruta Navardauskaite[1, 3, 4]
[1]Department of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania; [3]Coordinating Center for Rare and Undiagnosed Diseases Lithuanian University of Health Sciences Hospital Kauno Klinikos, Kaunas, Lithuania; [4]Department of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

Introduction
Poorly differentiated carcinoma (PDTC) is an aggressive and rare form of thyroid carcinoma that originates from follicular cells and accounts for only 1-3 percent of all thyroid carcinomas diagnosed[1]. Most of the limited instances of PDTCs have been observed in older individuals. Instances in the pediatric population are exceedingly rare[2].
Case report
This report refers 17-year-old female, who presented moderate hirsutism (scoring 8 points on the Ferriman-Gallwey scale), normal puberty development (Tanner stage B3P4), and regular periods. Upon physical examination, the patient exhibited an enlarged thyroid (IB degree), Laboratory examination showed normal levels of sex hormones, elevated antibodies against thyroid peroxidase and thyroglobulin, and thyroid-stimulating hormone concentration. Thyroid ultrasound revealed a right thyroid hypoechoic heterogeneous structure nodule, with microcalcifications and groups of them, measuring up to $2.7\times2.8\times4.1$ cm in size. A fine-needle aspiration biopsy and cytological examination of the mass found undetermined significance atypia (Bethesda category III). Due to the abundant presence of lymphocytes, lymphocytic thyroiditis was suspected. In consideration of a potential tumor process, it was decided to carry out a complete thyroidectomy. Histopathology determined high-grade PDTC of the right thyroid lobe. The patient underwent radioactive iodine therapy following the completion of thyroidectomy. The treatment was well tolerated, with no observed side effects noted. Following the completion of the treatment, a PET/CT scan with fluorodeoxyglucose (FDG) was performed, during which no focal pathological FDG accumulation was detected. There were not detected pathological variants in PTEN, PRKAR1A, APC, TP53, RET, DICER1 genes.
Conclusions
This case emphasizes the challenges in diagnosing and treating thyroid disorders in young patients. The successful management PDTC through thyroidectomy and radioactive iodine therapy is notable. The absence of FDG accumulation post-treatment indicates a positive therapeutic response. This underscores the significance of comprehensive assessment and collaborative care for rare thyroid conditions in adolescents.
Keywords: adolescent, poorly differentiated thyroid carcinoma, thyroidectomy, radioactive Iodine therapy
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EP794

Thyroid cancer incidence trends in lithuania 2018 – 2022. single-centre study

Kamilė Antanavičiūtė[1, 2], Raimonda Klimaitė[1, 2], Gabrielė Riškutė[2], Laura Arbatauskaitė[2] & Viktorija Pareikaitė[2]
[1]Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Endocrinology Department, Kaunas, Lithuania; [2]Lithuanian University of Health Sciences, Kaunas, Lithuania

Introduction
Epidemiological studies show that thyroid nodules (TN) are found on ultrasonography in 19-67% of patients, with a predominance in women, the elderly, and populations living in areas with insufficient iodine intake. Approximately 5-15% of nodules are malignant, of which 95% are well-differentiated thyroid carcinomas.
Material and methods
The medical history of 377 patients treated for thyroid carcinomas (TC) in the Hospital of Lithuanian University of Health Sciences Kaunas Clinics Endocrinology and Surgery departments from 2018 to 2022 were analyzed. The patient's medical history, fine needle aspiration (FNA) of the TN cytology results and histological findings of operative material were interpreted. Calculations were performed using IBM SPSS Statistics 28.0 package.
Results
The study population consisted of 79% women and 21% men with an average age of 52.5±16.1 years. TN of 91% of patients were evaluated using EU-TIRADS scale. For 93% of patients FNA was performed before a thyroid surgery. EU-TIRADS median of TN, of which FNA were performed, was 5 (4-5). On average, FNA was performed 1, 16 times per patient. Median disease duration, counting from TN detection to surgery, was 8, 5 months. Cytological and histological concordance was observed in 93, 3% of cases, with a concerning 50% error rate in diagnosing anaplastic TC. The majority of patients (89, 9%) were diagnosed with papillary carcinoma, and the predominantly observed stage was pT1a (39, 4%). The total prevalence of TC is shown in Table 1. By ultrasound cancer metastases were identified in 17.1% of cases, although after surgical material examination metastases were observed in 29, 2% of cases with 90% being locoregional and 10% distant.

Table 1: The prevalence of TC.

Type of TC	Percent (%)	Predominant stage of TC	Percent (%)
Papillary carcinoma	89, 9	pT1a	39, 4
Anaplastic carcinoma	3, 7	pT3b	50
Follicular carcinoma	3, 2	pT3a	70
Medullary carcinoma	2, 9	pT1b	54, 5
Thyroid leiomyosarcoma	0, 3	pT3RxG3	100

Conclusions
According to our study, FNA shows limitations in identifying anaplastic TC. Moreover, almost 30% of patients were diagnosed with metastases. It is essential to note that patients with TN must be strictly monitored, especially those who have suspicious TN.
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EP795

Medullary thyroid carcinoma – a 22-year case series from a tertiary hospital center

Tânia Carvalho[1], Mafalda Martins Ferreira[1], Joana Madeira[2], Sofia Lopes[1], Joana Saraiva[1], Patrícia Oliveira[1], Miguel Melo[1], Cristina Ribeiro[1] & Isabel Paiva[1]
[1]Centro Hospitalar e Universitário de Coimbra, Serviço de Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal; [2]Centro Hospitalar e Universitário de Coimbra, Serviço de Anatomia Patológica, Coimbra

Introduction
Medullary thyroid carcinoma (MTC) arises from thyroid parafollicular C cells and accounts for <5% of thyroid cancers. Nearly 25% occur in the context of multiple endocrine neoplasia type 2 syndrome (MEN2) or familial isolated MTC.
Objectives
Evaluation of clinical characteristics and evolution of patients with MTC.
Methods
Retrospective analysis of clinical records of patients with MTC diagnosed from 2001 to 2023.
Results
42 cases of MTC were identified. 27 (64%) were female. Mean age at diagnosis was 46.2±2.8 years (10-78). 35.7% of patients presented symptoms, mostly cervical swelling; two had diarrhea. 8 patients (19%) had a germline mutation in the RET proto-oncogene. 40 underwent total thyroidectomy, 6 of them in two surgical stages; 2 performed only lobectomy. 33.3% ($n=14$) had lymph node dissection - 5 of the central compartment, 9 central+ipsi/bi-lateral. 5 MEN2A patients performed prophylactic thyroidectomy. The median tumor size was 1 mm, 19% ($n=8$) being microcarcinomas. The most frequent location was the right lobe (42.9%); 33.3% ($n=14$) were multifocal. The remaining thyroid parenchyma exhibited nodular hyperplasia in 23.8% ($n=10$), chronic lymphocytic infiltration in 28.6% ($n=12$) and synchronous papillary microcarcinomas in 14.3% ($n=6$). Resection was R0 in most patients (90.5%). Nodal involvement was present in 28.6% (8 N1b and 4 N1a), and distant metastases in 7.1% ($n=3$). AJCC classification was I, II, III, IVA and IVC in 38.1% ($n=16$), 28.6% ($n=12$), 11.9% ($n=5$), 11.9% ($n=5$) and 7.1%($n=3$), respectively. Response to surgery was excellent in 71.4% ($n=30$), biochemical incomplete in 16.7% ($n=7$) and persistent structural disease in 11.9% ($n=5$). Stage I and II had higher probability of excellent response to surgery (93.8% and 100%, respectively) than stage III (40%) and IV (0%). All but one patient with nodal involvement ($n=12$) showed persistent disease. Among patients exhibiting excellent response, 5 (16.6%) experienced recurrence - 3 were only biochemical, and 2 MEN2A patients developed structural disease. While 59.5% ($n=25$) were cured, 35.7% ($n=15$) still have evidence of biochemical or structural disease. Seven patients (16.7%) required adjuvant therapies, 3 of whom are under tyrosine kinase inhibitors (selpercatinib or vandetanib). Deaths due to MTC occurred in 4.8% (2 patients).
Conclusions
Our center's outcomes showed a substantial rate of excellent response, especially in stages I-II, highlighting the importance of early detection and intervention. While the cure relies essentially on the surgical response, surveillance is necessary for potential recurrence, especially in MEN2 patients. Long-term clinical studies are vital to enhance our understanding of this rare malignancy.

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EP803

Diagnostic workup of breast cancer metastases in the thyroid gland

Aistė Kondrotienė[1], Roberta Buginyte[2] & Lina Pužauskienė[3]
[1]Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Lithuanian University of Health Sciences, Medical Academy, Kaunas, Lithuania; [3]The Hospital of Lithuanian University of Health Sciences Kauno Klinikos, Kaunas, Lithuania

Introduction
Metastatic thyroid tumors are infrequent, accounting for just 3% of all thyroid cancers. Interestingly, 7.8% of these metastases stem from breast cancer. Previous malignancies increase metastatic suspicions when thyroid nodules, possibly accompanied by cervical lymphadenopathy, are discovered. As our case emphasizes, diagnostics can be complex, necessitating specialized treatment and monitoring plans.
Case Presentation
A 55-year-old female presented with right supraclavicular masses, neck discomfort. She was diagnosed with left breast carcinoma in 2008, with subsequent successful treatments including a right mastectomy, chemotherapy, and radiation. Clinical Examination: A 1 cm nodule was found in the right breast with skin adhesion. Clustered lymph nodes appeared in the left supraclavicular region. Diagnostic Assessments: Ultrasound: 3.8×3 cm tumor in the right breast's outer quadrant and a hypoechoic mass in the liver. The left supraclavicular area had pathological lymph nodes. Chest X-ray: Identified a 4.7×5 cm mass in the right paratracheal region. Lab. Results: CEA 19, 1->74 pg/l (0-5, 8); Ca125 8, 8 kU/l (0-35); Ca19-9 5, 5 kU/l (0-37); Ca27.29 129, 8 (0-31). TSH 1.1 mU/l (0, 4-3, 6), FT4 11, 1 pmol/l (9-21, 07), FT3 5, 1 pmol/l (3, 34-5, 14), AntiTPO 3, 0 kU/l (0-3, 2), AntiTg 6, 1 kU/l (0-13, 6), calcitonin 1, 24 (0, 12-2, 8). Histopathology: infiltrative ductal breast carcinoma, G2 (ER+), (PR+), (HER2-). Computed Tomography (CT): Highlighted tumor presence in the right breast, pathological lymph nodes, and metastases in renal, hepatic regions, and bones. PET CT: Revealed low metabolic activity neoplastic lesions in the right breast and high metabolic activity lymph nodes suggestive of lymphoma. Thyroid Ultrasound: Several nodules, largest being 0.9×0.7 cm (TI-RADS 4), and a heterogeneous 1.2×0.6 cm zone with microcalcinate-like inclusions (TI-RADS 5) are in the right lobe. The left lobe has zones up to 2.6×1.3 cm with similar inclusions (TI-RADS 5). Pathological-enlarged lymph nodes are present on both neck sides, the biggest being 2.3×1.6 cm on the left. Fine needle aspiration

biopsy revealed breast ductal carcinoma metastases in the thyroid gland. Abdominal l/m biopsy result L: infiltrative ductal carcinoma G2 spread, HER2(-), ER+, PR-. Therapeutic Recommendations: A multidisciplinary team recommended chemotherapy with ribociclib and fulvestrant. Given the reducing size of thyroid metastases and no signs of tracheal or esophageal compression, thyroidectomy was deemed unnecessary.
Conclusion
Metastases in the thyroid often indicate a poor prognosis, negating surgical intervention for some. This case underscores the importance of distinguishing primary thyroid conditions from metastatic incidences due to differing therapeutic approaches and their subsequent impact on prognosis.

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EP806

Characteristics and incidence of papillary thyroid carcinoma among georgian reproductive-aged women

Nestan Bostoganashvili[1], Rusudan Kvanchakhadze[2], Shorena Tukvadze[2], Natia Chachava[3] & Badri Gvadzabia[3]
[1]University of Georgia, Tbilisi; [2]Georgian - American University; [3]National Institute of Endocrinology

Introduction
The incidence of thyroid cancer in women, especially in reproductive age seems to be significantly increasing in Georgia and generally, worldwide. Thyroid cancer is the third most common cancer after breast cancer and uterine cervical cancer, among women aged 25 to 45 years. Multiple epidemiological studies have shown, that the prevalence of thyroid cancer is higher in women in the reproductive age (18-49), which could be explained by reproductive and menstrual factors. Aim of presented study was to determine characteristics and incidence of papillary thyroid cancer (PTC) in Georgian reproductive aged females
Methods
Women aged 18–49 years ($n=3643$) diagnosed with PTC in 2015–2022 were identified from Georgian national Registry Database. For each age group (14-25, 26–35, 36-49) results were stratified by cancer stage, location, ethnicity. Age-adjusted average annual percentage changes in incidence have been estimated based on 5-year survival.
Results
In the 18-49 age group, from 2015 to 2019 incidence had been increasing, whereas 2020-2022 it had been mildly decreasing. In the particular period (2015-2022) 65.5 % of total cases was stage 1, 15.2 % - stage 2, 11.3 % stage 3, 7% stage 4. (other 2 % unidentified). 97.5 % of all cases was malignant, other 2 % was described as precancerous invasion. Incidence was lowest in 14-25, and highest in 36-49 age group. Highest incidence occurred in Tbilisi, the capital from 2015-2019 and in 2020-2022, which could be explained with high screening facilities. High incidence rates was seen in high-mountainous regions (like Svaneti), Regarding ethnicity, in 2015-2019 incidence of ethnical minorities (Russians, Azers, armenians etc) was almost 4 times higher compared to ethnically Georgians, whereas later, from 2019, incidence in ethnically Georgian women has been almost 3.5 fold higher. A-5 year survival was equally high- 95% and 94 %, respectively in stage 1 and stage 2, in both 2015-2019 and 2020-2022 years, stage 3 was insignificantly low 93% and 94.5% respectively, in 2015-2019 and 2022 years.
Discussion
Due to very high survival and other clinical characteristics, PTC seems to be not quite 'malignant' disease, however reasons of high incidence, especially in reproductive aged females needs to be investigated properly and possible preventive methods should be well determined. In this particular study, Incidence rate changes from 2015-2019 to 2020-2022 and differences in regions could also be explained with lack/ inability of screening on time because of social isolation in Covid19 pandemic period.

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EP809

Infiltration of the thyroid in advanced laryngeal cancers: a retrospective analysis

Heyfa Belhadj-Miled[1], Houas Jihene[1], Monia Ghammam[1], Maroua Ben Njima[1], Malika El Omri[1], Abir Meherzi[1], Mouna Bellakhdhar[1], El Ghali Wassim[2], Yosra Hasni El Abed[3], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT Department, Sousse, Tunisia; [2]Department of Anaesthesia, Sousse, Tunisia; [3]Farhat Hached Hospital, Departement of Endocrinology, Sousse, Tunisia

Introduction
Pharyngolaryngeal cancers can invade the thyroid either by direct extension or via the lymphatic or hematogenous pathways. These three types of extension explain the indications for thyroidectomy during pharyngolaryngeal surgery, mainly documented for laryngeal cancers.
Methods
This is a retrospective descriptive cross-sectional study of 46 patients who underwent total laryngectomy (TL) associated with a thyroid procedure at the Department of Otolaryngology (ENT) and Cervicofacial Surgery, Farhat Hached Hospital, Sousse, over a period extending from January 2012 to December 2022.
Results
The mean age of our patients was 59.1 years. The sex ratio was 22. The average consultation time was 10.9 months. Dysphonia was the main symptom, found in all patients. Thyroid surgery associated with laryngectomy was performed in all our patients: loboisthmectomy in 52.2% and total thyroidectomy in 47.8%. Invasion of the thyroid gland by laryngeal carcinoma was identified in 8 patients (17.4%). Invasion was macroscopic, by direct extension of the tumour, in 6 (75%) patients and microscopic in 2 (25%). Comparison between groups of patients with and without thyroid invasion revealed that patients with evidence of glandular invasion had the following characteristics: Higher rates of invasion of the following structures by the primary tumor: Anterior commissure ($P=0.047$), subglottis ($P=0.004$), cricoid cartilage ($P=0.002$), thyroid cartilage ($P=0.089$), piriform sinus ($P=0.052$). There were no statistically significant differences between the two groups with regard to gender, age, smoking status, T, N, M staging, tumour size, surgery, histological grade and presence of vascular emboli or peri-nervous sheathing.
Conclusion
Thyroid invasion should not be underestimated in advanced pharyngolaryngeal cancers. Preoperative CT scans are essential for its evaluation. Thyroidectomy should not be performed routinely.

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EP814

Lateral lymph node metastasis in papillary thyroid carcinoma: predictive factors and management

Sameh Mezri[1], chaima zitouni[1], Wadii Thabet[2] & Khemaies Akkari[1]
[1]Principal Military Hospital, ENT, Tunis, Tunisia; [2]Taher Sfar Hospital, Mahdia, Tunisia

Introduction
Papillary carcinoma is the most common histological type of thyroid carcinomas. Lymph node involvement is an important prognostic factor. But its management remains uncodified.
Objective
The aim of our study was to identify the predictive factors of lateral lymph node metastases in papillary thyroid carcinoma.
Methods
This is a retrospective study including 96 patients operated on for papillary thyroid carcinoma at our department from 2001 to 2021 with a minimum postoperative follow-up of two years with clinical, biological and ultrasound control.
Results
Our study included 23 patients with lateral lymph node metastases with a mean age of 42 years, slightly lower than that of group without lateral metastasis (48 years). The sensitivity and the specificity of neck ultrasound in identifying lateral metastatic nodes were 71% and 83% respectively. Total thyroidectomy was performed in all cases. Central neck dissection was performed in 59 cases. Metastatic nodes were found in 47% of cases. Lateral neck dissection was done either simultaneously ($n=21$) or 12 and 18 months later ($n=2$). All patients received additional radioactive iodine treatment with an average dose of 200 mci. In our study, we identified tumor capsular invasion ($P=0.04$) and recurrent lymph node invasion ($P=0.02$) as independent factors of lateral lymph node metastases.
Conclusion
Lymph node involvement is a determining prognostic factor in papillary thyroid carcinoma. Central dissection is required if the cancer is diagnosed before or during the surgery. In the presence of metastatic nodes or other risk factors, preventive or curative lateral dissection should be discussed.

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EP815

Patterns of thyroid cancer incidence and mortality in lithuania over 30 years period

Lina Zabuliene[1], Viktorija Maciuliene[2], Jurgita Urboniene[3] & Giedre Smailyte[4, 5]
[1]Faculty of Medicine, Vilnius University, Institute of Clinical Medicine, Vilnius, Lithuania; [2]Faculty of Medicine, Vilnius University, Vilnius, Lithuania; [3]Vilnius university hospital ' Santaros klinikos', Center of Infectious Diseases, Vilnius, Lithuania; [4]National Cancer Institute, Vilnius, Lithuania; [5]Faculty of Medicine, Vilnius University, Institute of Health Sciences, Vilnius, Lithuania

Background
The incidence and mortality rates of thyroid cancer (TC) vary across nations for reasons such as registry accuracy, diagnostic and management practices, care quality, and standardization methods. Risk factors for TC include genetic abnormalities, iodine intake, TSH levels, autoimmune thyroid disease, gender, lifestyle, and environmental pollutants. In 2005, a mandatory salt iodization program was implemented in Lithuania. This study aims to analyse TC incidence and mortality trends in Lithuania between 1990 and 2019.
Methods
All TC cases (ICD-10 code C73) reported to the Lithuanian Cancer Registry from 1990 to 2019 were used in this study. The Registry covers the entire population of Lithuania (2.79 million per 2019 census). Age-specific and age-standardized incidence and mortality rates were calculated using the direct method with the EU-27 + EFTA reference population[1]. A Joinpoint regression model was used to estimate the average annual percentage change (AAPC).
Results
Over a 30-year period, 7, 753 TC cases were diagnosed. The mean age of the patients was 53.57 ± 15.22 years, 84% were women. The median follow-up duration was 11.5 years. The age-standardized incidence rate of TC in males ranged between 1.42 and 4.95/100, 000. AAPC increased significantly by 6.8% (95% CI 4.4, 28.2) in 1990–2004, and the changes in AAPC was insignificant at 1.8% (95% CI -10.7, 3.6) in 2004–2019. The age-standardized incidence rate in female ranged from 3.75 to 20.51 cases per 100, 000, with a significant increase in AAPC of 9.3% (95% CI 7.9, 10.8) in 1990–2004, and significant decrease in AAPC of 2.8% (95% CI -5.3, -0.1) in 2004–2019. The male mortality rate for TC ranged from 0.53 to 3.38/100, 000, with slight change in AAPC of 4.8% (95% CI -0.1, 25) in 1990–2002, and insignificant decrease in AAPC of 5.9% (95% CI -17.7, 3.2) in 2002–2019. In females it ranged from 0.7 to 5.38 cases per 100, 000, with a significant increase in AAPC of 4.2% (95% CI 2.3, 6.6) in 1990–2006 and a significant decrease in AAPC of 12.5% (95% CI -16.1, -9.8) in 2006–2019.
Conclusions
Incidence and mortality increased until the early 2000s, whith a stable or declining trend thereafter. Since 2006, there has been a marked decrease in mortality, especially in women, associated with the salt iodization program. Further studies are needed to confirm the link between salt iodization and reduction in mortality.
Reference
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EP819

Predictive factors of recurrent and refractory disease in papillary thyroid cancers

Sameh Mezri[1], Chaima Zitouni[1], Ilyes Abid[1], Wadii Thabet[2] & Khemaies Akkari[1]
[1]Principal Military Hospital, ENT, Tunis, Tunisia; [2]Taher Sfar Hospital, Mahdia, Tunisia

Introduction
Papillary cancer accounts for 90 % of all thyroid cancers. Although this cancer has a good prognosis, some patients do not respond well to the conventional treatment (surgery and iodine radiation therapy).
Objective
The aim of this study is to identify predictive factors of persistent or refractory disease in papillary thyroid cancer.
Method
This is a retrospective study including 79 patients who underwent surgery for papillary cancer from January 2010 to December 2020, with a minimum follow-up period of 24 months. We divided them into two groups: The first group included patients with persistent or radioactive iodine (RAI) refractory disease, while the second group included disease-free patients. We conducted a statistical study in order to identify predictive factors of recurrence and refractory disease.
Results
Among our patients, 61 % were disease-free, 25, 6 % had persistent response and 12, 8 % had refractory response. Predictive factors of recurrent and RAI-refractory cancer were lateral lymph node dissection ($P = 0.049$), multifocal cancer ($P = 0.003$), nodal recurrence ($P = 0.032$), thyroglobulin level ($P = 0.02$) and cumulative doses of radioiodine ($P = 0.02$). On multivariate study, nodal recurrence and thyroglobulin level were predictive factors of recurrence or refractory disease.
Conclusion
In our study, nodal recurrence and thyroglobulin level were identified as independent factors of recurrent or refractory disease. These findings can contribute to adapt treatment strategies and follow-up protocols among high-risk patients.

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EP822

Preoperative biological markers in papillary thyroid carcinoma

Sameh Mezri[1], Chaima Zitouni[1], Wadii Thabet[2], Salah Menasria[1] & Khemaies Akkari[1]
[1]Principal Military Hospital, ENT, Tunis, Tunisia; [2]Taher Sfar Hospital, Mahdia, Tunisia

Introduction
Carcinogenesis results from a disturbance in the balance between apoptosis and cell proliferation. This process involves inflammatory cells, which play a pro- and anticarcinogenic role.
Objective
the aim of this study is to investigate the status of neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) as potential biomarkers in predicting the evolutionary profile of papillary thyroid cancers.
Methods
This is a retrospective study including 80 patients operated on for papillary thyroid cancer at our department between 2010 and 2019. We studied the predictive role of NLR and PLR in metastases, multifocal forms and recurrences.
Results
NLR and PLR were significantly higher in cases of extra-thyroidal invasion ($P = 0.04$), multifocal tumours ($P = 0.01$), locoregional or distant lymph node metastases ($P = 0.03$); unlike gender, age, tumor size, histological subtype or TNM stage.
Conclusion
NLR and PLR are inexpensive and easy to perform. They can also predict the evolutionary profile of papillary thyroid cancers.

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EP825

Medullary thyroid carcinoma presenting with carcinoid syndrome: a case report

Beril Turan Erdogan[1], Hatice Aksu[1], Burçak Cavnar Helvacı[2], Baris Saylam[3], Aynur Albayrak[4], Cevdet Aydin[5], Oya Topaloglu[5], Reyhan Ersoy[5] & Bekir Cakir[5]
[1]Ankara City Hospital, Department of Endocrinology and Metabolism, Ankara; [2]Ankara Etlik City Hospital, Department of Endocrinology and Metabolism; [3]Ankara City Hospital, Department of General Surgery, Ankara; [4]Ankara City Hospital, Department of Pathology, Ankara; [5]Yildirim Beyazit University Faculty of Medicine, Department of Endocrinology and Metabolism, Ankara

Introduction
Medullary thyroid cancer (MTC) is characterized by elevated calcitonin levels, stemming from genetic factors or occurring sporadically. Carcinoid syndrome involves symptoms triggered by substances released by tumors, such as hormones and amines. This case report details a patient who developed carcinoid syndrome linked to medullary thyroid cancer.
Case
A 77-year-old male presented with flushing, diarrhea, and dizziness. No other health issues or medication use were reported, except for flushing and hypotension during a hemorrhoid operation a year ago. While routine tests showed normal results, neck CT revealed calcified nodules in the thyroid and pathological lymph nodes. Calcitonin was elevated at 11312 pg/ml, CEA at 126 ng/ml. Thyroid ultrasound displayed a 19.1 × 21 × 35.9 mm calcified nodule with pathological cervical lymph nodes. Ga-68-DOTA-PET confirmed thyroid and

cervical involvement. Fine needle aspiration biopsy confirmed medullary carcinoma. Catecholamine and 5-HIAA levels were normal. Chromogranin was normal. Surgery was planned for MTC, involving bilateral total thyroidectomy and lymph node dissection. Sandostatin infusion was initiated for carsinoid symptoms 24 hours before surgery, continuing intraoperatively and 48 hours postoperatively, gradually decreasing over a week. Postoperatively, calcitonin was 639 pg/ml, CEA 110 ng/ml on day one. Three months later, similar symptoms recurred, with calcitonin at 2600 pg/ml . Re-operation confirmed MTC, with a 5 cm retrosternal mass in the right lobe. Postoperatively, calcitonin decreased to 312 pg/ml . Two months later, a patient with similar complaints had a calcitonin level of 261 pg/ml, and residual tissue? was observed in the right lobe on thyroid ultrasonography. A spherical lymph node with the largest size of 10 cm was identified in the right level IV. Biopsy results were non-diognastic, and calcitonin washouts results of 4.9 pg/ml and 15.2 pg/ml, respectively. Due to ongoing symptoms, the patient was readmitted with a preliminary diagnosis of carcinoid syndrome, and short-acting sandostatin was initiated. After the post-operative follow-up Ga-68 DOTA-PET, as regression and the absence of new metastases were observed, tyrosine kinase inhibitors were not considered. The patient was discharged with lanreotide 120 mg/month, and no attacks were observed following the treatment.

Conclusion

MTC can manifest with flushing in carcinoid syndrome. When diagnosing flushing, consider MTC, pheochromocytoma, pancreatic tumors, hyperthyroidism, and male hypogonadism. Treating carcinoid syndrome involves addressing the underlying disease, and also sandostatin relieves symptoms in these patients. Keep MTC in mind when patients present with flushing or carcinoid syndrome.

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EP826

Anaplastic thyroid carcinoma: 27-year study

Heyfa Belhadj-Miled[1], Houas Jihene[1], Ghammam Monia[1], Khalfi Oussama[2], El Omri Malika[1], Merherzi Abir[1], Bellakhdher Mouna[1], El Ghali Wassim[3], Hasni El Abed Yosra[1], Kermani Wassim[1] & Abdelkefi Mohamed[1]

[1]Farhat Hached Hospital, ENT Department, Sousse, Tunisia; [2]Radiology Department, Sousse, Tunisia; [3]Department of Anaesthesia, Sousse, Tunisia

Introduction

Anaplastic thyroid carcinoma, also known as undifferentiated thyroid carcinoma, is a rare, highly aggressive malignant tumor accounting for 2 to 3 percent of all thyroid gland neoplasms. Anaplastic thyroid carcinoma continues to be one of the most deadly diseases worldwide and carries a very poor prognosis. This study aimed to investigate the epidemiological, clinical, therapeutic, and evolutionary aspects of anaplastic thyroid carcinomas.

Materials and Methods

A retrospective study was conducted on 18 cases of anaplastic thyroid carcinomas collected and treated in our department over a 27-year period (1995-2022).

Results

In this comparative study involving 11 females and 7 males, the average age of participants was 62 years, ranging from 31 to 82 years. The average consultation delay was assessed at 4 months. Local compression symptoms were predominant, accounting for 83.3% of observed cases. Physical examination revealed goiters in 88.8% of patients, with an average size of 6 cm. Recurrent laryngeal paralysis was observed in 50% of patients, including 3 cases with bilateral involvement. Lymph node involvement was present in 77.7% of patients, while distant metastases were observed in 55.5% of cases. Ultrasound results indicated the presence of multinodular goiters in all participants (100%). Cervico-thoracic CT imaging (performed on 11 cases) revealed plunging goiters in 8 cases. Regarding management, emergency tracheotomy with biopsy was performed in 61.1% of patients, while the remaining 7 patients underwent total thyroidectomy with bilateral cervical dissection. Radiotherapy was administered to 14 patients, with 9 receiving palliative treatment. Patient outcomes demonstrated a high mortality rate of 77.7%, with survival less than one year. Three patients experienced local recurrence. However, one patient remains alive with complete remission, followed up for 14 years.

Conclusion

Anaplastic thyroid carcinoma is among the most aggressive cancers. Optimal management is still debated, and a standardized treatment strategy is yet to be established.

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EP829

Performance of ultrasound using Kwak-TIRADS in thyroid nodule risk stratification

Antonios Tsakountakis[1], Konstantina Vouzouneraki[2], Emmanouil Mastorakis[3] & Elena Drakonaki[4]

[1]School of Medicine, University of Crete, Heraklion, Greece; [2]Department of Public Health and Clinical Medicine, Umeå University, Sweden and Independent Endocrinology practice, Ierapetra, Greece; [3]Department of Cytopathology, General Hospital "Venizeleio and Pananio", Heraklion, Greece; [4]Department of Anatomy, School of Medicine, University of Crete & Independent Radiology Practice, Heraklion, Greece

Introduction

This study aims to assess the performance of ultrasound using Kwak-TIRADS as the primary diagnostic tool for estimating papillary thyroid carcinoma (PTC) risk in thyroid nodules within the high-prevalence region of Crete, Greece.

Methods

A retrospective analysis was conducted on 802 thyroid nodules collected between 2018 and 2021. Nodules were categorized based on Kwak-TIRADS and compared against the Bethesda System for Reporting Thyroid Cytopathology (BSRTC). TIRADS 4a/4b served as the cutoff for benign/malignant categorization. Bethesda II category was used as the benign standard reference, and Bethesda V & VI categories as the malignant. Ultrasound and cytology tests were performed by a single experienced radiologist and cytologist, respectively.

Results

Of 802 thyroid nodules, 549 (68.4%) were benign, and 185 (23%) were malignant on cytology. The majority of nodules ($n = 391$; 48.7%) were classified as TIRADS 4a. Overall accuracy stood at 76.9%. Concordance rates between TIRADS 2, 3, 4a, and Bethesda II were 81%, while for TIRADS 4b, 4c, 5, and Bethesda IV & V, it was 62.2%. Excluding TIRADS 4 subcategories improved accuracy to 93.6% and 77.3%, respectively. The probability of a malignant fine-needle aspiration cytology (FNAC) was 77.33%, 60%, 43.63%, 18.67%, 1.29%, and 0% for TIRADS 5, 4C, 4B, 4A, 3, and 2, respectively. The probability of a benign FNAC was 100%, 93.53%, 73.4%, 41.81%, 24.44%, and 9.33% for TIRADS 2, 3, 4A, 4B, 4C, and 5, respectively. Sensitivity, specificity, and positive likelihood ratio were 58.9%, 92.5%, and 7.89, respectively. Excluding TIRADS 4, sensitivity increased to 95%, and specificity to 96.9%.

Conclusion

The study affirms strong concordance between Kwak-TIRADS and BSRTC, endorsing ultrasound as an effective first-line tool for thyroid nodule risk assessment. Notably, considering more ultrasound and clinical data in TIRADS 4 subcategories may optimize diagnostic accuracy. Kwak-TIRADS, characterized by simplicity and implementability, emerges as a reliable method for thyroid malignancy risk stratification.

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EP830

Falsely elevated serum calcitonin levels

Tamara Janić[1], Mirjana Stojković[1, 2], Sanja Klet[1], Bojan Marković[1], Biljana Nedeljković Beleslin[1, 2], Jasmina Ćirić[1, 2] & Miloš Žarković[1, 2]

[1]Clinic of Endocrinology, Diabetes and Metabolic Diseases, University Clinical Center of Serbia, Thyroidology, Belgrade, Serbia; [2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Serum calcitonin (CT) screening of thyroid nodules is a highly sensitive test for early diagnosis of medullary thyroid carcinoma (MTC) and is used for initial diagnosis and post-surgical follow-up. MTC is neuroendocrine tumor derived from parafollicular C cells which produce calcitonin. It is a rare tumor, accounting for 5-10% of all thyroid carcinomas, with a favorable prognosis if diagnosed early. A 74-year-old patient was referred to our clinic due to elevated basal CT levels. Routine thyroid ultrasonography revealed hypoechoic nodule in the left lobe 14.5x9.1 mm, with multiple calcifications (TIRADS 4a), and several nodules up to 12 mm in the right lobe. The initial thyroid hormone status showed high CT (203 pg/ml ; ref. $<$9.52 pg/ml -ECLIA), confirmed by repetition in the same laboratory. During the additional diagnostic at our clinic, basal CT levels were measured by two different assays, and both showed normal findings of basal CT (CT 2.8 ng/l; ref. 1-10.1 ng/l-IRMA); CT $<$ 0.5 ng/l (0-9.1 ng/l-ECLIA). Due to suspicion of interference, we performed serial dilutions of the serum that showed linearity (dilutions: 1:1, 1:2, 1:5, 1:10; CT 2.8; 5.8; 10.4; 11.5 ng/l, respectively - IRMA). Also, calcium stimulation test was performed and calcitonin response was determined in both laboratories. Results showed normal response in both laboratories (IRMA: 2.8; 6.8; 10.8; 11.3; 5.0 ng/l; ECLIA: $<$0.5; 4.0; 5.3; 5.0; 3.2 ng/l). CEA was normal (4.4; 4.3 µg/l). Fine-needle aspiration biopsy of the suspicious nodule was performed, and cytopathology showed atypia of unknown

significance (Bethesda classification system III). Due to pathological lymphadenopathy of the left side of the neck and suspicious ultrasound characteristics of the thyroid nodule, the patient was referred to surgery. Total thyroidectomy and left neck dissection were performed. PH diagnosis: multifocal papillary thyroid carcinoma (PTC). Tumor 15x10x1 mm in the left lobe and isthmus with infiltration of the capsule and muscle, and one focus of PTC 3 mm in the same lobe, and 3/9 metastatic LN with extracapsular extension, left, in region III and IV. Control CT measured in the initial laboratory was still elevated postoperatively (151 pg/ml), while normal measured by IRMA (4.5 ng/l). Based on the results, we concluded that the falsely elevated CT observed in the first laboratory was due to immunoassay interference. Immunoassay interference in CT determination is uncommon, but it can affect the course of diagnosis and treatment, so it should be considered in cases of conflicting laboratory results. The right diagnosis may prevent patient from complex diagnostic and therapeutic procedures.

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EP831

Unintentional discovery of a second cancer amidst laryngeal carcinoma surgery: case report of two patients

Heyfa Belhadj-Miled[1], Houas Jihene[1], Monia Ghammam[1], Oussama Khalfi[2], Malika El Omri[1], Abir Meherzi[1], Mouna Bellakhdhar[1], El Ghali Wassim[3], Yosra Hasni El Abed[4], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT Department, Sousse, Tunisia; [2]Department of Radiology, Sousse, Tunisia; [3]Department of Anaesthesia, Sousse, Tunisia; [4]Department of endocrinology, Sousse, Tunisia

Introduction
The occurrence of a differentiated thyroid carcinoma alongside a squamous cell carcinoma of the larynx is a seldom-encountered clinical phenomenon. Typically, it presents as a histological surprise, as clinical examinations and thyroid gland scans often show no abnormalities. Limited clinical cases have been documented in the literature, and the management of such cases remains a subject of significant controversy.
Material and Methods
We conducted a retrospective study involving two patients who underwent surgery for epidermoid carcinoma of the larynx, where the unexpected discovery of papillary thyroid carcinoma occurred.
Results
Two patients, aged 63 and 68, both chronic smokers, sought medical attention for progressive dysphonia and recent-onset inspiratory dyspnea. Fibroscopic examination revealed distinct lesions: an ulcerating-burgeoning lesion on the left vocal cord, fixed in the first patient, and a lesion encompassing the entire right hemilarynx, fixed in the second patient. Biopsy confirmed infiltrating, moderately differentiated squamous cell carcinoma in both cases. Tumor staging was T4N0M0 for the first patient and T4aN1 cm1 with bone and lytic lesions for the second patient. Surgical interventions included total pharyngo-laryngectomy with bilateral functional lymph node curage for both patients. In addition, the first patient underwent a left loboisthmectomy, revealing papillary thyroid carcinoma on extemporaneous examination, leading to totalization with bilateral mediastino-recurrent curage. The second patient underwent an immediate total thyroidectomy. The final pathology indicated the coexistence of squamous cell carcinoma of the larynx with papillary carcinoma of the left thyroid lobe (3.2 cm) in the first case and multiple papillary microcarcinomas involving both thyroid lobes (0.3 to 0.8 cm) in the second case. Both patients received external radiotherapy in conjunction with treatment for squamous cell carcinoma. Additionally, both patients were recommended further iratherapy and underwent a single 100 mCi ablative treatment with white mapping on scanning.
Conclusion
The coexistence of differentiated thyroid carcinoma with squamous cell carcinoma of the larynx is a rare clinical finding, often surprising from a histological standpoint. Despite normal clinical examinations and thyroid scans, few cases have been reported in the literature, and the optimal management strategy remains a subject of significant controversy.

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EP832

Medullary thyroid cancer: case series presentation

Rachida Bouattay[1], nawres bouaziz[1], Safa Jemli[1], Mehdi Ferjaoui[1], Elkorbi Amel[1]. Naourez Kolsi[1]. Harrathi Khaled[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction
Medullary thyroid carcinoma (MTC) is a rare neuro-endocrine tumor arising from the parafollicular cells of the thyroid gland. MTC produces calcitonin, and elevated calcitonin level is an essential feature of this tumor. MTC constitutes approximately 4% to 10% of all thyroid cancers. The objective of our study is to discuss the clinical aspects and therapeutic modalities of MTC through our series with review of the literature.
Patients and Methods
This is a retrospective study involving 11 cases of medullary thyroid carcinoma, collected over a period of 21 years (2001-2021).
Results
The mean age was 43 years (ranging from 36 to 90 years). The sex ratio was 4.5 (9 males/2 females). The average consultation delay was 5 months. The primary reason for consultation was an anterior basicervical swelling in 81.8% of cases, dysphonia in 9.1% of cases, and bone pain in 9.1% of cases. Physical examination revealed an anterior basicervical swelling in all cases. Cervical lymphadenopathy was found in 63.6% of cases. Thyrocalcitonin levels were assessed in two patient and were found to be elevated. Neck ultrasound, performed for all patients, revealed thyroid nodules classified as EU TIRADS IV in 36.4% of cases and EU TIRADS V in 63.6% of cases. The diagnosis was made after fine needle aspiration in 45.5% of cases. All our patients underwent total thyroidectomy with central neck dissection. Eight patients had bilateral functional neck dissection in six cases. A total laryngectomy was indicated in one case, due to tumor extension to the trachea and cricoid cartilage. Adjuvent radiotherapy was performed in 9 cases. The final histologic exam showed locoregional nodal metastasis in seven patients. Distant metastases were found in 4 cases (pulmonary, hepatic, osseous, and nodal). The follow-up was marked by the absence of recurrence in 7 patients, superior mediastinal nodal recurrence in one patient, death in one case. Two patients were lost to follow-up.
Discussion/conclusion
Seventy-five percent to eighty percent of MTCs are sporadic, and the remainder is familial as part of multiple endocrine neoplasias (MEN) 2A, MEN 2B, and familial medullary thyroid cancer. Prophylactic thyroidectomy is recommended for patients with mutations that put them at high risk. Various tyrosine kinase inhibitors are approved for use in progressive, metastatic medullary thyroid cancer. Finally, prognosis depends on the age of the patient, histologic grade, and status of surgical resection. The five-year survival for stages 1 to 3 is 93% compared to 28% for stage 4.

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EP833

The value of SPECT-CT in the follow-up of patients with differentiated thyroid carcinoma

Houas Jihene[1], Heyfa Belhadj-Miled[1], Monia Ghammam[1], Oussama Khalfi[2], Malika El Omri[1], Abir Meherzi[1], Mouna Bellakhdhar[1], El Ghali Wassim[3], Yosra Hasni El Abed[4], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT Department, Sousse, Tunisia; [2]Department of Radiology, Sousse, Tunisia; [3]Department of Anaesthesia, Sousse, Tunisia; [4]Departement of Endocrinology, Sousse, Tunisia

Introduction
In the follow-up of differentiated thyroid cancer (DTC), essential tools include iodine-131 scintigraphic imaging, coupled with cervical ultrasound and thyroglobulin measurement. An additional valuable tool is single-photon emission computed tomography combined with computed tomography (SPECT-CT), which precisely localizes fixation anomalies observed during whole-body scans. The aim of our study is to demonstrate, through a case study, the diagnostic contribution of SPECT-CT in identifying mediastinal lymphadenopathy during the follow-up of papillary carcinoma.
Observation
A 29-year-old woman underwent a comprehensive treatment regimen for papillary thyroid carcinoma, including total thyroidectomy, bilateral mediastino-recurrent lymph node dissection, and adjuvant radioiodine therapy. The tumor was classified as pt1b N1b M0. Following two courses of 100 mCi radioactive iodine, a post-therapeutic scan revealed a moderately intense mid-cervical focus of uptake, along with a less intense superior mediastinal focus. The thyroglobulin Tg T4 off assay showed elevated levels (>500 ng/ml). Further investigation using hybrid imaging SPECT-CT focused on the cervicothoracic region provided a more detailed response to the elevated thyroglobulin. The mediastinal focus was identified as a roughly oval-shaped tissue mass measuring 45*32*20 mm lateral to the trachea, causing a mass effect on the pulmonary apex. Surgical exploration uncovered a 5 cm right mediastinal mass adjacent to the right brachiocephalic trunk. Additional functional right lymph node dissection with excision of the mediastinal mass was performed. The final histopathological

examination confirmed the metastatic nodal nature of the mediastinal lymphadenopathy.
Conclusion
SPECT-CT plays a crucial role in studying iodine-131 fixation anomalies in the context of DTC. It enables precise anatomical localization of lesions, enhances the detection of metastases overlooked by whole-body scans, and aids in assessing questionable fixation anomalies.

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EP834

Papillary carcinoma of the thyroid in patient with Graves' disease

Rachida Bouattay[1], Nawres Bouaziz[1], Amaidi Rami[1], Mehdi Ferjaoui[1], Elkorbi Amel[1], Naourez Kolsi[1], Harrathi Khaled[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction
The association of thyroid carcinoma with Graves' disease (GD) is considered rare. Over 85% of thyroid cancer in patients with GD was papillary thyroid carcinoma, although other histologic types including follicular, medullary, and anaplastic carcinoma could be found in some studies. We report here a series of cases of thyroid cancer discovered in patients with GD, in order to evaluate the incidence of thyroid carcinoma in patients operated on for GD and to identify criteria which may predict malignancy.
Patients and Methods
This is a retrospective study of patients who underwent surgery for Graves' disease between 2010 and 2021, and for whom the pathological study revealed a thyroid carcinoma.
Results
Among 51 patients operated on for Graves' disease, thyroid cancer was discovered in nine patients (17.6%). These were 9 women with an average age of 42 years (27 to 72 years). The indication for initial surgery was failure of medical treatment for Grave's disease in 6 cases (66.7%) and papillary carcinoma diagnosed by fine needle aspiration of a thyroid nodule classified EUTIRADS IV or V in 3 cases (33.3%). A total thyroidectomy with bilateral central neck dissection was performed in all patients; due to malignancy on frozen section examination. The final histological examination confirmed, in addition to characteristic Graves' lesions, the presence of a thyroid cancer. This one was a papillary microcarcinomas in 8 cases (88.7%) and a papillary carcinoma in one case (11.3%). Cancer was multifocal in only one patient. Furthermore, it was associated with lymph node metastasis in 8 patients. The nine patients underwent radioactive iodine therapy, with an average of 2-3 sessions per patient (100 mCi/session), until achieving a white cartography. The follow-up was marked by absence of recurrence in all patients.
Discussion/Conclusion
It was accepted that hyperthyroidism inhibited the development of neoplastic cells within the thyroid parenchyma. This concept is no longer accepted, even though the link between hyperthyroidism and cancer is controversial. The prevalence of thyroid cancer in Graves' disease varies in the series between 0.4% and 9.8%. Literature shows that the presence of thyroid nodule(s) in patients with GD (25-33% of cases) may be considered as an indication for surgery because it is a suggestive indication of cancer. The most adequate radical surgery in this situation is to perform a total thyroidectomy. It has the advantage of better adjusting postoperative substitutive opotherapy doses and allows for a therapeutic supplement based on radioactive iodine.

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EP835

Undifferentiated (Anaplastic) thyroid carcinoma: a report of 8 cases

Rachida Bouattay[1], Nawres Bouaziz[1], Mehdi Ferjaoui[1], Elkorbi Amel[1], Naourez Kolsi[1], Harrathi Khaled[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Objective
The epithelial cancers of the thyroid include papillary, follicular, hurtle and anaplastic. These are divided into well, poorly differentiated thyroid cancer and undifferentiated (or anaplastic) thyroid cancer (ATC). ATC is uncommon and very agressive entity. It is responsible for 7, 5% of all thyroid cancers. The aim of our study is to discuss the clinical aspects and therapeutic modalities of ATC through our series with review of the literature.
Patients and Methods
This is a retrospective study that collected patients taken care of in our department for ATC over a period of 30 years.
Results
Our series included 8 patients, comprising 7 females and one male, with a mean age of 69 years. The main reason for consultation was a rapidly-growing basicervical anterior and/or lateral cervical mass in all cases. Compressive signs were present in 3 patients. The average consultation delay was 3 months. Physical examination revealed a goiter with an average size of 5 cm, with tenderness in 3 cases. Jugulodigastric lymphadenopathy was associated in 5 cases and supraclavicular in one case. Indirect laryngoscopy performed for all patients showed laryngeal palsy in two patients. Ultrasound was performed for 6 patients and revealed a multinodular goiter classified as EUTIRADS IV in 3 cases and EUTIRADS V in 3 cases. Cervico-thoracic computed tomography was performed in 3 patients due to the presence of compressive signs. Total thyroidectomy with bilateral mediastino-recurential curage was performed in 4 cases. Lateral dissection was carried out in 3 cases and deemed impossible in two cases due to adhesion of lymph nodes to the esophagus and trachea. The tumor was considered unresectable in 3 cases. External radiotherapy was indicated in 6 cases, combined with radioactive iodine therapy in 3 cases due to the association with papillary carcinoma. The average follow-up duration was 6 months.
Discussion/conclusion
Anaplastic thyroid cancer remains one of the most deadly diseases. According to literature, patients with ATC have a median survival of 5 months and less than 20% survive 1 year. Early tumor dissemination results in 20-50% of patients having distant metastases and 90% having adjacent tissue invasion on presentation. This highlights the necessity for effective combined therapy. Resectable disease may benefit from a multimodal (surgery, IMRT for loco regional control, and systemic therapy) approach. However, a majority of patients present with unresectable locoregional disease. Early palliative care involvement is inclusive of life-prolonging therapies. ATC management demands rapid and integrated multidisciplinary decision making.

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EP837

Association between hyperthyroidism and differentiated thyroid cancer: association or coincidence? about 15 cases

Doaa El Bazi[1], Haraj Nassim Essabah[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital - Casablanca, Morocco Clinical Neuroscience and Mental Health Laboratory Faculty of Medicine and Pharmacy - Hassan II University, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
The association between hyperthyroidism and differentiated thyroid cancer has become increasingly frequent. The etiopathogenesis remains controversial. We report 15 cases of patients, in whom an incidental association with differentiated thyroid cancer was identified.
MaterialS and Methods
Retrospective study over a 37-year period (1986-2023) including 15 patients followed at the Department of Endocrinology and Diabetology for hyperthyroidism, in whom an incidental association with differentiated thyroid cancer was discovered on anatomopathological examination.
Results
The average age was 43.4 years, with a clear female predominance 11W/4M. Nine patients had a toxic nodule, four a basedow's goiters, and two had graves's disease, one of whom had a severe graves orbitopathy, who had benefited from corticosteroid boluses and decompression surgery. Total thyroidectomy was performed in all patients, with suspicion of malignancy in the preoperative evaluation in one patient. Histopathological examination revealed papillary carcinoma in four patients, microcarcinoma in nine patients, NIFT-P (Non-Invasive Follicular Thyroid neoplasm with Papillary-like nuclear features) in one patient, and papillary carcinoma with an insular component in one patient, who also had retro-orbital and spinal metastasis. Stage pT1a was the most frequent (9 patients). Iratherapy was indicated in four patients due to multifocality. The outcome was marked by remission in 93% of the patients. One death was recorded in the patient with insular carcinoma.

Conclusions
Based on our series and observations reported in the literature, hyperthyroidism does not guarantee the absence of cancer, and does not eliminate this possibility. The nature of thyroid nodules must be carefully assessed before surgery.

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EP838

Intra-Thyroid metastases of clear cell renal carcinoma - analysis of two complex cases

Sara Ribeiro[1], Juliana Gonçalves[1], Joao Carlos Almeida[1], Ana Varela[1] & Joana Queirós[1]
[1]São João Universitary Hospital Center, Porto, Portugal

Introduction
Intra-thyroid metastases are infrequent, comprising only 1-3% of all thyroid malignancies. Renal cell carcinoma, particularly of the clear cell type (CCRC), stands out as the predominant kidney malignancy and the most common primary source of intra-thyroid metastases, often manifesting several years post-diagnosis. This report highlights two cases of CCRC metastasis to the thyroid, both featuring deceptive cytological findings.
Case 1
A 60-year-old woman, post-right nephrectomy for a T1bN0M0 CCRC a year prior, exhibited a 3.5×2.4×6.4 cm nodule in the right thyroid lobe on ultrasound, characterized by hypoechoicity, internal vascularization, and irregular borders (TIRADS 5). Multiple isoechoic nodules, the largest measuring 1.6×1.4×2.3 cm (TIRADS 3), were evident in the left lobe. Fine needle aspiration revealed colloid, small epithelial cell clusters with round nuclei, and rare macrophages, indicative of follicular nodular disease. Incongruence between ultrasound and cytology, coupled with the lesion's size, prompted total thyroidectomy. Macroscopical evaluation of the surgical specimen unveiled a 4×4×2 cm lesion with a "nodule in nodule" configuration and hemorrhagic areas. Histopathological analysis of the lesion showed a tumor with solid growth pattern composed of cells with clear cytoplasm, positive for CD10, racemase, and PAX8. The absence of TTF1, thyroglobulin, chromogranin, synaptophysin, and calcitonin confirmed CCRC metastasis. Left lobe lesions were due to thyroid follicular nodular disease. Case 2: A 74-year-old woman, eight years post-left nephrectomy for CCRC, was referred for an Endocrinology appointment following right adrenalectomy for a suspicious mass seven years post-diagnosis. Physical examination revealed a cervical mass. Initial ultrasound unveiled a predominantly cystic nodule (4.5×2.6 cm, ACR-TIRADS 3). A subsequent evaluation six months later showcased a transformation into a predominantly solid, isoechoic nodule, 4.6 cm in diameter, with localized vascularity. Cytology suggested benign follicular disease. Owing to the development of compressive symptoms, right lobectomy was pursued. Histological analysis of both thyroid and adrenal lesions was compatible with CCRC metastasis.
Conclusions
Identifying metastatic CCRC through fine needle aspiration proves challenging due to overlapping clear cell features with other lesions (thyroid follicular neoplasms and intrathyroidal parathyroid tumors) and to the potential for coexistence with primary thyroid neoplasms ("tumor to tumor metastasis"). A thyroid nodule in a patient with a history of RCC should evoke a high index of suspicion, demanding comprehensive judgment based on ultrasonographic and cytological findings. Surgical resection may be warranted for definitive characterization.

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EP839

Chronic hashimoto's thyroiditis in patients with differentiated thyroid carcinoma- a case-control retrospective study

Adishah Çerma[1] & Agron Ylli[2]
[1]Kukës Regional Hospital, Internal Medicine, Kukës, Albania; [2]Mother Teresa University Hospital, Endocrinology, Diabetology and Metabolic Diseases, Tirana, Albania

Introduction
Co-occurrence of differentiated thyroid carcinoma (DTC) and chronic autoimmune thyroiditis (HT) is a debatable subject in many studies. It's noted that patients with HT have less aggressive tumors and a better prognosis, possibly related to the immune response against tumoral cells.
Aim
To evaluate demographic, clinical, laboratorial, histopathological parameters in patients with HT and DTC, compared to the patients without HT, focusing on differences in tumor aggressivity.
Methods
This study is a case-control retrospective study, where 106 patients were evaluated, 68 patients with HT and DTC and a control group of 38 patients without HT. The data are analyzed using IBM-SPSS v.24.
Results
Patients with HT and DTC were mostly females (95.6%) and of the age group 41-50 years old, with a mean age of 47.34 years old. In most of the patients, biopsy description was that of papillary carcinoma (52.9%), with predomination of classic variant. The majority of primary tumors in patients with HT were 0-2 cm (69.7%), unilateral (76.3%) and unifocal (68.2%). 66.1% of patients with HT had no capsular invasion, significantly less than the patients without HT (*P* 0.016). Vascular and extrathyroidal, despite being less frequent, had no statistical significance. Only 11.7% of the patients with HT have lymph node metastasis and advanced age proved to be the only relevant risk factor for that (*P* 0.002). None of the patients with HT had distant metastasis, which compared to the group without HT was statistically significant (*P* 0.05). All patient were treated with radioactive iodine and the most frequently used dose was 100 mCi (48.8%). Unlike the group without HT, all patients with HT took only one dose of radioactive iodine (*P* 0.021).
Conclusions
Patients with HT have some features which are less aggressive compared to those without HT as: less capsular invasion, lack of distant metastasis and less frequently treated with radioactive iodine. Because of their risk of malignancy, patients with HT should be monitored periodically.

Keywords: HT, differentiated thyroid cancer, tumor aggressivity
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EP846

Warthin-Type variant of papillary thyroid carcinoma: a case report

Rahal Amel[1]
[1]Bologhine Hospital, Endocrinology, Algiers, Algeria

Introduction
Warthin-like thyroid tumor (WLPTC) is a rare variant of papillary thyroid carcinoma characterized by a lymphoid stroma. Approximately 95 observations have been published in the literature. Like papillary carcinoma, Warthin-like thyroid tumors have a good prognosis. The key to diagnosis is anatomopathological examination. In this regard, we report a case of WLPTC because of its rarity.
Observation
Patient aged 56, known diabetic for 6 years on Glucophage. She has been followed up since 2012 (10 years ago) for hypothyroidism of autoimmune origin, and it was not until 1 year ago that an ultrasound examination revealed a thyroid of heterogeneous hypoechoic echostructure, with the presence of two supra-central nodules (right and left), classified EU TIRADS 5. Cytopuncture strongly suggestive of carcinoma on thyroiditis. The patient underwent surgery 6 months later, consisting of total thyroidectomy with bilateral central lymph node curage. Anatomopathological examination of the right and left lobes showed a malignant tumour proliferation of epithelial nature and predominantly papillary architecture. The papillae were of variable size, with a richly lymphocytic axis bordered by an epithelium of large polygonal cells with abundant granular eosinophilic cytoplasm, and enlarged nuclei with ground-glass chromatin and irregular incisure nuclear membranes. These nuclei show overlapping and moderate anisokaryosis. The stroma is squirrel-like and fibroinflammatory, with local calcospherites. This appearance corresponds to a papillary thyroid carcinoma variant warthin like class PT2m 0N+/22N, Mx. Six-month postoperative follow-up was without incidents.
Conclusion
The aim of this work is to outline the clinical, histological and immunohistochemical features, as well as the differential diagnoses and prognosis of this rare entity.

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EP851

Rare find of giant lymph node metastasis due to papillary thyroid microcarcinoma

Alida Nicoleta Dumitru[1] & Alina Sucaliuc[1]
[1]National Institute of Endocrinology, IV, Bucharest, Romania

Introduction
Papillary microcarcinoma is a malignant disease of the thyroid measuring less than 1 centimeter at its highest dimension. It has a good prognosis with a small rate of metastasis and giant adenopathies with rapid growth are a rare find.
Case report
We present the case of a 75-year-old male patient, who recently underwent surgery for massive laterocervical adenopathy, measuring 50/38.5/48.5 mm in diameters, with rapid growth (in approximately three months), well defined, in close contact with right internal jugular vein. Histological exam revealed cystic metastasis of thyroid papillary carcinoma and immunohistochemical stains were positive for paired-box gene 8 (PAX8), cytokeratin 19 (CK 19), thyroid transcription factor 1 (TTF 1), Thyroglobulin (Tg), p40 with Ki67 proliferation index of 15%. Preoperative full body CT scan did not find other distant tumors, so no associated distant metastasis. He was admitted in our department in good physical condition and thyroid ultrasound disclosed three heterogenous microfoci in the right thyroid lobe, of 0.1 mm in the largest dimension. Biochemical exams showed normal thyroid function and negative calcitonin. Total thyroidectomy was performed and histological exam confirmed the presence of a 0.25/0.1 cm, non-encapsulated, lymphovascular and perivascular invasive papillary thyroid microcarcinoma. Post surgery, ultrasound found paratracheal thyroid tissue, confirmed by the 131I Thyroid scintigraphy. Therapy with 100 micrograms of Levothyroxine was initiated with good adaptation to therapy. Postoperative follow-up included non-stimulated thyroglobulin of 0.04uUi/ml, stimulated thyroglobulin of 3.14 uUi/ml, antithyroglobulin antibodies in the normal range. The next step was to administer 50mCi radioiodine. Unfortunately, the patient was lost to follow up.
Conclusions
One should consider papillary microcarcinoma when it comes to giant lymph nodes with rapid growth.

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EP878

Challenging thyroid storm in pregnancy case report

Hemmat El Haddad[1], Heba Murad[1], Nehal Hamdy[1], Rokaya Abdel Aziz[1], Heba Moustafa[1], Randa Salam[1], Mohamed Magdy[1], Fady Nagy[1] & Ahmed Atef[1]
[1]Cairo University, Internal Medicine, Endocrinology, Cairo, Egypt

Introduction
Thyroid storm is a rare complication of hyperthyroidism. In pregnant patients can cause spontaneous abortions, fetal demise. Aggressive treatment is needed.
Case report
26 years female 20 weeks pregnant; Graves' disease for five years, was on carbimazole but she discontinued since she became pregnant Shortly after that, she started to complain with progressive dyspnea at less than ordinary effort, bilateral lower limb swelling, increase in abdominal girth, 10 days ago, she developed lower abdominal pain and severe vaginal bleeding, Spontaneous abortion of her twins occurred The patient was orthopnea, pulse 105 /mint, temp 38c, RR 25/mint, BP 150/90 and generalized edema, she was admitted to the Gynecological ICU for stabilization and further management Exophthalmos, staring look, Pallor, Neck veins: congested pulsating Hb 8.5 g/dl, TSH: 0.005 μIU/ml (normal range: 0.55–4.78), Free T3: 7 pg/dl, Free T4 = 3 ng/dl Ejection fraction: 48%. The patient was diagnosed as a case of thyroid storm (based on clinical manifestations and low TSH 0.005) complicated by congestive heart failure. Treatment was given (Inderal 40 mg/12 hour carbimazole 1 mg/day, hydrocortisone 1 mg/8 hours, Fursemide infusion, Spironolactone 1 mg/day, Ramipril 1 mg. The general condition of the patient partially improved and then she was discharged from ICU. Improvement of her condition on carbimazole 1 mg/day however TSH was 0.05 thyroidectomy was done on thyroxin replacement
Conclusions
Thyroid storm in pregnancy is a medical emergency needs high index of suspicion and early management by a multidisciplinary team Thyroidectomy may be the only option in selected cases like our case.

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EP881

Early detection and management of hypocalcaemia after total thyroidectomy

Dewan Mahmud Hasan[1]
[1]Bangladesh Specialized Hospital, Otolaryngology & Head-Neck Surgery, Dhaka, Bangladesh

Background
After total thyroidectomy Hypocalcemia is the most frequent complication. Serum calcium levels are reliable only 48–72 hours postoperatively. Now a day's measurement of iPTH as an early predictor of postoperative hypocalcemia is practiced in many centers.
Objectives
To share our experience for the diagnosis and treatment of post-operative transient and permanent hypoparathyroidism after total thyroidectomy and to assess the ability of iPTH in predicting postoperative hypocalcemia.
Methods
Our total number of patients is 84. iPTH level was measured on 1st postoperative day. Patients were followed up for 1 to 6 months post operatively. Unfortunately, we lose a big number of our patients from follow up.
Results
iPTH on the first postoperative day equal to or less than 15 pg/ml were found to be norm calcemic. iPTH less than 10 pg/ml were disturbed parathyroid hormone metabolism. Hypocalcemia is the most common complication recognized in patients of total thyroidectomy. Around 50% of patients who suffer from transient hypoparathyroidism develop permanent hypoparathyroidism. Measurement of iPTH after surgery is the mainstay of early identification tool in our country though combining postoperative iPTH and serum calcium level can entail more accurate result.
Conclusion
Measurement of iPTH on first postoperative day allow accurate prediction of postoperative parathyroid function in 99% cases. Morbidity due to hypoparathyroidism can be reduced by appropriate dose adjustment of supplemental therapy & lifelong follow up. Till date calcium & vitamin D is the drug of choice.

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EP884

Thyroiditis revealing a rare congenital anomaly: about 3 cases

El Omri Malika[1], Jemli S[1], Bellakhdher Mouna[1], Meherzi Abir[1], Houas Jihene[1], Ghammem Monia[1], Ach Taieb[2], Kermani Wassim[1] & Abdelkefi Mohamed[1]
[1]ENT Department Farhat Hached Hospital, Sousse, Tunisia; [2]Endocrinology Department Farhat Hached Hospital, Sousse, Tunisia

Introduction
Fourth branchial lesions are a rare cause of inflammatory neck masses in children. The aim is to emphasize the pathophysiology, clinical features, and therapeutic modalities of the fourth branchial cleft cyst. We report three cases of fourth branchial arch cysts complicated by superinfection, collected in our ENT and neck surgery department.
Results
There were three male children aged of 4, 6 and 18 years old respectively. They consulted our department foran acute basicervical swelling in one case and an isolated acute left cervical swelling in another case. The swelling was associated with torticollis in the third case. Physical Examination found a basicervical inflamed mass whose size varied between 4 and 8 cm. Cervical ultrasound showed a basicervical abscess pushing the homolateral thyroid lobe, hypopharyngoscopy suggested a piriform sinus fistula in two cases. Computed tomography scan revealed a left lateral thyroid cystic mass in one case. All our patients underwent intravenous antibiotics therapy. Surgical drainage of the abscess was required in two cases. In a later step, we performed chemical cauterization of the fistula within piriform sinus in two cases and hemithyroidectomy in three of them. Postoperative outcomes were favorable without any recurrence for the all the cases.
Conclusion
The fourth branchial cyst are unfrequent congenital anomalies occurring in 2% to 4%. This case highlights the significance of including congenital anomalies, especially rare etiologies, as a potential differential diagnosis when assessing pediatric neck masses.

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EP894

Abnormal liver function tests in patients with graves' disease

Ibtissem Oueslati[1, 1], Cherchir Faten[2], Sabrina Ayari[1], Arige Abid[1], Meriem Yazidi[1] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Endocrinology, Tunis, Tunisia; [2]La Rabta University Hospital, Endocrinology, Tunis, Tunisia

Introduction
In patients with Graves' disease, uncontrolled thyrotoxicosis causes liver dysfunction in 37 to 78% of cases. This is commonly revealed by abnormal elevation of liver enzymes including hepatic cytolysis and cholestasis. The aim of the present study was to determine the prevalence of liver dysfunction and its associated factors in patients with Graves' disease.
Methods
This was a monocentric retrospective study including 108 patients with hyperthyroidism secondary to Graves' disease. Patients with previous history of liver diseases were excluded. Baseline clinical and biological data were collected.
Results
The mean age at the diagnosis of Graves' disease was 45.9 $\pm$ 13.9 with a sex-ratio (F/M) of 1.9. Biochemical investigations revealed hepatic cytolysis and cholestasis in 20.6 and 33.3% of cases, respectively. The elevation of alkaline phosphatase was the most common abnormality (26.7 %). FT4 level ($P<0.001$), creatinine clearance ($P=0.036$) and transaminase levels ($P<0.001$) were significantly higher in patients with cholestasis compared with those without cholestasis. Moreover, male gender (O$r=1.7$, $P=0.045$), smoking (O$r=4.0$, $P=0.002$), and regular alcohol consumption (O$r=5.6$, $P=0.027$) were associated to cholestasis. Alcohol consumption ($P=0.013$) was also associated with an increased risk of cytolysis. Patients with hepatic cytolysis had higher levels of FT4 ($P=0.044$), alkaline phosphatase levels ($P=0.019$) and GGT levels ($P<0.001$) than those without cytolysis.
Conclusions
Graves' disease is associated with a considerable risk of liver dysfunction. The present study showed that gender, smoking alcohol consumption and the severity of hyperthyroidism significantly interfere with liver dysfunction.

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EP896

Diagnostic challenges to differentiate central hyperthyroidism (Resistance to thyroid hormone and TSHoma): a case report

Navya Basavaraju[1], Elaf Al-Samaraaie[1], Catherine Jones[1] & Probal Moulik[1]
[1]Royal Shrewsbury Hospital, United Kingdom

Introduction
The term syndrome of 'inappropriate secretion of TSH' was originally coined to indicate two forms of central hyperthyroidism-resistance to thyroid hormone (RTH) and thyrotropin (TSH)-secreting pituitary adenomas (TSHomas). We present such a case that poses a diagnostic challenge.
Case
A 44-year-old female presented with fatigue post COVID infection four months ago. Thyroid function tests (TFT) revealed high thyroid-stimulating hormone (TSH) 6.1 mU/l (range:0.3-4.2) with raised free thyroxine (fT4) 25.1 pmol/l (range:11-22) and free triiodothyronine (fT3) 7.1 pmol/l (range:3.1-6.8). She denied palpitations, weight loss, bowel changes, or menstrual irregularities. She was not on any regular or over the counter medications. She has 2 children and no family history of thyroid disorders. On examination, BMI 1 kg/m^2, pulse 70beats/min, regular, clinically euthyroid, no palpable goitre, visual fields normal. She had normal TSH at 1.1 mU/l and 3.1 mU/l, checked 14years and 4years back. Blood investigations showed normal anterior pituitary profile including short synacthen test. Repeat TFT's revealed a similar pattern and assay interference was ruled out by DELFIA for TSH, Atellica for fT3 and radioligand binding assay for familial dysalbuminaemic hyperthyroxinemia (FDH) negative in two referral laboratories. Serum glycoprotein alpha subunit (α-GSU) was 0.37IU/l (range: <3.0). Pituitary MRI scan showed a 1 mm anterior pituitary microadenoma. Thyroid pertechnetate scan suggested increased thyroid uptake. TRH (thyrotropin-releasing hormone) stimulation test showed less than 1.5-fold rise in TSH at 20minutes from baseline. T3 suppression test showed partial suppression of TSH at day 10. She is awaiting results of genetic testing for thyroid hormone receptor β (TRβ) gene mutation and somatostatin analogue suppression test.
Discussion
Assay interference should be first excluded with high fT4, fT3 and TSH prior considering other causes. RTH and TSHoma are rare and differentiating the two could be challenging. RTH is inherited as autosomal dominant in 80% of cases, with mutation in TRβ in majority. TSHoma accounts for 1% of all pituitary tumours, with prevalence of one per million, 80% being macroadenomas. Alpha-subunit is raised in TSHoma in 70% cases. TRH stimulation test with more than fivefold increase in TSH is suggestive of RTH while in TSHoma there is an attenuated (no greater than 1.5-fold increase) response in TSH. In T3 suppression test, TSH suppression occurs in RTH while absent in TSHoma. Response to Octreotide LAR, but not short acting single octreotide injection, is seen in TSHoma, but not RTH.
Conclusion
A panel of clinical, biochemical, radiological, dynamic testing, and genetic analysis, help to differentiate between RTH and TSHoma.

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EP897

Treatment-Induced myopathy in a patient with graves' thyrotoxicosis

Amina Al-Qaysi[1], Nwe Aung[2] & Chitrabhanu Ballav[2]
[1]Stoke Mandeville Hospital; [2]Stoke Mandeville Hospital, Endocrinology & Diabetes, Aylesbury, United Kingdom

Introduction
Thyrotoxicosis as well as its treatment with Carbimazole (CBZ) or Propylthiouracil (PTU) have been reported to result in myopathy. Onset of myalgia during the treatment of thyrotoxicosis may cause a diagnostic challenge in distinguishing the thyrotoxic from the drug-induced myopathy. We report such a case where myopathy was induced by treatment with both CBZ and PTU.
Case report
We report the case of a 26-year-old Chinese lady presenting with palpitations due to Graves' thyrotoxicosis (TSH <0.01 mIU/l, Free T4 52.4 pmol/l, TSH receptor antibodies 7.1 IU/ml, and Anti-Thyroid Peroxidase antibodies >1000 IU/ml). She developed myalgia, muscle cramps and weakness involving the upper and lower limbs with significantly elevated Creatine Kinase (CK) of 2651 U/l (normal range 29 – 168 U/l) when she was commenced on CBZ 40 mg daily. The MRI scan of all limbs showed normal muscle bulk with no evidence of myositis. Although her free thyroid hormones settled with CBZ, her symptoms did not respond to reducing the dose to 20 mg daily. Changing the treatment to PTU 100 mg twice daily resulted in a transient improvement of symptoms and a reduction of the CK level. Her serum potassium, calcium, and renal functions were within normal ranges. The muscle cramps and myalgia recurred while on PTU in two weeks with high CK despite normal free thyroid hormones and completely suppressed TSH. Her TSH receptor antibody level remained elevated throughout the course of treatment. Since she had myopathy with both antithyroid agents, she has been referred for total thyroidectomy.
Conclusion
We report a patient with Graves' thyrotoxicosis who developed myopathy during anti-thyroid drugs treatment. High CK and normal potassium levels are reported more frequently in drug-induced myopathy, unlike Grave's myopathy which often presents with normal CK and hypokalemia. This alongside the sequence of symptom onset may help distinguishing between the two conditions.

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EP899

Transient thyrotoxicosis and hypothyroidism after combination therapy with pd-1 and ctla-4 inhibitors for cervical cancer

Ketevan Lomidze[1, 2], Nino Kikodze[1], Marine Gordeladze[3], Tinatin Chikovani[1] & Nino Charkviani[3]
[1]Tbilisi State Medical University, Immunology, T'bilisi, Georgia; [2]Israeli-Georgian Medical Research Clinic Healthycore, Clinical Trials Department, Tbilisi, Georgia; [3]Tbilisi State Medical University, Endocrinology, T'bilisi, Georgia

Introduction
Mono or combination therapy with immune checkpoint inhibitors for malignancies causes thyroid dysfunction in the form of overt or subclinical hypothyroidism, or thyrotoxicosis. Thyrotoxicosis phase is often transient and in some cases so short that it cannot be diagnosed in time and the patient is examined late when hypothyroidism is confirmed. We describe a case of Cervical Cancer woman who developed transient thyrotoxicosis and later hypothyroidism after combination treatment with CTLA-4 and PD-1 inhibitors.
Case Presentation
A 60-year-old postmenopausal female developed transient thyrotoxicosis-TSH- <0.005 (NR: 0.3-4.0 micro IU/ml) and 2 weeks later Hypothyroidism TSH-220 micro IU/ml 2 months after immunotherapy. The only complaints she

had was palpitation and increased blood pressure. Her Anti-TPO was positive, but Anti-Tg and TRab were negative. Initial therapy for thyrotoxicosis was performed with propranolol and after the development of hypothyroidism L-thyroxine replacement therapy was started.
Conclusions
Autoimmune thyroid dysfunctions can be induced by immune checkpoint inhibitors treatment: anti-PD-1, anti-CTLA-4, and anti-PD-L1. An elevated level of clinical suspicion is required for the diagnosis of endocrinopathies due to an upward trend in endocrine disorders among cancer patients receiving immunotherapy. Early management of ICI-induced endocrinopathies improves the quality of oncopatients' life and continuity of anticancer treatment.

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EP900

Exploring the spectrum: complications of hyperthyroidism - insights from a series of 29 cases

Raida Ben Salah[1], Siddiqa Soomauroo[2], Faten HadjKacem[2], Ahmad Ridwaan Auckburally[3], Abdelmuhaymen Missaoui[2], Wiem Feki[3], Mouna Mnif[2], Sameh Marzouk[1], Mohamed Abid[2], Nabila Rekik[2] & Zouheir Bahloul[1]
[1]Hedi Chaker University Hospital, Department of Internal Medicine, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [3]Hedi Chaker University Hospital, Department of Radiology, Sfax, Tunisia

Introduction
Overt hyperthyroidism is the result of excessive production of thyroid hormones. The diagnosis is made on the basis of clinical characteristics and the diagnosis of certainty is made by hormone assay, combining low TSH with increased thyroid hormones. If the hyperthyroidism is left untreated, symptoms progress and can lead to complications that may jeopardize life prognosis.
Patients and Methods
A retrospective study involving 29 patients with primary hyperthyroidism was conducted. We identified various complications associated with hyperthyroidism.
Results
We enrolled 29 patients with overt hyperthyroidism, among which 18 women and 11 men. The mean age at diagnosis was 35.5 years. Weight loss, tremor and hypersudation were the most frequent clinical findings. In all patients, we found a goitre, while exophthalmos was found in only 11 patients. The mean TSH level was 0.14 µUI/l. The mean free T4 level was 54.68 pmol/l. Graves' disease was the most common diagnosis in our study. The TSH-receptor antibodies (TrAb), the thyroid peroxidase antibodies (TPOAb) and the thyroglobulin antibodies (TgAb) were positive in 19, 27 and 14 patients respectively. Nineteen patients presented with complications. The most frequent complications were metabolic such as dyslipidaemia and poorly controlled diabetes in 9 patients each, as well as haematological complications such as anaemia in 9 cases as well. Neuromuscular complications, that were observed in 5 patients included amyotrophy of the lower limbs and thyrotoxic myopathy and the cardiovascular complication was cardiothyreosis and arrhythmia by atrial fibrillation in 5 patients. Neuropsychiatric complications were found in 2 patients and liver failure in one patient.
Conclusion
Hyperthyroidism is a prevalent thyroid condition characterized by an overproduction of thyroid hormones. Graves' disease is the most common cause of hyperthyroidism. Since thyroid hormone exerts physiological effects on various organ systems, the symptoms and signs of hyperthyroidism encompass manifestations affecting multiple organs. If hyperthyroidism is not treated or managed properly, it can escalate into a severe condition known as a thyroid storm. Prolonged untreated or inadequately treated hyperthyroidism are linked to a heightened risk of acute cardiovascular events, atrial fibrillation, ischemic stroke and increased mortality.

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EP902

Thyroid storm requiring plasma exchange and urgent thyroidectomy - an atypical presentation of de quervain's thyroiditis

Nikhel Sachdev[1]
[1]Singapore General Hospital

Background
De Quervain's thyroiditis is a transient inflammatory thyroid disorder, characterized by neck pain, a tender goiter and a triphasic clinical course of thyroid function evolution.
Clinical Case
A 21-year-old male presented to the emergency department with 5 days of fever, agitation, palpitations, diarrhea and cough. He had a significant past medical history of aplastic anemia, in remission after an allogeneic stem cell transplant a year ago. Thyroid function test revealed a free T4 of 67.1 pmol/l (reference range 8.8 – 14.1 pmol/l) with a thyroid stimulating hormone (TSH) of $<$ 0.1 mU/l (reference range 0.65 – 3.1 mU/l). TSH receptor antibody was negative. On physical examination, he was confused, restless and diaphoretic. He had a non-tender goitre. He was diagnosed with thyroid storm and had a Burch Wartofsky Score of 60. He was treated with oral propylthiouracil (PTU), oral Lugol's iodine, oral propranolol and intravenous hydrocortisone. Unfortunately, he developed profoundly deranged liver function which persisted even after switching PTU to carbimazole, precluding further use of anti-thyroid drugs (ATDs). ATDs were stopped and he was started on oral colestyramine and lithium. He subsequently underwent three cycles of plasma exchange (PLEX) prior to undergoing a total thyroidectomy. Intraoperative findings were that of a vascular and mildly enlarged fibrotic thyroid. Histopathology of the resected thyroid revealed a granulomatous thyroiditis. Microbiological investigations, including acid-fast bacilli smears, were negative.
Conclusion
De Quervain's thyroiditis may present atypically with the absence of neck pain or tenderness. The thyrotoxicosis is usually mild and temporary, but rarely may be associated with life-threatening manifestations including thyroid storm. PLEX is an effective bridge to safe definitive therapy for patients with thyroid storm in whom ATDs are ineffective or contraindicated.

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EP904

Acute perforated viscus complicating thyroxicosis: a case series

Pei lin Chan[1], Qing Wei Lim[2], Wei Hang Lim[2], Adib Fikri Bin Azalan[2] & Jean Mun Cheah[2]
[1]Hospital Umum Sarawak, Kuching, Malaysia; [2]Bintulu Hospital, Bintulu, Malaysia

Introduction
In cases of emergent surgical conditions, pre-medication of patients with thyrotoxicosis is required to reduce the patient's risk of thyroid storm in the perioperative and postoperative state. Perforated viscus with concurrent thyrotoxicosis is rarely reported. We report 2 cases of thyrotoxicosis and acute abdomen with perforated viscus.
Case 1
A 27-year-old gentleman with underlying hyperthyroidism, presented with central epigastric pain for 3 days duration. He did not have any gastrointestinal losses. On assessment, blood pressure was stable, temperature was 38°C and patient was tachycardic at 144 beats/minute. He had fine tremors and a generalized tender abdomen with guarding. ECG showed sinus tachycardia while chest radiograph revealed air under the diaphragm. Bedside abdominal ultrasound showed free fluid in the Morrison's pouch. His Free T4 was raised at 68.1 pmol/l (12-22) with suppressed TSH $<$0.005 mIU/l (0.27-4.2). He was started on rectal propylthiouracil and intravenous hydrocortisone. To optimize his condition prior to surgery, a peritoneal drain was inserted for temporary source control while plasmapheresis was done. Post plasmapheresis FT4 dropped to 1 pmol/l and he proceeded for exploratory laparotomy. Rectal PTU was continued until patient was allowed orally. He recovered well and was discharged with oral carbimazole.
Case 2
A 46-year-old construction worker with no prior medical illness, presented with 1 day history of epigastric pain. He had a history of chronic analgesia use. An initial chest radiograph done at primary care found air under the diaphragm and he was referred to hospital. On assessment he had a mild goiter and abdomen was tense and guarded. His temperature was 38°C, BP 137/89 and heart rate was 130 beats/minute. Bedside ultrasound showed free fluid in the abdominal cavity. His FT4 was elevated at 90.1 pmol/l with TSH $<$0.005 mIU/l. He developed fast atrial fibrillation requiring intravenous infusion amiodarone. Prompt treatment with intravenous hydrocortisone and rectal propylthiouracil was initiated. He was not able to proceed with surgery as patient was deemed unstable due to the atrial fibrillation with rapid ventricular response. Plasmapheresis was done and repeated FT4 post plasma exchange was 51 pmol/l. He subsequently underwent emergency exploratory laparotomy however post-surgery he had persistent fast AF requiring multiple synchronized cardioversions. His blood investigations showed worsening septic parameters and he eventually succumbed a day after surgery.
Conclusion
The presence of a compromised gastrointestinal tract requires alternative routes of administrating vital medications in thyrotoxicosis and utilization of other modalities of treatment such as plasmapheresis.

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EP912

A rare etiology miming a thyroid nodule: report of a case and literature review

Amel Elkorbi[1], Nawres Bouaziz[1], Mahdi Ferjaoui[1], Rachida Bouatay[1], Naourez Kolsi[1]. Harrathi Khaled[1] & Jamel Koubaa[1]
[1]مستشفى فطومة بورقيبة بالمنستير, Monastir, Tunisia

Introduction
Thyroid swelling is habitually a thyroid nodule, however sometimes it reveal to be another pathology that we did not expect. We aim through this case and literature revue discuss the diagnostic errance in front of thyroid mass that it correspond to a cyst of the fourth cleft.
Material and method
We report a case of cyst of the 4th cleft in adults managed in our department that presented as a thyroid nodule.
Case report
This is a 58-year-old man, with no notable pathological history, referred to our department for a right basicervical swelling evolving over two months. There was no signs of infection nor compression. Clinical examination revealed a painless 4 cm-sized mass located in the right basicervical region. It was mobile with swallowing conferred to the diagnosis of thyroid nodule. No other cervical mass was found. The rest of the ENT examination was normal. Cervical ultrasound showed a right laterocervical cystic mass closely to the right thyroid lobe sized 68×42×35 mm. Fine needle aspiration suggested the diagnosis of a branchial cyst. The patient underwent a hypopharyngoscopy that did not show any fistulous orifice of the piriform sinus. A right loboisthmectomy with the cyst excision was then performed. Histopathological examination confirmed the diagnosis of a cyst of the 4th cleft. No recurrence was observed after three years of follow-up.
Discussion/Conclusion
The fourth cleft cyst is a congenital malformation that is a challenging for the pratician. It is habitually revealed at an early age and frequently presented as a thyroid abscess. Endoscopy is necessary to research an eventual internal orifice of the fistula that explained the infection. In our case, the cyst has mimed a thyroid nodule and the absence of history of infection is explained by the absence of the internal orifice. Treatment is surgical, however cauterization of the internal orifice can be an alternative in cases of surinfected cyst when dissection closely to the recurrent nerve seems to be laborious.
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EP957

Cervical pulmonary hernia: a differential diagnosis of thyroid nodule to keep in mind

El Omri Malika[1], Jemli S[1], Bellakhdher Mouna[1], Meherzi Abir[1], Houas Jihene[1], Ghammem Monia[1], Ach Taieb[2], Kermani Wassim[1] & Abdelkefi Mohamed[1]
[1]ENT department Farhat Hached hospital, Sousse, Tunisia; [2]Endocrinology department Farhat Hached hospital, Sousse, Tunisia

Introcduction
Pulmonary herniation is defined as a protrusion of the lung and its pleural layers beyond the normal limits of the rib cage. It can be cervical, intercostal or diaphragmatic. Cervical hernia develops from the apex of the lung and represents approximately one third of pulmonary hernias and 60% of congenital lesions e report a case of cervical pulmonary hernia, in order to discuss the epidemiological etiopathogenic and clinical particularities of this entity.
Observation
It was a 38 year old man smoker with chronic cough with the medical history bilateral inguinal hernia and umbilical hernia that were surgically treated He consulted our department for a right side-cervical swelling evolving for 2 years which increased in size when coughing. Physical examination revealed a right side-cervical swelling of 7 cm long axis which manifested itself during coughing. The remainder of the ENT examination was unremarkable. The cervical CT scan concluded that there was a cervical lung herniation due to the abnormal presence of lung tissue at the cervical level. The patient was referred to the vascular and thoracic surgery department for surgery.
Conclusion
Cervical pulmonary hernia is a rare clinical entity; its often difficult diagnosis is facilitated by chest CT scanning. It is almost always lateralized to the right with a possible deviation of the trachea towards the left. Their appearance results from the conjunction of a weakening of wall resistance and an increase in intrathoracic pressure. Chronic cough, emphysema, physical exertion promote the appearance of these hernias.

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EP958

Macro-TSH: a case report

Najoua Lassoued[1], Souissi Mariem[1], Abdelkafi Yassmine[1], Alzeer Mahmoud[1], Alaya Wafa[1] & Sfar Mohamed Habib[1]
[1]Taher Sfar University Hospital, Endocrinology Department, Mahdia, Tunisia

Background
Macro-TSH, a rare condition, should be considered in asymptomatic patients presenting with a biological profile of subclinical hypothyroidism, thus avoiding unnecessary treatment. We report the case of a patient with macro-TSH.
Case Presentation
A 41-year-old man was transferred from the Cardiology Department for further exploration of elevated TSH. He has been hospitalized for acute decompensation of heart failure. A thyroid workup revealed a TSH of 45.5 µUI/ml, verified twice after three and six months with normal Free T4 level. There was no history of taking amiodarone or iodized products. The patient had no clinical signs of hypothyroidism on examination. Anti-thyroid peroxidase antibodies and antithyroglobulin antibodies were negative. Ultrasound showed thyroid hypotrophy, and scintigraphy revealed homogeneously increased fixation. The diagnosis of macro-TSH was most likely. Unfortunately we could not find any laboratory that could do TSH chromatography. We decided not to prescribe hormone replacement therapy. The evolution was marked by the persistence of a high TSH without any clinical or biological repercussions.
Discussion/Conclusion
Isolated elevation of TSH in the absence of thyroid symptoms can be very rarely caused by a macromolecule formed between TSH and immunoglobulins (macro-TSH), confounding the interpretation of thyroid function test results. The biochemical profile mimics subclinical hypothyroidism and may lead to inappropriate LT4 treatment. No immunoassay can reveal the presence of macro-TSH. Gel filtration chromatography is the state of-the-art method for detection of macro-TSH. Unfortunately, this test is expensive and not widely available

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EP960

Atypical subacute thyroiditis associated with papillary thyroid carcinoma in a case of Graves' disease

Müge Keskin[1, 2], Kübra Solmaz[3], Cevdet Aydın[4], Ferit Taneri[5], Banu Bilezikci[6], Oya Topaloglu[4], Reyhan Ersoy[4] & Bekir Cakır[4]
[1]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [3]Ankara Bilkent City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [4]Ankara Yildirim Beyazit University Faculty of Medicine, Endocrinology and Metabolism, Ankara, Turkey; [5]Ankara Güven Hastanesi, Department of General Surgery, Ankara, Turkey; [6]Ankara Güven Hastanesi, Department of Pathology, Ankara, Turkey

Aim
In patients with papillary thyroid carcinoma (PTC), the incidence of subacute thyroiditis (SAT) is thought to be more frequent than estimated. The incidence of thyroid cancer is between 2.3% and 21.1% in Graves' Disease (GD).
Case
A 31-year-old female patient applied with complaints of amenorrhea and hair loss in the 10th postpartum month. There was no history of COVID-19 infection, but Biontech vaccine were administered two years ago. Her family history revealed GD in her sister. On physical examination, blood pressure was 120/1 mm/Hg, pulse rate was 83 beats/min. Laboratory values were TSH: <0.1 mU/l (0.55-4.78), freeT4:2.1 ng/dl (0.89-1.76), freeT3:11.1 ng/l (2.3-4.2), antithyroglobulin:2.7 IU/ml (<13), antithyroidperoxidase: 10235 U/ml (<60), thyroid stimulating immunglobulin: 6.34 IU/l (0.1-0.55), TSH receptor antibody: 3.63 IU/l (<1.5). The patient refused thyroid scintigraphy because of breastfeeding. She admitted with severe pain over the right thyroid lobe the next day. There was tenderness in the right thyroid area and the body temperature was 37.5°. Thyroid US revealed hypoechoic heterogeneous areas in the superior anterior and the inferior anterior regions of the right lobe, a 16x24x1 mm isoechoic nodule with areas of cystic degeneration in the superior region and a 22x38x1 mm conglomerated isoechoic nodule with areas of cystic degeneration in the inferior region of left lobe. In laboratory analysis, TSH: <0.1 mU/l, freeT4:2.1 ng/dl (0.89-1.76), freeT3:15.1 ng/l (2.3-4.2), sedimentation rate: 1 mm/hour(0-20), CRP:8.1 mg/l (0-5). Her pain regressed and CRP values returned to normal after one week with NSAID treatment. However, since thyrotoxicosis did not resolve (TSH: <0.1 mU/l (0.55-4.78), free T4:3.05nd/dl(0.89-1.76), free T3: 18.1 ng/l (2.3-4.2), methimazole treatment was started. On the control thyroid US, heterogeneous hypoechoic areas

have resolved. The thyroid FNAB cytology result of the dominant nodule in the left lobe was suspecious for follicular neoplasia and hurtle cell type. The patient underwent bilateral total thyroidectomy, and an infiltrative follicular subtype PTC 0.1 cm in diameter was observed in the right lobe in addition to hyperplastic colloidal nodules in non-tumor thyroid tissue.
Conclusion
SAT can be seen rarely in patients with PTC. In the literature, there are cases diagnosed with GD after SAT, cases of SAT concurrent with GD, and cases of concurrent GD and SAT after COVID-19 infection. Considering that the incidence of combinations of these three diseases is very rare, our patient is the first case in the literature with all three diagnoses.

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EP961

Management of thyroid nodule in pregnancy

Furhana Hussein[1], Gideon Mlawa[1], Sivatharjini Priya Sivarajasingam[1], Lina Eltayieb[1], Elizabeth Philips[1], Josie O'Heney[1], Chineze Otigbah[1], Godwin Simon[1] & Rabia Mahmood[1]
[1]Queen's Hospital, London, United Kingdom

Introduction
Thyroid cancer is one of the common malignancies diagnosed in pregnancy and the management of thyroid nodules in pregnancy is the same as in non-pregnant patients. Ultrasound thyroid and FNA are necessary in the investigations of any thyroid nodule.
Case presentation
A 39-year-old woman of Eastern European descent presented to the joint obstetric-endocrine clinic complaining of dysphagia and swollen neck at 34 weeks gestation. Her past medical history included hypothyroidism, psoriatic arthritis and depression. Family history was noteworthy for thyroid cancer – her mother had thyroid cancer treated with total thyroidectomy and radioactive iodine therapy. In addition, the woman herself was 2 years of age and exposed to the Chernobyl nuclear disaster. An Ultrasound (USS) thyroid revealed a right-sided solid thyroid nodule (U3-U4) measuring 9x8x1 mm and fine needle aspiration (FNA) confirmed follicular lesion Thy3F. She had a successful right hemithyroidectomy 4 weeks postpartum. The histology confirmed classic features of papillary carcinoma 1 mm staged as pT1b N0 R0. She was discussed in the thyroid MDT and the outcome was for TSH suppression, surveillance and not for completion thyroidectomy.
Discussion
Pregnant women with thyroid cancer can be asymptomatic and studies have suggested pregnancy increases the risk of developing new thyroid nodules. Pregnancy can also cause an increase in the size of pre-existing thyroid nodules by up to 50%. Development of new nodules is up to 20%. A detailed history of suspected thyroid nodules should be taken including a family history of thyroid cancer. A thorough examination of the thyroid gland should be performed followed by an USS thyroid to characterize the thyroid nodule. FNA is safe in pregnancy and can be performed in any trimester. Counselling is an important part of the management of thyroid nodules in pregnancy to allay anxiety and distress. Regular (4-6 weeks) monitoring of thyroid function tests is essential and the FT4, FT3, TSH range is trimester dependent.
Conclusion
The management of thyroid nodules in pregnancy depends on whether the nodules are benign or malignant and if the pregnant mother is symptomatic. For malignant nodules, surgical intervention is ideal in the second trimester or post-partum. Hence, an MDT approach is important. The TSH range should be maintained at 0.2-2.0mIU/l.

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EP966

Right jugular vein agenesis. a challenging case for experienced endocrine surgeons

Ángel Luis Sánchez Álvarez[1], Laura García García[1], M. Isabel Gutiérrez Giner[1], Ana Tejera Hernández[1], Jorge Loro Pérez[1] & Magel Fernández Alfonso[1]
[1]Complejo Hospitalario Universitario Insular Materno Infantil, General and Digestive Surgery, Las Palmas de Gran Canaria, Spain

Introduction
Jugular vein agenesis is an extremely rare condition and its prevalence is not well-established. Case reports in the medical literature are limited, emphasizing the rarity of this anatomical variation.
Case Presentation
Agenesis of the jugular vein is a rare anatomical variation characterized by the congenital absence or significant underdevelopment of the jugular vein, an essential vascular structure in the venous drainage of the head and neck. Although rare, this condition can have notable clinical implications defying expectations in medical evaluation and surgical practice. We present the amazing case of a patient with agenesis of the right jugular vein and hypertrophy of the contralateral vein. In lateral cervical dissections, the internal jugular vein is a main anatomical reference to perform the procedure. This is a 60-year-old woman with a diagnosis of medullary thyroid carcinoma and a calcitonin of 331 pg/ml . After being presented to a multidisciplinary committee it was decided to perform Total Thyroidectomy associated with bilateral central and bilateral lateral cervical dissections.. During the approach to the left lateral compartments, a highly dilated internal jugular vein with a transverse diameter of more than 3 cm was observed. When approaching the right lateral compartments, the carotid sheath was completely released from the posterior belly of the digastric muscle to the clavicle, with identification of the carotid artery and vagus nerve without being able to identify the right internal jugular vein. Intraoperatively, the images of the preoperative studies were reviewed with the Radiology Department confirmed the absence of the right internal jugular vein. Finally, the procedure was completed without incident and the patient was discharged within 24 hours.
Discussion
The case of jugular vein agenesis highlights the uniqueness and complexity of anatomical variations in the vascular system. Although this condition is exceptional, its recognition is crucial for accurate clinical evaluation and appropriate management of affected patients. The absence of the jugular vein can complicate common surgical procedures, such as vascular access, and is of vital importance in those where it constitutes an anatomical reference or in locally advanced tumors that require vascular resection where if it is not taken into account, it can have disastrous consequences for the patient. Complete understanding of the patient's specific anatomy and detailed planning are important elements in the success of the surgical intervention. Cervical endocrine surgery should be performed by experienced surgeons to identify possible anatomical variants and reduce the comorbidity of surgery.

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EP967

Unveiling the multifaceted presentation of a rare case: a complex intersection of anti-TPO positive graves' disease, raised CA-125, and severe dilated cardiomyopathy with myxedema in a zimbabwean migrant woman

Sargunann Naidu Krishnasamy Naido[1] & Faizan Rao[1]
[1]Royal Bournemouth Hospital, Diabetes and Endocrinology, Bournemouth, United Kingdom

Case presentation
This detailed case report delves into the complex clinical trajectory of a 37-year-old Afro-Caribbean woman hailing from Zimbabwe, who presented with a diverse array of symptoms. Among these were diarrhea, tremor, anxiety, abdominal distension, amenorrhea and a staggering unintentional weight loss of 1 kg over the past year. Notably, her medical history features a previous open left-sided salpingectomy undertaken for a ruptured ectopic pregnancy. The persistence of diarrhea, initially attributed to a chronic intestinal infection, led to her relocation to the UK in early 2023. Following a referral to the Gynae-Oncology team due to elevated CA-125 levels, a meticulous examination ensued to probe the possibilty of gynaecological malignancy. The speculum test yielded normal findings, and bimanual palpation failed to reveal any palpable masses. Remarkably, the patient, abstinent for over a year, declined a pregnancy test. Despite negative results from contrast-enhanced computed tomography of the chest, abdomen, pelvis (CTCAP), with specific consideration given to the differential diagnosis of struma ovarii, the gynae-oncology multidisciplinary team (MDT) dismissed ovarian cancer as the likely diagnosis, prompting further exploration of alternative causes. Subsequent referral was made to the endocrine team for symptoms suggestive of hyperthyroidism and neck swelling, the patient exhibited normal anti-TSH receptor antibodies but a significant elevation in anti-TPO antibodies. Biochemical analysis confirmed hyperthyroidism, prompting the initiation of treatment with carbimazole and propranolol by the GP. Subsequent imaging, CTCAP and computed tomography pulmonary angiography (CTPA), revealed a substantial right-sided pleural effusion and ascites, generalized soft tissue edema, hyperdense gastro-intestinal tract and negative for pulmonary embolism. This necessitated therapeutic thoracocentesis, which, upon analysis of the pleural fluid, revealed a transudative lymphocytic effusion, effectively excluding malignancy as a contributing factor to the observed symptoms. Surprisingly, further cardiac investigations unraveled an additional layer of complexity: severe non-ischemic dilated cardiomyopathy with reduced ejection

fraction. This manifested as impaired left ventricular function, dilation in all cardiac chambers and valvular regurgitations possibly complicated by a late diagnosis of long-standing autoimmune hyperthyroidism. In conclusion, early detection of autoimmune hyperthyroidism is imperative, considering the characteristic symptoms. The presence of anti-TPO antibodies and myxedema, typically associated with Hashimoto's thyroiditis, adds diagnostic intricacy. Notably, this presentation can also occur in Graves' disease where severe heart failure with myxedema becomes a complication of long-standing hyperthyroidism. This highlights the crucial role of vigilant clinical suspicion, recognizing diverse manifestations, and swift diagnosis of hyperthyroidism, emphasizing the need for interdisciplinary collaboration in addressing complex clinical scenarios.

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EP968

Experience of using tocilizumab for the treatment of glucocorticoid-resistant graves orbitopathy

Tatsiana Mokhort[1], Volha Shyshko[2], Kseniya Palavinkina[2], Alena Mokhort[1] & Natalya Likhorad[3]
[1]Belarusian State Medical University, Endocrinology, Minsk, Belarus; [2]Minsk City Clinical Endocrinological Center, Minsk, Belarus; [3]1th City Clinical Hospital, Endocrinology, Minsk, Belarus

Objective
to evaluate the efficacy of tocilizumab (TZM) in the treatment of glucocorticoid-resistant Grave's orbitopathy (GO).
Materials and Methods
3 patients with GO on the background of compensated Graves' disease were observed. Treatment of GO was initiated with methylprednisolone (total doses of 8, 000-13, 1 mg) without significant clinical effect with a CAS of 4 points. After that TZM was administered three times intravenously once a month at a dose of 8 mg / kg.
Results
The table shows the results of the initial CAS values (1) and the results of the examination 1 month after the end of therapy (2). We registered decrease of GO severity: reduction of proptosis, ophthalmotonus depletion and involution of thickness of oculomotor muscles. All patients noted a significant improvement in their quality of life, but 2 patients had minor leukopenia.
Conclusion
TZM has been shown to be effective in reducing CAS in patients with glucocorticoid-resistant GO, so it can be used to reduce the inflammatory process and severity in patients with GO.

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EP969

A rare cause of hyperthyroidism in hashimoto disease

Samir Mkaouer[1], Elyes Kamoun[1], Nadia Khessairi[1], Meriem Yazidi[1], Oueslati Ibtissem[1], Fatma Chaker[1] & Chihaoui Melika[1]
[1]La Rabta University Hospital, Endocrinology Department, Tunis, Tunisia

Introduction
Hashimoto's thyroiditis is the most frequent cause of hypothyroidism with a relative increased risk of thyroid lymphoma compared to healthy subjects. Hyperfunctioning nodules are rarely malignant. We report the case of a rare association of thyroid carcinoma, a hyperfunctioning nodule and Hashimoto thyroiditis.
Observation
We report the case of a 40-year-old female patient treated with L-thyroxine for hypothyroidism due to Hashimoto thyroiditis for 3 years. Thyroid ultrasonography was performed due to suspicion of thyroid nodule at the clinical examination and showed a 13 mm EUTIRADS 3 thyroid nodule, which increased in size to 27 mm after 12 months. Fine needle aspiration showed a benign cytology. During monitoring, TSH levels dropped to 0.005 mIU/l after withdrawal of L-Thyroxine. Thyroid scintigraphy showed a solitary hyperfunctioning nodule. The patient had a total thyroidectomy following suspicion of carcinoma on extemporaneous examination. The definitive pathological examination of that nodule concluded to a 1 mm vesicular thyroid carcinoma within the nodule.
Conclusion
The association of a solitary hyperfunctioning nodule and Hashimoto's thyroiditis is rarely described in the literature. The majority of autonomous nodules are benign. However, in case of clinical or ultrasound criteria of malignancy, surgery is required and can reveal malignancy.

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EP970

Case report: nivolumab induced dual hypophysitis and secondary hyperthyroidism

Geraint Worby[1], Brittany Cole[1], Mae Tan[1] & Umer Qazi[1]
[1]Watford General Hospital, United Kingdom

A gentleman in his 70s with a background of atrial fibrillation, hypertension, and mesothelioma undergoing immunotherapy via Nivolumab and Ipilimumab, presented with general unwellness, fevers, confusion, and headaches. He had no prior endocrine history but was found to have significantly deranged thyroid function tests. He was treated for thyrotoxicosis and an impending thyroid storm with carbimazole. He remained treatment resistant for several days, with continuous delirium, fast atrial fibrillation, refractory hypotension, and persistent pyrexia. His treatment was therefore switched to PTU with addition of Lugol's iodine, IV beta blockers, and IV hydrocortisone. The source of his thyrotoxicosis was hypothesised to be due to amiodarone, immunotherapy, or Jod Basedow effect post contrast. His TFTs started to improve after about 1 week of this treatment regimen. His medications were reduced to prevent hypothyroidism and he was discharged appropriately with a plan in place for urgent follow up. Days later, he was readmitted with hypotension; therefore, his carbimazole was reduced and prednisolone was added. The patient's TFTs normalised while in hospital and he was discharged on a low dose of carbimazole and prednisolone with repeat bloods and endocrine follow up. The discussion revolves around the potential effect of immunotherapy on hormones, and distinguishing at what level the effect is taking place. At the level of the thyroid, the increased free T4 and T3 causes negative feedback on the pituitary gland to suppress TSH in an attempt to counteract this. Similarly, if the effect is on the pituitary itself, the TSH may be dually suppressed in this manner. To distinguish whether the pituitary was also being affected, it was necessary to observe the changes in TSH as the other thyroid hormones normalised. If TSH reverted to normal levels when free T4 and T3 were within range, it is unlikely that the pituitary gland was contributing to the suppressed TSH, and much more likely that it had been low as a result of negative feedback from the elevated levels of T4 and T3 that were being produced by the thyroid gland. Additionally, we tested the other pituitary hormones to look for other derangements in values. We found that once the patient's T4 and T3 were within normal ranges, the TSH gradually also went back to normal. This suggests that the derangement occurred primarily at the level of the thyroid, as pituitary involvement would have continued to suppress TSH despite the correction on T4 and T3.

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(Abstract EP968)

Table 1: Summary of Analytical Results

Symptoms	Patient 1		Patient 2		Patient 3	
	1	2	1	2	1	2
Spontaneous retrobulbar pain	1	-	1	-	1	-
Pain on attempted upward gaze when moving the eye-balls up or to	1	-	1	-	1	-
Redness of the eyelids	-	-	1	-	-	-
Redness of conjunctiva	1	-	1	-	-	-
Swelling of the eyelids	1	-	1	1	1	-
Inflammation of the caruncle and/or fold	1	-	1	-	1	-
Swelling of conjunctiva (chemosis)	1	-	1	-	-	-

EP990

Papillary thyroid microcarcinomas and lymph node metastases: [about 20 cases]

Khouloud Boujelben[1], Fatma Hamza[2], Feriel Touzi[1], Elleuch Mouna[1], Dhoha Ben Salah[1], Yasmine Elloumi[1], Islam Jardak[2], Mohamed Maaloul[2], Mouna Mnif[1], Fatma Mnif[1], Charfi Nadia[1], Faten Hadj Kacem[1], Fadhel Guermazi[2], Khalil Chtourou[2], Abid Mohamed[1] & Rekik Nabila[1]
[1]Hedi Chaker Hospital, Endocrinology Department, Tunisia; [2]Habib Bourguiba Hospital, Nuclear Medicine Department, Sfax, Tunisia

Introduction
Papillary thyroid microcarcinomas (PTMC) usually manifest a slow progression, commonly displaying local-regional extension, contributing to a generally favorable prognosis. However, certain instances are complicated by lymph node metastasis, a pivotal factor influencing therapeutic strategies. The aim of this study was to evaluate the epidemiological, clinical, and histological characteristics of patients with PMCT and lymph node metastasis.
Patients and Methods
We performed a retrospective study and selected 20 patients who were diagnosed with Papillary Thyroid Microcarcinoma (PTMC) and had lymph node metastasis. These patients had undergone at least one total thyroidectomy and were referred to the nuclear medicine department of Habib Bourguiba Hospital for radioiodine therapy.
Results
In our study, there were 17 females and 3 males, resulting in a sex ratio of 5.66 The mean age was 43.4 years, ranging from 11 to 87 years Therapeutically, 13 patients underwent upfront total thyroidectomy, while lobectomy was performed in 7 patients. Totalization in the same procedure occurred in 6 cases, and later, after obtaining the definitive histological result, in only one patient. Histologically, the final examination revealed a diagnosis of classic papillary carcinoma in 85% of cases, with vesicular dedifferentiation noted in only 15%. The size of the tumor focus varied from 1 mm to 1 mm, averaging 4.1 mm. The tumor was multifocal in 17 cases. Capsular invasion was identified in 40% of cases, often associated with vascular emboli in 3 instances. All patients underwent a tracer dose scan with an average thyroglobulin (TG) level of 23.1 ng/ml. Hormonal replacement therapy was prescribed for all participants.
Conclusions
The detection of lymph node metastases heightens the risks of distant recurrence, justifying an exhaustive therapeutic strategy. Moreover, Surveillance should not be constrained temporally, as late recurrences remain a plausible occurrence

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EP1026

A case of giant toxic nodular goiter with dyspnea by pulmonary hypertension and obstructive symptom

Irida Kecaj[1], Ergita Nelaj[1], Ilir Gjermeni[1], Kei Xhixhabesi[1] & Ina Refatllari[2]
[1]University Hospital Center, Internal Medicine, Tirana, Albania; [2]University Hospital Center, Cardiology, Tirana, Albania

Introduction
Giant multinodular goiter (MNG) is a heterogeneous clinical disorder that can be asymptomatic or can cause compression of surrounding structures, and when it is accompanied by obstructive symptoms such as dyspnea, it carries an indication for surgery. Pulmonary hypertension is one of the most important complications of untreated hyperthyroidism, that can be reversible under treatment.
Case presentation
We present a case of 75 years old female with a giant MNG with a rapid increase in size within 3 years, with atrial fibrillation, palpitations, breathlessness on exertion and dyspnea. She is diagnosed with toxic nodular goiter since 60 years old, not regularly treated. Computed tomography scan of the neck shows a gross enlargement of thyroid. The trans-thoracic cardiac ultrasound shows dilatation of left atrium, right ventricular dilatation, pulmonary hypertension, with no evidence of pulmonary embolism in angio-ct. The fine needle aspiration suggested MNG with adenomatous nodules and toxic changes. She was treated with 20 mg methimazole daily; after 4 weeks the patient's palpitations improved but still complained shortness of breath. To check the heart status and pulmonary hypertension, following the treatment of thyrotoxicosis, the patient underwent echocardiography, and the pulmonary pressure was significantly reduced. A total thyroidectomy was performed and the gland was dissected successfully.
Conclusion
Pulmonary hypertension, associated hyperthyroidism, is a common complication, usually reversed after treatment of thyroid disease. Surgical management is recommended for goiters with compressive symptom, in aim to improved breathing and swallowing outcomes after thyroidectomy. With careful preoperative testing and thoughtful consideration of the type of anesthesia, including the type of intubation, preparation for surgery can be optimized.

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EP1029

Methimazole-Resistant graves' disease: a case report

Meriem Adel[1], Marwa Chiboub[1, 2], Ons Smairi[1], Manel Jemel[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technology, Endocrinology, Tunis; [2]Tunisia, Endocrinology, Tunis, Tunisia

Introduction
Graves' disease (GD), the most common cause of hyperthyroidism, is an organ-specific autoimmune disease. Initial treatment of GD is based on antithyroid drugs (ATDs). However, few cases of resistance to ATDs have been described in the literature. Here, we report a GD patient who suffered from resistance to ATDs requiring an early definitive therapy.
Case presentation
A 30-year-old female patient was referred to our institution for management of resistant thyrotoxicosis. She had no significant medical or surgical history. The diagnosis of Graves' disease was established based on clinical signs of thyrotoxicosis, goiter and eye signs. Laboratory findings objective high free thyroxine (FT4) concentrations, low TSH concentration and positive levels of TSH receptor autoantibody. Initial treatment involved prescribing 1 mg of Methimazole and 1 mg of Propranolol. However, despite good compliance, FT4 levels remained elevated for few months. Corticosteroid therapy at a dose of 30 mg of prednisolone was added for one month but thyroid function tests remained unchanged. Therefore, the patient was given 3 boluses of 1 mg of Solumedrol per day in combination with Methimazole 40 mg/d. seven days later, FT4 levels decreased to 39.8 pmol/l. In the presence of a FT4 level close to the normal range, the patient underwent definitive treatment. She received 15 mCi of radioactive iodine. The biological control one month after radioiodine therapy revealed a normal level of FT4 with decreasing clinical signs.
Discussion
For many years, ATDs have been the primary treatment for Graves' disease due to their ability to swiftly achieve euthyroidism with a lower likelihood of progressing to permanent hypothyroidism compared to alternative therapies. The occurrence of resistance to ATDs is uncommon, and the mechanisms behind such resistance remain unclear due to limited cases. Potential etiologies encompass malabsorption, elevated metabolism, drug antibodies, and irregularities in the intrathyroidal accumulation or action of the drugs. The approach to handling resistance to ATDs is not yet clearly defined. Alternative approaches have been suggested for such situations, including Lugol's solution, lithium carbonate, cholestyramine, and plasma exchange. These aim to achieve prompt euthyroidism before administering definitive treatment.
Conclusion
Managing resistance to ATDs in GD remains a complex issue due to the lack of well-defined diagnostic methods and established secure treatment approaches.

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EP1033

The role of one stop clinic to support patients with thyroid eye disease (TED)

Keiko Carter[1], Bashir Mahamud[2], Mohammad Saleki[3], Ayan Mohamed[4], Furhana Hussein[5], Catherine Man Yan Cheung[6] & Gideon Mlawa[7]
[1]Queen's Hospital, Endocrine and Diabetes Department, Romford, United Kingdom; [2]Queen's Hospital, Acute Medicine, Romford, United Kingdom; [3]Queen's Hospital, Endocrine and Diabetes, Romford, United Kingdom; [4]Queen's Hospital, United Kingdom; [5]Queen's Hospital, Endocrine and Diabetes, United Kingdom; [6]Queen's Hospital, Romford, United Kingdom; [7]Queen's Hospital, Endocrine and Diabetes, Acute Medicine, Romford, United Kingdom

Background
The causes of thyrotoxicosis include hot and Graves disease. Graves' disease can be associated with Graves eye disease, and thus have a psychological impact on the patient. The treatment of thyrotoxicosis includes medical therapy, surgical therapy, and radioiodine treatment. Treatment of thyroid eye disease includes both medical and surgical therapy in a multidisciplinary setting. Medical treatment using steroids may worsen hyperglycaemia in patients with existing diabetes. Steroid-induced

hyperglycaemia is not uncommon. Baseline HBA1C, fasting glucose, and regular monitoring for hyperglycaemia are required in patients on steroids.
Aims
- To establish BM monitoring patterns on non-diabetic patients with thyroid eye disease receiving steroids.
- To establish whether management corresponds with national guidance.
- To develop a consensual pathway for thyroid eye disease patients requiring steroids
- To present a retrospective study in the management of thyroid eye disease in the acute setting

Methods
- Retrospective study/audit using clinic letters and patients notes
- Baseline Fasting glucose done- 100%
- Baseline HBA1C done 100%
- Follow-up fasting glucose and HBA1C done 100%

Results
- 8 Patients analysed were identified.
- 7 patients had their baseline HBA1 checked,
- 50% had their HBA1C months after starting the steroids and
- 62% had their HBA1C checked after finishing the treatment

Discussion
- Treatment of thyroid eye disease includes both medical and surgical therapy in a multidisciplinary setting.
- Medical treatment using steroids may worsen hyperglycaemia in patients with existing diabetes. Steroid-induced hyperglycaemia is not uncommon.
- Baseline HBA1C, fasting glucose, and regular monitoring for hyperglycaemia are required in patients on steroids.
- At present no structured MDT approach to managing these patients. A 'One Stop Shop' with ophthalmology & endocrinology to manage these patients

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EP1038

Unmasking graves' disease: navigating the complexities of diagnosis, treatment, and beyond

Raida Ben Salah[1], Siddiqa Soomauroo[2], Faten Hadjkacem[2], Abdelmuhaymen Missaoui[2], Ahmad Ridwaan Auckburally[3], Wiem Feki[3], Mouna Mnif[2], Sameh Marzouk[1], Mohamed Abid[2], Nabila Rekik[2] & Zouheir Bahloul[1]
[1]Hedi Chaker University Hospital, Department of Internal Medicine, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [3]Hedi Chaker University Hospital, Department of Radiology, Sfax, Tunisia

Introduction
Graves' disease (GD), an autoimmune disorder predominantly impacting the thyroid gland, can extend its effects to various organs, such as the eyes and skin. It stands as the leading cause of hyperthyroidism. It is defined by the pathognomonic combination of thyrotoxicosis, goitre and exophthalmos. The aim of this study was to identify the characteristics of GD.
Patients and Methods
A retrospective study involving 31 patients with primary hyperthyroidism was conducted.
Results
We enrolled 29 patients with overt hyperthyroidism, among which 19 was diagnosed with GD. There were 10 men and 9 women. The mean age at diagnosis was 35.5 years. Weight loss and tremor were the most predominant symptoms noted in 64.5% and 58% of cases respectively. In all patients, we found a goitre, while exophthalmos was found in only 11 patients. The mean TSH level was 0.14 µUI/l. The mean free T4 level was 54.68 pmol/l. The TSH-receptor antibodies were positive in all cases. Dyslipidaemia, poorly controlled diabetes and anaemia were observed in 9 patients each. All patients were treated with a beta-adrenergic blocker. Corticosteroid therapy was initiated in 2 patients who had malignant Graves' orbitopathy. Eleven patients were treated with only antithyroid drug (ATD) and 17 with radioactive-iodine treatment (RAI). RAI was used after failure of or intolerance to ATD in 9 patients and a second course of RAI was indicated in 2 patients. Only one patient had a total thyroidectomy, indicated because of resistance to ATD, poor socioeconomic conditions, association with type 1 diabetes mellitus and the patient's young age. Neutropenia secondary to ATD, requiring discontinuation of this treatment and recourse to RAI was observed in one patient. The outcome was considered favourable in 18 patients, with clinical and biological euthyroidism and improvement of the complications caused by the hyperthyroidism itself or by its treatment. One patient died.
Conclusion
GD is a systemic condition that impacts various organs, presenting with diverse symptoms. The optimal management involves a collaborative approach by an interprofessional healthcare team. While antithyroid drugs can control symptoms, they don't provide a cure, resulting in common relapses. Radioactive iodine is often the preferred approach to address the condition. Hyperthyroidism poses significant short and long-term health risks, emphasizing the importance of early recognition and timely intervention.

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EP1039

Ultrasound assessment of thyroid gland size in young healthy men in the Minsk city

Elena Brutskaya-Stempkovskaya[1], Alena Yurenia[2], Volha Shyshko[1, 2], Ulyana Vauchankova[1] & Vladislav Dembski[1]
[1]Belarusian State medical University, Belarus; [2]Minsk City Clinical Endocrinology Center, Belarus

Background
Normal thyroid size varies across populations depending on age and gender. The results of assessing the normal size of the thyroid gland in young healthy men in Belarus population have not been published yet.
Materials and methods
A retrospective cross-sectional study was conducted. We studied 138 men 18-28 years old without endocrine pathology who applied to the Minsk City Clinical Endocrinology Center in 2023. The aim of the study is to establish the normal size of the thyroid gland among healthy young men. The study included patients with normal echogenicity of the thyroid gland, without increased thyroid blood flow, without a severe disturbance of the echostructure (cyst-like formations with a diameter of less than 5 mm were assessed as normal). Patients with cervical lymphadenopathy were excluded from the study. Statistical processing of the results was carried out using the Statistica 10 program (StatSoft, USA).
Examination
thyroid ultrasound, TSH, FT4, ATPO, height, weight, BMI.
Results
Average age was 21.9±2.42 years, height was 180 (175-186) sm, weight was 78 (64-95) kg, BMI was 22.1 (19.6-24.4) kg/cm^2. TSH level was detected 3.14±1.01 µIU/ml, FT4 – 17.1 (14.9-20.1) pmol/l, ATPO -13.9 (7.3-22.1) IU/ml. The average volume of the right lobe was 5.45±2.13 cm^3, the left lobe of the thyroid gland was 5.39±1.74 cm^3. The width of the isthmus was 2.4 (2.1-2.7) cm. Minimum registered total thyroid volume was 4.1 cm^3, maximum registered total thyroid volume was 25, 4 cm^3. The total thyroid volume was recorded 10.7 (6.7-17.9) cm^3.
Conclusion
As a result of the study, the total thyroid volume was recorded as 10.7 (6.7-17.9) cm^3 in young healthy men 18-28 years old without a history of endocrine diseases in the city of Minsk.

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EP1040

Ultrasound thyroid size in young healthy women in the minsk city

Elena Brutskaya-Stempkovskaya[1], Ihar Tarasik[2], Katsiaryna Dziachko[2], Volha Bohdan[1], Anastasiya Tubolets[1], Mikhail Vasiliuchak[1] & Aliona Mikhailava[1]
[1]Belarusian State medical University; [2]Minsk Clinical Consulting and Diagnostic Center, Belarus

Normal thyroid size in women varies between populations, and depends on the age. The results of assessing the normal size of the thyroid gland in young healthy fertile women in Belarus population have not been published yet.
Materials and methods
A retrospective cross-sectional study was conducted. We studied 122 fertile women 18-44 years old without endocrine pathology who applied to the Minsk Clinical Consultative and Diagnostic Center in 2023. The aim of the study is to establish the normal size of the thyroid gland among healthy young women. The study included patients with normal echogenicity of the thyroid gland, without increased thyroid blood flow, without a severe disturbance of the echostructure (cyst-like formations with a diameter of less than 5 mm were assessed as normal). Patients with cervical lymphadenopathy were excluded from the study. Statistical processing of the results was carried out using the Statistica 10 program (StatSoft, USA).
Examination
thyroid ultrasound, TSH, FT4, ATPO, height, weight, BMI.
Results
Average age was 32.0±7.25 years, height was 166 (162-170) sm, weight was 64 (56-73) kg, BMI was 22.4 (19.2-24.7) kg/cm^2. TSH level was detected 2.15 (1.46 -

3.04) μIU/ml, FT4 – 16.3 (15.2-18.8) pmol/l, ATPO -18.0 (11.8- 31.6) IU/ml. The average volume of the right lobe was 5.1 ± 1.69 cm^3, the left lobe of the thyroid gland was 5.5 ± 1.86 cm^3. The width of the isthmus was 2.5 (2.0-2.9) cm. Minimum registered total thyroid volume was 3.4 cm3, maximum registered total thyroid volume was 25, 2 cm^3. The total thyroid volume was recorded 9.7 ±3.13 cm^3. Frequency range 5-95% was detected 5.8-16.4 cm^3.
Conclusion
The result of the study demonstrated the total thyroid volume was recorded 5.8-16.4 cm^3 as normal in young healthy fertile women 18-44 years old without a history of endocrine diseases in the city of Minsk

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EP1041

Subclinical hyperthyroidism: exploring etiologies, clinical profiles and outcomes

Baltagi Myriam[1], Sawsen Essayeh[2], Imen Rojbi[2], Ibtissem Ben Nacef[2], Sabrine Mekni[2], Rihab Laamouri[2] & Karima Khiari[2]
[1]Tunisia, Endocrinology, Tunisia; [2]

Introduction
Subclinical hyperthyroidism (SH) is defined by normal thyroid hormone levels and reduced thyroid-stimulating hormone (TSH) concentration. It still raises intriguing questions about its clinical impact, management and outcomes. The aim of our study was to determine the underlying etiologies of SH, its clinical features and its outcomes in Tunisian patients.
Methods
We conducted a retrospective study at Charles Nicolle Hospital, including 46 patients with subclinical hyperthyroidism. Clinical data and paraclinical parameters were collected for analysis.
Results
The mean age of patients was 67 ± 8 years, with a female predominance (26women against20 men). Patients were managing health conditions, including 60% with type 2 diabetes, 42% with hypertension, 56% with dyslipidemia, and 8% with coronopathy. The majority of diagnoses (49%) for subclinical hyperthyroidism were incidental, discovered through routine medical analyses. Hashitoxicosis emerged as the most prevalent etiology, accounting for 32%, followed by Graves' disease at 21%, and multinodular goiter at 5%. In the majority of cases, the therapeutic decision involved a conservative approach, opting to monitor patients without initiating treatment. SH resolved spontaneously in 35% of cases.
Conclusion
In summary, our study emphasizes the importance of individualized approaches in addressing this condition, considering its varied etiologies and the potential for spontaneous resolution. Wait-and-See approach can be an interesting therapeutic alternative when hashitoxicosis is the suspected cause.

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EP1043

Radiation thyroiditis after radioactive iodine treatment

Hatice AKSU[1], Yaşar Aydoğmuş[1], Narin Nasiroğlu imga[1], Nazim Coşkun[2], Hüsniye Başer[3], Oya Topaloğlu[4], Reyhan Ersoy[3] & Bekir Çakir[3]
[1]Ankara City Hospital, Endocrinoloogy and Metabolism, Ankara, Turkey; [2]Ankara City Hospital, Nuclear Medicine, Ankara, Turkey; [3]Ankara Yildirim Beyazit University Faculty of Medicine, Endocrinoloogy and Metabolism, Ankara, Turkey; [4]Ankara Yildirim Beyazit University Faculty of Medicine, Ankara, Turkey

Radioactive iodine therapy (RAI) is a treatment method used to in cases of Graves' disease(GD), toxic multinodular guatr and solitary toxic nodüle and residual tissue after thyroidectomy or in the treatment of metastases capable of capturing iodine. The biological basis of the treatment is the inhibition of follicle cell functions. Side effects such as thyroid swelling, radiation thyroiditis and sialadenitis are rare. Radiation thyroiditis tends to occur within two weeks after RAI administration and is generally asymptomatic in most patients. Approximately % 1-5 of patients with GD develop radiation thyroiditis after RAI treatment. Radiation causes ınflammation that develops as a result of exposure of a large residual tissue to a high radiation dose may cause tenderness in the thyroid tissue or neck, erythema and edema, pain when swallowing, rarely airway obstruction, and in some patients, a thyrotoxic state. Symptoms generally begin 1-10 days after treatment. Pain and tenderness in the thyroid and neck area are mild and disappear within 3-7 days. There may be a temporary hyperthyroidism attack at this time. Mild symptoms are usually relieved with non-steroidal anti-inflammatory drugs. In more severe cases, corticosteroid treatment (30 mg/day prednisone) provides rapid relief of symptoms. In case of thyroid storm, symptoms can be controlled with corticosteroids, if severe adrenergic symptoms are accompanied by beta blockers and if necessary antithyroid drugs. Here we will present a case of radiation tyroditis developing after Graves Diseaes(GD). A 71-year-old patient with a diagnosis of Graves' disease was treated with 20 mcı radioactive iodine due to elevated liver function tests under antithyroid drug therapy. 1 week after radioactive iodine treatment, she was admitted to our outpatient clinic with complaints of pain in the throat and difficulty swallowing. Thyrotoxicosis was detected in the tests. Oral cavity looked natural and sensivity was detected in the neck area. No respiratory distress was detected. Newyl developed tracheal stenosis was detected on the cervical graphy. Color doppler pattern 3 and edema in the thyroid gland was detected on the ultrasonography. The patient 's complaıns were primarily evaluated as thyroiditis secondary to radıoactive iodine treatment. The patient was started on oral methylprednisolone sodıum succinate, non-steroidal anti-inflamatory and betablocker treatment. The patient's complaints regressed under treatment. In conclusion, radiation thyroiditis is a complication of RAI for the treatment of GD and may cause morbidity. Radiation thyroiditis should be suspected as the etiology of patients presenting with neck pain and difficulty swallowing immediately after RAI.

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EP1044

A spontaneous remission of Hashimoto's thyroiditis

Oumeyma Trimeche[1], Bilel Ben Amor[1], Ekram Hajji[1], Matiem Souissi[1], Ines Bayar[1], Sana Abid[1], Héla Marmouch[1], Hanene Sayadi[1] & Inès Khochteli[1]
[1]Fattouma Bourguiba University hospital, Monastir, Tunisia

Introduction
Hashimoto's thyroiditis (HT) is one of the most frequent endocrine diseases worldwide that is typically irreversible. Herein we report the case of a woman who had spontaneous remission of hypothyroidism while discussing the potential mechanisms underlying this unusual evolution.
Case report
T.C. is a 44-year-old woman with no familial history of thyroid diseases nor autoimmune conditions. She has no particular personal medical history. She consulted our Endocrinology department the first time in September 2021, with clinical signs suggestive of hypothyroidism such as asthenia, chronic constipation, myxedema and alopecia. Hormonal evaluation confirmed the diagnosis of primary hypothyroidism: elevated Thyroid stimulating hormone (TSH = 206 μui/ml) and low thyroxine (FT4 = 2.29 pmol/l). Thus, she was put on 100 μg per day of Levothyroxine. Her cervical echography showed hypotrophic gland with normal vascularization. Her anti thyroperoxidase antibodies were elevated 120 ui/ml (normal < 50) as well as her anti TSH receptor antibodies > 40 UI/l (normal < 1.8). She initially reported resolution of her symptoms. Shortly after, her TSH began to fall. As a result, her levothyroxine dose was diminished until completely stopping it after two years. On last check up, she was asymptomatic, had a TSH of 0.14 μui/ml and an FT4 of 10.3 pmol/l. Intriguingly, her anti TSH receptor became negative. Ultrasound was normal at last control.
Discussion
There are some hypotheses that can explain this intriguing phenomenon: cessation of medications susceptible of inducing hypothyroidism, high iodine exposure and disappearance of blocking anti TSH receptor antibodies, which in our case seems the most plausible cause.

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EP1064

Recurrence of papillary microcarcinoma after 7 years of surgical treatment

Tamar Shervashidze[1], Rusudan Kvanchakhadze[2], Irakli Phagava[1], Liana Jashi[3], Khatuna Chakvetadze[4] & Badri Gvadzabia[5]
[1]David Abuladze Georgian Italian Clinic, Endocrinology, Tbilisi, Georgia; [2]David Aghmashenebeli University of Georgia, Tbilisi, Georgia; [3]Batumi Shota Rustaveli State University, batumi, Georgia; [4]EVEX Kutaisi Emergency Referral Hospital, kutaisi, Georgia; [5]National Institute of Endocrinology, Tbilisi, Georgia

Background
Papillary microcarcinoma (PMC) of the thyroid is defined as papillary thyroid carcinoma (PTC) measuring ≤1 cm., Survival after surgery for papillary thyroid microcarcinoma is greater than 99%. The chances of a recurrence of thyroid cancer after surgery are between 2-4%.
Case Presentation
9 years old boy was consulted by an endocrinologist in 2012. 6-5-1 mm thyroid nodule revealed. Thyroid antibodies and thyroid hormones were in normal ranges. He was administered 100 mg of iodine supplementation. An ultrasound examination of the thyroid gland was performed once in 6 months. In 2016, the isoechoic nodule of 9 x 6 mm, with microcalcifications was determined. FNA was performed-papillary carcinoma was detected. A total thyroidectomy was planned. Histomorphological examination of the postoperative material confirmed the presence of papillary microcarcinoma Radioiodine therapy was not performed. Thyroglobulin level was within the desired range after surgery and annually <0.2 ng/ml 2016-2021. Thyroid hormone levels were maintained within the recommended target range of 0.5-2.0 ng/ml. In 2023 an increase in TG, anti-TG, and the presence of pretracheal lymph nodes with reduced echogenicity were detected. An aspiration biopsy with cytological examination of the lymph node was performed - a secondary lesion of papillary carcinoma. On June 9, 2023, the patient underwent reoperation and radioiodine therapy.
Conclusions
After total thyroidectomy, long-term follow-up was conducted for more than 5 years with positive results. Nevertheless, in the process of observation, a tendency of TG increase was revealed, not within the limits of the recommendations >1 ng/ml, which did not indicate the risk of disease recurrence. However, with additional studies conducted, tumor metastasis was discovered and excised in time

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EP1078

Deep cervical lymph node metastasis of thyroid cancer: a case report

Houas Jihene[1], Heyfa Belhadj-Miled[1], Monia Ghammam[1], El Ghali Wassim[2], Malika El Omri[1], Abir Meherzi[1], Mouna Bellakhdhar[1], Yosra Hasni El Abed[3], Wassim Kermani[1] & Mohamed Abdelkafi[1]
[1]Farhat Hached Hospital, ENT Department, Sousse, Tunisia; [2]Department of Anaesthesia, Sousse, Tunisia; [3]Department of Endocrinology, Sousse, Tunisia

Introduction
Follicular thyroid cancer is the second most common differentiated thyroid cancer and accounts for approximately 10–15% of all thyroid cancers. It tends to invade blood vessels and metastasise by haematogenous spread to distant sites, most commonly to the bones and lungs. The incidence of distant metastasis in follicular thyroid cancer has been reported as 6–20%. Metastases to the retropharyngeal lymph nodes are extremely rare. the aim of this work is to document a rare case of retropharyngeal metastasis from a follicular carcinoma of the thyroid and to describe its evolutionary characteristics.
Materials and Methods
We present the case of a patient who underwent surgery at our ENT department for a follicular carcinoma of the thyroid, with the discovery of a voluminous retropharyngeal metastasis during follow-up.
Observation
We report the case of a 60-year-old woman followed for thyroid goiter, clinically and biologically euthyroid. Ultrasound revealed a multinodular goiter without suggestive signs of malignancy. The patient underwent total thyroidectomy due to dysphagia. The final pathological examination confirmed a follicular carcinoma of the right lobe of the thyroid classified as T3NoM0. Additional radioactive iodine therapy was indicated. The course was marked by the appearance, six months later, of nodal metastases in the IIA and IIB chain with thrombosis of the right internal jugular vein. The patient underwent a right radical neck dissection. During follow-up, an increase in serum thyroglobulin levels was noted despite adequate radioiodine therapy. Clinical examination revealed no abnormalities. A cervical ultrasound returned normal results. A CT scan revealed a large right retropharyngeal mass measuring 4 cm, suggestive of retropharyngeal lymph node metastasis associated with a costal bone metastasis. The patient passed away one month later.
Conclusion
The incidence of distant metastasis after total thyroidectomy for thyroid cancer is between 7% and 23%. Although rare, retropharyngeal lymph node metastasis should be considered during the follow-up of thyroid carcinomas.

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EP1079

New case of papillary thyreoglossal cyst carcinoma, in the absence of clear guidelines, what should be do?

El Jadi Hamza[1] & Moustaghit Imane[2]
[1]Oued Eddahab Military, Endocrinology and Metabolic Diseases, Agadir, Morocco; [2]Oued Eddahab Military, Endocrinology and Metabolic Diseases, Agadir, Morocco

Thyroglossal tract cyst carcinoma (TTC) is a rare pathological situation, The challenge is mainly in the surgical management. We report a new case of papillary TTC in a 51 year old female patient, not suspected preoperatively and confirmed postoperatively by histological analysis of the resected specimen. The therapeutic strategy was completed by a total thyroidectomy with adjuvant treatment with radioactive iodine and hormone restraint therapy. The outcome was favorable after 7 years of follow-up. The incidence of TTC carcinoma is unknown, probably in the order of 1%. Since Brentano's first description in 1911, only about 300 cases have been published, mostly as case reports or small serie. The papillary type is the most common and is found in about 83% of cases. The other types are mixed papillary-vesicular carcinomas (8%), squamous cell carcinomas (6%), a few cases of Hûrthle cell, vesicular, anaplastic and squamous cell carcinomas. No cases of medullary carcinoma have been described. In the absence of clear guidelines, the management of TTC depends on the clinical situation and the experience of the treating team. TTC carcinoma is a rare entity with an overall good prognosis. Its management is still a matter of debate between those who are satisfied with excision of the cyst and others who opt for a more aggressive treatment. In all cases, it is necessary to stratify the risk of recurrence in order to identify the modalities of subsequent follow-up. With this work, we add a new observation of a rare carcinoma with the expectation that further studies will be done to standardize the therapeutic procedure and improve the prognosis.
Keywords: papillary carcinoma, thyroglossal tract cyst, thyroid surgery, iratherapy.
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EP1089

Specificities of papillary thyroid carcinoma in males

Neni Dezoumbe[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Ibn Rochd University Hospital, Endocrinology, Diabetology, Metabolic Diseases, and Nutrition, Casablanca, Morocco

Introduction
Thyroid cancers in males are rare forms characterized by their aggressiveness and frequent association with locoregional or distant metastases. Objective To describe the clinical and biological characteristics of papillary thyroid carcinomas in male subjects.
Materials and Methods
We conducted a descriptive cross-sectional study involving all male patients followed for papillary thyroid carcinoma at the endocrinology department of Ibn Rochd University Hospital in Casablanca from 1986 to 2023. Univariate statistical analysis was performed for all variables using Excel 2017.
Results
The male gender accounted for 45 patients, representing a prevalence of 4.4%. The mean age was 50 years, with a history of familial thyroid neoplasia in 6.6% of cases. The most common presenting complaint was multi-heteronodular goiter in 45% of cases. The average tumor size was (0.2–6.2 cm). All patients underwent total thyroidectomy, with lymph node dissection performed in 20% of cases. Radioiodine therapy was indicated in 59% of patients. Papillary carcinoma was the histological type in all cases, classified as high risk in 51.4% of cases. Follow-up revealed 25% locoregional recurrences and distant metastasis (pulmonary) in 5% of patients. Prognosis was significantly correlated with tumor size and locoregional or distant metastases at the time of diagnosis.
Discussion
Thyroid cancers in male subjects are rare and aggressive forms. Their major prognostic impact influences subsequent management, as reported in the literature.

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EP1111

Toxic adenoma in a patient with hashimoto's thyroiditis. a case report and review of the literature

Marjeta Kermaj[1], Ana Selaj[1], Violeta Hoxha[1], Klodiana Poshi[1], Dorina Ylli[1] & Agron Ylli[1]
[1]UHC " Mother Tereza", Endocrinology, Tirana, Albania

Introduction
Thyroid nodules are common in Hashimoto's Thyroiditis (HT) patients. They are usually hypo-functioning or "cold" areas on the scan. Presentation as a functioning "nodule" is extremely unusual. Warner reported the first case of Hashimoto's thyroiditis and hot nodule in 1971. This rare condition has been previously reported in a few cases too. We present a 55-year-old woman with toxic adenoma and Hashimoto's Thyroiditis with local compressive signs.
Case report
The patient presents in outpatient consultations with difficulty in breathing and swallowing for 3 months and an enlarged thyroid gland. Physical examination: Mild signs of hyperthyroidism. Enlarged thyroid gland. Laboratory tests: TSH 0.019 (0.3-4.5) and Ft3, Ft4 twice the normal values. Anti TPO 208.14 IU/ml (<5.5) Calcitonin = 0.50 (<6.4), Anti TG = 218.5 (<115). WBC = 7.1 k/ul (4 - 10.5), Neutrophils = 3.7 k/ul (1.6-7.56), ALT= 28 U/l (<55), AST= 21 U/l (5-34). Thyroid ultrasonography: The entire left lobe had increased dimensions, occupied by a nodule with cystic degeneration inside with dimensions over 60 mm, that displaces the trachea to the right. The right lobe was reduced in size and had bilateral reactive laterocervical lymph nodes. Thyroid Schinti scan with tc99m showed a hot nodule occupying the entire left lobe of the thyroid with a total uptake of 4.6% (0.35-3.65), with inhibition of the right lobe. Ct scan neck with contrast iv, showed: The left lobe of the thyroid with increased dimensions, transformed into a nodular structure with necrotic degeneration inside, and dimensions of 66×62 mm, extending to the jugular fossa with displacement of the trachea to the right and compressing it. It was concluded that the diagnosis was toxic Adenoma with local compressive signs in a patient with Hashimoto's Thyroiditis. Under treatment with methimazole 1 mg 2×1 tablets for 6 weeks, TSH, Ft4, and Ft3 were within normal range. Because of compressive signs, the patient performed a total thyroidectomy and the biopsy showed: chronic lymphocytic thyroiditis.
Conclusion
Our case confirms that Toxic adenoma can be associated with Hashimoto's Thyroiditis. Schinti scans with Tc99m help determine the function of nodules and the decision for definitive treatment.

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EP1162

Intrathyroidal CMT with high level of calcitonin

Miruna-Alicia Ungureanu[1], Ramona Dobre[1, 2], Andreea Manole[1], Anca Andrei[1], Iulia-Florentina Burcea[1, 2], Dan Octavian Alexandrescu[1] & Catalina Poiana[1, 2]
[1]National Institute of Endocrinology "C.I. Parhon"; [2]University of Medicine and Pharmacy "Carol Davila"

Introduction
Medullary thyroid carcinoma (MTC) is defined as a rare neuroendocrine tumor originated from the parafollicular C cells of the thyroid, noted for the ability of secreting calcitonin and other peptides. MTC poses a high risk of mortality if left untreated as the tumoral cells can invade nearby tissues, lymph nodes, lymphatic or blood vessels and, ultimately, other organs. Calcitonin is key in the evaluation and treatment protocol as its basal serum levels tend to be proportional with the tumor size and the extent of metastasis. Thus, targeted surgical treatment holds an important role in the therapeutic management of this disease. We present the case of a patient with low suspicion of MTC but with high suspicion of distant metastatic disease due to increased levels of serum calcitonin.
Clinical case
A 34 years old male patient, with a previous history of a 'cold' thyroid nodule in the left thyroid lobe and a serum calcitonin level of 1025 pg/ml with no significant clinical signs discovered during examination. Thyroid ultrasound described a solitary, hypoechoic, irregular macronodule in the left thyroid lobe with no suspicious lymph nodes. The family history was negative for MTC or MEN-related diseases. Fine needle aspiration biopsy confirmed the diagnosis and calcitonin wash-out level was higher than 200000 pg/ml, serum CEA levels of 56.56 ng/ml. Screening for primary hyperparathyroidism, pheochromocytoma and ectopic Cushing's syndrome was negative. Germline RET mutation is awaited. The high level of calcitonin imposed additional imaging like cervical, thorax and abdominal computed tomography which revealed no evidence of local invasion, secondary lesions. The therapeutic decision was based on calcitonin levels and involved complete removal of the thyroid along with extensive prophylactic bilateral cervical lymph node dissection (central and lateral compartments). The results of the histopathological exam confirmed the diagnosis of CMT in the thyroid nodule but no affected lymph nodes. Seven days after surgery, the patients serum calcitonin levels dropped significantly to 4.35 pg/ml, with the CEA levels lowered to 29.13 pmol/l.
Conclusion
An optimistic prognosis of a patient with MTC is usually rare. Although an agreement on the subject of prophylactic lymph node dissections in the absence of secondary lesions does not exist, ultimately, the only chance of increasing the survival rate remains surgery. In this particular case with very high levels of calcitonin of an intrathyroidal CMT, a rapidly declining level of calcitonin after one-week post-surgery offers early evidence of remission.

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EP1179

A foreign body of the thyroid gland

Yuriy Aleksandrov[1] & Vasiliy Semikov[2]
[1]Yaroslavl State Medical University, Surgery, Yaroslavl, Russian Federation; [2]I.M. Sechenov First Moscow State Medical University, Surgery, Moscow, Russian Federation

Patient R., 66 years old. Diagnosis: A foreign body of the thyroid gland. Anamnesis: On 01.12.2023, I ate fish. After swallowing a piece of fish, I felt discomfort in the neck area, a feeling of a foreign body appeared. On 02.12.2023, she turned to an otolaryngologist. During laryngoscopy, it was found that the fish bone stuck into the wall of the esophagus at the level of the larynx. During endoscopic removal, the bone broke off. It was possible to extract a fragment up to 2 cm long. The patient was allowed to go home. The patient had a feeling of a foreign body. The patient performed a CT scan of the neck organs. It was found that a foreign body passed through the wall of the esophagus into the right lobe of the thyroid gland. The length of the formation is 25 mm, the width is 2 mm. The patient was hospitalized in the thoracic department of the regional clinic. In FGDS, damage to the esophageal mucosa has not been established, and no foreign body has been detected. CT scan did not reveal signs of mediastinitis. On 13.12.2023, the patient was discharged with recommendations to contact a specialized center. Treatment at a specialized center on 12/18/2023: the patient's condition is satisfactory, laboratory parameters are normal. A control ultrasound revealed an inflammatory reaction around a foreign body of the thyroid gland with the threat of purulent strumitis and mediastinitis. The patient is hospitalized. A control ultrasound revealed a pronounced migration of a foreign body (up to 1 mm) towards the vascular bundle of the neck on the right. The distance from the acute end of the foreign body to the carotid artery on the right was 2 mm. On 12/19/2023, an operation was performed: removal of a foreign body of the thyroid gland and soft tissues of the neck. During the revision, it was found that the foreign body migrated to soft tissues, while there was a pronounced scarring process involving the thyroid gland and neck muscles associated with tissue damage by the sharp end of the foreign body and local bleeding. Intraoperative ultrasound was used in the search for a foreign body. The foreign body (fish bone 25 mm) was completely removed, and the patient received antibiotics in the postoperative period. The patient was discharged from the hospital for 5 days in a satisfactory condition.

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EP1180

Heterogeneous clinical outcomes in two separate cases of advanced differentiated thyroid cancers

Massimiliano Mazza[1], Chiara Parazzoli[1], Vittoria Favero[1, 2], Carioni Emanuela[1], Alberto Falchetti[1], Erika Grossrubatscher[1], Bendetta Zampetti[1], Iacopo Chiodini[1, 2] & Paolo Dalino Ciaramella[1]
[1]Ospedale Niguarda Ca' Granda, Milan (Italy), Endocrinology Unit; [2]Department of Biotechnology and Translational Medicine, University of Milan, Milan (Italy)

Background
Among differentiated thyroid cancers, follicular thyroid carcinoma (FTC) is the second most prevalent, representing 10-15% of cases. Histopathological features, tumour size, multifocality, presence of lymphnode metastasis at diagnosis are the most impacting features affecting clinical outcome. Tumour microenvironment (TME) may have an important ancillary role for disease progression. We present two cases of FTC with biochemical and structural persistence of disease, with different clinical outcomes and timing of disease progression.
Case report
Case 1 In November 2008, an 81-year-old male underwent total thyroidectomy for a FTC measuring 6 cm with capsular invasion. A 100 mCi radioactive iodine therapy (RAI) was administered. Whole-body scintigraphy (WBS) revealed radioiodine hyperaccumulations in both lung fields, leading to multiple RAI sessions (cumulative dose of 700 mCi). In 2014, after a fourth RAI, WBS highlighted small focal hyperaccumulations in the left lung field. In 2015 at

SPECT, a small hyperaccumulation projecting to the liver was observed. In 2021, computed tomography (CT), showed the growth of the hepatic lesion, which was surgically removed. Six months later, multiple subpleural pulmonary nodules were revealed at CT. The patient refused tyrosine kinase inhibitor treatment. Over a 14-year follow-up period, the patient enjoyed a satisfactory quality of life until June 2023 when an uncontrolled disease progression, with bone and cerebral metastasis, led to a fatal outcome. Case 2 In March 2017, a 70-year-old female underwent total thyroidectomy, diagnosed at biopsy as a Hurthle cell carcinoma, followed by 100mCi RAI treatment. In 2018 a thyroid ultrasound identified a cervical anechoic nodule, negative on WBS. Thyroglobulin levels exhibited a consistent increase. A thorax CT scan revealed pulmonary nodules, inactive at WBS. At FDG-PET scan hypercaptation was observable in thyroidal (compatible with residual disease), paratracheal and paraesofageal region. Patient started lenvatinib at low-dose due to poor compliance, systemic adverse effects and low body weight (46 kg). Over a four-year follow-up period, the patient exhibited an unexpected rapid disease progression with a fatal outcome (pulmonary, hepatic and pancreatic metastases).
Conclusions
Patients with FTC may have indolent persistence of disease for several years with an unexpected rapid progression of disease, independent from the histotype and disease extension at diagnosis. These observations suggest a possible role of the TME in influencing the disease outcomes. Future research on the TME complex interactions and its effects on disease outcome, is warranted. This would allow for a more nuanced approach, potentially modulating the TME and improve treatment outcomes.

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EP1181

Debulking surgery in locally advanced papillary thyroid carcinoma

Laura García García[1], M. Isabel Gutiérrez Giner[1], Ángel Luis Sánchez Álvarez[1], Ana Tejera Hernández[1], Jorge Loro Pérez[1] & Magel Fernández Alfonso[1]
[1]Complejo Hospitalario Universitario Insular Materno Infantil, General and Digestive Surgery, Las Palmas de Gran Canaria, Spain

Introduction
Thyroid cancer is the most common endocrine neoplasia, with papillary thyroid carcinoma (PTC) being the subtype that represents 75 - 80% of cases; with an indolent character and a 10-year survival rate greater than 90%. Vascular infiltration is very rare in this type of tumors, which usually spread through the lymphatic route. The treatment of choice continues to be surgery with adjuvant radioiodine based on the risk stratification of recurrence and radiotherapy in very selected cases.
Case Presentation
We present the case of a 78-year-old male patient with a grade III goiter at the expense of the left thyroid lobe with an intrathoracic component and Bethesda IV FNAC, anticoagulated for left jugular vein thrombosis. Presented in a multidisciplinary committee, a total thyroidectomy was decided. During surgery, a 10 cm locally advanced tumor mass was observed that infiltrated the esophagus and was closely adhered to the internal jugular vein. During the process, there is a loss of signal from the recurrent laryngeal nerve (RLN), so the total thyroidectomy is not completed while awaiting the definitive pathological result. The final pathology confirmed infiltrative follicular variant papillary carcinoma with extrathyroidal extension and vascular and lymphatic infiltration (pT3b). Subsequent surgery involved a totalizing right lobectomy and adjuvant 1131 treatment. Follow-up showed increased thyroglobulin, cervical remnants with a left internal jugular vein tumor thrombus, and suspicious lymph nodes in the left compartment ll. An exploratory cervicotomy revealed a large tumor thrombus affecting the entire cervical extension of the left internal jugular vein, requiring resection with spinal nerve preservation. Intraoperatively, a tumor mass infiltrating the pharyngoesophageal junction was observed, necessitating debulking surgery, leaving a small tumor due to the risk of pharyngeal fistula, excision of pathological lymphadenopathy at the level of compartment II. Subsequently, the tumor bed was marked with clips for adjuvant radiotherapy.
Discussion
Surgery remains crucial in managing recurrent thyroid cases unresponsive to radioactive iodine treatment. Locally advanced thyroid neoplasms are rare, requiring individualized management in clinical committees and specialized centers with experienced endocrine surgeons.

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EP1182

Clinical progression and differential diagnosis of an uncommon delayed-onset thyroid eye disease in a patient with graves' disease: a case report

Abdel Mouhaymen MISSAOUI[1], Nadia Charfi[1], Siddiqa Soomauroo[1], Souhir Maalej[1], Rihab Khochtali[1], Mohamed Abid[1] & Nabila Rekik[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology, Sfax

Introduction
Thyroid eye disease (TED) is the major extra-thyroidal manifestation of Graves' disease (GD). The delayed onset of TED after hyperthyroidism resolution and the decline in TRAb levels is a rare occurrence, necessitating the exclusion of other underlying orbital inflammatory diseases.
Case Report
A 59-year-old non-smoking female patient presented with thyrotoxicosis symptoms (fatigue, palpitations, resting tremors) persisting for three months, along with a homogeneous elastic goiter and no orbital abnormalities. Laboratory investigations revealed primary hyperthyroidism (TSH < 0.01 mIU/l; FT4 = 38.7 pmol/l, 1.8xULN), with positive TRAb at 9 IU/ml (3xULN), strongly indicating GD. The patient was treated with methimazole 7.5 mg/day for 11 months, resulting in clinical improvement, normalization of thyroid function, and a decrease in TRAb levels to 3.59 IU/ml. In the 12th month of treatment, bilateral exophthalmos, eyelid retraction, and bilateral diplopia, predominantly affecting the left eye, emerged. The orbitopathy was inactive (activity score 2/7) but severe. Given the favorable clinical, biochemical, and serological evolution of GD, and the absence of smoking, we aimed to exclude underlying orbital inflammatory disease. Immunological investigations ruled out IgG4-related disease and granulomatosis with polyangiitis. Orbital MRI revealed bilateral fusiform swelling with abnormal signal and intense enhancement of the extraocular muscles. Inflammation was primarily located in the left inferior rectus muscle. The insertions of the extraocular muscles on the eyeballs were spared, ruling out idiopathic orbital myositis (IOM). Delayed-onset TED was confirmed, and the patient continued methimazole treatment with a high-dose corticosteroid regimen (6 weekly boluses of 750 mg of methylprednisolone), leading to the resolution of the patient's diplopia.
Discussion
TED is the most common orbital inflammatory condition. Its delayed onset is rare, occurring in 7% of non-smokers and 20% of smoking individuals with GD. Its primary differential diagnosis is IOM. The distinctive features of TED include the presence of thyroid dysfunction, positive TRAb, painless bilateral involvement, and preservation of extraocular muscle insertions on the eyeballs.
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EP1183

Iodine-induced hyperthyroidism after long-term use of povidone-iodine: a report of two cases

Laura Stirane[1, 2, 3], Viktorija Preobrazenska[1, 2], Natalija Fokina[2] & Lauma Jaunozola[2]
[1]University of Latvia; [2]Pauls Stradiņš Clinical University Hospital, Department of Endocrinology, Riga, Latvia; [3]Rezekne Regional Hospital

A 60–year-old male and 24–year-old female presented to the endocrinologist with hyperthyroidism of unknown cause. A 60-year-old male was admitted to the Department of Endocrinology with fatigue, dyspnoea, increased sweating, and anxiety. Hyperthyroidism was diagnosed with TSH < 0.0008 mIU/l [reference range: 0.3500 – 4.9400], FT4 – 4.03 ng/dl [reference range: 0.89 – 1.76] and FT3 – 12.96 [reference range: 2.3-4.2]. The patient had a history of congenital heart disease, myocardial infarction, dilated cardiomyopathy, Cardiac Resynchronisation Therapy with Defibrillator device implantation, aortic valve replacement, and because of progression of chronic heart failure (NYHA class IV) the HeartMate 3 Left Ventricular Assist Device (LVAD) implantation two years ago. A 24-year-old female visited the endocrinologist in an Outpatient clinic. She complained about nausea and vomiting almost every day, fatigue, and hand tremor. The blood test showed hyperthyroidism: TSH < 0.008 mIU/l, FT4 – 4.4 ng/dl and FT3 – 12.49 pg/ml . Since the age of 3, the patient has been diagnosed with Wolff–Parkinson–White syndrome and left ventricular hypertrophy, later repeated episodes of ventricular and supraventricular arrhythmia, including radio-frequency ablation performed at the age of 14. Subsequently Danon disease

was confirmed by genetic testing. At the age of 22 - a cardioverter-defibrillator was implanted due to ventricular tachycardia and because of progression of chronic heart disease (NYHA class IV) the Heart Mate3 LVAD was implanted. Antithyroid antibodies (TSH receptor antibodies, anti-thyroid peroxidase antibodies) were negative in both patients. They had no personal or family history of thyroid disease. Both patients had no exposure to iodine-containing contrast media, Amiodarone, or iodine supplementation over the past two years. Thyroid ultrasound findings were similar for both - mild diffuse changes in the thyroid gland that could be consistent with chronic autoimmune thyroiditis. Thiamazole 30 mg daily was initiated without improvement. The female patient was evaluated to exclude struma ovarii. Possible iodine sources were reviewed again, and it was determined that Povidone-iodine solution was used for the Heart Mate3 LVAD entry point disinfection daily. Povidone-iodine was discontinued for both patients, and Thiamazole therapy 30 mg daily was continued for one more month and then decreased to 10 mg daily. Following this, both patients felt better, their symptoms of hyperthyroidism settled. A gradual improvement and normalization of thyroid hormone tests was observed within two months and Thiamazole was discontinued. We hypothesize that using Povidone-iodine long-term could cause iodine overdose and hyperthyroidism.

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EP1184

Polyglandular autoimmune syndrome

Mariam Khachatryan[1]
[1]Dilanyan Clinic, Endocrinology, Moscow, Russian Federation

Polyglandular autoimmune syndromes (PAS) are rare group of diseases, which characterised by association of two or more autoimmune endocrine disorders in a single patient. Often PAS is combined with autoimmune damage of non-endocrine organs. Type 3 PAS includes combination of autoimmune thyroid disease and other autoimmune conditions. The adrenal cortex is not involved. This type of PAS typically affects middle aged women. The cause is still unclear. In this case study I describe a patient with Hashimoto's thyroiditis, latent autoimmune diabetes in adults, vitiligo, miasthenia gravis. Case study: A 68-year old female presented to the endocrinology outpatient department with complains of high blood glucose level, dropping of one eyelid, weakness in the hands in the last 3 month. She also noticed that antidiabetic drugs were not effective about 2-3 month. The patient had been diagnosed with Hashimoto's thyroiditis about 5 years before, and with diabetes mellitus type 2 about 1 year before. It was suggested as a latent autoimmune diabetes in adults and initiated insulin therapy. Laboratory tests showed high level of acetylcholine receptor antibody, anti-insulin antibody, GADA, IAA, ICA. So patient had diagnosed with PAS type 3. Treatment of PAS type 3 includes lifelong hormone replacement of any glandular failure. It is very important that patients with PAS type 3 are monitored closely to detect any glandular problems early.

Keywords: polyglandular autoimmune syndrome, Hashimoto's thyroiditis, miasthenia gravis, latent autoimmune diabetes in adults.

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EP1194

Thyroid surgery under local anesthesia in a selected group of patients our experience

Md Safi Ullah[1]
[1]Noakhali, Otolaryngology and HNS, Noakhali, Bangladesh

Objective

To find out the safety and fusibility of Thyroid surgery in a selected group of patients under local anesthesia. The aim of the study was to share our experience in case of home and total thyroidectomy in ENT foundation hospital and different clinics of Dhaka, Bangladesh.

Case Study: Materials and Methods

All the patient was admitted to the hospital with clinically significant goiter selected for surgical treatment (2%) xylocaine with adrenaline was used for infiltration anesthesia. Before the operation, the patient had received 1 mg per kg body weight intravenous pethidine slowly Diazepam 1 mg iv. In case of need in a selected group of patients iv ketorolac is sometimes needed.

Result

Haeme thyroidectomy performs there is no remarkable complication (Intra and post-operative) Except 3 cases (three patients postoperative scar two case Reactionary Hemorrhage mean duration of procedure is about 90 minutes The follow-up medical stay was three days. All the patients were in good general condition on the day of discharge from the hospital.

Conclusion

Surgery for thyroid swelling in a selected group of patients may be an alternative where General Anesthesia is not available and in patients contraindicated for medical reasons.

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EP1207

Papillary thyroid carinoma in children: features and management

Ahmed Boukhalfa[1], Salma El hilali[1], Sana Rafi[1], Ghizlane El Mghari[1] & Nawal El Ansari[1]
[1]Mohamed VI University Hospital Center, Marrakech, Morocco, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Introduction

Differentiated thyroid carcinoma is the most common pediatric endocrine malignancy (0.5–3% of all childhood malignancies) with papillary thyroid carcinoma (PTC) being the most common type. Children have higher rates of cervical lymph node metastases, distant metastasis and recurrence. We report the case of a patient who presented a thyroid nodule whose exploration revealed PTC, to illustrate clinical, ultrasonographic and therapeutic features.

Clinical Case

Nine years-old patient, with no personal history, admitted for thyroid nodule whose evolution dated back 2 years with, on current ultrasound, a right lobar nodule, 28×17 mm (initially 17×17), oval, isoechoic, heterogeneous with multiple scattered micro-calcifications, mixed vascularization classified Eu-tirads 4 with jugulo-carotid and sub-mandibular nodes of sub-centimetric size. Clinically, no signs of dysthyroidism and was hemodynamically and respiratorily stable. Biological thyroidien tests was normal. A thyroid cytopunction revealed a follicular nodule with epithelial atypia of undetermined significance (category III). The child underwent right lobo-isthmectomy with extemporaneous sampling revealing papillary carcinoma, totalization performed with bilateral central lymph node curage In the post-operative period, the child began to experience clincal signs of hypocalcemia; peri-labial tingling, paresthesias, needles with a positive chvosteak sign in the presence of corrected calcemia at 78 mg/l. Intravenous calcium replacement was initiated, followed by oral replacement. Substitutive and inhibitory treatment has been initiated and will be adjusted according to the risk of recurrence. Patient scheduled for iratherapy 131-I* in one month.

Discussion

Children with PTC have shown a significantly higher local and regional recurrence over time when they undergone a loboisthmectomy compared to those who underwent total thyroidectomy. the high rate of multifocality (42–65%) reported in children with differentiated thyroid cancers have influenced others to recommend total thyroidectomy for all children with disease limited to the thyroid (1, 2). In view of the higher rate of cervical metastasis among children, ATA recommends prophylactic central compartment neck dissection (CCND) (1). Higher rates of post-thyroidectomy hypocalcemia among children when compared to adults is well recognized (3). CCND, extrathyroidal extension and the presence of nodal disease in the neck are the reported risk factors. Recurrence rate was significantly reduced when RAI therapy was performed.

Conclusion

PTC in children is characterized by the frequency of cervical and distant lymph node metastases and recurrences after treatment compared with adults, which justifies the use of total thyroid surgery with lymph node dissection followed by iratherapy, thus guaranteeing a better prognosis.

Keywords: PTC, chidren, metastases, total thyroidectomy, iratherapy.

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EP1209

Effect of central obesity indices on ultrasound and fine needle aspiration features of thyroid nodule

Bilal Natiq Nuaman[1, 2], Sanad Asaad Abd Al -Hussein[3], Mohammed Sami Turki[4] & Mahmood Shakir Khudhair[2]
[1]AL-Iraqia University, College of Medicine; [2]Baghdad, Baghdad, Iraq; [3]Najaf, Najaf, Iraq; [4]Hillah, Hillah, Iraq

Background
Obesity and thyroid neoplasia are common endocrinological diseases in the world and Iraq, and risk factors of this cancer are usually unmodifiable but there are some evidences that obesity is associated with increasing prevalence of many malignancies due to proposed pathophysiological mechanisms. Numerous research assessed the connections between thyroid disease outcomes and obesity, but only a small number took TBSRTC into account. The relationship between obesity and TIRADS is briefly discussed in a few published papers, while the great majority of studies investigating this relationship depend on BMI. To the best of my knowledge, no studies have examined the impact of central obesity on thyroid ultrasonography and FNA results in Iraq. Therefore, this study examined the relationship between thyroid FNA results in Iraqi patients and central obesity indicators as waist circumference and waist-height ratio.
Aim of the study
To Examine the effects of indexes of central obesity on cytological abnormalities of thyroid nodule FNA and risk of malignancy. To Assess the effectiveness of central obesity indices in predicting malignant TNs.
Patients and Methods
Patients with suspicious thyroid nodules who performed FNA at the cytology unit of AL Imamain AL-Kadhimain Medical City between October 2022 and April 2023 were considered for this cross-sectional research. who indicated for FNA according to ACR-TIRADS Criteria (grades TR3-TR5) and had Biochemical 'euthyroidism'
Results
There was a significant association between TBSRTC categories and WtC and WtHR categories ($P<0.0001$). But, there was a no significant association between Bethesda classes (benign vs non-benign) and WtC classes (normal vs central obesity) ($P=0.071$), and there was no age or gender difference between benign and non-benign classes, P 0.502, 0.121, respectively. The efficacy of central obesity indices in predicting malignant TNs was assessed using ROC curve analysis, which revealed that the sensitivity, specificity, and AUC of WtHR at a cutoff value of 0.61 were (66.7%, 64.2%, 0.714; respectively), while those for WtC in females were (82.4%, 68.1%, 0.767; respectively) at a cutoff value of 99 cm, and those for WtC in males were (75.0%, 66.7%, 0.646; respectively) at a cutoff value of 105 cm. The sensitivity and specificity of WtHR alone increased to 76.2% and 66% when WtHR and WtC were combined to assess the risk of malignancy.
Conclusion
The TIRADS and BETHSDA categories of TNs are highly correlated with central adiposity indices, particularly in the elderly.

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EP1219

Difficulties in the management of basedow's disease in children: a case study

Rahal Amel[1]
[1]bologhine hospital, endocrinology, algiers, Algeria

Introduction
Graves' disease is a rare and severe condition, affecting mainly younger children. Its appropriate management in children remains a subject of controversy in pediatric endocrinology, and the optimal duration of medical treatment to induce remission of the disease, as well as the indications for alternative therapies, remain to be defined.
Observation
This is a 15-year-old child who presented at the age of 13 years and 10 months with typical clinical signs of Graves' disease associated with exophthalmia. Clinical and paraclinical data led to the diagnosis of Graves' disease. Follow-up was difficult: the patient was noncompliant and took his treatment irregularly. Hyperthyroidism induce: osteopenia and disturbed liver function; exophthalmias without inflammation. Because of non-compliance of treatment, we opt for total thyroidectomy.
Conclusion
Positive diagnosis of Graves' disease in children is often easy, but poses difficulties in management. The well-codified medical treatment is unfortunately often very poorly accepted in children, making the duration of treatment long and often imposing radical treatment in these situations.

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EP1220

Euthyroid graves' orbitopathy

Nino Turashvili[1]
[1]High Technology Medical Centre, University Clinic, Tbilisi, Georgia

Background and aims
Graves's disease is associated with specific eye signs that is called as Graves'orbitopathy or ophthalmopathy (GO). GO usually occurs with hyperthyroidism. However it can be sometimes develop several years before the hyperthyroidism. The aim of this presentation is to describe the clinical case of a 48-year-old female patient with euthyroid Graves' orbitopathy.
Case report
A 48-year old woman presented to the clinic with a few weeks history of exophthalmos. She did not report history of thyroid disease. She was not taking any medication and was not a smoker. Her TSH and FT4 - within normal reference ranges: TSH- 1.1 (*n* 0.27-4.2 mIU/l), FT4-1.2 (*n* 0.93-1.7 ng/dl). The level of anti-TSHR was elevated: Anti-TSHR-1.94 (n <1.5 U/l). Ultrasonographically, the volume of the thyroid gland was normal. She was referred to an ophthalmologist. A computed tomography (CT) scan of the orbits showed typical findings of GO. Local therapy measures (artificial tears) and supplementation of selenium was advised for mild case of GO. Currently, the patient is on regular follow-up. She still remains euthyroid.
Conclusion
Graves orbitopathy (GO) usually occurs with hyperthyroidism. However, the patient can sometimes present without thyroid dysfunction in which case it is called euthyroid Graves' orbitopathy.

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EP1222

Coexistence of primary hyperparathyroidism and thyroid papillary carcinoma: about two cases

Gorgi Khaoula[1], Lamya Echchad[1], Cheibatta Zakaria[1], Rifai Kaoutar[1], Iraqi Hinde[1] & Gharbi Mohamed El Hassan[1]
[1]Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Primary hyperparathyroidism represents a commonly encountered endocrine disorder characterized by the dysregulated secretion of parathyroid hormone (PTH), often associated with a parathyroid adenoma. The simultaneous occurrence of primary hyperparathyroidism with non-medullary thyroid carcinoma is infrequent. Our cases bring attention to this atypical connection, emphasizing the unique nature of this rare association.
Cases
In Case 1, a 63-year-old female patient, presenting a history of recurrent bilateral renal lithiasis, was admitted for the management of primary hyperparathyroidism. The localization workup favored a left inferior parathyroid nodule associated with a multiheteronodular goiter classified as Eutirads 5. Subsequent intervention included left lower parathyroidectomy combined with total thyroidectomy. Anatomopathological examination revealed a parathyroid adenoma and identified a thyroid papillary microcarcinoma measuring 0.6 x 0.7 mm Case 2 involves a 66-year-old female patient with chronic renal failure at the dialysis stage, concurrently treated for primary hyperparathyroidism. The localization workup revealed a right parathyroid nodule alongside suspicious multiheteronodular nodules classified as Eutirads 4. The patient underwent total thyroidectomy associated with right parathyroidectomy. Anatomopathological study confirmed a parathyroid adenoma and disclosed a thyroid papillary carcinoma classified as PT1bNxMx.
Discussion & Conclusion
The co-occurrence of non-medullary thyroid carcinoma and hyperparathyroidism is considered rare, and the underlying mechanisms of this association remain inadequately understood. A potential hypothesis suggests a connection rooted in embryological origins and shared genetic factors, possibly exacerbated by elevated parathyroid hormone levels, diminished vitamin D levels, and hypercalcemia, resulting in heightened levels of angiogenic growth factors. While this association is infrequent, it should not be disregarded during the preoperative phase. A thorough acknowledgment of this dual pathology is crucial for ensuring optimal management of both conditions

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Late Breaking

EP1226

Assessment of sarcopenia in patients with diabetes mellitus, considering body composition

Elena Makhlina[1], Yana Navmenova[1], Oksana Kononova[1] & Tatiana Mohort[2]
[1]Gomel State Medical University, Chairs Internal Medicine No. 1 with courses in endocrinology and hematology, Gomel, Belarus; [2]Minsk, Endocrinology, Minsk, Belarus

Objective
To assess the features of the manifestation of sarcopenia (SP) in patients with diabetes mellitus (DM), taking into account the body composition.
Materials and study methods
The study included 87 patients with DM (29 men - 33% and 58 women - 67%). The average age of patients was 41.59 ± 11.84 years and duration of diabetes was 12.51 ± 6.39 years. The study included anthropometric measurements: mass body index (BMI), waist circumference (WC), shin circumference (SC). Muscle strength (MS) was determined using hand dynamometry, and muscle function (MF) was assessed using a 4-meter walking speed test. Taking into account WC, patients were divided into 2 groups: the first group ($n=45$) WC less than 80 cm for women and less than 94 cm for men and the second group ($n=42$) with WC exceeding these target parameters taking into account gender. Statistical processing of the data array was performed using the statistical program «Statistica 10.0» (StatSoft, GS35F-5899H). The level $P<0.05$ is considered as a criterion for the statistical confidence of the results.
Study results and discussion
When assessing SP parameters in patients with DM, the groups differed significantly in muscle mass (MM) assessed by SC (SC first group 35.00 [34.00; 36.00]cm, second group 38.00 [37.00; 39.00] cm) and MF (first group 4.00 [4.00; 4.00] points, second group 3.00 [3.00; 4.00] points) $P<0.05$. There were no significant differences in MS between the groups (first group 27.27 [20.50; 37.00] kg, second group 21.00 [18.00; 31.50] kg) $P>0.05$. There was a decrease in MM in 14% of patients in the first group and in 8% of patients in the second group. A decrease in MF prevailed in patients in the second group (62%), while in the first group a decrease in MF was not noted. The decrease in MS prevailed in patients in the second group (first group – 29%, second group – 46% of patients) $P<0.05$.
Conclusions
Decreased MS (46% of patients) in patients with DM, which determines the probability of SP, and decreased MF (62% of patients) were noted in patients with WC and BMI exceeding the target values, and decreased MM prevailed in patients with WC and BMI corresponding to the target normal values.

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EP1227

Patient perception of unmet needs for multiple endocrine neoplasia (MEN) in germany

Rosemarie Schubert[1,2], Petra Bruegmann[1,2], Jo Grey[2,3], Johan de Graaf[4], Juliet Fleischer[5], Helga Schmelzer[1], Philipp Drewitz[2] & Ludwig Schaaf[2,6]
[1]Netzwerk Hypophysen - und Nebennierenerkrankungen e.V., Fürth, Germany; [2]European MEN Alliance e.V., München, Germany; [3]The Association for Multiple Endocrine Neoplasia Disorders (AMEND), Tonbridge, Kent, United Kingdom; [4]Nederlandse Hypofyse Stichting, Nijkerk, Netherlands; [5]Ludwig-Maximilians-Universität München, Institut für Statistik, München, Germany; [6]München Klinik Schwabing, München

The German Network for Pituitary and Adrenal Disorders (Netzwerk Hypophysen- und Nebennierenerkrankungen e.V.) conducted a nationwide survey on unmet needs of patients with multiple endocrine neoplasia (MEN) in Germany. The study aimed to identify unmet needs in patient care and quality of life, as well as potential areas for improvement.
Methods
The survey was based on a questionnaire developed by the European MEN Alliance (EMENA) and was distributed by the German Patients' Advocacy Group using the European Commission's EU Survey platform among group members, physicians, and social media. A total of 73 responses were analysed.
Results
Of the responses analysed, 23% ($n=17$) were from patients or their parents and carers aged 39 years or younger, and 77% ($n=56$) were from those aged 40 years or older, of whom 34% were male. 54 cases of MEN1, 10 cases of MEN2A, 6 cases of MEN2B, and 3 cases of MEN4 were included. Just under 50% of all cases were managed by a multidisciplinary team and were not aware of reference centres. The time to diagnosis is rated as too long (30%), psychological help is missing (40%). Approximately one-third of the participants indicate their GP's knowledge of their disease as poor. More than half of the participants rate the communication among the physicians as suboptimal. The involvement of endocrine nurses is not well recognized and is unknown to many (57%). Unmet needs according to patients include biomarkers to predict new tumours or recurrence (28%), more clinical trials (20%), digital tools for quick screening results (18%), faster tests and scans, and self-monitoring of hormones in the blood. It is noteworthy that 60% of the MEN patients are not registered in any research database, despite almost all respondents (93%) being interested in registries. They hope for new knowledge about the disease and treatments. About 45% are not members of a patient group, although meetings with fellow patients are described as important (62%). The results of the survey indicate that German patients generally perceive the quality of medical care to be good. However, there are some unmet needs regarding access to reference centres, research registries and membership of patient organisations. In particular, the access to psychological help and communication between the different doctors involved in the care of MEN patients needs improvement.

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EP1228

Primary bilateral macronodular adrenal hyperplasia caused by a novel variant in the ARMC5 gene

Mariana Lopes-Pinto[1], André M Travessa[2,3], Ema Paula Ricca Lacerda Nobre M Caetano[1,3] & Ana Paula Barbosa[1,3]
[1]Unidade Local de Saúde de Santa Maria, Hospital de Santa Maria, Endocrinology Department, Lisbon, Portugal; [2]Unidade Local de Saúde de Santa Maria, Hospital de Santa Maria, Medical Genetics Department, Unidade Local de Saúde de Santa Maria, Hospital de Santa Maria, Lisbon, Portugal, Lisbon, Portugal; [3]Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, Lisbon, Portugal

Introduction
Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH) represents <2% of all causes of Cushing's Syndrome (CS). Clinical course is insidious, with adrenal bilateral macronodules and gradual cortisol excess, only rarely presenting with overt CS. The pathophysiology remains unclear in most cases; however, pathogenic variants in the onco-supressor ARMC5 gene are described in 25-50% of PBMAH and may confer a more severe clinical course.
Objectives
To report a new germline variant in the ARMC5 gene associated with PBMAH.
Case Report
A 34-year-old woman presented with exuberant CS phenotype including progressive weight gain, facial hair growth, plethoric face, dorsocervical and supraclavicular fat pads and easy bruising. She had been diagnosed with prediabetes and hypertension. Serum morning cortisol was 46.1 µg/dl (N: 6.2-18) and ACTH was <1 pg/ml. Morning cortisol after 1 mg overnight dexamethasone suppression test was 37.9 µg/dl, 24 h urinary cortisol was 6825 µg/24 h (N:124-581), while salivary cortisol kept circadian rhythm. Androgen and mineralocorticoid hypersecretion were excluded. Androgen and mineralocorticoid hypersecretion were excluded. Adrenal CT scan documented evident bilateral adrenal enlargement with multiple hypodense macronodules that reached a maximum diameter of 67 mm and 49 mm. No aberrant receptors were identified following a stimulation tests protocol. The patient showed good biochemical response to metyrapone and was submitted to unilateral adrenalectomy of the largest adrenal gland. Histopathologic evaluation revealed adrenal cortex macronodular hyperplasia, compatible with the diagnosis of PBMAH. There was an evident clinical response after surgery, with improved well-being, CS phenotype regression and weight loss. Additionally biochemical response with normalization of cortisol levels was achieved. One year after surgery, hydrocortisone replacement was resumed. Given the clinical diagnosis, a Next Generation Sequencing (NGS) panel including the ARMC5 and KDM1A genes was performed, and identified a novel germline variant in heterozygosity in the ARMC5 gene, c.169G>T p. (Gly57), leading to a premature stop codon. This new variant is classified as likely pathogenic. The recurrence risk for offspring is 50%.
Discussion and Conclusions
We report a case of PBMAH with a new germline variant in the ARMC5 gene, c.169G>T p.(Gly57), diagnosed due to overt CS and successfully treated with unilateral adrenalectomy. Genetic assessment of patients with PBMAH and family members may allow an early diagnosis of CS, minimize complications, and contribute to a better management and follow-up of PBMAH patients.

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EP1229

Steroidogenesis inhibitors in mild/subclinical cushing's syndrome: results from a retrospective cohort of patients

Alessandro Bavaresco, Filippo Ceccato, Pierluigi Mazzeo, Martina Lazzara, Giacomo Voltan, Irene Tizianel, Alessandro Mondin & Mattia Barbot
University of Padova, Endocrinology Unit, Padua, Italy

Cushing's syndrome (CS) is a severe disease associated with elevated morbidity and mortality rates, up to four times higher than those of general population. Whether the positive effects of cortisol-lowering medications is widely documented in overt CS cases, its impact on mild or subclinical CS remains unclear since limited clinical investigations have been performed in patients with subclinical hypercortisolism. In this study, we retrospectively analysed clinical data from patients with mild CS treated with either Ketoconazole or Metyrapone. Inclusion criteria were: serum cortisol levels after dexamethasone suppression test >50 nmol/l, slight increase of urinary free cortisol (UFC) levels (<2 times the upper limit of normal) and/or impaired circadian rhythm of cortisol. Our aim was to evaluate the effects of steroidogenesis inhibitors on UFC, late-night salivary cortisol (LNSC), ACTH, metabolic parameters, and blood pressure in these patients. Twenty-five patients (20F and 5 M) met the inclusion criteria, with 12 diagnosed with adrenal CS and 13 with Cushing's Disease. Fifteen patients were treated with Metyrapone and ten with Ketoconazole. Significant reduction in UFC levels were observed after 6 (median [IQR] levels 120 [65 – 162] nmol/24 h, *P* 0, 021) and 12 months of treatment (74 [48 – 146], *P* 0, 008) compared to baseline (178 [116 – 255], along with a reduction in LNSC (baseline 3.7 [3.4 – 5.1] nmol/l, 12 months 2.7 [1.7 – 3.6] *P* 0, 022) and increase in ACTH levels at 12 months (baseline 17.7 [6.7 – 43.8] ng/l, 12 months (33 [7.9 – 58.5], *P* 0, 033). However, metabolic parameters such as glucose, HbA1c, LDL cholesterol, waist circumference and blood pressure did not change over time. The subgroup analysis of patients treated with Metyrapone also showed an improvement of glucose metabolism both at 6 and 12 months. Conversely, patients treated with Ketoconazole did not experience any of these changes. Additionally, we considered patients treated for more than 12 months. Sixteen patients were included, with follow-up period which ranged from 13 to 125 months. We observed a significant reduction in UFC, total cholesterol, LDL (baseline 124 [102.75 – 144.3] mg/dl, last follow-up 87.2 [75.7 – 111.3], *P* 0, 028) and an increase in ACTH levels. To conclude, metyrapone might be considered to control mild/subclinical CS. Although no metabolic effects were observed after 6-12 months of treatment, an improvement in lipid profile was observed in patients treated for a longer period. Further studies are needed to evaluate the metabolic and cardiovascular implications of medical therapy in these patients.

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EP1230

Audit on management of addison's disease in pregnancy

Masato Ahsan[1,2], Emma Bremner[1], Diane Todd[1], Chandrima Roy[1], Miles J Levy[1,2], Shailesh Gohil[1,2] & Narendra Reddy[1,2]
[1]Leicester Royal Infirmary, United Kingdom; [2]University of Leicester, United Kingdom

Background
Primary adrenal insufficiency or Addison's disease (AD) is characterized by glucocorticoid and mineralocorticoid deficiency due to lesion of the adrenal glands through different mechanisms (1). Addison's disease is a risk factor for adverse maternal and neonatal outcomes. Close monitoring is required for these patients during the intrapartum and postpartum periods.(2)
Objective
Retrospective evaluation of the management of Addison's disease in pregnant patients, focusing on adherence to guidelines, monitoring practices, and maternal and fetal outcomes.
Methods
Retrospective data was collected after reviewing medical records of pregnant patients with diagnosed Addison's disease.
Results
$n=7$, mean age of 27, mean BMI at booking 30.5, 100% patients were on Hydrocortisone and Fludrocortisone, All pregnancies were spontaneous, 15% patient had hospital admission with adrenal crisis within one year prior to the pregnancy, 2 patients had miscarriage (at 6th week and 8th week) and both of them prior to first antenatal visit, 70% patient had successful outcome of pregnancy and among them all were reviewed in endocrine antenatal or maternal medicine clinic. None of the patient was reported to have gestational hypertension or pre-eclampsia. Mean Sodium was 137 (lowest 128 and highest 142), Potassium was 4.8 (lowest 4.2 and highest 5.6). Among the 70% pregnancy, all of them reached the term and all had NVD. Labour was induced in 1 patient. Average birthweight of the babies was 2900 grams (highest 3500 gram and lowest 2300 grams). Neonatal seizure or neonatal hypoglycaemia was reported in none of the babies.
Conclusion
This audit highlights the importance of stringent adherence to management protocols for Addison's disease during pregnancy. Pregnant individuals with Addison's disease require ongoing monitoring throughout pregnancy and postpartum by multidisciplinary teams. It is crucial to provide patient education and specialized monitoring to prevent complications arising from inadequate or excessive replacement therapy during this time. Timely referral to hospital services facilitating collaboration between Endocrinology and Obstetrics is essential.

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EP1231

Autoimmune endocrinopathies associated with the use of immune checkpoint inhibitors: a clinical case of a combination of isolated secondary adrenal insufficiency and diabetes mellitus

Laura Ebanoidze, Ekaterina Pigarova, Larisa Dzeranova, Elena Przhiyalkovskaya & Lyudmila Ibragimova
Endocrinology research centre, st. Dmitry Ulyanov, 11, Moscow, Russian Federation

Introduction
Endocrinopathies are one of the most common autoimmune adverse events (AIAEs) causing severe toxic complications during the use of checkpoint inhibitor therapy (CPI).
Clinical Case
A patient with complaints of hyperpigmentation of the skin of the back in August 2022 an excisional biopsy was performed and pigmented epithelioid cell melanoma with tumor growth along the resection margin was verified. In December 2022, CT revealed metastases in the right axillary and supraclavicular lymph nodes, the right lung, the right scapula and the right groin area - mts skin melanoma of the back T4aN3M1 b (R1), and therefore therapy with pembrolizumab (a human monoclonal antibody IgG4 kappa that selectively blocks PD-1) was initiated. In August 2023 with manifestations of asthenic syndrome, dyspepsia (nausea, vomiting), an increase in venous blood glucose to 14-16 mmol/l, an endocrinologist at the place of residence diagnosed type 2 diabetes mellitus and recommended taking metformin and glimepiride. Due to the lack of improvement in general well-being the patient was hospitalized to an emergency department with diabetic ketoacidosis where insulin therapy was initiated (insulin glargine 14 units at night, short-acting insulin 3-4 units before main meals) with subsequent stabilization of the condition, but continuous persistence of asthenia and hypotension.. Subsequently, based on low values of ACTH and blood cortisol as well as 24-hour urine cortisol, secondary adrenal insufficiency was identified, for which hydrocortisone was prescribed. Due to the lack of compensation for adrenal insufficiency, the drug was replaced with prednisolone at a dose of 7.5 mg $\rightarrow$ 5 mg/day. Later, due to severe hypotension on either glucocorticoid therapy (BP 80/40 mm Hg), fludrocortisone 0.05 $\rightarrow$ 0.1 mg was added to therapy. In November 2023 during hospitalization in the endocrinology hospital, his lab tests showedlow levels of C-peptide – 0.0035 ng/ml (1.1-4.4), insulin – 1.42 mU/ml (2.6-24.9), absense of antibodies to GAD – 0.2 U/ml (0-10), insulin – 2.68 U/ml (0-10), tyrosine phosphatase <1 U/ml (0-10) and positive islet cell antibodies – 2.6 U/ml (0-1). Insulin therapy was optimized, glycemic levels were stabilized within individual target values. According to hormonal analysis: ACTH – 2.77 pg/ml (7.2-63.3), cortisol – 41.42 nmol/l (171-536). MRI of the brain visualized heterogeneity of the adenohypophysis and the developing "empty" *sella turcica*.
Conclusion
Considering the etiological features of the occurrence of AIAEs during the use of CPI, a multidisciplinary approach is required for comprehensive and effective management of patients, minimizing complications and fully implement the therapeutic potential of this treatment method.

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EP1232

Angiogenesis in benign and malignant thyroid pathologies based on the vascular endothelial growth factor (VEGF) and CD34 markers activities

Tamuna Gvianishvili & Liana Gogiashvili

Ivane Javakhishvili Tbilisi State University, Alexandre Natishvili Institute of Morphology, Department of Clinical and Experimental Pathology, Tbilisi, Georgia

Angiogenesis is critical for tumor growth and metastatic spread. Vascular Endothelial Growth Factor (VEGF) is the most potent inducer of neovascularization, and its increased expression is associated with worse clinical outcome in many diseases. The aim of our work was to evaluate the dynamics of VEGF and CD34 molecular morphology with Follicular Epithelial Dysplasia (FED) in Thyroid neoplasm and autoimmune pathology. These markers allow accuracy distinguishing between pseudoneoplastic hypertrophy (Graves' disease) and neoplasia (Papillary Thyroid Carcinoma (PTC)). 36 patients in equal amounts were evaluated: Hashimoto's Thyroiditis (HT) ($n=12$), Graves' disease ($n=12$), PTC ($n=12$), which had undergone total thyroidectomy or lobectomy. Immunohistochemical reaction with VEGF-138 and CD34 antibody (Leica Novocastra, UK) and routine H&E diagnostic treatment were used. As a result, molecular analysis using data, obtained from Immunohistochemistry, VEGF expression was markedly lower in Graves' disease and HT, than in PTC. But there was no significant association between CD34 expression and thyroid pathology variants. Consequently, incidence of FED correlate with VEGF activity rate. Based on the above mentioned observation, neovascularization/angiogenesis play a crucial role for the growth and metastatic spread of neoplasms and is comparable to each other. We hypothesize that the thyroid tumors in early stage of carcinogenesis (precursor lesion) is characterized by well-developed vasculo- and angiogenesis and became secondary objective of our research.

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EP1233

Features of pregnancy after simultaneous pancreas-kidney transplantation in patient with type 1 diabetes mellitus (clinical case)

Madina Yevloyeva, Darya Savitskaya, Anastasia Severina, Natalia Trubitsyna & Minara Shamkhalova
Endocrinology Research Centre, Moscow, Russian Federation

Introduction
Simultaneous pancreas-kidney transplantation (SPKT) is the best way to restore normoglycemia and renal function in patients with type 1 diabetes mellitus (T1D) and end-stage renal disease (ESRD). Pregnant patients after SPKT are a high-risk group for adverse events/loss fetal and transplantation organs. These risks are significantly reduced due to pregnancy planning, regular monitoring of the woman and fetus condition with timely correction of immunosuppressive therapy, maintaining blood pressure (BP) and glycemia, choosing the optimal birth time, mode of delivery.
Case Description
A 34-years-old woman with T1D (for 25 years) and ESRD underwent successful SPKT in 2021 in preparation for pregnancy. Graft function was preserved during treatment in endocrinology hospital in 2022: HbA1c = 5.6%, estimated glomerular filtration rate 80.9 ml/min, normoalbuminuria. All necessary conditions for successful planned pregnancy outcome were discussed. A transplantologist adjusted immunosuppressive therapy: mycophenolic acid was replaced by azathioprine (teratogenic effect), the patient continued taking methylprednisolone and tacrolimus (his concentration was maintained within the target values). A 16-week pregnant patient was admitted to an endocrinologic hospital because of BP episodic elevating up to 160/90 mmHg in 2023. The transplanted kidney function corresponded to stage 3a microalbuminuric CKD. Blood glucose levels was found to be higher than the target values for pregnant women during diet therapy (HbA1c = 5.6%, glycemia range: 4.6-9.3 mmol/l). Insulin (glargine) therapy was recommended due to failure to achieve the glycemic targets, which injections were refused by the patient. BP stabilized by optimal methyldopa dose selection. Glycemic target were ensured by diet therapy in the future. A 34-week pregnant patient was hospitalized in a nephrology ward because of increased creatinine level (175 μmol/l). After consultation with transplantologist it was decreased to 140 μmol/l due to reduction of the tacrolimus dose. A cesarean section was performed during the planned hospitalization to the maternity hospital at 38 weeks of pregnancy. The child birth weight was 3320 g, height - 52 cm, Apgar score 8-8 points. Creatinine, urea and blood glucose values of mother and child were normal in the postnatal period.
Conclusion
Pregnancy management in patients after SPKT should begin at the planning stage with the correction of immunosuppressive therapy and careful monitoring graft function. Such patients should be monitored by a multidisciplinary team (endocrinologist, nephrologist, obstetrician, transplantologist) in order to ensure a favorable pregnancy and delivery course with minimization of potential risks for mother and child. The success of these measures proves the experience of our patient.

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EP1234

Patient with MEN1 gene deletion and the classic triad of MEN-1 components

Rustam Salimkhanov[1], Victoria Vishnyakova[1], Ekaterina Kim[1], Anastasia Lavreniuk[1], Anna Eremkina[1], Timofei Vizerov[2], Marina Utkina[1] & Natalia Mokrysheva[1]
[1]Endocrinology Research Centre, Moscow, Russian Federation; [2]Research Centre for Medical Genetics, Moscow, Russian Federation

Introduction
Multiple endocrine neoplasia syndrome type 1 (MEN-1) is an autosomal dominant disorder caused by germline mutations in the *MEN1* gene encoding menin. *MEN1* mutations are mainly represented by deletions/insertions, nonsense, splice site or missense mutations and can be detected by DNA sequencing. MEN-1 generally includes parathyroid, adenohypophysis, and pancreatoduodenal neuroendocrine tumors.
Clinical Case
Patient S., 26-years-old female, admitted with morbid obesity (BMI – 49, 5 kg/m^2), weakness, vertigo, high blood pressure and irregular menstrual cycle. Primary hyperparathyroidism (PHPT) was diagnosed at 23 (2020): PTH – 481.6 pg/ml (15-65), $Ca_{adj.}$ – 3.0 mmol/l (2.15-2.55). The patient underwent selective parathyroidectomy (histologic confirmation of adenoma) with postoperative PTH and blood Ca normalization. Three years later, laboratory tests revealed PHPT relapse: PTH – 158.0 pg/ml (15-65) with a high-normal $Ca_{adj.}$ – 2.55 mmol/l (2.15-2.55), normophosphatemia – 0.8 mmol/l (0.74-1.52), normocalciuria – 5, 65 mmol/d (2.5-8.0). Screening for PHPT complications excluded nephrocalcinosis/nephrolithiasis, gastric and duodenal ulcer disease. DXA showed decreased bone mineral density in L_{1-4} below age-expected values: -2.9 SD (Z-score). Imaging techniques (US;^{99m}Tc-sestamibi scintigraphy with SPECT-CT) visualized left upper, right lower and upper abnormal parathyroid glands (PGs) (maximum size 1.6x0.85x0.5 cm) in typical locations. In 2023, S. had a surgical removal of three altered PGs with remission achievement. Histological analysis verified hyperplasia and adenoma. Therapy after discharge included alfacalcidol and Ca supplements. We diagnosed the patient with hyperprolactinemia – 1526 mEd/l (64-365). Brain MRI revealed an endosellar pituitary microadenoma (6x8 mm). Dopamine receptor agonist therapy was prescribed. Laboratory tests showed hypergastrinemia – 3283.0 pg/ml (13.0-115.0), chromogranin A elevation –34.6 nmol/l (<3.00). Contrast-enhanced CT scan detected multiple pancreatoduodenal tumors (maximum size 2.0x2.0x2.0 cm) with focal SSTR2 overexpression at PET-CT with ^{68}Ga-DOTA-TATE, confirming its neuroendocrine origin. Considering clinical findings genetic analysis was performed identifying mutation in the *MEN1* (an extended deletion in the heterozygous state of HG38:chr:11 chromosome with approximate boundaries 64804062-64810384 and p. 6322 bp, including 2-10 exons of the *MEN1* gene (NM 130799.2). We used chromosomal microarray analysis as a reference method: microdeletion in chromosome 11 (67901 base pairs), imbalance region genes – *MEN1*, *MAP4K2*, *CDC42BPG*, *EHD1*.
Conclusions
There is currently no conclusive data on the genotype-phenotype correlation of MEN-1. Small or large deletions of the *MEN1* gene are rare and have been described previously as pathogenic. Deletions of other genes are also of interest. Presumably they may affect the clinical manifestations of the disease.

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EP1235

Use of bidirectional Mendelian randomization to unveil the mutual associations of Helicobacter pylori infection and autoimmune thyroid diseases

Kai Wang & Qinnan Zhang
Shanghai Fifth People's Hospital, Fudan University, Department of Endocrinology, Shanghai

Previous observational studies found associations between *Helicobacter pylori* infection and autoimmune thyroid diseases (AITDs), but the causal nature of this association is still uncertain. We investigated the causal effect of 6 crucial antibodies against *H. pylori* on AITDs using a bidirectional Mendelian randomization (MR). We found anti-*H. pylori* OMP significantly increased the

risk of hyperthyroidism and Graves' disease (GD). In addition, our reverse MR analysis indicated hyperthyroidism could increase the levels of CagA and OMP antibodies. We also observed causal roles of GD on anti-*H. pylori* OMP. Our analyses indicate the mutual effects of *H. pylori* infection and AITDs, suggesting the existence of a gut-thyroid axis. These results also provide evidence of the bidirectional causal association between anti-*H. pylori* OMP with hyperthyroidism and GD, resulting in a vicious circle.

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EP1236

Insufficient bone mineralization to sustain mechanical load of weight in obese boys: a cross-sectional study

fabienne Emeriau, Amsellemn Jager Jessica, Bouhours-Nouet Natacha, Donzeau Aurelie, Rouleau Stephanie, Rerat Solene, Labarre Emmanuelle, Levaillant Lucie & Regis Coutant
Angers University Hospital Center, Angers, France

Context
The increase in bone mineral content (BMC) and density (BMD) measured by dual-energy X-ray absorptiometry (DXA) in obese children may not sustain the mechanical load associated with weight, and the factors influencing bone mineralization are not well known.
Objective
We described bone mineralization in overweight- obese (ow/ob) and lean (non-ow/non-ob) boys in relation to body composition.
Methods
Cross-sectional study in the Pediatric Endocrinology Unit of Angers University Hospital. Two-hundred-forty-nine ow/ob boys aged 8-18 underwent DXA and insulin, testosterone, and IGF-1 measurements. Bone mineralization was compared with data obtained from 301 lean boys of similar age and height from the NHANES study from 2011 to 2015, using the same DXA model. Path analyses were performed to evaluate the factors associated with total body less head (TBLH) BMC.
Results
The mean age and height-adjusted difference in TBLH-BMC between obese and lean boys was 241 ± 20 g/cm^2. Each 1 kg/m^2 increase in BMI was associated with $+39 \pm 6$ g of TBLH-BMC in lean subjects vs. $+25 \pm 3$ g in obese subjects ($P < 0.05$). Each 1 kg/m^2 increase in lean BMI (LBMI) was associated with $+78 \pm 5$ g of TBLH-BMC in lean and obese boys, and each 1 kg/m^2 increase in fat mass index (FMI) was associated with a decrease of 9 ± 3 g of TBLH-BMC. These findings suggest that the rise in TBLH-BMC observed in obese boys cannot sustain the increased mechanical load associated with weight. The Path analyses for TBLH-BMC Z-score in lean boys shows that TBLH-BMC Z-score was directly influenced by LBMI and height Z-scores (positively) and indirectly influenced by testosterone, FMI, and height Z-scores (positively, mediated through LBMI Z-score). And the path analyses for TBLH-BMC Z-score in obese boys shows that TBLH-BMC Z-score was directly influenced by LBMI and height Z-scores (positively) and indirectly influenced by insulin, height Z-scores (positively, mediated through LBMI Z-score), indirectly influenced by IGF-1, testosterone, and insulin Z-scores (positively, mediated through height and LBMI Z- scores). Finally, FMI Z-score indirectly influenced TBLH-BMC Z-score both positively (through LBMI Z-score) and negatively (through its negative impact on IGF-1 and testosterone Z-scores).
Conclusion
Bone mineralization in obese children and adolescents, although increased in response to the increased mechanical load of weight, did not follow the same positive relationship with BMI as that observed in lean boys. Lean body mass, had a similar positive relationship with bone mineralization in obese and lean boys, whereas fat mass had a negative impact.

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EP1237

Therapeutic options in the control of refractory hypercalcemia due recurrent parathyroid carcinoma: a case series

Olga Spasskaya, Ekaterina Kim, Rustam Salimkhanov, Anastasiia Lavreniuk, Anna Eremkina & Natalia Mokrysheva
Endocrinology Research Centre

Introduction
Parathyroid carcinoma (PC) is one of the rarest malignant endocrine neoplasms (0.005% of all oncological diseases). PC relapses in 40-60% cases. The severity of the disease is determined by life-threatening hypercalcemia. Surgery is the gold treatment standard of primary tumors and distant metastases, but if it is contraindicated there are few options to control life-threatening hypercalcemia.
Case 1
A 36-year-old-woman with a recurrent parathyroid carcinoma (PC) after multiple surgeries was admitted with symptoms of hypercalcemic crisis. Laboratory test revealed severe hypercalcemia - 4.62 mmol/l (2.15-2.55), elevated PTH - 265 pmol/l (2.0-9.4), hypophosphatemia - 0.58 mmol/l (0.74-1.52) while taking zoledronic acid 4 mg/month for 11 months and cinacalcet 90 mg/day (further dose titration lead to dyspepsia). The PET-CT with 18-FDG showed metastases in both lungs, pleura, multiple bones and liver. Due to ineffectiveness of previous therapy, we initiated denosumab 120 mg/28 days with a significant clinical and laboratory improvement. 3 months later Ca adj. was 2.6 mmol/l without cinacalcet therapy.
Case 2
A 70-year-old woman with a PC relapse and distant lung metastases complaining of muscle weakness, adynamia, bone pain and hoarseness was hospitalized in our Centre. Laboratory examination showed hypercalcemia - 4, 04 mmol/l, increased PTH - 1148 pg/ml and low eGFR (CKD-EPI) - 32 ml\min\1.73 m^2. We initiated infusion therapy, cinacalcet and denosumab 60 mg with the achievement of normocalcemia - Ca adj. 2.26 mmol/l on the 14th day. She was discharged under cinacalcet 60 mg/day. 6 months later she was admitted again with symptomatic hypercalcemia - Ca adj. 4, 13 mmol/l and reduced eGFR (CKD-EPI) - 27 ml/min/1.73 m^2. We started infusion therapy, titrated cinacalcet to 90 mg/day and provided injection of denosumab 60 mg. 7 days after Ca adj. was 2.9 mmol/l, eGFR (CKD-EPI) - 42 ml/min/1.73 m^2. Failure to achieve significant calcemia reduction we prescribed denosumab 120 mg/28 days with cinacalcet titration to 120 mg/day under regular laboratory follow-up
Conclusion
Managing a recurrent PC is challenging. Denosumab is a therapy of choice in bisphosphonate/calcimimetics refractory hypercalcemia and low eGFR.

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EP1238

Characteristics of prolactin macroadenomas:a cross-sectional analytical study of 40 cases

Farah Ayechi[1], Hanene Sayadi[1], sana abid[1], Raoua Naouar[1], Ghassen Belkahla[2], Atef Ben Nsir[2], Bilel Ben Amor[1], Ekram Hajji[1], Ines Bayar[1], Héla Marmouch[1], Inès Khochteli[1], Mahdi Darmoul[2] & Gema Martinez Tames[3]
[4]Fattouma Bourguiba Hospital, endocrinology and internal medicine department, monastir; [2]Fattouma Bourguiba Hospital, Neurosurgery department, monastir; [3]Hospital Valle del Nalon, Servicio de Endocrinología y Nutrición, Spain

Introduction
Macroprolactinoma is a rare pathology often considered benign. However, its singularity lies in its potential to become highly invasive, threatening both functional and vital prognosis by infiltrating surrounding structures.
Patients and methods
We conducted a monocentric, cross-sectional, analytical study of patients followed for confirmed prolactinoma at the endocrinology-internal medicine and neurosurgery departments of the Fattouma Bourguiba University Hospital, Monastir, from January2000 to March2022.
Results
Our study population comprised 24men and 16women (sex ratio (M/F)1.5) with a mean age at diagnosis of 41 ± 15.3 years. Men were significantly older than women ($P < 0.001$). The mean time to diagnosis was 1.9 ± 0.68 years. The main circumstances of discovery were: headache (47.5%), visual disorders (65%), galactorrhea (22.5%), menstrual cycle disorders (50% of women) and erectile dysfunctio (41.66% of men). The clinical signs most frequently encountered in both sexes were headache (70%), reduced visual acuity (60%) and visual field impairment (65%). In women, galactorrhea-amenorrhea syndrome was the most frequent clinical sign: galactorrhea was noted in 75% of patients, and secondary amenorrhea was present in 56.25% of cases. In men, erectile dysfunction (58.33%) and decreased libido (33.33%) were the most common signs. Median prolactinemia was 399 ng/ml[291.4 - 1075] and mean tumor size was estimated at 28.25 ± 11.85 mm. Extra-sellar extension was observed in 82.5% of cases, with invasion of the cavernous sinus in 62.5% of our patients. In our series, macroprolactinoma was complicated by pituitary deficiency in 85% of patients, involving the gonadotropic axis in 72.5% of cases. The metabolic impact showed the presence of: overweight or obesity (55%), prediabetes (15%), unrecognized diabetes (2.5%), hypertriglyceridemia (7.5%)and hypercholesterolemia (27.5%). Treatment with dopaminergic agonists resulted in tumor reduction and disappearance in 77.5% and 15% of cases respectively, and normalization of

serum PRL levels in 65% of cases. Complete remission was achieved in 15% of our patients, more frequently in women than in men, with a statistically significant difference ($P=0.01$). At the end of our study, we noted a similar serum PRL concentration whatever the type of treatment received, and an absence of significant difference between the mean rate of tumor reduction in the case of surgical treatment compared with that of medical treatment ($P=0.2$). Among the factors associated with the use of surgery found in our work, only initial tumour size was correlated with surgical treatment.
Conclusion
Macroprolactinoma is a rare and potentially serious disease. Prolonged and regular multidisciplinary collaboration is essential for optimal management of these patients. Thus, a multicentric study and the creation of a national registry are needed to better codify the management of this pathology.

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EP1239

Symptomatic hypocalcemia and hypomagnesemia in a 72 year-old woman, chronic user of pantoprazole

Alba Hernandez-Lazaro[1], Ricardo Jose de Leon-Durango[2], Borja Santana-Ojeda[2], Inmaculada Molinero-Marcos[2], Carmen Acosta-Calero[3], Claudia Arnas-Leon[2,4], Agnieszka Kuzior[4], Paula Gonzalez-Diaz[5], Maria del Pino Perez-Garcia[6] & Francisco Javier Martinez Martin[2,4]
[1]Parc Taulí University Hospital, Endocrinology & Nutrition, Sabadell, Spain; [2]University Hospital of Gran Canaria Dr. Negrín, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [3]University Hospital of Gran Canaria Dr. Negrín, Cardiology, Las Palmas de Gran Canaria, Spain; [4]Hospitales San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [5]University Hospital of Gran Canaria Dr. Negrín, Emergency Medicine, Las Palmas de Gran Canaria, Spain; [6]Centro de Salud El Calero, Family & Community Medicine, Telde, Gran Canaria, Spain

Introduction and Objectives
Proton-pump inhibitors (PPI) are some of the most commonly prescribed drugs, and they are generally well tolerated. However, their long-term use has been associated with adverse effects such as acute interstitial nephritis, Clostridium difficile infection. pneumonia, and (controversially) bone fractures, cardiovascular disease and dementia. The acidification of the intestinal milieu may interfere with TRMP6-mediated active absorption of magnesium in the intestinal mucosa. There have been several reports of symptomatic, even life-threatening (because of severe arrhythmia) hypomagnesemia associated with chronic use of PPIs. We hereby report a case of symptomatic hypocalcemia and hypomagnesemia in a patient which was resolved after switching pantoprazole to famotidine, in order to raise awareness about this uncommon adverse effect.
Methods
Review of the patient's clinical records and of the relevant literature
Results
A 72 year old woman with history of obesity, hiatal hernia and gastroesophageal reflux, chronically treated with pantoprazole (>3 years) was admitted in the hospital emergency room with tingling and paresthesia in both arms and hands after an episode of acute gastroenteritis with vomiting and diarrhoea; Mild hypocalcemia (7.9 mg/dl) and severe hypomagnesemia (0.6 mg/dl) were detected, but her EKG showed no significant anomalies. Intravenous magnesium sulphate was administered and the patient's symptoms were alleviated. She was discharged with calcium, magnesium and cholecalciferol supplements and referred to our Endocrinology clinic, after one month with new lab tests. The patient reported fatigue and occasional cramps and numbness in both hands but the Trousseau and Chvostek tests were negative. Plasma calcium, phosphate, PTH and calcifediol were normal but magnesium remained low (0.9 mg/dl) in spite of reported good compliance with the supplements and no new episodes of vomiting and diarrhoea. In a 24-h urine collection, calciuria was normal but magnesiuria was low. PPI-related hypomagnesemia with secondary hypocalcemia was suspected; the patient was switched from pantoprazole 40 mg to famotidine 20 mg daily. In the follow up visit after 3 months there were no symptoms and lab tests were normal; calcium, vitamin D and magnesium supplements were withdrawn.
Conclusions
Severe symptomatic hypomagnesemia is an uncommon adverse effect associated with the chronic use of PPIs, and it is resistant to the use of oral magnesium supplements. PPIs are probably overused, and deprescription should be considered in chronic users unless there is a clear justification. H2 blockers can be used as an alternative to PPIs if needed.

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EP1240

Exploring experiences of patients with adrenal insufficiency (AI) using parenteral hydrocortisone injection device to manage adrenal crisis: a qualitative interview study

Aldons Chua[1,2], William Drake[1], Heather Yoeli[2], Patrick Oyibo[2], Umesh Dashora[3], David Till[3], Martin Cartwright[2] & Sofia Llahana[2]
[1]St Bartholomew's Hospital, Endocrinology, London, United Kingdom; [2]City, University of London, London, United Kingdom; [3]East Sussex Healthcare NHS Trust, Hastings, United Kingdom

Background
Adrenal Insufficiency (AI) is an inadequate production of cortisol hormone from the adrenal glands. The most common form is secondary AI (suppression of the hypothalamic-pituitary-adrenal axis), with a prevalence of approximately 300 cases per million. Patients with AI require lifelong corticosteroid replacement, which poses a risk of a life-threatening adrenal crisis (AC) event. AC presents with low blood pressure, hypoglycaemia and even loss of consciousness. This causes a significant burden, not just to families but also to the healthcare system. To prevent AC-related complications and even death, patients with AI need an urgent hydrocortisone 100 mg intramuscular injection. The United Kingdom (UK) Society for Endocrinology released an updated clinical guidance in 2016, including a new emergency steroid alert card. "Patient education" is also emphasised as an essential tool. However, studies showed that up to 50% of AC-related hospitalisations are preventable with effective patient self-management. However, numerous studies still report barriers to effective patient self-management during AC.
Objective
This study aimed to explore experiences of patients with adrenal insufficiency (AI) during an adrenal crisis (AC), and to identify barriers and enablers on the use of hydrocortisone injection device in self managing AC.
Methods
This is a qualitative study using 1:1 semi-structured interview. Participants were recruited through patient advisory groups (Addison's Disease Self-help Group and the Pituitary Foundation) in the UK. Eligible participants were interviewed via Microsoft Teams online platform, transcribed verbatim and analysed using thematic analysis with NVivo software.
Results
Twelve White European females from various geographical locations in the UK, with confirmed diagnosis of secondary/tertiary AI participated. All participants possess an emergency hydrocortisone injection and report at least one AC episode per year. Only one participant successfully self-injected hydrocortisone. Participants reported self-management during AC is mainly affected by complexity of the disease. But, over time, understanding and confidence developed. Challenges with the use of hydrocortisone injection have been highlighted and compared to other modalities i.e., EpiPens and insulin pens. The current tools and training were beneficial to most participants, but some find the teaching session confusing. Concerns were also raised on healthcare professional's lack of understanding in managing AC, especially in emergency departments. With the support available, i.e., next of kin, participants were able to manage AC at home.
Conclusion
This study highlights the need for an easier-to-prepare hydrocortisone injection device and more structured teaching provision not just for patients, but also for health care professionals.

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EP1241

Graves' disease following subacute thyroiditis: a rare occurrence

Nergis Basmacı & Seda Hanife Oguz
Hacettepe University School of Medicine, Endocrinology and Metabolism, Ankara, Turkey

Background
Subacute thyroiditis (SAT) is typically a self-limiting condition, with patients usually returning to normal thyroid function after healing. However, very rarely, Graves' disease (GD) may develop following SAT.
Case presentation
A 50-year-old female patient presented to an outside internal medicine outpatient clinic with anterior neck pain, fatigue, and subclinical fever symptoms. Her medical history included a diagnosis of psoriatic arthritis and she was receiving weekly methotrexate along with folate replacement. Firstly, the patient was given oral antibiotics that failed to relieve the symptoms. Laboratory tests revealed thyrotoxicosis [TSH: 0.096 uIU/ml (0.38-5.33 uIU/ml), fT4: 28.6 pmol/l (7.8-14.4 pmol/l), fT3: 7.9 pmol/l (3.8-6 pmol/l)]; and elevated acute phase reactants

[eritrocyte sedimentation rate (ESR): 28 (0-20), C-reactive protein (CRP): 48 mg/l (0-5 mg/l)]. Both anti-thyroglobulin (Anti-Tg Ab, 602 IU/ml (0-40 IU/ml), and anti-thyroid peroxidase antibodies (Anti-TPO Ab, 28 IU/ml (0-9 IU/ml) were positive, while the thyroid stimulating immunoglobulin (TSI) was undetectable. She was then consulted to endocrinology outpatient clinic. On physical examination, she had a diffuse tender goiter and no symptoms of orbitopathy. Ultrasonographic examination revealed enlargement in the thyroid gland, and patchy heterogenous areas with decreased vascularization on color Doppler imaging, consistent with SAT. Treatment with methylprednisolone 16 mg/day was initiated, which led to instant symptom relief. The dosage was gradually reduced and the medication was eventually discontinued after 4 weeks. One month after cessation of treatment, thyroid function tests were normal. However, after an additional 2 months, the patient presented with complaints of anterior neck pain, palpitations, sweating and hair loss. Thyroid examination revealed mild tenderness, and thyroid function tests showed subclinical hyperthyroidism (TSH: 0.2 mIU/l, fT_4: 14.5 pmol/l, fT_3: 5.4 pmol/l). Both ESR and CRP levels were in normal range. However, TSI level was 1 IU/l (<0.1 IU/l), inciting a suspicion of GD. A thyroid scintigraphy was performed which demonstrated diffuse radioisotope uptake with reduced counting time. In addition, increased vascularity was observed on color Doppler imaging. The patient was therefore diagnosed with GD following SAT.
Conclusions
This case highlights the unusual onset of GD following subacute SAT. Although the pathogenic pathways have yet to be uncovered, the inflammatory environment of SAT might trigger an immunological response, resulting in the onset of GD. Clinicians must be mindful for GD in individuals with persistent hyperthyroidism after SAT remission, especially in patients with a history of other autoinflammatory disorders, as in our case.

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EP1242

Clinicopathological features of inflamed rathkes cleft cysts: a case series

Annabelle Hayes[1,2], Julia Low[2], Nicholas Shoung[2], Sebastain Fung[2] & Ann McCormack[1,2,3]
[1]UNSW Sydney, School of Medicine, Sydney, Australia; [2]St Vincent's Hospital Sydney, Darlinghurst, Australia; [3]Garvan Institute of Medical Research, Darlinghurst, Australia

Background
Rathkes cleft cysts (RCC) are present in up to 20% of autopsy studies but only a minority necessitate surgical treatment[1]. Inflammation of the RCC wall may act a trigger for disease progression, resulting in development of clinical symptoms and prompting investigation and surgical management[2,3]. The significance of inflammation of RCC is thought to be three-fold: the development of classical symptoms including headache, visual disturbance or pituitary hormone disturbance, secondly, a predisposition to rupture or apoplexy, and thirdly, it is thought to increase rate of RCC recurrence[1].
Objective
To review and characterize clinical presentation, histological and radiological findings in a series of patients with inflamed RCC.
Methods
We conducted a retrospective case series of 25 cases of RCC, which had undergone surgical management between April 2016 and November 2022. Histopathology and radiology were independently reviewed by neuropathologist and neuroradiologist, and case notes were reviewed for clinical and biochemical data.
Results
25 cases were reviewed: 19 demonstrated inflammation of either the RCC cyst epithelium ($n=10$), cyst wall ($n=17$) (Rathkes cystitis) or anterior pituitary (adenohypophysitis) ($n=10$), 6 cases were not inflamed; mean age was 47 years (± 19 years); 72% were female, consistent with literature. Preoperative features included pituitary dysfunction (64%), headache (64%), visual disturbance (20%) and polyuria/polydipsia (4%). Most (67%) patients experienced symptoms for less than 1 year. Four patients presented with apoplexy. Headache was present in 90% of patients with adenohypophysitis vs 47% cases without pituitary involvement ($P=0.027$) and all 9 cases where adenohypophysitis was chronic. Pituitary dysfunction was not associated with cystitis (69% vs 67% p=ns) or adenohypophysitis (44% vs 33% P=ns). Rathkes cystitis was associated with loss of posterior bright spot (71% vs 14% $P=0.013$).
Conclusion
Headache but not pituitary dysfunction was associated with adenohypophyseal inflammation. A trend of increasing headache prevalence was seen with increasing degree of inflammatory infiltrate within RCC.
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EP1243

Severe spontaneous long-lasting hypoglycaemia. Differential diagnostic challenges thorough a case report

Gergő Csitári[1], Bettina Varga[1] & Gábor Simonyi[1,2]
[1]DBC-SZIEOK, Metabolic Center, Budapest; [2]Szent Imre University Teaching Hospital, Metabolic Center, Budapest, Hungary

In our presentation we would like to demonstrate a complex case with severe spontaneous long-lasting hypoglycaemic episodes that were observed for more than 48-hours. Later the continuous parenteral glucose need was promptly ceased. A 78-years-old hypertensive non-diabetic patient came to our hospital with hypoglycaemic coma. His unconsciousness were cured prehospitally by parenteral glucose replacement. However hypoglycaemic comas (GCS 1-2-1) were observed several times in the ER and upon admission so he were treated by intravenous glucose perfusor. In the first 24-hours he needed 420 grams (!) of glucose intravenously to avoid unconsciousness and to maintain the patient's blood glucose level around 3-4 mmol/l. Unsuppressed, moreover elevated serum insulin and C-peptide levels were measured simultaneously with the hypoglycaemic episodes. Our patient was in good physical condition, he was neither obese nor malnourished. He negated any alcohol and antidiabetic drug consumptions despite multiple interrogations. His wife had T2DM but she was on fix dose combination of metformin and vildagliptin. Staging CT and abdominal MRI scans did not revealed any obvious malignancy nor insulinoma or any GEP-NET-like alteration. On the third observational day our patient's parenteral glucose need started to decreased and later it ceased. Therefore a casualty of sulfonylurea abuse was clinically assumed, so we sent blood and urine samples to the laboratory of toxicology for sulfonylurea derivates. The findings showed 87, 5 ng/ml gliclazide in the blood and traces of gliclazide from the urine with liquid chromatography and tandem mass spectrometry which could also be an artefact. Once we received these results we asked again the patient and his family whether they had ever taken gliclazide on its marketed brand names. Then they confirmed that they had gliclazide in their home, although it was prescribed only for his wife's peri-contrast media days despite metformin and they proved that only those 4 pills were missing. Thus, we dared to perform a 72-hours fasting test which ended with a negative result, consequently the likelihood of insulinoma finally could be excluded. We asked the family to keep the above mentioned unnecessary drug far away from our patient and from his wife to avoid similar accidents. The patient was discharged but he needs further urologic and cardiologic follow up due to elevated PSA levels and sinus bradycardia with left bundle branch block.

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EP1244

Improvement in albumin excretion in patients with type 2 diabetes mellitus labelled as metformin-intolerant after rechallenge with extender-release metformin

Jennifer Maria Perez-Rivero[1], Alba Hernandez-Lazaro[2], Ricardo Jose de Leon-Durango[3], Carlos Rios-Gomez[3], Borja Santana-Ojeda[3], Inmaculada Molinero-Marcos[3], Claudia Arnas-Leon[3,4], Carmen Acosta-Calero[5], Agnieszka Kuzior[4] & Francisco Javier Martinez Martin[3,4]
[1]Centro Salud Escaleritas, Family & Community Medicine, Las Palmas de Gran Canaria, Spain; [2]Parc Taulí University Hospital, Endocrinology & Nutrition, Sabadell, Spain; [3]University Hospital of Gran Canaria Dr. Negrín, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [4]Hospitales Universitarios San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [5]University Hospital of Gran Canaria Dr. Negrín, Cardiology, Las Palmas de Gran Canaria, Spain

Introduction and Objective
Metformin is still a mainstay of treatment in patients with type 2 diabetes mellitus (T2DM), but in 10-25% of them there are persistent gastrointestinal disturbances that worsen their quality of life, lead to poor compliance and treatment withdrawal, and ultimately result in worse health outcomes. Extended-Release Metformin (XRM) is much better tolerated, and since 2005 is recommended in the

well-respected British NICE guidelines for the treatment of T2DM in patients with gastrointestinal disturbances related to the use of metformin. However in Spain XRM was not available until 2022, after the expiration of the patent of sitagliptin, when a generic combination of XRM/sitagliptin (1000/50 mg) became available, while monocomponent XRM is still not available. We undertook to study whether in patients with T2DM, labeled as metformin-intolerant and treated with a DPP4 inhibitor but insufficiently controlled, the switch from the DPP4 inhibitor to the XRM/sitagliptin combination could improve their glycemic control and renal function.
Design & Method
Patients with T2MD, with HbA1c $>7\%$ but $<9\%$; estimated GFR >45 ml/min/1.73 m^2, labeled as metformin-intolerant and treated with full dose of a DPP4 inhibitor were recruited and, after informed consent, switched to XRM/sitagliptin 100/50 mg beginning with one daily pill, and after one month increasing the dose to 2 daily pills if there were no significant tolerance issues. Fasting glycaemia, HbA1C, estimated GFR (CKD-EPI equation) and albumin/-creatinine ratio in a morning urine sample were measured before and 3-4 months after the switch. As albumin/creatinine values are not distributed normally, they are given as median (interquartile range) and compared by Mann-Whitney's U test
Results
72 such patients were recruited; 12 did not tolerate the combination, 8 tolerated only one pill, and 52 tolerated both pills. Fasting glucose was reduced from 175 ± 34 to 129 ± 23 mg/dl ($P<0.05$) with one pill and to 121 ± 21 ($P<0.01$) with 2 pills. HbA1c was reduced from 8.3 ± 1.0 to $7.7\pm0.8\%$ ($P<0.05$) with one pill and to 7.4 ± 0. GFR was unchanged: 57 ± 16 to 59 ± 16 ml/min/1.73 m^2 7. Albumin/creatinine quotient was reduced from 39 (17-78) to 29 (14-66) mg/gr ($P=0.029$). There was a significant positive correlation between albumin/creatinine change and HbA1C change (Spearman's rho: 0.47, $P<0.001$).
Conclusions
The switch from DPP4 inhibitor to the XRM-sitagliptin combination was well tolerated in a large majority of the patients, improved significantly the glycemic control and reduced urinary albumin excretion; this reduction seems to be partly driven by the improvement in glycemic control.

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EP1245

Cutaneous lymphoid hyperplasia in a male patient with type 3 polyglandular autoimmune syndrome - a rare association

Daniel Cosma[1], Horatiu Silaghi[2] & Cristina Alina Silaghi[3]
[4]Horezu City Hospital, Diabetes, Nutrition and Metabolic Diseases Outpatient Clinic, Horezu, Romania; [2"]Iuliu Hatieganu" University of Medicine and Pharmacy, 5th Department of Surgery, Cluj-Napoca, Romania; [3"]Iuliu Hatieganu" University of Medicine and Pharmacy, Endocrinology Department, Cluj, Romania

Cutaneous lymphoid hyperplasia (CLH) is a spectrum of benign conditions characterized by reactive B- and T-cell cutaneous lymphocytic infiltrates. The most common presentation of reactive CLH is as a solitary red skin papule, nodule, or plaque but 10–15% of patients present with more generalized or multifocal skin lesions. A 40-year old male, initially diagnosed with type 1 diabetes mellitus (DM), with a family history of autoimmune thyroid disease, vitiligo and type 2 DM, asked transfer to our service for specific treatment and monitoring. Based on detailed personal history, labs exams (positive antibodies and normal C-peptide value) and clinical evolution, the diagnosis was changed to latent autoimmune diabetes of the adult (LADA) in the context of a polyglandular autoimmune syndrome type 3 by association with vitiligo and Hashimoto thyroiditis. The physical examination revealed a round erythematous lesion on the right shoulder with positive Darier sign (sugestive for a mastocytoma), localized prurit after stimulation, 3 other circular lesions on the abdomen and telangiectasia on the epigastric area. The patient was directed to a university hematology center for further investigations, where the CHL diagnosis was established based on the tryptase and β-2 microglobulin within normal values, lack of the pAsp816Val mutation and the histopathological examination. Despite denying the diagnosis of systemic mastocytosis, the patient received treatment with an antihistamine agent and sodium cromoglycate with progressive titration up to 10 capsules/day with some improvements in gastrointestinal and urinary symptoms. The antihyperglycemic therapy consists of Metformin and basal insulin. To our knowledge, this is the first case of CLH in a patient with type 3 polyglandular autoimmune syndrome composed of LADA, Hashimoto thyroiditis and vitiligo.

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EP1246

Insights into beckwith-wiedemann syndrome: exploring the clinical spectrum and tumor surveillance in four case reports

Denisa-Isabella Tănasie[1], Elena Braha[2], Camelia Procopiuc[2], Aura-Madalina Boboc[1,2], Carmen Iordachescu[2], Adriana Padure[2] & Iuliana Gherlan[1,2]
[1]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [2]C.I. Parhon National Institute of Endocrinology, Bucharest, Romania

Introduction
Beckwith-Wiedemann Syndrome (BWS), a genetic imprinting disorder linked to 11p15, showcases overgrowth traits, including macrosomia, macroglossia, and abdominal wall defects. Characterized by specific genotype-phenotype correlations and recognized as a cancer predisposition syndrome (nephroblastoma, hepatoblastoma, neuroblastoma and adrenocortical carcinoma), our four case reports provide insights into varied clinical presentations.
Case reports
Case 1: a 1-year and 4-month-old boy conceived through *in vitro* fertilization was diagnosed with BWS at 11 months. MLPA detected maternal hypomethylation (11p15-IC2). Notable physical features include macroglossia and a forehead flat hemangioma. Literature supports a 10-fold BWS risk with assisted-reproduction-technology, potentially indicating milder phenotype (Carli D *et al*, 22). Case 2: We examine a 2-year and 6-month-old girl with suspected BWS identified prenatally due to macroglossia, omphalocele, and polyhydramnios. At 1-day old, she underwent surgical intervention for omphalocele. BWS was confirmed at 6 months through MLPA, revealing the same submolecular type as in case 1 (IC2-LoM). Case 3: We introduce a 2-year and 7-month-old girl. Neonatally, the phenotypic features, with macroglossia, transient hypoglycemia and ear lobe creases raised suspicion of BWS. By 1 year and 6 months, she had surgical reduction for macroglossia, and, over time, the diastasis of the rectus abdominis resolved spontaneously. At 2 years, an orthopedic exam revealed a leg length discrepancy, suggesting shoe lift usage. The patient's clinical score is 7 points, exceeding the diagnostic threshold for BWS without molecular confirmation (Brioude *et al*., 18). Case 4: a 1-year and 3-month-old girl presented with neonatal hypoglycemia and hyperinsulinism (elevated insulin and C-peptide levels). Central adrenal insufficiency (low cortisol, lower normal range ACTH) was treated with hydrocortisone. An early ultrasound revealed a left adrenal tumor that later resolved, likely due to adrenal hemorrhage. Genetic tests, including WES and MLPA, showed no evidence of congenital hyperinsulinism or BWS-associated deletions/duplications. Like case 3, the clinical score is 7 points (including macroglossia, ear pits), negating a need for molecular confirmation. Repeated suprarenal ultrasound demonstrated no tumor formations on both sides. In all four cases, the tumor screening consists of serum alpha-fetoprotein (AFP) levels and abdominal ultrasound every three months, were within normal limits. IC2-LoM, found in 2 of our cases is associated with the lowest tumor risk, being the most frequent.
Conclusion
Given the complex genetics and diverse phenotypes associated with BWS, a multidisciplinary team approach is essential. This collaborative effort aims to coordinate various aspects of care throughout childhood, particularly highlighting the need for tumor surveillance.

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EP1247

Sociodemographic and socioeconomic factors of patients with adrenal insufficiency and their influence on glucocorticoid dosage and the occurrence of adrenal crisis

Milena Haase[1], Peter Kropp[2], Catharina Bullmann[3] & Birgit Harbeck[1,3]
[1]University Medical Center Hamburg-Eppendorf, III. Department of Medicine, Hamburg, Germany; [2]University of Rostock, Institute for Medical Psychology and Medical Sociology, Rostock, Germany; [3]MVZ Amedes Experts, Endocrinology, Hamburg, Germany

Introduction
Patients with primary, secondary or tertial adrenal insufficiency are usually treated with a glucocorticoid substitution therapy adjusting dosages to align with the circadian rhythm. Despite those attempts, finding the correct dosage individually seems challenging, influenced not only by the complexity of circadian rhythms but also by various other factors. Approximately 6-8% of adrenal insufficiency patients still experience adrenal crises every year, which is associated with an increased mortality. While it is known that social circumstances significantly impact disease development, the current therapy primarily focuses on glucocorticoid substitution, which makes it necessary to

implement a different approach in therapy considering physiological and sociodemographic factors.
Material and Methods
Patients with primary, secondary or tertial adrenal insufficiency were included in the study. They were handed out questionnaires to collect demographic data, quality of life, symptoms of depression and anxiety as well as social integrity and social support data. The data analysis was conducted using Excel and SPSS.
Results
61 participants (77% females, 23% males) with primary (47.5%), secondary (47.5%), or tertiary (4.9%) adrenal insufficiency took part in this study.. The results indicate lower health-related quality of life in adrenal insufficiency patients compared to the normative sample. The collected data from the sum of the questionnaires, in particular SCL90-R, SF-36 and AddiQol, suggest a significant correlation between lower health-related quality of life, respectively depressive symptoms, and increased occurrence of adrenal crises. For better comparability, the analysis included not only the overall number of experienced adrenal crises but also the number of crises within the last year. There was no observed correlation concerning individual glucocorticoid dosage.
Conclusions
The study underscores ongoing challenges faced in the therapy of adrenal insufficiency. The results of our study confirm a networthy association between lower health-related quality of life, including depressive symptoms and inadequate social support, and an increased incidence of adrenal crises. Although glucocorticoid dosage didn't show a significant correlation, improving social conditions may reduce substitution requirements and adrenal crises frequency, which could have a positive impact on overall well-being and disease outcomes. This study highlights the importance of considering socioeconomic and sociodemographic factors in treatment of adrenal insufficiency.

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EP1248

Primary aldosteronism in patient with autosomal dominant polycystic kidney diseases: diagnostic and therapeutic challenge

Kammoun Fatma[1], Ibtissem Ben Nacef[1], Sabrine Mekni[1], Sawsen Essayeh[1], Rihab Laamouri[1], Werfili Mariem[2], Mchirgui Nadia[1], Karima Khiari[1] & Imen Rojbi[1]
[1]Charles Nicolle Hospital, Endocrinology, Tunis, Tunisia; [2]Charles Nicolle Hospital, Laboratory of Renal Pathology LR00SP01, Tunis, Tunisia

Introduction
Hypertension is often associated with autosomal dominant polycystic kidney disease (ADPKD). The pathogenesis of hypertension is complex, including intrarenal activation of the renin-angiotensin-aldosterone system (RAAS), arterial stiffness endothelial dysfunction, increased sympathetic nervous system activity and endothelin-1 secretion. However a secondary cause of hypertension should be suspected in presence of hypokaliemia and resistant hypertension.
Case report
A 51-year-old woman with a 30-year history of ADPKD was admitted to our hospital because of inadequate control of blood pressure. She had a family history of polycystic kidney disease, with an affected father and brother. The patient was diagnosed with hypertension secondary to ADPKD at the age of 35, she received treatment with betablockers, calcium blockers and angiotensin converting enzyme inhibitor. At physical examination the blood pressure was 160/100 mm Hg (no difference between arms); heart rate was 70 beats/min and body mass index was 28.48 kg/m^2. Laboratory findings revealed mild hypokalemia 3.4 mmol/l with inappropriate kaliuresis 53, mmol/24H, increased serum creatinine at 110 umol/l with an estimated glomerular filtration rate (GFr) : 50 ml/min. After therapeutic adjustement, management of hypokalemia and normal salt diet, endocrine evaluation revealed high plasma aldosterone concentration at 583 pg/ml $>$200 pg/ml, suppressed plasma renin activity, aldosterone/renin ratio of 74, 36 $>$23 confirmed the diagnosis of primary aldosteronism (PA). Abdominal computer tomography (CT) without contrast revealed an adenoma in the left adrenal gland of 13 mm. The surgical excision of the adenoma was considered but it was excluded due to the difficult surgical approach, and therefore the patient started spironolactone (a mineralocorticoid-receptor blocker) at 50 mg once daily. After medical treatement, the patient's blood pressure normalized (120/80 mmHg) as did her serum potassium level (4.0 mmol/l) without impairment of kidney function.
Discussion
The diagnosis of primary aldosteronism in a patient with polycystic kidney disease is challenging because: the renal cysts may obscure an adrenal adenoma; polycystic kidney disease itself is often complicated by hypertension and hypokalemia can be obscured by renal insufficiency. The association of ADPKD and PA is rare but once the coexistence of hypokalemia and resistant hypertension is identified in ADPKD patients, a secondary cause of hypertension should be considered, like PA.

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EP1249

Prevalence and characterization of sexual dysfunctions in male patients with hyperprolactinemia in a national registry

Antonio De Fraia[1], Elisa Maseroli[2], Emilia Sbardella[3], Cristina de Angelis[1], Marianna Minnetti[3], Renata Simone Auriemma[1], Rita Indirli[4], Caterina Golinelli[5], Angelo Cignarelli[6], Linda Vignozzi[2], Giovanni Corona[7], Andrea Isidori[3] & Rosario Pivonello[1]
[1]Università Federico II di Napoli, Naples, Italy, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia ed Andrologia, Unità di Andrologia e Medicina della Riproduzione, Sessualità e Affermazione di Genere (Fertisexcares), Italy; [2]Università di Firenze, Florence, Italy, Dipartimento di Scienze Sperimentali Cliniche e Biomediche "Mario Serio"; [3]Università La Sapienza di Roma, Rome, Italy, Dipartimento di Medicina Sperimentale; [4]University of Milan, Milan, Italy, Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy - Department of Clinical Sciences and Community Health; [5]University of Modena and Reggio Emilia, Modena (Italy), Department of Biomedical, Metabolic and Neural Sciences; [6]Università degli Studi di Bari "Aldo Moro", Dipartimento di Medicina di Precisione e Rigenerativa e Area Jonica - (DiMePRe-J);[7]AUSL di Bologna, U.O. di Endocrinologia e Malattie del Ricambio Ospedale Maggiore Bellaria, AUSL di Bologna, U.O. di Endocrinologia e Malattie del Ricambio Ospedale Maggiore Bellaria

Hyperprolactinemia is frequently accompanied by sexual dysfunctions, represented by decreased libido, erectile dysfunction and ejaculatory disorders. Moreover, cabergoline (CAB), used for treatment of hyperprolactinemia, is known to influence sexual function. Aim of the study was to evaluate sexual function in males with hyperprolactinemia under medical therapy. Data were retrieved from GONADIS, a national registry on gonadal status and reproductive and psycho-sexual function in patients affected by pituitary and adrenal disorders, promoted by SIAMS–SIE–AME. Twenty-three male patients aged 25-76 yrs (median age: 49 yrs) with diagnosis of hyperprolactinemia and on therapy with CAB were evaluated. Pharmacological anamnesis, hormonal parameters and standardized questionnaires investigating sexual function (SIEDY, Androtest, IIEF-15, PEDT, MHQ and BDI) were assessed; the cohort was then stratified in "uncontrolled" and "controlled" patients, the latter defined by PRL $<$16, 5 ng/ml. In overall cohort, 12/23 (52.2%) reached disease control. In overall cohort CAB dose negatively correlated with MHQ-A (r=-0. 652; P=0. 016), MHQ-O (r=-0, 0615; P=0, 025), MHQ-S (r=-0.618; P=0.024), MHQ-D (r=-0.561; P=0, 046) and MHQ-I (r=-0.600; P=0.030) score. In patients with uncontrolled disease, CAB dose positively correlated with IIEF-15 overall satisfaction domain score (r=0.829; $P<0.021$) and PRL level negatively correlated with IIEF-15 intercourse satisfaction domain score (r=-0.811; $P<0.027$); in patients with controlled disease, CAB dose negatively correlated with MHQ-S (r=-0.788; $P<0.028$) and MHQ-H (r=-0.716; $P<0.03$) score. Our study highlighted that in patients with uncontrolled disease, a worse disease control (i.e. higher PRL levels), is associated with a worse intercourse satisfaction, and that CAB treatment positively impacts on overall satisfaction; this should encourage a tighter disease control by increasing CAB dose. In controlled disease, CAB dose positively impacts on somatization and hysteria traits, which might contribute to general and sexual health. This happens regardless of PRL levels, suggesting that it might be due to its dopaminergic properties.

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EP1250

Gonadis national registry on gonadal status in pituitary and adrenal disorders: prevalence and characterization of sexual dysfunctions in male patients with acromegaly

Francesco Garifalos[1], Tiziana Feola[2], Noemi Fralassi[3], Cristina De Angelis[1], Marianna Minnetti[2], Rosa Pirchio[1], Linda Vignozzi[3], Annamaria Colao[1], Giovanni Corona[4], Andrea Isidori[2] & Rosario Pivonello[1]
[1]Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia ed Andrologia, Unità di Andrologia e Medicina della Riproduzione, Sessualità e Affermazione di Genere (FERTISEXCARES), naples; [2]Dipartimento di Medicina Sperimentale, rome; [3]Dipartimento di

Scienze Sperimentali Cliniche e Biomediche “Mario Serio”, florence; [4]Endocrinology Unit, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy - Department of Clinical Sciences and Community Health, bologna

The potential independent role of growth hormone (GH) excess in sexual dysfunction of acromegalic male patients is poorly characterized. The aim of the current study was to evaluate the sexual function, in adult males with acromegaly, stratifying the cohort in “uncontrolled” and “controlled” disease. Data were retrieved from GONADIS, a national registry on gonadal status and reproductive and psycho-sexual function in patients affected by pituitary and adrenal disorders, promoted by SIAMS - SIE - AME. Sixty male acromegalic patients aged 18-73 yrs (mean age: 51.4 $\pm$13.4 yrs) were evaluated. In the overall cohort, 34/60 (56.6%) patients had reached disease control; 10/23 (43.4%) had ED at IIEF, 26/34 (76.4%) BPH, 17/37 (45.9%) varicocele, 7/37 (18.9%) testis hypotrophy, 17/47 (36.1%) hypotestosteronemia. Controlled disease patients had significantly higher age ($P=0.021$), disease duration ($P=0.003$), IIEF-15 total score ($P=0.011$), IIEF-erectile function (IIEF-EF) ($P=0.008$), IIEF-orgasmic function (IIEF-OF) ($P=0.021$), IIEF-Sexual desire (IIEF-SD) ($P=0.006$) and IIEF-Overall satisfaction (IIEF-OS) ($P=0.012$), and lower serum levels of insulin ($P=0.022$), HOMA index ($P=0.046$), glycated hemoglobin ($P=0.013$), IGF-1 ($P<0.001$) and GH ($P<0.001$). Controlled disease patients had a lower prevalence of ED ($P=0.001$). Correlation analysis in overall cohort highlighted that IIEF-EF score negatively correlated with free anxiety (MHQ-A) ($r=-0.470$; $P=0.015$) and depression (MHQ-D) ($r=-0.503$; $P=0.009$) traits, serum IGF-1 levels ($r=-0.308$; $P=0.025$); IIEF-OF ($r=-0.460$; $P=0.031$), IIEF-SD ($r=-0.542$; $P=0.009$) and IIEF-OS ($r=-0.515$; $P=0.014$) scores negatively correlated with serum IGF-1 levels. SIEDY scale 1 score correlated positively with age ($r=0.386$; $P=0.02$) and negatively with Peak Systolic Velocity at penile-US ($r=-0.423$; $P=0.016$). Linear regression analysis with age, testosterone, IGF-1, MHQ-A and MHQ-D scores as independent variables failed to identify a main independent predictor of IIEF-EF score.

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EP1251

Nearly asymptomatic hypophosphatasia: a clinical case report

Ekaterina Pigarova[1,2], Aurika Asanova[1,2], Elizaveta Drachuk[1,2] & Larisa Dzeranova[1,2]
[1,2]Endocrinology Research Centre, Moscow, Russia

Introduction
Hypophosphatasia is a group of inherited disorders characterized by the impaired mineralization of bones and/or teeth and low serum alkaline phosphatase (ALP) activity. It is caused by a mutation in the ALPL gene encoding the isoenzyme of ALP resulting in a loss of function. Since an early age of onset is usually associated with a more severe disease, and a late age – with a mild course of the disease, the manifestation of the disorder ranges from a life-threatening condition occurring at birth, characterized by severely impaired bone mineralization and seizures, to young adults with premature tooth loss without other symptoms. Relatively little data is available on the prevalence and clinical features of hypophosphatasia in adults.
Clinical case
An 18-year-old female (weight 56 kg, height 160 cm, BMI 21.9) with complaints of weakness, pain in the legs and joints, darkening in the eyes. Development in childhood and adolescence proceeded without any special features. Considers herself sick since the age of 16, when swelling and tenderness of the left ankle and knee joints appeared without x-ray changes. At the same time, the patient was diagnosed with infectious mononucleosis, after which she noted an increase in general weakness, periodic increases in body temperature to 37.2 0C, loss of appetite, pain in the bones and joints. CRP, ASLO, RF – negative, biochemical indicators, parameters of bone and calcium-phosphorus metabolism were normal except for the detected decrease in ALP to 13-15 U/l (40-150) and a pronounced deficiency of vitamin D - 9 ng/ml (30-100). The diagnosis of hypophosphatasia was confirmed: a pathogenic nucleotide variant *chr1:21563115C>A* was detected in a heterozygous state in the ALPL gene. According to DEXA of the whole body, BMD, taking into account the skull, corresponds to the age norm: -0.5 SD (Z-criterion);BMD excluding the skull corresponds to the age norm: -0.7 SD. According to lateral morphometry, no data were obtained for vertebral deformities and compression fractures. Teeth, hair, nails without any features. A detailed collection of family history revealed similar symptoms of joint pain in the mother with a decrease in ALP to 20 U/l (35-105).
Conclusions
Despite low ALP activity the patient does not demonstrate the typical clinical indications of hypophosphatasia, as evidenced by the absence of manifestations in the mother. The observed symptoms could possibly be the result of mononucleosis. Other genetic, epigenetic, or non-genetic factors influencing illness progression may explain circumstances where it is difficult to demonstrate a link between a pathology’s genotype and phenotype.

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EP1252

Diagnosis of adult GHD: new diagnostic tests

Kevin Yuen
Phoenix, Neuroendocrinology and Neurosurgery, Phoenix, United States

Although diminished height velocity and short stature are important clinical markers to consider testing for GHD in children, the signs and symptoms of GHD are not always so apparent in adults. Furthermore, quality of life and metabolic health are often impacted in adults with GHD; thus, making an accurate diagnosis is important so that appropriate GH replacement therapy can be offered to these patients. However, the diagnostic work up of adult GHD can be challenging and made more complicated by the episodic and pulsatile nature of endogenous GH secretion, concurrently modified by age, gender, and body mass index. Hence, GH stimulation testing is required to establish the diagnosis, and should only be considered if there is a clinical suspicion of GHD and the intention to treat if the diagnosis is confirmed. One or more GH stimulation tests may be required, but existing methods of testing can be inaccurate, difficult to perform, and imprecise. Furthermore, there are caveats when interpreting test results including individual patient factors, differences in peak GH cut-offs (by age and test) and testing time points. For now, the insulin tolerance test (ITT) remains the gold standard test, while the glucagon stimulation test is its reasonable alternative. Following its validation against the ITT, together with its safety, reproducibility and good patient tolerability, the macimorelin test gained approval in the US in December 2017 but its use was limited due to its cost and its distribution in the US was discontinued in May 2023. In Europe, macimorelin (renamed ghryvelin) was approved in January 2019 becoming the newest diagnostic test for adult GHD. Cost withstanding, given the ease of conducting this test and good patient tolerability, the oral macimorelin test has the potential of becoming the preferred GH stimulation test for diagnosing adult GHD in Europe.

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EP1253

Exploring the relationship between metabolic dysfunction-associated steatotic liver disease and osteoporosis

Marin Pecani[1,2], Marzia Miglionico[1], Michele Mallamace[3], Gabriele Angeloni[3], Antonia Barbitta[3], Stefania Basili[4] & Paola Andreozzi[3]
[1]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy; [2]Sapienza University of Rome; [3]Sapienza University of Rome, Policlinico Umberto I University Hospital, Rome, Italy; [4]Sapienza University of Rome, Department of Translational and Precision Medicine, Roma, Italy

Background and aims
Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) and Osteoporosis are two silent prevalent metabolic conditions. MASLD involves fat accumulation in the liver, along with at least one of five specified cardiometabolic criteria, while excluding other liver diseases or secondary causes. Osteoporosis is a systemic skeletal condition characterised by reduced bone mass, leading to increased fracture risk. The relationship between MASLD and decreased bone mineral density remains uncertain. Therefore, this study aims to explore the association of bone mineral density in patients with and without MASLD.
Methods
Subject’s demographics, medical history, and laboratory test findings were collected. MASLD diagnosis was done according to the new consensus statement definition and the guidelines outlined by EASL–EASD–EASO. Dual-energy X-ray absorptiometry (DEXA) was used to evaluate bone mineral density (BMD), and Osteoporosis diagnosis followed the criteria outlined by World Health Organization (WHO). Statistical analysis was performed, with significance determined for P values <0.05.
Results
106 consecutive individuals were investigated for osteoporosis. The study population had a mean age of 63.55 years and consisted of 83 (78.3%) females

and 23 (21, 7%) males. Osteoporosis was identified in 26 (24.5%) patients, while osteopenia and vertebral fracture were present in 54 (50.9%) and 10 (9.4%) patients respectively. Hypertension was the most prevalent condition, affecting 70 (66%) individuals, followed by dyslipidemia in 53 (50%), impaired fasting glucose 19 (17.9%) and type 2 diabetes 14 (13.2%). MASLD was present in 43 patients (40.6%). When comparing individuals with MASLD to those without MASLD, no statistically significant differences were found in age ($P=0.865$), gender ($P=0.285$), smoking status ($P=0.143$), hypertension ($P=0.503$), dyslipidemia ($P=0.166$), or impaired fasting glucose ($P=0.237$). However, there were statistically significant differences between the two groups observed in type 2 diabetes prevalence ($P=0.012$), Body Mass Index (BMI) ($p<0.001$), and Vitamin D levels ($P=0.008$). There were no significant differences between the two groups regarding osteoporosis ($P=0.106$), osteopenia ($P=0.665$), and vertebral fracture ($P=0.178$).

Conclusion

Individuals with MASLD showed reduced levels of vitamin D, increased body mass index, and higher type 2 diabetes prevalence than those without MASLD. However, this study did not reveal an increased association between MASLD and conditions like osteoporosis, osteopenia, or vertebral fractures.

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EP1254

Etiological profile of young diabetes mellitus in south indian population

Sadishkumar Kamalanathan[1], Kg Rashmi[1], Jayaprakash Sahoo[1], Dukhabandhu Naik[1], Jabasteen J[2], Aaron Chapla[2] & Nihal Thomas[2]
[1]JIPMER, Endocrinology, Puducherry, India; [2]CMC, Endocrinology, Vellore, India

Background & objective

In contrast to Caucasians of European origin, the aetiology of diabetes mellitus (DM) in young adults in other ethnic groups, including Indians is likely to be heterogeneous and difficult to determine. This study was undertaken to determine the aetiology of DM in the young South Indian population.

Methods

In this ambispective study, 144 South Indian young-onset diabetes (age at onset 12-35 years; duration <5 years) were studied. Diabetes secondary to steroid intake, gestational diabetes and secondary to endocrine diseases like acromegaly, and Cushing's disease were excluded. Fasting and post-prandial plasma glucose, fasting lipid profile, fasting and stimulated C-peptide, islet cell antibodies ICAs [glutamic acid decarboxylase 65 (GADA), tyrosine phosphatase (IA-2Ab) and zinc transporter-8 (ZnT8Ab)] and pancreatic imaging using abdominal radiography was performed in all patients. Clinically suspected MODY subjects were subjected to targeted next generation sequencing for 13 MODY genes.

Results

The prevalence of type 2 diabetes (T2DM) and type 1 diabetes (T1DM) was 59.02% (85/144) and 29.16% (42/144) respectively, followed by fibrocalculous pancreatic diabetes (2.77%). Other rare types included MODY (2.08%), ketosis-prone type 2 DM (2.08%), diabetes secondary to lipodystrophy (1.38%), syndromic diabetes (1.38%), diabetes secondary to pancreatic disease (2.08%). The median (IQR) fasting c-peptide was 1.83(1.3, 2.62) vs 0.27(0.023, 0.66) ng/ml [$P<0.0001$] while stimulated C-peptide was 4.38(2.82, 5.95) vs 0.43(0.093, 1.55) ng/ml[$P<0.0001$] in T2DM and T1DM respectively. ICA was positive in 73.80% of T1DM and 5.8% of T2DM. Among T1DM subjects, the ICA positivity for GADA, IA-2Ab and ZnT8Ab was 61.90% (26/42), 21.42% (9/42) and 1.66% (7/42) respectively. GADA+ IA-2Ab positivity was found in 7.14%, and GADA+ZnT8Ab positivity was found in 9.52%. and only one T1DM subject was found to be positive for IA-2Ab+ZnT8Ab. For diagnosis of T1DM, the addition of IA-2Ab increased the yield in three subjects, while ZnT8 didn't add to the yield. MODY was diagnosed in 2.08% (3/144) subjects, one subject was positive for a novel heterozygous ABCC8 (NM_000352.6): c.1591A>G. *P* (Thr531Ala) gene missense variant with unknown significance. Other two MODY subjects were positive for heterozygous ABCC8 (NM_000352.6): c.917G>A p. (Arg306His) gene missense mutation and a rare heterozygous PDX1 (NM_00209.4): c.670G>A *P* (Glu224Lys) gene variant with unknown significance respectively.

Conclusion

The aetiology of diabetes in young adults was heterogeneous, with T2DM more common than T1DM. Testing for islet antibodies and C-peptide along with targeted genetic testing in this age group helps in the correct etiological diagnosis of diabetes.

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EP1255

A case of langerhans cell histiocytosis accompanying hypothalamus, mastoid bone and liver involvement

Saadet Acar, Berrin Çetinarslan, Zeynep Cantürk, Alev Selek, Emre Gezer, Damla Köksalan, Özlem Alkan & Fatma Öktem
Kocaeli Üniversitesi Tıp Fakültesi, Endocrinology and Metabolic Diseases, Kocaeli, Turkey

Introduction

Langerhans cell histiocytosis (LCH) is a multisystem neoplastic disease with primarily bone and skin involvement. Although its pathogenesis is still not fully understood, LCH lesions contain clonal CD 207+ dendritic cells with the frequently identified BRAF V600E mutation and an inflammatory component. Although isolated central nervous system involvement is extremely rare, a common site of involvement is the hypothalamic-pituitary axis.

Case

A 35-year-old female patient applied to us with complaints of headache, excessive water retention, vomiting, weakness and amenorrhea in the last two months. There was no additional disease in his medical history other than hyperlipidemia. There was no history of previous surgery or head trauma. On physical examination, there was a fluctuating disorientation in place and time. The patient had panhypopituitarism and hypernatremia at the time of admission. It was determined that the patient, who was subjected to water restriction, had central diabetes insipidus. Contrast-enhanced cranial MRI revealed 19x10x17 mm a mass in the hypothalamus and diffuse contrast enhancement. PET-CT showed increased FDG uptake in the pituitary locus (SUV-max: 19.4), posterior of the left mastoid (SUV-max: 12.4) and hepatıc segment 8 (SUV-max 8.4). Temporal MRI showed mass lesions extending to the petrous sinus with signal characteristics similar to hypothalamic lesions. Liver dynamic MRI showed T2A hyperintense lesions with progressive contrast enhancement, the largest of which was 12 mm in diameter in the subcapsular area of segment 8. Thereupon, the patient underwent mastoid and liver biopsy. The biopsy result showed widespread monocyte infiltration with acidophilic cytoplasm and stained pozitifly with S100 and CD1a. The patient was referred to the oncology clinic for treatment.

Conclusions

Multisystemic diseases such as Langerhans cell histiocytosis should be considered in the differential diagnosis of patients with a hypothalamic mass, and other systemic involvements should also be investigated.

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EP1256

Factors associated with high glycemic variability in adolescents with type 1 diabetes

Faten Mahjoub, Ines Bani, Nadia Ben Amor, Ramla Mizouri & Jamoussi Henda
Institut De Nutrition, Tunis, Tunisia

Factors associated with high glucose variability in patients with type 1 diabetes

High glycemic variability is recognized as a risk factor for degenerative complications and hypoglycemia. The factors affecting glycemic variability in diabetic patients need to be clarified. Our aim was to determine factors associated with high GV in adolescents patients with type 1 diabetes.

Method

This is a cross-sectional analytical study, conducted at the National Institute of Nutrition in Tunis during the year 2022, including adolescents with type 1 diabetes, who underwent continuous glucose monitoring for 6 days. We analyzed the continuous glucose monitoring CGM data for each patient and we calculated the coefficient of variability (CV)by dividing the SD by the mean glucose and multiplying by 100 to get a percentage.

Results

Our study included 90 patients with type 1 diabetes, of which 53 are girls and 37 are boys. The average age was $16.6\pm2.$, and the mean duration of diabetes was 6.7 ± 3.5 years. The average CV was $40\pm12\%$, and 62, 2% of patients had a CV greater than 36%. The age of patients, and duration of diabetes were positively correlated with CV ($P=0.001$ and $P=0.002$ respectively), however, age at onset of diabetes was negatively correlated with CV ($r=-0.3$; $P=0.004$). Patients with higher glycemic variability took significantly higher doses of basal insulin ($P=0.03$). Patients on insulin analogues had a significantly lower CV than patients on NPH insulin ($P=0,\ 021$). A significant association was observed between the presence of lipodystrophy and a cv $>36\%$ ($P=0,\ 024$). However, no statistically significant relationship was found between the presence of autoimmune diseases such as adrenal insufficiency, celiac disease and hypothyroidism) and glycemic variability.

Conclusion
Several factors are involved in the genesis of glycemic variability in type 1 diabetics. Recognizing these factors enables us to act on modifiable factors to limit glycemic variability.

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EP1257

«Is there disparity in gestational diabetes care in Switzerland?»

Nina Kägi-Braun[1], Kutz Alexander[2] & Löf Marie[1]
[1]Karolinska Institute, Sweden; [2]KSA Kantonsspital Aarau, Aarau, Switzerland

Background
Lifestyle interventions as well as pharmacological therapy are strong measures to prevent adverse pregnancy and birth outcomes in women with gestational diabetes (GDM). Social determinants of health and consequent health disparities can affect a successful GDM management. This includes inequality in health care and education quality, economic stability as well as environmental factors. However, in high-income countries, these social determinants of health have rarely been studied even though gestational diabetes prevalences as well as social inequities are a rising health care problem.
Aim
Therefore, our aim is to investigate whether the association between GDM and adverse maternal outcomes is modified by insurance classes, regional area, or citizenship.
Methods
This is a population-based retrospective cohort study, using Swiss claims data from the Federal Statistical Office from January 2012 to December 2021. All delivery hospitalisations in Swiss hospitals were included and stratified according to maternal gestational diabetes status. The primary endpoint is a composite endpoint of adverse pregnancy (hypertensive disorders), delivery (induction of labor, instrumental or surgical delivery, obstetric traumata, other complications) and puerperal (infections, venous complications, other complications) outcomes defined by ICD-10 and CHOP codes. Secondary outcomes are the single components of the primary outcome.
Results
Of the identified 850, 414 delivery hospitalisations between 2012 and 2021, 7.3% of the pregnancies were affected by GDM. Women with GDM were more likely to be publicly insured, more often born outside of Switzerland and lived more often in a region with a high urban population. GDM patients had higher risk of an adverse obstetric outcome overall (OR 1.14, 95% CI 1.12-1.16). This association remained stable in the citizenship or insurance status subgroups but not in the regional area subgroup where we found a more pronounced association in women living in a canton with higher proportion of rural population (rural canton OR 1.18, 95% CI 1.14-1.23 vs urban canton OR 1.12, 95% CI 1.11-1.15, *P* for interaction 0.043).
Conclusion
We found no evidence for health disparity in relation to insurance status and citizenship in Switzerland. If there is no treatment inequality or if these variables are not adequate proxies for health disparities remains unknown. The finding that women from a more rural canton were at higher risk for GDM-related outcomes might be of importance in further improving nation-wide GDM care.

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EP1258

Atypical manifestation of parathyroid carcinoma in patient with RET and CYP24A1 mutations: a case report

Aurika Asanova, Ekaterina Kim, Anna Eremkina, Ekaterina Pigarova & Natalia Mokrysheva
Endocrinology Research Centre, Moscow, Russia

Introduction
Parathyroid carcinoma (PC) is one of the rarest endocrine malignancies. Most PCs are sporadic, sometimes occurring in the framework of familial primary hyperparathyroidism (PHPT). PHPT due to PC is usually characterized by significantly increased PTH levels, severe hypercalcemia, larger tumor size and a higher incidence of disease complications.
Clinical case
A 56-year-old male C. presented with an accidental formation at the posterior contour of the right thyroid gland lobe 10x9x9 mm according to US in 2017 (correlated with ST scan). Mineral metabolism parameters were assessed for the first time after a year: PTH 13.67 pmol/l (1.6-6.9), hypercalcemia - Ca 2.86 mmol/l (2.12-2.6), *P* and daily calciuria were not determined. PHPT complications included recurrent urolithiasis (first manifesting at age 25), osteopenia in L1-L4 (-2.2 SD T-score). C. did not notice loss of height, gastric and duodenal ulcers. There was no family history. In 2019 the patient underwent selective parathyroidectomy followed by mild asymptomatic hypocalcemia (Ca 2.15 mmol/l). At discharging he was prescribed cholecalciferol 2000 IU. Histological examination revealed atypical parathyroid tumor (APT) with fibrous bands, hemorrhages and foci suspicious for capsular invasion. After immunohistochemistry (IHC) the diagnosis was reclassified as PC based on capsular invasion and the presence of tumor cells in the surrounding fatty tissue. Ki-67 was 9%, there was positive parafibromin expression. Regular follow-up confirmed normocalcemia and PTH within the reference ranges. We recommended gene panel sequencing associated with hereditary forms of PHPT that revealed heterozygous mutations with uncertain significance variants: in the *RET (c.3052C>T:p.L1018F)* and *CYP24A1 (c.37G>A:p.A13T)* genes. The patient is currently in remission of the disease. DEXA scans showed positive dynamics in the BMD (L1-L4 -1 SD) There are no clinical symptoms of MEN2 syndrome. Liquid chromatography–mass spectrometry did not reveal any changes in the vitamin D metabolites similar to *CYP24A1* mutation.
Conclusions
Patients with solid masses near the typical location of the parathyroid glands should be examined for PTH and Ca. Morphological diagnosis of ATP requires additional IHC. In the present case the mild clinical course of PC and tumor's small size are noteworthy. The identified mutations with unknown pathogenicity are also of particular interest because they have not been previously described in patients with PC.

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EP1259

Langerhans cell histiocytosis presenting spinal cord compression after diabetes insipidus diagnosis: a case report

Zeliha Yarar[1] & Hülya Kaynak[2]
[1]Tokat State Hospital, Department of Endocrinology and Metabolism, Tokat, Turkey; [2]Meram Faculty of Medicine, Necmettin Erbakan University, Department of Endocrinology and Metabolism, Konya, Turkey

Introduction
Langerhans cell histiocytosis (LCH) is a proliferative disease that origins from dentritic cell family. LCH most commonly affects bones and skin, but it can also involve the other systems and organs. Lytic bone lesions are the most common findings in LCH, LCH can involve any bone; the most common sites are skull and femur. In rare case, lytic osseous lesions occur in the spine. Diabetes insipidus (DI) is the most frequent endocrine abnormality associated with LCH and it can occur prior to, concomitant with or after the diagnosis of LCH. Here, we report a rare case of LCH at spinal vertebra in an adult patient with present neurological deficits.
Case Report
A 33-year-old woman presented with 3 months history of back pain, weakness in the lower extremities and unable to walk for 2 days. She had no history of fever, weight loss. The patient's medical history was unremarkable for trauma or other bone diseases. Three years before admission, the patient was diagnosed with central DI and desmopressin treatment was started. The etiologic cause of DI could not be found. On physical examinations, she rated the back pain as visual analogue scale 8 and localized tenderness over the C7-T1 spinous process was showed. Muscle strength in lower limbs was slightly decreased (3-4/5). Pathological reflexes were negative for both legs. And there were no sensory abnormalities. Her body temperature was normal, and there was no inflammatory focus in other systems. Laboratory tests including blood cell count, serum electrolytes, renal and liver function tests, erythrocyte sedimentation rate, and C-reactive protein did not reveal any abnormalities. Computed tomography showed a defined osteolytic lesion involving the the vertebral body C7, T1 and L2. Magnetic resonance imaging revealed a continuous enhancing epidural lesion located C7-T1 level with spinal cord compression. Because of motor weakness, and cord compression, the patient underwent posterior laminectomy. Histopathological examination showed that neoplastic cells which were positive for S-100, CD 68 and CD-1a. These features confirmed the diagnosis of LCH. After surgery, the patient showed a progressive improvement in motor function. The patient underwent chemotherapy with prednisolone and vinblastine.
Conclusion
We reported a rare case of adult spinal LCH with epidural involvement and neurological compression. The patient was treated succesfully vertebral resection and chemotherapy. Although extremely rare, LCH should be considered when there are epidural lesions with spinal cord compression in adults and it can be seen years after DI diagnosis.

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EP1260

Papillary thyroid carcinoma revealed by toxic goiter: a case report

Hajar Azagouagh, Karimi Meryem, Talbi Dounia, Sebbar Ghizlane, Rifai Kaoutar, Iraqi Hind & Mohamed Elhassan Gharbi
Chu Ibn Sina, Endocrinology, Rabat, Morocco

Introduction
A toxic goiter is a goiter that functions autonomously, causing hypersecretion of thyroid hormones, and is almost always benign. We report here the case of a toxic goiter that revealed the presence of papillary thyroid carcinoma.
Observation
Patient aged 68, with a history of arterial hypertension, followed for hyperthyroidism on a toxic goitre, with a thyroid scintigraphy showing an enlarged thyroid gland with intense uptake on the right side, an ultrasound scan showed a multiheteronodular goiter with nodules classified EUTIRADS 3 and 5. Antithyroid antibodies were negative, which led to her being put on TSA and beta-blockers, and the patient underwent surgery after euthyroidism. Pathological examination revealed an invasive variant vesicular papillary carcinoma of the right lobe of the thyroid measuring 1.5 cm long, with the presence of vascular emboli, and an invasive variant vesicular papillary microcarcinoma of the left lobe of the thyroid measuring 0.5 cm long, with the presence of vascular emboli. The tumour was classified as PT2NxMx at intermediate risk of recurrence. Iratherapy was considered and the patient was put on hormone replacement therapy with l. Thyroxine.
Discussion and conclusion
Differentiated thyroid carcinoma usually occurs in euthyroidism. The association of papillary thyroid carcinoma with hyperthyroidism is exceptional. The prevalence of this association varies from 0.2 to 8.3%. This has led to widely adopted recommendations by several expert groups not to perform cytopuncture on these lesions. Our case has shown that the risk of malignancy in toxic goitres is not zero, hence the need to resort to cytopuncture in the presence of elements in favour of malignancy.

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EP1261

Liver injury after I131 administration

Irina Tica
"Ovidius" Faculty of Medicine, Constanta, Romania, IInd Medical Department, Constanta, Romania

Hepatic effects of I131 administration in endocrine disorders are not mentioned in drug's recipe and are rarely described in medical literature. We present the case of a 32 years old woman who was admitted and investigated for myalgias, arthralgias, asthenia and elevated transaminases (ALAT = 482.22 UI/l). The patient was diagnosed in 2022 with autoimmune thyroiditis and a dominant nodule (TIRADS 4) in the right lobe. Thyroidectomy was performed in 2023 and multifocal, partially incapsulated papillary carcinoma was detected. Three months after thyroidectomy, a dosage of 30 mCi of I131 was administered. Five months after thyroidectomy, the patient was admitted for the previous symptoms. After multiple and extensive investigations, using the Roussel Uclaf Causality Assessment Method scaler, the diagnosis of drug (I131) induced liver injury was considered. After conventional hepatoprotective treatment failed to improve patient's status, corticoid treatment was used, with a benefic outcome. Even if liver injury is not cited as an adverse effect of I131 administration, it must be taken into consideration. The manifestations start after a long time (3-6 weeks) post-exposure and they do not respond to conventional hepatoprotective treatment but to corticotherapy.

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EP1262

Clinical and biochemical characteristics of pheochromocytoma

Anna Lugovskaya & Irena Ilovayskaya
Moscow Regional Research and Clinical Institute, Department of Neuroendocrine Diseases, Moscow, Russian Federation

Introduction
Pheochromocytomas (PCCs) or adrenal paragangliomas are neuroendocrine non-epithelial catecholamine-producing tumors with a wide range of cardiovascular, metabolic, neurological manifestations, which may complicate the early diagnosis of the disease in some cases.
Materials and methods
We analyzed data from 89 patients (58 women, 31 men, median age 52 years) with histologically and immunohistochemically verified PCCs including 4 patients with bilateral PCCs.
Results
The most common symptom was hypertension which was observed in 78 (85%) patients including 67 (73%) patients with paroxysmal hypertension, and 11 (12%) patients with sustained hypertension. Median blood pressure (BP) was 200/107mm Hg, the majority (75%) of patients had BP grade III (ESH/ESC 2018). Episodes of tachycardia were observed in 34 (37%) patients. The other most common symptoms were headaches ($n = 47$, 51%), pain in the lumbar region ($n = 20$, 22%) and sweating ($n = 16$, 17%). According to biochemical data, mixed type of secretion predominated (59%), noradrenergic type (25%) and adrenergic type (8%) were rare. Interestingly, we did not observe catecholamine hypersecretion in 8% cases patients despite the subsequent verification of PCCs. Perhaps they had dopamine type of secretion which is currently not available in routine clinical practice. We could not find any obvious correlation between hypertension course and biochemical catecholamine profile. According to CT data of PCCs, the size varied from 1.5 cm to 20 cm (median 4.75), native density - from +9HU to +96HU (median +39HU). Lesion's size was >4 cm in most of the patients (75%), however, CT-density <+10HU was a more accurate marker of pheochromocytoma.
Conclusion
In our cohort of patients, BP grade III (ESH/ESC 2018) predominated regardless of the type of catecholamine secretion. We could not find any obvious correlation between hypertension course and biochemical catecholamine profile. The absence of catecholamine hypersecretion does not exclude the presence of pheochromocytoma in patients with arterial hypertension and an adrenal tumor. Pheochromocytoma should be considered in adrenal lesions of high native CT-density.

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EP1263

Nutritional status in patients with eating disorders after hospital admission

Delia Lavinia Marginean, Carmen Zurera Gomez, María Ángeles Gálvez, Ángel Rebollo-Román & Concepción Muñoz
Hospital Reina Sofía, Endocrinología y Nutrición, Córdoba, Spain

Introduction
Eating disorders (ED) are prevalent psychiatric conditions with significant nutritional implications, posing a risk of life-threatening illness for patients. The chronic and recurrent nature of these disorders, along with normal laboratory test results, present challenges in their management and ongoing monitoring, which typically focuses on weight changes. Techniques like determining the phase angle using bioimpedance analysis or conducting functional muscle tests such as dynamometry can be valuable for monitoring the progression of these patients.
Objective
To evaluate changes in anthropometric measures (weight and body mass index), muscle function and body composition in patients with ED after hospital admission.
Methods
Patients with at least one hospital admission in the last three years. Anthropometric data, bioimpedance and dynamometry data were collected. Statistical analyses were performed with SPSS version 25.
Results
Eighteen cases were included, 100% women with a mean age of 24 + 7.15 years. Anthropometric data at admission: weight 40.59 + 6.17 kg and BMI 14.70 + 1.45 kg/m^2. The 61.1% presented low phase angle (<5.5º). Dynamometry on admission: right arm 20.62 + 4.99 kg and left arm 19.27 + 6.35 kg. After 33.16 + 27.58 days of admission, a significant increase in weight was observed with a mean at discharge of 44.14 + 6.42 kg ($P < 0.05$) and BMI of 16.18 + 1.78 kg/m^2 ($P < 0.05$). At discharge, 55.6% continued with low phase angle. Improvements in functional muscle testing were observed, with right arm dynamometry of 23.71 + 5.00 kg ($P = 0.11$) and left arm dynamometry of 22.24 + 4.91 kg ($P = 0.22$) not significant.
Conclusions
The study population did not show significant alterations or improvements in the analytical parameters after admission, which is consistent with findings in the literature. These findings are more commonly observed in other eating disorders such as bulimia nervosa. Additionally, the phase angle did not exhibit significant improvement after admission, despite being previously reported by other authors. However, dynamometry did show improvement, even though the baseline values were not pathological. This study suggests that BMI and weight are sensitive parameters for determining the timing of admission and confirming the clinical stability of the patients.

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EP1264

Results of bariatric surgery in a third level hospital in the last 5 years

Eduardo Torrecillas del Castillo, Mercedes Peinado Ruiz, María del Castillo Tous Romero, Reyes Rave García, Eduardo Domínguez-Adame Lanuza, Juan Manuel Cáceres Salazar & María Asunción Martínez Brocca
Hospital Universitario Virgen Macarena, Sevilla, Spain

Aim
Describing bariatric surgery (BS) interventions in our center in the last five years, complications and effectiviness in weight loss and resolution of comorbities.
Methodology
Prospective descriptive study on a cohort of people who underwent BS surgery at Virgen Macarena University Hospital, a tertiary hospital of the Public Health System of Andalusia, between January 2018 and May 2023. Patients who underwent revision surgery with a first previous surgery were excluded. Description of demographic characteristics, complications, weight evolution, comorbidities associated with obesity (diabetes, arterial hypertension and OSA) and their remission after BS up to two years later. Quality criteria based on AEC and SECO recommendations.
Results
217 patients, average age 46.55 years, 156 women (71.9%) Median follow-up time between surgery and last check-up 19.8 months. Most common surgery: vertical sleeve gastrectomy (77.88%), 21.66% gastric bypass. Surgery complications: early complications 23 cases (10.6%), 1 death (0.46%). Reintervention before 30 days 5.06%. Revision surgery: 5.52%, GERD most common cause. Initial average weight 140.7 kg (SDS 23.42). Initial BMI 51.36 kg/m^2, 14.5% weight loss in preparation for surgery. Average weight after one year 83.97 kg (SDS 14.10). Average weight after 2 years 83.29 (SDS 14.77), loss of 40.8% of weight and 79.2% of excess overweight. Average weight after 5 years 87.5 kg (SDS 14.5), weight loss of 37.8%. Comorbidities before BS: Diabetes mellitus (DM) 64 (29.5%), prediabetes 28 (12.9%). Average oral drugs for + GLP1a 2.01 (70.3% of patients with GLP1 analogues). 13 patients with insulin (20.6%, 64 IU/day on average, SDS 40.55). Arterial hypertension (AHT) 113 cases (52.1%), average number of drugs for control 2.03. OSA with CPAP 126 patients (58.1%). After BS: DM remission 69.8%. Insulinization 3 patients (1.38%), 12.55 IU/day on average (SDS 12.14). Cessation of aGLP1 in 97.77%. AHT remission 68.1%. Withdrawal of CPAP in patients with OSA 49.2%.
Conclusions
We observed good initial weight loss data, highlighting a high percentage of loss in the preoperative period and maintenance of the percentage obtained after the intervention. Sleeve vertical gastrectomy was the most used technique. The percentage of remission of comorbidities after BS is high two years after surgery. Greater follow-up is needed to evaluate definitive data on weight loss, medium-long term complications, evolution of comorbidities, need to reintroduce drugs due to comorbidities and revision surgery.

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EP1265

Diagnostic challenges: suspected adrenal myeloid sarcoma

Kouloud Hachani[1], Sabrine Mekni[1,2], Sawsen Essayeh[1,2], Rihab Laamouri[1], Meriem Werfelli[1], Nadia Mchirgui[1], Karima Khiari[1], Imen Rojbi[1,2] & Ibtissem Ben Nacef[1,2]
[1]Charles Nicolle Hospital, Tunis, Tunisia; [2]Laboratory of Renal Pathology LR00SP01, Tunis, Tunisia

Introduction
Myeloid sarcoma is a rare etiology of adrenal tumors, with both diagnostic and therapeutic difficulties. This clinical case highlights the diagnostic challenges inherent in the coexistence of these two pathologies, underscoring the complexity of their management.
Case report
We present the case of a 40-year-old woman with a history of polycystic ovary syndrome since her youth. She was referred to our department to explore adrenal incidentaloma as a CT scan of the abdomen showed a 55 × 49 mm heterogeneous adrenal mass with a density of 35 HU. Investigations revealed a suspicious, non-secreting mass, with morning cortisol levels after a 1-mg overnight dexamethasone suppression test at 22 nmol/l and normal Urinary metanephrins and normetanepherins, testosterone and SDHEA levels. Clinicobiological assessments and CT chest-abdomen-pelvis excluded metastasis from another cancer. The patient was referred to the urology department for total adrenalectomy, but she developed (2month later) bicytopenia, presenting with anemia at 5 g/dl and thrombocytopenia at 50, 000 / microliter. Faced with the hematological emergency, surgery and biopsy could not be performed, and the patient was referred to the hematology department. The diagnosis of acute myeloid leukemia was established, and the patient underwent chemotherapy (protocol combining intensive induction chemotherapy, and consolidation treatment). The course was marked by a significant decrease in adrenal tumor size by 47% in the adrenal CT scan follow up. Given this evidence, the most probable diagnosis appears to be myeloid sarcoma of the adrenal gland.
Conclusion
Myeloid sarcoma can develop before the onset of acute myeloid leukemia (Aml), concurrently with AMl, or during Aml relapse. Its localization in various organs is possible, however, adrenal localization remains rare. Diagnosis can be concluded by clinical and evolutive evidence, but definitive confirmation always relies on histopathology.

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EP1266

LHX4 mutation: new perspective

Stefania Munari, Rebecca Vitella, Rossella Gaudino & Franco Antoniazzi
Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy

Background
Growth is a multifactorial trait, in which about 80% are determined by genetic factors. The pituitary plays a central role and some of the transcription factors can be involved in isolated or combined deficits: they orchestrate the ontogeny of the gland, maintain the differentiated state and mediate the coordinated expression of specific cell type. Among them, *LHX4* mutations can manifest as a combined pituitary hormone deficiency and are associated with an ectopic posterior pituitary and/or a sella turcica defect. Its mutations are associated with variable expressivity and incomplete penetrance.
Case presentation
We describe a patient with growth failure. Regular pregnancy without problems reported at prenatal ultrasounds. Term-born: weight 3040g (-1.1 SDS), length 48 cm (-1.5 SDS), head circumference 33 cm (-1.5 SDS). No dysmorphisms. At the age of three, sleep apneas are reported with an obstructive sleep apnea syndrome (OSAS) with central predominant component of mild degree at the polysomnography. At the age of four, we evidenced a growth slowdown (height -2.7 SDS, with TH -1, 2 SDS). We excluded celiac disease, hypothyroidism, GH deficiency (GHD), chromosomopathy and *SHOX* gene alteration. Bone age was delayed by about 1 year. Due to persistence of growth failure, we performed a genetic analysis that revealed a mutation in the *LHX4* gene c.250C>T p.(Arg84Cys), which was subsequently detected in the father (final height 168 cm). No other deficits in pituitary hormone function were found. The brain MRI showed no abnormalities in the hypothalamic-pituitary region nor other encephalic defects were detected. At the age of 6, 8, we started a trial therapy with rhGH 27 mg/kg/day, but due to behavior disorder (anger outbursts) and the lack of improvement in growth rate with the therapy the treatment was suspended after 6 months.
Conclusions
Our patient has a mutation that is already described as putative, but he doesn't present the typical clinical features: he doesn't have any pituitary deficit nor any alteration at the brain MRI. His short stature can't be explained by a GHD, moreover the trial treatment with rhGH didn't work. Further studies are needed to elucidate the relationship between short stature and the *LHX4* mutation. The central OSAS could be related to the *LHX4* mutation since studies on mice demonstrated a ventral motor neuron defect that impair respiratory movements, associated whit lung hypoplasia. This could be a possible manifestation in humans which let us widen the clinical manifestation associated with such mutation.

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EP1267

The influence of hyperglycemia on clinical and biochemical parameters in patients with acute myocardial infarction

Mehriban Rizaeva[1] & Zulaykho Shamansurova[2,3]
[1]Bukhara State Medical Institute, Endocrinology, Bukhara, Uzbekistan; [2]Central Asian University Medical School, Endocrinology, Tashkent, Uzbekistan; [3]Institute of Biophysics and Biochemistry at the NUUz, Metabolomics, Tashkent, Uzbekistan

Introduction
Hyperglycemia is often elevated in patients with acute myocardial infarction (AMI) and is a prognostic indicator. According to a number of researchers, the risk differs between women and men. The purpose of our study was to study the effect of hyperglycemia on clinical and biochemical parameters in men and women with AMI.

Materials and methods
The study was conducted on 92 patients admitted to the intensive care unit of the cardiology center in Bukhara. Of these, 65% are men and 35% are women, aged from 42 to 84 years. Among them, 16 patients had a history of type 2 diabetes. All subjects were measured for BMI, SBP, DBP, general blood count, urine test, glycemia, HbA1c, ALT, AST, blood urea and creatinine levels, and coagulation parameters according to a coagulogram.
Results
The results showed that AMI was more common in men (1.78 times) compared to women, while the increase in glycemia was observed in women by 1.87 times higher compared to the group of men. BMI, SBP, DBP, and blood biochemical parameters did not differ significantly in the group of men and women. However, the dependence on glycemia assessed by correlation showed an average correlation between BMI in the group of men with normoglycemia, while in women this relationship was positive in both the group with normoglycemia and hyperglycemia. A positive correlation was found between the parameters of SBP, leukocytes, blood platelets, with proteinuria, prothrombin index, D-dimer. Interestingly, a positive correlation with glycemia was detected with both normo- and hyperglycemia; there was a weak correlation with BDNF levels.
Conclusions
AMI is more common in men than in women. At the same time, clinical and laboratory parameters did not differ significantly. A correlation was found with BMI, SBP, blood leukocyte level, blood D-dimer, and a weak correlation was noted with blood BDNF level, which suggests their consideration as prognostic criteria for the prognosis of AMI.

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EP1268

Using a SGLT2 inhibitor does not modify the efficacy and tolerability of extended-release metformin in patients with type 2 diabetes

Borja Santana-Ojeda[1], Alba Hernandez-Lazaro[2], Ricardo Jose de Leon-Durango[1], Inmaculada Molinero-Marcos[1], Agnieszka Kuzior[3], Claudia Arnas-Leon[1,3], Jennifer Maria Perez-Rivero[4], Marta Martin-Perez[5], Paula Gonzalez-Diaz[6] & Francisco Javier Martinez Martin[1,3]
[1]University Hospital of Gran Canaria Dr. Negrín, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [2]Parc Taulí University Hospital, Endocrinology & Nutrition, Sabadell, Spain; [3]Clinica San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [4]Centro Salud Escaleritas, Family & Community Medicine, Las Palmas de Gran Canaria, Spain; [5]Clínica Cajal, Family & Community Medicine, Las Palmas de Gran Canaria, Spain; [6]University Hospital of Gran Canaria Dr. Negrín, Emergency Medicine, Las Palmas de Gran Canaria, Spain

Introduction and Objectives
The tolerance of extended-release metformin (XRM) is superior to that of conventional metformin. XRM is recently available in Spain as a fixed combination with sitagliptin, but not in monotherapy. There are no data yet on how additional antidiabetic treatment can modify the effects of the XRM/sitagliptin combination. After assessing the efficacy and tolerability of XRM/sitagliptin in patients with T2DM labelled as metformin-intolerant and treated with a DPP4 inhibitor (DPP4i), we performed additional analyses in order to assess if additional treatment could modify these results.
Patients and Methods
Consecutive patients with T2DM, HbA1c $>7\%$ and GFR (CKD-EPI) >45 mL/min/1.73m^2 labelled as metformin-intolerant due to gastrointestinal symptoms, and treated with a DPP4i were switched to the 50 mg sitagliptin plus 1000 mg XRM combination, taking 1 pill daily in the first month and afterwards 2 pills if the tolerance was good. Tolerance data were obtained by questionnaire in the follow-up visit. All Included patients granted informed consent.
Results
29 patients previously treated with SGLT2i (17 with empagliflozin, 8 with dapagliflozin and 4 with canagliflozin) could be pooled and analyzed vs. 43 not treated with any SGLT2i. No patient was treated with metformin (due to assumed intolerance); all were treated with DPP4i (by protocol) but none with a GLP-1ra (due to incompatibility with iDPP4); 5 patients were treated with insulin, 4 with gliclazide, 3 with repaglinide and 3 with pioglitazone; these drugs were unsuitable for analysis due to sample size. There were no significant differences for the reductions in fasting glycemia (without SGLT2i: 36 ± 16 mg/dl with 1 pill, 45 ± 17 mg/dl with 2 pills; with SGLT2i 32 ± 16 mg/dl with 1 pill, 40 ± 13 mg/dl with 2 pills) or in HbA1c (without SGLT2i: $0.64\pm0.30\%$ with 1 pill, $0.95\pm0.32\%$ with 2 pills; with SGLT2i $0.59\pm0.28\%$ mg/dl with 1 pill, $0.91\pm0.30\%$ with 2 pills) induced by the switch from DPP4i to XRM/sitagliptin in patients with vs. without previous SGLT2i treatment. There were also no significant differences for tolerance: without SGLT2i: 8 patients (18.6%) did not tolerate the rechallenge, and 5 (11.6%) tolerated only 1 pill; with SGLT2i, 4 (13.8%) did not tolerate, and 3 (10.3%) tolerated only 1 pill.
Conclusions
A large majority of the patients with T2DM labelled as metformin-intolerant and treated with DPP4i tolerated XRM/sitagliptin, and their fasting blood glucose and HbA1c significantly improved. The concomitant use of iSGLT2i did not modify these results. Other antidiabetic treatments could not be meaningfully analyzed.

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EP1269

Rechallenge with extended-release metformin in patients with type 2 diabetes labelled as metformin-intolerant: satisfaction and its determinants

Ricardo Jose de Leon-Durango[1], Alba Hernandez-Lazaro[2], Carlos Rios-Gomez[1], Borja Santana-Ojeda[1], Inmaculada Molinero-Marcos[1], Agnieszka Kuzior[3], Claudia Arnas-Leon[1], Jennifer Maria Perez-Rivero[4], Debora Maria Garcia-Alamo[5] & Francisco Javier Martinez Martin[1,3]
[1]University Hospital of Gran Canaria Dr. Negrín, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [2]Parc Taulí University Hospital, Endocrinology & Nutrition, Sabadell, Spain; [3]Clinica San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria; [4]Centro Salud Escaleritas, Family & Community Medicine, Las Palmas de Gran Canaria, Spain; [5]Hospital Virgen Macarena, Laboral Medicine, Sevilla, Spain

Introduction and Objectives
Extended-release metformin (XRM) is recently available in Spain as a fixed combination with sitagliptin, but not in monotherapy. Its tolerance is clearly superior to that of conventional metformin, and since 2005 the NICE guidelines for type 2 diabetes mellitus (T2DM) recommend its use in patients with metformin-caused gastrointestinal disturbances. We assessed the efficacy and tolerability of XRM/sitagliptin in patients with T2DM previously labelled as metformin-intolerant and treated with a DPP4 inhibitor (DPP4i), and additionally analyzed the data for patient satisfaction.
Patients and Methods
Consecutive patients with T2DM, HbA1c $>7\%$ and GFR (CKD-EPI) >45 mL/min/1.73m^2 labelled as metformin-intolerant due to gastrointestinal symptoms, and treated with a DPP4i were switched to the 50 mg sitagliptin plus 1000 mg XRM combination, taking 1 pill daily in the first month and afterwards 2 pills if the tolerance was good. The mean reductions in HbA1c were 0.6% with 1 pill and 0.9% with 2 pills (both $P<0.01$). The patients were contacted for a short web-based questionnaire in order to assess their satisfaction with the switch from DPP4i to the XRM/sitagliptin combination. This was categorically expressed choosing one of 5 icons conventionally considered as representing "very poor, poor, fair, good or very good" satisfaction (Likert scale); there was also an option for "no opinion". Tolerance data were obtained by questionnaire in the follow-up visit. All Included patients granted informed consent.
Results
Satisfaction data could be obtained from 70 of a total 72 patients, 62 through the web, 5 by phone and 3 presentially, but the questioner was never the prescribing physician. 39 (55.7%) of the patients reported "very good" satisfaction, 14 (20.0%) "good" satisfaction, 9 (12.6%) "fair" satisfaction, 4 (5.7%) "poor" satisfaction, 2 (2.9%) "very poor" satisfaction, and 2 (2.9%) reported no opinion. 51 patients (73%) tolerated 2 tablets of XRM/sitagliptin (1000/50 mg); 8 (11%) tolerated 1 tablet and 11 (16%) did not tolerate any. A backwards stepwise logistic regression identified the lack of adverse effects as the only independent predictor of "good" or "very good" satisfaction, while the changes in HbA1c, fasting glucose, body weight, etc. did not predict satisfaction.
Conclusions
A large majority of the patients with T2DM labelled as metformin-intolerant and treated with a DPP4i tolerated the XRM/sitagliptin combination. Patient satisfaction with the switch was high, with 3/4 of them reporting it as "good" or "very good", and was driven by the absence of adverse effects.

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EP1270

Should acromegaly disease activity be considered while using anti-diabetic treatment among patients with acromegaly and diabetes?

Adnan Zaina[1] & Kassem Sameer[2]

[1]Bar-Ilan University, Azrieli Faculty of Medicine, Division of Endocrinology and Metabolism, Israel; [2]Technion - Israel Institute of Technology, Haifa, Israel

Management of type 2 diabetes (T2DM) has advanced since introducing sodium-glucose co-transporter 2 inhibitors (SGLT2i) with their protective cardiovascular and renal effects. However, in acromegaly patients with diabetes, the SGLT2i class is less attractive among endocrinologists because of the increased risk of diabetic ketoacidosis (DKA), and the use of incretin-based therapy as second-line treatment after metformin is more considered. This review aims to discuss the role of SGLT2i in diabetes management in acromegaly.
Methods
A comprehensive Medline/PubMed and Embase search was performed between 2012-2022 using the terms acromegaly and diabetes, SGLT2i in acromegaly, DKA in patients with acromegaly with and without SGLT2i use.
Results
Database evidence regarding the use of SGLT2i in acromegaly patients with diabetes is scanty. Previously reported data disclosed that in most cases, DKA was not related to SGLT2i, and this complication was reported as a presenting manifestation in most patients with uncontrolled acromegaly and diabetes. It is worth mentioning that GH and IGF-1 levels were markedly elevated in all reported cases of developed DKA. In contrast, in our previously reported data, the use of SGLT2i in controlled acromegaly was safe and without adverse events. Therefore, in this review, we consider acromegaly disease activity an essential criterion in the proposed algorithm for diabetes management in acromegaly patients, particularly when considering treatment with SGLT2i.
Conclusion
We recommend using SGLT2i among patients with controlled acromegaly and diabetes, following the T2DM recommendation guidelines. However, SGLT2i could be considered cautiously among partially controlled acromegaly patients and not recommended in poorly controlled patients. In these cases, incretin-based therapy is more favorable for patients, at least until the availability of future studies demonstrating SGLT2i safety also in this context.
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EP1271

The short and long-term potential negative effects of thyroxine therapy in children and adolescents

Ashraf Soliman, Nada Alaaraj, Noor Hamed, Shayma Mohamed & Fawzia Alyafei
Hamad General Hospital, Doha, Qatar

Introduction
This review aims to systematically analyze and summarize the findings from research articles regarding the potential short-term and long-term side effects of L-thyroxine therapy in children and adolescents. The selection criteria for the studies included their focus on the negative effects of thyroxine therapy related to thyroid health, cognitive function, cardiovascular health, bone health, and cancer risk in pediatric populations.
Results of the Review
Summary of Research Findings on Thyroxine Therapy, Thyroid Health, and Associated Risks in Children and Adolescents

(Abstract EP1271)

Study Focus	Findings	Authors	Year
Neurocognitive Function in Hypothyroidism	Short-term thyroxine therapy did not significantly affect neuropsychological function in children with compensated hypothyroidism.	Aijaz *et al.*	2006
Cardiovascular Side Effects of Thyroxine Therapy	Potential adverse effects include shortening of systolic time intervals, increased frequency of atrial premature beats, and possible left ventricular hypertrophy, manageable with appropriate dosage adjustments.	Bartalena, Bogazzi, & Martino	1996
Bone Health in Long-term Thyroxine Therapy	Long-term use of thyroxine can affect bone density and mass, mitigable with careful monitoring.	Bartalena, Bogazzi, & Martino	1996
Thyroxine Therapy in Down Syndrome	Thyroxine treatment improved growth and potentially development in Down syndrome children with congenital hypothyroidism.	van Trotsenburg *et al.*	2005
Cognitive and Behavioral Outcomes in Juvenile Hypothyroidism	Mild behavioral symptoms and poorer school achievement may occur in children treated with L-thyroxine for juvenile acquired hypothyroidism.	Rovet, Daneman, & Bailey	1993
Autoimmune Hyperthyroidism Characteristics	Prepubertal children are more severely affected at presentation and require longer therapy for remission.	Shulman *et al.*	1997
Thyroid Cancer Outcome after Chernobyl	Favorable responses to radioiodine therapy in Chernobyl-exposed Belarusian children and adolescents with thyroid cancer.	Reiners *et al.*	2013
Thyroid Cancer Risk and Serum TSH	Increased thyroid cancer risk in children especially vulnerable to ionizing radiation.	Ron *et al.*	1995
Neurocognitive Functions in Subclinical Hypothyroidism	Impacts on attention in children and adolescents with subclinical hypothyroidism.	Ergür *et al.*	2012
Thyroxine Therapy in Nodular Goiter	L-thyroxine treatment associated with decreased frequency of papillary thyroid cancer in nodular goiter patients.	Fiore *et al.*	2010

Conclusions
The review highlights that while thyroxine therapy is crucial for the management of hypothyroidism and associated conditions in pediatric populations, careful consideration is necessary to mitigate potential adverse effects. These include, but are not limited to, cardiovascular side effects, impacts on bone health, cognitive function, and growth. The findings underscore the importance of tailored and monitored thyroxine therapy in children and adolescents to balance therapeutic benefits against potential risks.
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EP1272

Dilated cardiomyopathy: an unusual revelation of autoimmune hypothyroidism; case report

Ikrame Qasdi, Hasna Ouirar, Kaoutar Elmoatamid, Fatima Toulali, Kaoutar Rifai, Iraqi Hinde & Mohamed Elhassan Gharbi
Ibn Sina University hospital, Endocrinologie et maladies métaboliques, rabat, Morocco

Introduction
The occurrence of Dilated Cardiomyopathy (DCM) and hypothyroidism induced systolic dysfunction is rare, especially when it presents as an initial manifestation of hypothyroidism Case We report the case of a 57-year-old patient, a known chronic smoker, who was admitted to the emergency department reporting asthenia, NYHA class III dyspnea, cardiac angina, and periorbital oedema. The ECG reveals a regular rhythm at 50 bpm and diffuse low voltage with firstdegree atrioventricular block. Biologically, the initial assessment showed normal renal and hepatic function. TSH was elevated at 228 mIU/l, T4 was low, and anti-TPO and anti-TG were significantly positive. Cervical ultrasound findings pointed towards a pseudo-nodular thyroid indicative of thyroiditis, along with features of bi-ventricular dilated cardiomyopathy presenting moderate left ventricular dysfunction and an ejection fraction of 45% on echocardiography. The Coronary angiography yielded normal results, while cardiac MRI revealed dilated cardiomyopathy with a dilated left ventricle. The patient underwent heart failure management, with a stepwise introduction of thyroid hormone replacement therapy using L-thyroxine, leading to a favorable clinical, biological, and radiological progression
Discussion
Dilated cardiomyopathy is a weakening and stretching of the heart muscle, resulting in a diminished capacity for effective blood pumping. Although it can have diverse factors, such as genetic causes, viral infections, and metabolic issues, it can also have an association with thyroid disorders, including hypothyroidism. Treating hypothyroidism can enhance cardiac function gradually in numerous cases.
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EP1273

When an ectopic and hyperfunctional thyroid nodule appears 2 decades after subtotal thyroidectomy: A case report

Hasna Ouirar, Ikrame Qasdi, Caimae Zouna, Amal Riad, Kaoutar Elmoatamid, Fatima Toulali, Ghizlane Sabbar, Kaoutar Rifai, Iraqi Hinde & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco

Introduction
A toxic thyroid nodule refers to a nodule that functions autonomously, causing an overabundance of thyroid hormones. It is generally considered non-malignant. Making a decision regarding surgery in hyperthyroid patients necessitates the accurate localization of the toxic region. Here we report a case of an intrathoracic toxic thyroid nodule causing hyperthyroidism with a normally functioning cervical thyroid nodule.
Case
A 63 year-old female underwent subtotal thyroidectomy in 2000 for a multinodular goiter with preservation of the upper left pole, and postoperative course was marked by permanent hypoparathyroidism requiring replacement therapy. The pathological examination revealed a benign condition. Subsequently, in 2019, a toxic nodule developed and was treated with radioiodine therapy without improvement. Confronted with ongoing clinical and biochemical hyperthyroidism, Ultrasonographic assessment of thyroid bed showed an isoechoic left nodule measuring 17×13 mm. Thyroid scintigraphy employing 99m technetium displayed intense and heterogeneous uptake projecting into the anterior and middle mediastinum. Cervico-thoracic CT imaging disclosed a mediastinal lesion, indicating a possible ectopic thyroid nodule. The patient was treated with graded doses of Carbimazole, but partial response was provided. A left lobectomy and removal of an intrathoracic goiter were performed. Results of the histopathological evaluation are currently being processed
Discussion
Radionuclide scintigraphy is valuable in confirming suspected or clinically evident thyroid tissue that is extending into mediastinum. The possibility of the existence of external thyroidal tissue should be kept in mind in such suspicious cases. Intrathoracic goiters are generally considered an indication for surgery; radioiodine therapy remains a choice for those who cannot be operable because of advanced systemic disease or other reasons.

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EP1274

From high dose Insulin therapy to dual oral therapy: recovery from glucotoxicity after acute pancreatitis and severe ketoacidotic hyperglycaemia

Hassan Al Sahaf[1], Lama AlMahrous[2] & Azmi Mohammed[3,4]
[1]Johns Hopkins Aramco Healthcare Dhahran, Dhahran, Saudi Arabia; [2]Johns Hopkins Aramco Healthcare Dhahran, Internal Medicine, Dhahran, Saudi Arabia; [3]Johns Hopkins Aramco Healthcare Dhahran, Endocrinology, Dhahran, Saudi Arabia; [4]County Durham and Darlington NHS Foundation Trust, United Kingdom

Significant hyperglycaemia suppresses beta cell replication and cell cycle progression. Acute beta cell failure is caused by several mechanisms involving oxidative and endoplasmic stress leading to DNA damage response (collectively termed glucotoxicity) [(1)]. Short-term glycaemic control unmasks the regenerative potential of beta cells, leading to recovery and potentially weaning off Insulin therapy [(1, 2, 3)]. We present a case of a 62-year-old woman with type 2 diabetes mellitus for four years, on metformin (2g daily) and Empagliflozin (25 mg daily), who presented with acute abdomen secondary to acute pancreatitis, severe ketotic hyperglycaemia (glucose 477 mg/dl) and acidaemia (pH: 7.31, anion gap 20 mEq/l). She was managed medically with intravenous insulin infusion and IV therapy, then converted to multiple daily injections (MDI). Her laboratory results indicated high lipase; low C-peptide coupled with high glucose. CT abdomen was unremarkable apart from signs of pancreatitis. Following stabilization over a few days in the hospital, she was discharged on glargine, meticulously adjusted to 42 units daily, and NovoRapid up to a maximum of 16 units with meals. Empagliflozin was initially suspended for a few weeks to mitigate the risk of rebound ketonemia. Over the subsequent eight weeks, a methodical reduction in her insulin doses was pursued until the need for MDI was eliminated. HbA1c 4.85% was achieved without troublesome hypoglycaemia on glucose monitoring with Freestyle libre (2). Presently, her diabetes is managed effectively with metformin and Empagliflozin 10 mg daily. This case highlights the complex risks of glucotoxicity stemming from severe hyperglycaemia that causes acute beta cell failure. Acute pancreatitis exacerbated insulin deficiency in this case. SGLT2 inhibitors increased the risk of ketonemia due to pronounced insulin deficiency and resistance. They can also lead to dehydration through glucosuria, hinder ketone elimination, heighten the glucagon-to-insulin ratio, and promote ketogenesis [(4)]. Interestingly, the effects of glucotoxicity were reversible following 6-8 weeks in a normoglycemic setting with adequate Insulin therapy, illustrating the potential for beta-cell functional recovery, eventually leading to insulin therapy cessation. In conclusion, this narrative underscores the criticality of recognizing and addressing glucotoxicity in patients with type 2 diabetes who may present with acute pancreatitis. It illustrates the importance of vigilant management strategies, including short-term insulin therapy, to reverse the adverse effects of glucotoxicity.

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EP1275

Graves' disease associated with primary biliary cholangitis: a case report

Karimi Meryem, Hajar Azagouagh, Hasna Ouirar, Rifai Kaoutar, Iraqi Hind & Mohamed Elhassan Gharbi
Ibn Sina Rabat, Endocrinology, Rabat, Morocco

Introduction
Graves' disease is an autoimmune thyroid disease that is frequently associated with other autoimmune diseases. In our case, we report a rare association with primary biliary cholangitis.
Case report
A 38-year-old patient, with no particular medical history, has been followed for Graves' disease for 14 years, initially treated with carbimazole with poor therapeutic compliance and irregular follow-up. The evolution was marked by the onset of cutaneous-mucosal jaundice. Laboratory tests showed hepatic cholestasis with cytolysis and pancytopenia, persisting after discontinuation of treatment. Hepatic ultrasound was unremarkable. Liver biopsy confirmed primary biliary cholangitis. The patient was started on ursodeoxycholic acid with rapid medical preparation for definitive treatment.
Discussion and Conclusion
The disturbance of liver function tests in Graves' disease may be correlated with thyrotoxicosis or secondary to treatment with synthetic antithyroid drugs, or it may be due to primary biliary cholangitis, which should always be considered in cases of hepatic cholestasis.

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EP1276

A rare association between cushing's disease and primary biliary cirrhosis: about a case report

Arige Abid, Bchir Najla, Annam Benchhida, Yosra Abderrahim, Dorra Dorraelguiche, Zouaoui Chadia & Haroun Ouertani
Tunis Military Hospital, Endocrinologie, Tunis, Tunisia

Introduction
Cushing's disease is a rare disorder caused by the hypersecretion of corticosteroids. Primary biliary cirrhosis (PBC) is a chronic autoimmune cholestatic hepatopathy characterized by destruction of the bile ducts and the presence of m^2-type anti-mitchondrial antibodies. We report a rare association between cushing's disease and primary biliary cirrhosis.
Observation
The patient was 38 years old, with recent history of diabetes and dyslipidemia, was admitted to our department of endocrinology for suspicion of a Cushing syndrome. The physical examination showed facial erythrosis, filling of the supra-scalvicular hollows, presence of a buffalo hump and facio-truncular fat distribution but not catabolic signs. Diagnosis of ACTH-dependent cushing's syndrome biologically was made on the basis of lack of plasma cortisol response to low dexamethasone suppression test at 516 nmol/l (above 50 nmol/l), and high ACTH value at 69.4 confirmed by a second assessment at 100 pg/ml. High-dose Dexamethasone Suppression test cortisol level decrease greater than 50% after 8 mg of dexamethasone (from 728 to 315 nmol/l), suggesting Cushing disease. Pituitary MRI showed a 6 mm micro-adenoma. She underwent a transphenoidal adenomectomy with post operative remission. Moreover, the biological work -up showed cytolysis at 1.5 time the upper limit with cholestasis. Viral serologies and autoimmune antibodies were carried out, showing positive anti-mitochondrial m^2 ACs and negative viral serologies. Abdominal ultrasound revealed no abnormalities. A liver biopsy was performed, showing epithelioid granulomas with neoductular proliferation, confirming the diagnosis. The patient was treated by ursalvan,
Conclusion
Cushing's syndrome has been associated in the literature to several liver diseases, hepatic steatosis being the most common. coexistance between cushing's disease and primary biliary cirrhosis (PBC) is uncommon and has been little reported Common physiopathology must be investigated.

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EP1277

Heterozygous type 1 familial hypercholesterolemia patient with a rare LDL receptor mutation and the efficacy of evolocumab in the management of consequent hyperlipidemia

Olivera Boskovic[1] & Edina Hubanic[2]
[1]Clinical Center of Montenegro, Endocrinology, Podgorica, Montenegro; [2]Bijelo Polje, General Hospital-Internal medicine department, Bijelo Polje

Heterozygous (monoallelic) familial hypercholesterolemia (HeFH) is a monogenic disorder that affects one in 300 people. The majority of cases of FH are caused by inherited mutations in the LDLR gene, which encodes the LDLR. Less commonly, the heterozygous FH phenotype can be caused by mutations in other genes, specifically PCSK9, which encodes proprotein convertase subtilisin/kexin type 9. As many as 30% of patients do not survive their first myocardial infarction (MI). We present a HeFH patient with a rare mutation of LDLr. A 67-year-old woman with FH has been treated for the past 30 years with statins in the maximum tolerated dose. Last 10 years, on Rosuvastatin 40 mg, and cholesterol absorption inhibitor Ezetimibe 10 mg. Her past history revealed that she underwent percutaneous coronary interventions (PCI) with stent implantation on the left anterior descending artery 15 years ago and carotid endarterectomy. Her family history included premature coronary artery disease: her brother had MI in his forties, required the placement of 3 bypasses. Both daughters have FH. For determining the presence of a hetero or homozygous form of FH for the purpose of applying appropriate therapy, molecular genetic diagnostics using Next Generation Sequencing method was conducted. The analysis included all coding sequences (exons) and boundary exon/intron sequences in genes defined according to phenotypic characteristic present in the patient. The clinical target encompassed nine genes in the panel for FH. The conducted analysis revealed the presence of a likely pathogenic heterozygous variant in the LDLr gene c.858C > A, p. (Ser286Arg), NM 000527.5. This variant has an expected allelic frequency of 0.0028%. Following the results, she became eligible for treatment with a PCSK9 inhibitor, and she was approved for adjuvant biweekly treatment with Repatha® (evolocumab) 140 mg. Follow-up results showed a reduction: total cholesterol from 4.93 to 3.9 mmol/l; and LDL-C from 2.59 to 1.48 mmol/l. Treatment with PCSK9 inhibitor was combined with Rosuvastatin 20 mg and Ezetimibe 10 mg daily. We confirm the observations that, in compound heterozygous HeFH patients who receive stable background lipid-lowering treatment and do not undergo apheresis, biweekly treatment with evolocumab 140 mg was well tolerated and significantly reduced LDL-C.

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EP1278

Cardiovascular protection with a novel nutraceutical based on mulberry leaf, fenugreek, inulin, laciplantibacillus plantarum A14, chromium, zinc and niacin

Claudia Arnas-Leon[1,2], Jennifer Maria Perez-Rivero[3], Sara Andrada-Diaz[4], Alba Hernandez-Lazaro[5], Ricardo de Leon-Durango[2], Carlos Rios-Gomez[2], Borja Santana-Ojeda[2], Inmaculada Molinero-Marcos[2], Agnieszka Kuzior[1] & Francisco Javier Martinez Martin[1,2]
[1]Hospitales San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [2]University Hospital of Gran Canaria Dr. Negrín, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [3]Centro Salud Escaleritas, Family & Community Medicine, Las Palmas de Gran Canaria, Spain; [4]Bioksan Naturalmente juntos Sl, Medical Advisor, Las Palmas de Gran Canaria, Spain; [5]Parc Taulí University Hospital, Endocrinology & Nutrition, Sabadell, Spain

Introduction and Objectives
The prevalence of prediabetes in the adult Spanish population is close to 15%. People with prediabetes are not only at high risk of developing T2DM but also at high cardiovascular risk. Several drugs, including metformin, glitazones, GLP-1RAs and SGLT2is have been found to reduce the incidence of diabetes in this population, but none is currently licensed with this indication. In particular α-glucosidase inhibitors such as acarbose have been shown to significantly reduce the risk of progression to T2DM but also the risk of developing hypertension and major cardiovascular events (STOP-NIDDM trial). The white mulberry (Morus Alba) leaf contains 1-deoxynojirimycin, a powerful α-glucosidase inhibitor. A novel neutraceutical based on Reducose, a patented standardized white mulberry leaf extract, containing also fenugreek, inulin, Lactiplantibacillus plantarum A14, chromium, zinc and niacin (for better efficacy and tolerance) has been developed for the treatment of prediabetes. We undertook an open trial to validate the tolerability and efficacy of this nutraceutical including markers of cardiovascular and metabolic risk.
Methods
We are actively recruiting adult subjects with prediabetes, excluding those with morbid obesity, concomitant serious diseases, alcoholism, addictions, present or planned pregnancy. After obtaining baseline anthropometry and lab tests and giving informed consent, they take a pill of the nutraceutical daily before lunch with a glass of water. Follow- up visits are scheduled after 3-4 and 6-7 months. Presently we have 15 subjects who have completed the first follow-up visit for this preliminary analysis. The targets are: estimated 10-year cardiovascular risk (SCORE2), lipid profile, systolic BP, BMI, fasting glucose and insulin, HOMA2-IR and tolerability (questionnaire). Stats were made by paired t-test.
Results
In 15 subjects (2/3 women, age 54.2 ± 6.6 years, 20% active smokers), the SCORE2 changed from to 4.09 ± 1.98 to 3.63 ± 1.83% ($P = 0.002$); cHDL from 46.5 ± 9.5 to 49.1 ± 8.9 mg/dl ($P = 0.002$), triglycerides from 183.6 ± 59.4 to 155.9 ± 52.8 mg/dl ($P = 0.009$); SBP from 138.1 ± 16.1 to 131.7 ± 13.4 mmHg ($P = 0.002$); HOMA2-IR from 1.42 ± 0.32 to 1.19 ± 0.17 ($P = 0.029$); fasting glucose from 105.5 ± 11.9 to 99.5 ± 7.7 mg/dl ($P = 0.015$); fasting insulin from 10.6 ± 2.4 to 8.89 ± 1, 31 μU/ml ($P = 0.028$); HbA1c from 6.07 ± 0.28 to 5.93 ± 0.24% ($P = 0.023$). Total cholesterol, cLDL and IMC did not change significantly. There were no serious tolerability issues and no patient has withdrawn from the study so far.
Conclusions
These are very preliminary but promising results for the novel neutraceutical with significant reductions both for cardiovascular and for metabolic risk.

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EP1279

A rapid and concise dual-mode aptasensor for ultrasensitive detection of 17β-estradiol

Fengfeng Zhao
Zhongda Hospital, School of Medicine, Southeast University, Center of Clinical Laboratory Medicine, Nanjing, China

Objective
Pollution of endocrine disrupting chemicals has become a global issue. As one of the hormonally active compounds, 17β-estradiol produces the strongest estrogenic effect when it enters the organism exogenously including food intakes, bringing potential harmfulness such as malfunction of the endocrine system. Therefore, in order to assure food safety and avoid potential risks of 17β-estradiol to humans, it is of great significance to develop rapid, sensitive and selective approaches for the detection of 17β-estradiol in food matrices.
Method
Molecular recognition elements are valuable tools for rapidly and selectively binding to target proteins. Aptamers, commonly referred to as chemical antibodies, are one such category of molecular recognition elements, exhibiting several advantages such as smaller size, stability, cost-effectiveness, easy modification, low immunogenicity, and scalability for production. As a result, aptasensors combined with diverse detection technologies offer a promising alternative for the detection of clinical biomarkers across various sample types, enabling rapid and direct analysis. A developed freezing method has proven to be remarkably simple and efficient through gold nanoparticles (AuNPs) functionalized with thiolated DNA and poly (A)-tagged DNA. When the AuNPs are coated with polymers and DNA sequences, aggregation of AuNPs becomes reversible after freezing and thawing. Building upon this freezing-directed approach, the bioprobes based on AuNPs have been successfully implemented in a variety of detection systems, including colorimetric, fluorescence, and lateral flow assays. Inspired by this, we propose and demonstrate a rapid and concise dual-mode aptasensor (named RCPA) for reliable detection of 17β-estradiol.
Result
The RCPA strategy shows ultrahigh sensitivity to 17β-estradiol determination due to high binding affinity of aptamers, with the limit of detection of 0.018 ng/ml. The total detection time of 17β-estradiol in milk or serum is less than 30 min with small sample consumption (about 50 μ L) due to the rapid magnetic separation of apt@MNP. In addition, the proposed biosensor exhibits a high specificity for 17β-estradiol quantitative detection. On the other hand, the freeze-thaw mode provides a visual and concise detection method.
Conclusion
Therefore, this work provides a promising and concise strategy to rapid and ultrasensitive detection of 17β-estradiol for broader patients and more urgent cases.

KeyWords: Aptasensor, 17β-estradiol, Detection, Gold nanoparticles
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EP1280

Relation between hormonal and metabolic status in persons affected by the chnpp accident with parathyroid disordres

Valeriia Praporschikova[1], Irina Muraviova[1,2] & Dmytro Afanasyev[1,2]
[1]SI «National Research Center for Radiation Medicine of the NAMS of Ukraine», Radiation Endocrinology, Kyiv, Ukraine; [2], Kyiv, Ukraine

Objective
assessment of endocrine system profile featuring hormonal and metabolic parameters in persons affected by the ChNPP accident with parathyroid disorders.
Methods and results
Patients treated in the Department of Radiation Endocrinology in 2019-2020 were selected ($n=150$) by the method of blind sampling in accordance with the study objective. Study sample included the 100 subjects (50% females, 50% males) were affected by the ChNPP accident. The comparison group included 50 patients (55% males, 45% females) not exposed to ionizing radiation. The age of study subjects ranged from 37 to 75 years with 60.2 ± 9.8 years in average. Incidence of parathyroid hyperplasia among persons affected by the ChNPP accident was in twice higher vs the comparison group (41% and 20% respectively) against the background of the same serum level of vitamin 25(OH)D. Average level of parathyroid hormone among the ChNPP accident patients with parathyroid hyperplasia was significantly higher vs. the comparison group (57.2 ± 2.87 and 31.88 ± 4.82 respectively, $P<0.05$). Mean level of vitamin 25(OH)D in subjects with parathyroid hyperplasia was significantly lower than in cases of no such a disorder (14.36 ± 2.31 and 28.32 ± 6.48 respectively, $P<0.05$). Relationships between the hormones and metabolic profile using the correlation- regression analysis showed a significant negative effect of secondary hyperparathyroidism on comorbid conditions, namely the endocrine component of arterial hypertension, dyslipidemia, osteopenia and metabolic syndrome. Using multivariate analysis, a reliable relationship was established between the vitamin 25(OH)D deficiency and astheno-neurotic, anxiety-depressive syndromes ($F=83.811$; $P=0.0001$), autoimmune thyroiditis, hypothyroidism ($F=8.1802$; $P=0.0001$), type 2 diabetes mellitus and metabolic syndrome ($F=16.428$; $P=0.0001$). Also the multivariate analysis provided a reliable confirmation of the negative impact of hyperparathyroidism on arterial hypertension and arrhythmia ($F=8.8469$; $P=0.0007$), osteopenia ($F=16.208$; $P=0.0001$).
Conclusions
Secondary hyperparathyroidism has a negative effect on the course of concomitant endocrine disorders and comorbid conditions.

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EP1281

Abstract withdrawn

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EP1282

Temporal and masseter muscle evaluation by MRI provides information on muscle mass and quality in acromegaly patients

Angelo Milioto[1,2], Giuliana Corica[1,2], Federica Nista[3], Claudia Campana[2], Anna Arecco[2], Lorenzo Mattioli[2], Lorenzo Belluscio[2], Diego Ferone[1,2], Alberto Tagliafico[3,4] & Federico Gatto[1]
[1]Endocrinology Unit, IRCCS Ospedale Policlinico San Martino, Genoa, Italy; [2]Endocrinology Unit, Department of Internal Medicine and Medical Specialties (DIMI) and Centre of Excellence for Biomedical Research (CEBR), University of Genova, Genoa, Italy; [3]Radiology Section, Department of Health Sciences (DISSAL), University of Genova, Genoa, Italy; [4]Department of Radiology, IRCCS Ospedale Policlinico San Martino, Genoa, Italy

The impact of GH/IGF-1 levels on skeletal muscle in patients with acromegaly is still matter of debate. Recently, temporal (TMT) and masseter muscle thickness (MMT) have emerged as reliable indicators of muscle mass, as well as patients' functional status/prognosis in various clinical context – especially in the oncologic setting. This study aims to investigate the potential correlations between TMT/MMT and patients' demographic and clinical characteristics. A retrospective longitudinal analysis was conducted at a single tertiary center for pituitary diseases. Sixty-nine patients diagnosed with acromegaly, each with at least one brain/sella turcica MRI scan and matched clinical data, were included. The primary outcomes assessed were TMT, MMT, and muscle fatty infiltration (evaluated using the modified Goutailler score) at baseline (69 MRIs) and over time (total of 182 MRIs). The median time between first to last available MRI was 49 months. Results revealed that, at baseline, males had significantly higher TMT and MMT compared to females ($P=0.001$ and $P=0.016$, respectively). A direct association between TMT and MMT was observed (β 0.508, $P<0.001$). TMT was positively correlated with IGF-1 ×ULN ($P=0.047$), while MMT showed positive correlations with IGF-1 ×ULN ($P=0.001$), patient weight ($P=0.015$), and height ($P=0.006$). The presence of hypogonadism or impaired glucose metabolism did not significantly correlate with TMT or MMT. No significant difference in TMT and MMT has been observed when comparing patients with active cancers, with cancers in remission, and those with a negative clinical history for malignancies. Considering all available MRIs, sex and IGF-1 ×ULN emerged as significant determinants of both TMT and MMT in multivariable analysis (female sex: β -0.345/-0.426, $P<0.001$; IGF-1 ×ULN: β 0.257/0.328, $P<0.001$). Patients defined at risk of sarcopenia - by sex-specific TMT cut-offs – had IGF-1 ×ULN levels significantly lower compared to individuals classified as having normal muscle status ($P=0.016$). At longitudinal evaluation, patients with uncontrolled acromegaly at baseline exhibited a significant reduction in MMT over time ($P=0.044$). Notably, considerable fatty infiltration was observed in 34-37% of MRIs, with age identified as the main determinant (temporal muscle: OR 1.665; $P=0.013$; masseter: OR 1.793; $P=0.009$). In conclusion, male patients with higher IGF-1 values demonstrated thicker temporal and masseter muscles, indicative of greater muscle mass compared to other patients.

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EP1283

Estimation of thyroid diseases in type 1 DM women living in iodine deficiency region

Mushtariy Makhkamova[1], Mukima Karimova[1], Nigora Ibragimova[2], Muhammadrasul Muhammadsiddikov[1] & Zulaykho Shamansurova[3,4]
[1]Fergana Medical Institute of Public Health, Endocrinology, Fergana, Uzbekistan; [2]Fergana Regional Endocrinologic Dispensary, Endocrinology, Fergana, Uzbekistan; [3]Central Asian University Medical School, Endocrinology, Tashkent, Uzbekistan; [4]Institute of Biophysics and Biochemistry at the NUUz, Metabolomics, Tashkent, Uzbekistan

Iodine deficiency diseases are one of the wide problems seen in the geografically iodine deficiency regions and associated with a large number of people. The goal of our investigation was study of frequency of the thyroid diseases in women with type 1 Diabetes Mellitus (DM1) whose living in Ferghana valley, the iodine deficiency region of Uzbekistan.
Materials and methods
In 120 female patients in age from 18^h to 36 years old with type 1 diabetes blood glucose, HbA1c, TSH, free T4, antiTPO level were measured, thyroid glands were palpated and ultrasound were performed.
Results
Thyroid gland enlargement were found at palpation in all observed woman, with DM1 and in 92.5% without DM1. Estimation of thyroid status showed euthyroidism in 58% DM1 group and 85% without DM, hypothyroidism were registered in 42% woman with DM1 and 15% without DM1. Thyroid glands ultrasound showed in DM1 group 5% woman had nodular, 3.3% mixed goiter and 20% had autoimmune thyroiditis. In group without DM1 nodular goiter were detected in 2.5%, mixed in 3% and autoimmune thyroiditis in 10% woman. In case of nodular and mixed goiter ultrasound results clissified by TIRADS showed 55% TIRADS 1 and 2, 45% TIRADS 3, 4, 5 in DM1 group, whereas in woman without DM TIRADS 1 and 2 seen in 82% and TIRADS 3 and 4 in 18%.
Conclusion
In woman with DM1 lived in iodine defficiency region thyroid diseases were highly presented as a 2 times more nodular goiter and 2 times more autoimmune thyroiditis. Moreover, mallignancy signs incresed by TIRADS on ultrasound imaging. Effective elimination of Iodine defficiency is important in woman with DM1.

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EP1284

Neurosurgery treatment for macroprolactinomas: a retrospective study

Raoua Naouar[1], Hanene Sayadi[1], Sana Abid[1], Ghassen Belkahla[2], Atef Ben Nsir[2], Bilel Ben Amor[1], Ekram Hajji[1], Ines Bayar[1], Héla Marmouch[1], Inès Khochteli[1], Mahdi Darmoul[2] & Gema Martinez Tames[3]
[1]Fattouma Bourguiba Hospital, Endocrinology and Internal Medicine Department, Monastir, Tunisia;[2]Fattouma Bourguiba Hospital, Neurosurgery Department, Monastir, Tunisia; [3]Hospital Valle Del Nalon, Endocrinology Division, Monastir, Tunisia

Introduction
The management of prolactinomas, whatever their size, is based on medical treatment with dopamine agonists (DA). The latter allows clinical improvement with efficient control of prolactin secretion and tumor growth. Pituitary surgery or radiotherapy are adjuvant therapies in case of neurologic complication or lack of response to DA.
Patients and methods
We conducted a monocentric analytic study of patients followed for confirmed prolactinomas at the endocrinology-internal medicine and neurosurgery departments of the Fattouma Bourguiba University Hospital, Monastir, from January 2000 to March 2022.
Results
Among the factors associated with the necessity for surgery, only initial tumor size was correlated with surgical treatment. Indeed, the average initial tumor size in operated patients was 34.5 ± 8.44 mm versus 26.16 ± 12.19 mm in non-operated patients. However, there was no difference in the normalization of prolactin level (90% versus 93%, $P = 0.4$) nor in the rate of reduction in tumor size in response to surgery compared to those under medical treatment (53% versus 57%, $P = 0.2$).
Conclusion
DA have traditionally been the primary treatment for the majority of prolactinomas, with surgery considered the second line therapy. Complete surgical removal of invasive macroprolactinomas is technically difficult and structural healing is rare and is not without risks. It should be reserved for cases of inadequate response to medical therapy or in cases of emergency.

Table 1. Factors related to the use of pituitary surgery

Factors	Surgical managment $n=10$	p
Gender male	5 (50%)	0.39
Age at diagnosis	38.5 ± 11.78	0.66
Prolactin level (ng/ml)	639.9	0.09
Initial tumor size (mm)	**34.5 ± 8.44**	**0.02**
Pituitary apoplexy	2 (20%)	0.12
Tumor invasion	6 (60%)	0.79
T2-weighted MRI signal		
Hypersignal	8 (80%)	0.35
Hyposignal	1 (10%)	0.23
Isosignal	1 (10%)	0.21

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EP1285

Impact of type 1 Diabetes on growth, puberty onset and retardation

Shakhnoza Babamukhamedova[1] & Zulaykho Shamansurova[1,2]
[1]Central Asian University Medical School, Endocrinology, Tashkent, Uzbekistan; [2]Institute of Biophysics and Biochemistry t the NUUz, Metbolomics, Tashkent, Uzbekistan

Introduction
In some cases pubertal growth and sexual maturation and relating normal physiology can be disturbed and retarded by chronic disease as like Diabetes Mellitus (DM). According to International Diabetes Federation Atlas in 2013 approximately 5, 00, 000 known cases of children with T1DM (0–14 years) worldwide, where 50-60% of cases are diagnosed before the age of 15. Insulin deficiency in T1DM presented with age in childhood and visible peaks at the time of puberty can affected growth and puberty onset delay. We analysed data from literature by compare cases of growth and puberty delay in people with T1DM if there any majority of applicable mechanisms of growth and puberty retardation which are related with disease specific mechanisms.
Material and methods
A case-control study with 20 type 1 Diabetes Mellitus patients, who were 14-18 years old on the other hand 20 healthy age-matched participants were included as a control group. The stage of sexual maturation - Tanner's stage, hormonal profile - follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and total testosterone measured and the growth parameters, including the weight, height, and BMI respectively for both groups.
Results
The major criteria, its impact on linear growth, development and puberty onset, especially in those with poor glycemic control. T1DM was a cause of retardation of puberty as about one-quarter (25%) of the boys were sexually immature by Tanner's chart (did not reach stage V) comparing with control group, where 90% of volunteers were sexually mature regarding their age. Moreover, prolactin, testosterone, BMI, height and weight parameters were low in diabetic group comparing with control. Authors proposed well known fact the insulin affects central nervous system and involved reproduction. It is tend to be consequences of hypoinsulinemia or delayed release of GnRH, with subsequent delayed release of sex hormones. IGF-1 stimulates growth and puberty, also directly regulates GnRH which was in the decreased range because of hypoinsulinemia. When main risk factors were calculated poor glycemic control, low FSH and LH to cause pubertal and normal growth delay in these patients.
Conclusion
Children and adolescent with T1DM those with poor glycemic control showed remarkably delayed puberty (90%) and lower growth (25%) parameters, also accompanied with lower sex hormones level. Adequate insulin therapy with education should be necessary part of treatment in patients with T1DM.

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EP1286

Diabetes mellitus and endometrial carcinoma: risk factors and etiological links

Zebo Karabaeva[1] & Zulaykho Shamansurova[1,2]
[1]Central Asian University Medical School, Endocrinology, Tashkent, Uzbekistan; [2]Institute of Biophysics and Biochemistry at NUUz, Metabolomics, Tashkent, Uzbekistan

Introduction
Diabetes mellitus (DM) has emerged as a significant global health concern, contributing to increased mortality and complications, thereby adversely affecting overall quality of life. The incrising incidence of DM, particularly type-2 DM (T2DM), correlates with rising rates of various cancers, suggesting a potential direct link between DM and cancer. Mounting evidence suggests DM as a potential contributor to the heightened incidence of endometrial cancer (EC) and underlines its association with poor prognosis. Early intervention with metformin is anticipated to serve as an effective adjuvant alternative for EC, thereby offering new avenues for preventive and therapeutic strategies targeting glucose metabolism. Epidemiological studies affirm hyperglycemia as an independent risk factor for EC development. Patients with DM face a doubled risk of progressing to EC, possibly due to the conducive environment for the growth and invasiveness of EC cells in high-glucose settings. However, the etiological relationship between DM and EC remains unclear, and the precise biological mechanisms linking the two are not well understood. As existing treatments fail to prevent or delay EC progression, exploring early and effective prevention through glucose metabolism interventions holds promise for innovative targeted therapeutic interventions in EC, carrying substantial medical and social value.
Materials and Methods
A comparative analysis was conducted through a systematic search over the past two years, combining and analyzing published data from MEDLINE, EMBASE, PubMed, and Research Gate.
Results
Most epidemiological studies indicate a strong association between EC and T2DM. Analysis of T2DM's impact on cancer risk and mortality reveals a significant increase in both morbidity and mortality for EC. Early-stage DM, aside from T2DM patients, shows a 4.9% increased risk of EC. T1DM is also linked to an elevated risk of EC. Additionally, DM emerges as an independent risk factor for EC mortality. Biological Mechanisms: Increasing evidence suggests that insulin resistance (IR) and hyperinsulinemia, mediated by insulin and insulin-like growth factors, influence endometrial cells and signaling pathways, such as PI3K, MAPK/ERK, and VEGFR, promoting angiogenesis and EC occurrence. Chronic inflammation factors like TNFα, IL-6, and COX-2 contribute to carcinogenesis.
Conclusion
This study enhances the understanding of the complex relationship between DM and EC, offering a global perspective on the effects of DM on EC through various

mechanisms. It emphasizes the clinical application of antidiabetic medications for EC, providing valuable insights for future research and therapeutic strategies.

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EP1287

Epidemiological, clinical, paraclinical, and preoperative complication of primary hyperparathyroidism: a moroccan single center experience

Lamiae Zarraa[1], Rania El Amel[1], Siham Rouf[1,2] & Hanane Latrech[1,2]
[1]Endocrinology-Diabetology and Nutrition Department CHU Mohamed VI, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy Mohammed Premier University Oujda, Morocco, Oujda; [2]Morocco, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy Mohammed Premier University Oujda, Morocco, Oujda

Introduction
Primary hyperparathyroidism is a common endocrinopathy associated with autonomous hypersecretion of PTH by one or more parathyroid glands. This work aims to study the epidemiological, clinical, biological, radiological, and therapeutic profile of primary hyperparathyroidism, as well as its preoperative complications.
Material and methods
A retrospective descriptive study of 50 patients followed at the Endocrinology-Diabetology-Nutrition Department of Mohammed-VI-University-Hospital-Center-Oujda-Morocco for primary hyperparathyroidism. Data were collected from medical records and analyzed using SPSS-V21 software.
Results
The mean age was 55.24 ± 12.9 years, with a clear female predominance in 78% of cases, 79% of whom were menopausal. The circumstances of discovery were dominated by bone pain, recurrent renal lithiasis and abdominal pain, and were fortuitous in only 29% of cases. Biologically, hypercalcemia was found in 84% of cases, with a mean of 127 ± 24 mg/l, and hypercalciuria in 74%. The mean PTH1-84biointact value was 408 ± 586 pg/ml and vitamin D deficiency was observed in 62% of patients. Cervical ultrasonography was carried out in all our patients, localizing the tumor in 88%, thoracic CT objective a medial ectopic parathyroid tumor in 2 cases, and SestaMIBI scintigraphy was performed in nine patients whose cervical ultrasonography failed to localize the parathyroid adenoma. Osteoporosis and renal lithiasis were the main preoperative complications, occurring in 34% and 32% of cases in our series respectively; there was a high prevalence of brown tumours in 18% of cases; 90% of patients underwent surgical treatment, 13% of them complicated by hypocalcemia. Anatomopathological findings were in favor of parathyroid adenoma in 88.6%, parathyroid hyperplasia in 5.8%, and parathyroid carcinoma in 2.9%.
Conclusions
Primary hyperparathyroidism is responsible for altered phosphocalcic metabolism and is a frequent cause of hypercalcemia. Etiologies are dominated by parathyroid adenoma, with a clear female predominance, and treatment is mainly surgical.

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EP1288

Hypocalcemia revealing digeorge syndrome: case report

Cheibete Zakaria, Mariem Cheikh & Mohamed Elmoctar
Rabat, Endocrinology, Rabat, Morocco

DiGeorge syndrome is a genetic abnormality caused by a microdeletion of chromosome 22. Chromosome 22q1 1.2 microdeletion was first identified in 1992 [1-3] as the common genetic anomaly associated with a range of conditions previously known as DiGeorge or velocardiofacial syndrome, usually presents later in childhood, often leading to hypernasal speech caused by cleft palate, submucous cleft palate, or velopharyngeal insufficiency. Both disorders share similar clinical features, such as conotruncal heart defects and mildly dysmorphic facial characteristics. The term CATCH 22 (cardiac defect, abnormal facies, thymus hypoplasia, cleft palate, hypocalcemia, and chromosome 22 microdeletion) was coined to encompass both conditions. Usually, the age of diagnosis varies between birth and 16 years. The overall prevalence of DiGeorge's syndrome is 1 in 5950 births. Approximately 13% of patients receive a diagnosis at the age of 15 or older, with most of them being identified through familial genetic studies. In adulthood, the presence of hypocalcemia as a result of pseudohypoparathyroidism (PH) is often the primary indicator of the disorder. Adults with PH typically exhibit developmental delays, psychiatric issues, and cardiac anomalies. Additionally, there may be an increased risk of early-onset Parkinson's disease. The majority of patients experience hypocalcemia (49-80%), which can manifest at any age. Hypocalcemia is caused by PH, which is characterized by congenital parathyroid aplasia or hypoplasia We report in this work the case of a 17-year-old Moroccan male who has a PTH-dependant hypocalcemia revealed by DiGeorge Syndrome. Our aim is to emphasize the importance of considering that chromosome 22q11.2 deletion syndrome is not a rare occurrence and may manifest later in life with such abnormalities.

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EP1289

Leydig cell tumors in a postmenopausal women: case report

Kammoun Fatma[1,2], Sabrine Mekni[1,3], Sawsen Essayeh[3,4], Rihab Laamouri[3,4], Werfili Mariem[3], Mchirgui Nadia[4], Karima Khiari[3,4], Imen Rojbi[3,4] & Ibtissem Ben Nacef[3,4]
[1]Charles Nicolle Hospital, Endocrinology, Tunisia; [2]Charles Nicolle Hospital, Laboratory of Renal Pathology LR00SP01, Tunis; [3]Charles Nicolle Hospital, Laboratory of Renal Pathology LR00SP01, Tunis, Tunisia; [4]Charles Nicolle Hospital, Endocrinology, Tunis, Tunisia

Introduction
Virilizing ovarian tumors (VOT) are a rare cause of hyperandrogenism in postmenopausel women. Leydig cell tumors (LCTs) are rare sex-cord stromal tumors as they account for less than 0, 1 % of all ovarian tumors, and although they occur at any age, approximately one-fourth of them present after menopause. We report a clinical case of Leydig cell tumor in a postmenopausal woman.
Case-report
A 75-year-old woman, with a personnel history of type 2 diabetes mellitus, hypertension, and dyslipidemia presented with sudde nonset of virilization, hirsutism, androgenetic alopecia, and deep voice. On physical examination, she had positive signs of virilization, including temporal balding, coarse hair with a Ferriman-Galleway score of 36. The baseline laboratory values were as follows: DHEA-sulfate 35 µg/dl (normal range 15-220 µg/dl); androstenedione, 525 ng/dl (normal: 20-310 ng/dl); and total testosterone, 3.85 ng/ml (normal 0.03-0.4 ng/ml). On pelvic ultrasound, the patient's right ovary was enlarged but the echostructure was normal and there were no other findings. Pelvic MRI revealed a low-intensity mass in the right ovary measuring 35 mm. The patient underwent exploratory laparotomy with bilateral salpingo-oophorectomy. Histopathologic examination of the resected ovaries revealed a Leydig cell tumor of the right ovary. Six weeks later, her serum testosterone and androstenedione levels, normalized to the normal range for women. Four months after surgery, the patient showed significant improvement in hirsutism and virilization symptoms.
Conclusion
Although LCT is rare and difficult to diagnose biochemically or with imaging studies, androgen-secreting tumors should be considered in postmenopausal women with hyperandrogenism and hirsutism.

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EP1290

Diagnosis of MEN-1 syndrome with multiple tumor locations and a rare genetic mutation

Anastasios Tsitsimpis[1], Kasiani Papadimitriou[1], Vasiliki Papanikolaou[1], Maria Rigana[1], Konstantinos Barkas[2], Konstantinos Nastos[3] & Andromahi Vryonidou[1]
[1]Korgialeneio-Benakeio Red Cross General Hospital, Department of Endocrinology & Metabolism – Center of Diabetes, Athens, Greece; [2]General Hospital "Agios Panteleimon", Neurosurgery Clinic, Athens, Greece; [3]General Hospital "Attikon", 3rd Surgical Clinic, Athens, Greece

Introduction
Most of pituitary adenomas are sporadic, with only 5% of them attributed to genetic mutations and syndromes such as Multiple Endocrine Neoplasia type 1 (MEN-1). However, how easy is it for a doctor to suspect it when there is no known family history?
Case Presentation
A 36-year-old patient with no personal or family history presented to our Endocrine Department reporting intermittent episodes of unconsciousness during the last 48 hours. The episodes lasted a few minutes without preceding aura or postictal phenomena. Biochemical analysis showed Glu = 44 mg/dl, without accompanying symptoms. Brain imaging with CT revealed pathological tissue

within the pituitary fossa with suprasellar and parasellar extension, without evidence of bleeding or optic chiasm compression. Further hormonal and imaging testing of the pituitary revealed a non-functioning adenoma measuring 2.3×3×2 cm on MRI, with concomitant thyrotroph and corticotroph axes deficiency. Despite hydrocortisone replacement therapy, the patient had consistently low fasting morning glucose levels (Glu < 45 mg/dl) with inappropriately high insulin levels (Ins = 9 IU/mmol), without neuroglycopenic symptoms. Prolonged fasting test confirmed endogenous insulin hypersecretion. Abdominal CT described an invasive lesion in the pancreas body. Endoscopic ultrasound identified a 2 cm mass in the uncinate process, a 3 cm mass between the body and the tail, and two smaller (< 1 cm) satellite lesions. Cytology confirmed a pancreatic NET with characteristics of insulinoma. Additionally, biochemical analysis revealed elevated corrected calcium (11.9 mg/dl) and PTH = 238 pg/ml levels, and 25OHD3 < 8 mg/dl, indicating primary hyperparathyroidism. Neck ultrasound confirmed the presence of a parathyroid adenoma measuring 15.4×6.6×8 mm. Based on these findings, the diagnosis of MEN-1 syndrome was established and confirmed by genetic testing, detecting the rare nucleotide change c.467G > A heterozygosity in exon 3 of the MEN-1 gene. PET CT with Ga-68 showed no other lesions. The patient underwent initially transsphenoidal adenectomy and pathology report revealed "a well differentiated endocrine tumor consisting of a population of neoplastic cells expressing hormones (β-FSH, β-LH, PRL), with Ki-67 = 7% and absence of menin expression". Then parathyroidectomy, thyroidectomy, total pancreatectomy, splenectomy, and cholecystectomy took place. Histology revealed parathyroid hyperplasia consistent with MEN-1 and a pancreatic NET G2 with Ki-67 = 5%, well-confined, without peripancreatic lymph node involvement.

Discussion

Many cases may seem to have an obvious diagnosis, but patience and persistence in clinical observation can reveal an underlying rare syndrome, while genetic testing serves as the confirmation. A multidisciplinary approach is crucial for the optimal management of patients with rare diseases.

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EP1291

Endocrine disorders associated with prader-willi syndrome: a case report

Mariem Cheikh, Mohamed Elmoctar, Cheibete Zakaria, Diehah Isselmou, Rifai Kaoutar, Hinde Iraqi & Gharbi Mohamedelhassan
Ibn Sina Hospital, Endocrinology, Rabat, Morocco

Introduction

Prader Willi syndrome is a rare and complex genetic disease, with numerous implications on metabolic, endocrine, neurologic systems, with behavior and intellectual difficulties. Many patients with PWS manifest short stature due to growth hormone deficiency. These individuals also present with hypothalamic dysfunction, leading to several endocrinopathies such as hypogonadism, hypothyroidism, central adrenal insufficiency, with reduced bone mineral density. Our case illustrates the value of early genetic diagnosis.

Observation

A 21-year-old patient, diagnosed since the age of 12 with prader willi syndrome, presented with impubirism and severe statural retardation. Investigations revealed GH deficiency, hypogonadotropic hypogonadism complicated by severe osteoporosis and central hypothyroidism. The patient was substituted by l thyroxine and testosterone.

Discussion and conclusion

Prader-Willi syndrome is a complex genetic disorder caused by lack of expression of the paternally inherited chromosome 15q11-q13. Previous epidemiologic studies have estimated the incidence of PWS from 1 in 10, 000 to 1 in 30, 000 live births disorder It is characterized by hypothalamic-pituitary deficiency, severe neonatal hypotonia, early-onset hyperphagia, hypogonadism, mental retardation and morbid obesity, sometimes complicated by diabetes. Children diagnosed with Prader-Willi syndrome should receive GH treatment from 3 to 6 months of age. Several clinical guidelines recommend that thyroid function be assessed at the time of diagnosis of Prader-Willi syndrome, and once a year thereafter. Confirmation of the disease is necessary for early management of endocrinological manifestations, in particular early GH supplementation. Proper management of PWS patients requires a multidisciplinary team approach. It is important for pediatric endocrinologists to be aware of the recommendations for screening and monitoring of variou.

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EP1292

Effectiveness of the transition process in adolescents with chronic endocrinological disorders: experience of the transition clinic in verona, italy

Stefania Munari[1], Rossella Gaudino[2], Sabrina Vantini[2], Alessandro Ferruzzi[2], Thomas Zoller[2], Marta Arrigoni[2], Roberto Castello[2] & Franco Antoniazzi[2]
[1]Azienda Ospedaliera Universitaria Integrata Verona, Pediatria, Verona, Italy; [2]Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy

Background

Literature data indicate that up to 36.8% of patients with chronic endocrinopathies, occurring in children, abandon follow-up visits in adulthood, with the risk of major long-term consequences for their health. For this reason, it is essential that their transfer to an adult physician takes place through a well-structured transition process in order to ensure continuity of care. With this goal, the Transition Clinic of pediatric endocrine pathologies of AOUI Verona was born in 2010, first in Italy.

Aims

From the analysis of subjects transiting to our clinic from 2010 to 2019, the main objective of this work has been to assess the effectiveness of the transition process by measuring adherence to follow-up visits, experience and satisfaction with the transition process, the perception of their self-management skills and the assessment of the quality of life of these patients.

Subjects and Methods

50 patients with 9 different chronic endocrinopathies were included in this study. Clinical data have been collected through the consultation of medical records. Subjects have been offered an online, anonymous questionnaire. Adherence to follow-up visits was assessed by the detection of the last control visit. Satisfaction with the transition process was measured through an Analog Visual Scale (VAS). Evaluation of the perception of one's own self-management skills and quality of life was carried out through the "On Your own feet – Self-Efficacy Scale" (OYOF-SES) and SF-36®, respectively.

Results

For the first time a drop-out rate of 26% was found, with a significant variability among the individual endocrinological diseases analyzed (from 0% for Turner syndrome and Klinefelter syndrome up to 100% for hypoparathyroidism) and transited properly. 82% of the transited subjects were satisfied with their experience at the Transition Clinic, with a grade 6 (average 7.9 ± 2.4 SD). There was a good capacity for self-management, with high scores obtained at OYOF-SES (average 96.98 ± 13.30 SD). The perceived quality of life is also overall good, except for mental health, which was significantly lower than the reference healthy population.

Conclusions

Despite the improvement in the dropout rate and the results in terms of self-management and quality of life obtained by the Transition Clinic of AOUI in Verona, constant analysis and implementation of individualized transition process are necessary to ensure their optimum effectiveness.

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EP1293

The impact of metabolic and hormonal alterations on sexual and psychological function in women with polycystic ovary syndrome

Nunzia Verde, Federica Sorice, Roberta Scairati, Cristina de Angelis, Francesco Garifalos, Davide Menafra, Antonio de Fraia, Luigi Santella, Alessandro Mazzarella, Renata Simona Auriemma, Annamaria Colao & Rosario Pivonello
Università di Napoli "Federico II", Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia ed Andrologia, Unità di Andrologia e Medicina della Riproduzione, Sessualità e Affermazione di Genere (Fertisexcares), Naples, Italy

The current study evaluated the impact of metabolic and hormonal alterations on sexual and psychological function in women with Polycystic Ovary Syndrome (PCOS). Fifty consecutive women aged 24.16 ± 5.97 years with a diagnosis of PCOS were recruited; metabolic and hormonal parameters were measured and questionnaires related to sexual function (Female Sexual Function Index-FSFI) and psychological traits (Middlesex Hospital Questionnaire-MHQ, Body Uneasiness Test A and B-BUT A and B)were administered. Correlation analysis was performed by Spearman test, intragroup comparison by Mann-Whitney test. Mean FSFI total score was 12.5 ± 26.6 with a prevalence of sexual dysfunction of 34%. Anxiety was detected in 76%, phobia in 50%, obsession in 42%, somatization in 50%, depersonalization in 84%, and hysteria in 66% of patients.

Body image concern positively correlated with BMI and Waist Circumference (WC) ($P=0.031$; $P=0.022$) and depersonalization positively correlated with WC ($P=0.035$). Positive Symptom Distress Index-PSDI positively correlated with Ferriman-Gallwey score ($P=0.016$). FSFI total score ($P=0.009$; $P=0.019$), desire ($P=0.017$; $P=0.049$), arousal ($P=0.012$; $P=0.028$), lubrication ($P=0.011$; $P=0.022$), orgasm ($P=0.03$; $P=0.008$) and satisfaction ($P=0.013$; $P=0.016$) negatively correlated with insulin and HOMA-IR. Positive Symptom Total-PST positively correlated with insulin ($P=0.015$). Global Severity Index-GSI ($P=0.048$), weight phobia ($P=0.04$), thighs ($P=0.0443$) and legs ($P=0.008$) negatively correlated with prolactin levels. Pathological somatization ($P=0.011$), body image concern ($P=0.036$), WC ($P<0.0001$), Hip Circumference-HC ($P<0.0001$), insulin ($P=0.012$) and HOMA-IR ($P=0.003$) were significantly worse in overweight/obese($n=25$), compared to normal-weight($n=23$) patients; no difference in any of assessed parameters was detected based on the presence/absence of insulin resistance. The results of the current study highlighted that sexual and psychological function of PCOS patients might be negatively influenced by insulin resistance and that higher PRL levels were associated with reduced body satisfaction. The underlying mechanism might rely in the known negative impact of insulin resistance on clitoral vascular flow, namely increased vascular flow resistance. A timely and individualized therapy is necessary not only for the resolution of **metabolic** complications but also to improve **psycho-sexual** health of patients affected by PCOS.

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EP1294

Population characteristics of thyroid carcinoma in children and adolescents living in conditions of iodine deficiency in the republic of uzbekistan

Shakhlo Muratova & Madina Sattorova[1,1]
Republican Specialized Scientific and Practical Medical Center of Endocrinology named after Academician Y.Kh. Turakulov, Tashkent

Introduction
Thyroid cancer (TC) is a rare disease in childhood, with an incidence of 0.2 to 5 cases per million per year or higher [Neiva F., 2012, Tuli G, 2023]. The incidence of malignancy among thyroid nodules in children is about 16%, which is about three times higher than in adults [Vaisman F., 2011, Yeker R.M., 2022]. Lymph node metastases (40–80%) and distant metastases (25%) are also much more common in the pediatric population [Zirilli G., 2018, Thomas JK., 2021]. One of the important factors for the high risk of TC is iodine deficiency, which persists in Uzbekistan, although thanks to ongoing prevention, its prevalence has decreased by more than 2.5 times over the past 20 years [Ismailov S.I., 2018].
Objective
To assess the incidence of TC in children and adolescents based on admission to a tertiary hospital in the Republic of Uzbekistan.
Materials and methods
A retrospective study of 13, 509 medical histories and outpatient records of children and adolescents who received outpatient and inpatient treatment at the clinic of the RSSPMCE named after Academician Y.Kh. Turakulov for the period from 2016 to 2022 was conducted.
Results
During this period, 27 children with TC were identified, of which 24 were girls (89%) and 3 boys (11%), the gender distribution was 8.1:1. The average age was 17.5 ± 2.7 years. TC was most common among school-age patients (44.4%), in second place - among university students (26%), then among lyceum students (14.8%), college (11.1%), and among working people (3.7%). In all children, palpation revealed grade 2 goiter, with 66.7% (18) of children diagnosed with nodular goiter, and 33.3% (9) with multinodular goiter. Total thyroidectomy was performed in 75% (18) of cases, subtotal - 16.7% (4), and 2 patients underwent hemithyroidectomy (8.3%). Histological examination of native thyroid tissue in all children we studied revealed differentiated TC; papillary TC was diagnosed 2 times more often than follicular carcinoma. There were no cases of medullary and anaplastic TC. Radioiodine ablation with I131 was performed in only 20.8% of children.
Conclusion
TC remains a pressing and little-studied problem. Most often, children are diagnosed with papillary TC with a solid euthyroid node in adolescence, while in girls it is detected 8 times more often. The average TI-RADS values in children with TC according to ultrasound data are 4.2 ± 0.2, histological examination data are 4.14 ± 0.34 according to Bethesda. Further population-based prospective studies of TC in the pediatric population are necessary.

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EP1295

Evaluation of body image and eating behavior disorders in pregnant women

Yosra Hasni[1,2], Wiem Saafi[1,2], Aya Mlayah[3], Hamza Elfekih[1,2], Syrine Chelly[2,4], Meriem Ghardallou[2,5] & Latifa Lassoued[2,4]
[1]Hospital F. Hached, endocrinology, Sousse, Tunisia; [2]Ibn El Jazzar Medical Faculty of Sousse, Sousse, Tunisia; [3]College Science And Technology Health De Sousse, Sousse, Tunisia; [4]Hospital F. Hached, gynecology, Sousse, Tunisia; [5]Hospital F. Hached, epidemiology, Sousse, Tunisia

Introduction
During pregnancy, women experience various physiological changes that can impact them psychologically. Lifestyle modifications such as eating behaviors and physical activity during this period are major determinants of pregnancy outcomes, child development, and maternal health. Also, body transformations during this period could reactivate concerns regarding body image and introduce anxiety, body dissatisfaction, and eating behavior issues. The aim of our study was to assess the relationship between body image and eating behaviors in pregnant women.
Methods
We conducted a cross-sectional study that involved 194 pregnant women. We administered a questionnaire to explore their sociodemographic characteristics, gynecological-obstetric history, and current pregnancy. In addition, we assessed the nutritional status of these women using the FIGO checklist, evaluated their body image using the BAQ, and screened for eating disorders using the SCOFF tool.
Results
Our study found that 95.5% of the participants had an unhealthy diet that required further revision with a nutritionist. Among pregnant women, 66.5% consumed fruits and vegetables in moderation, while whole foods were the least consumed. More than half (58.8%) of the women in our study consumed pastries five times a week. The mean score for the Body Attitude Questionnaire (BAQ) was 140.7 ± 17, with scores ranging from 87 to 200. Additionally, 32% of the women were found to be at risk of developing an eating disorder based on the results of the SCOFF. Although there was no significant association between the SCOFF and the BAQ, the SCOFF was positively correlated with some subscales of the BAQ.
Conclusion
Our results stress the need for evaluating the nutritional status of pregnant women and monitoring their psychological well-being to address the risk of developing eating disorders.

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EP1296

Case report: acute intestinal pseudo-obstruction as a rare complication of pheochromocytoma

Yi Yi Aung, Ching Man Li & Sherif Ghieth
University Hospitals Plymouth Trust, Department of Endocrinology and Diabetes, Plymouth, United Kingdom

Phaeochromocytoma is a rare tumour of the adrenal gland medulla characterized by excess catecholamine release. Classic presentation includes paroxysms of hypertension and adrenergic symptoms such as headache, sweating, shortness of breath, and tachycardia. In severe cases, patients might develop hypertensive crises and cardiomyopathy. We present a case of intestinal pseudo-obstruction as a rare complication of phaeochromocytoma which responded only to surgical resection of the tumour. A 76-year-old lady presented to A&E with progressive shortness of breath, chest discomfort, and collapse following a new introduction of a beta blocker. Initial assessment revealed tachypnoea, low oxygen saturation, and high blood pressure. CT pulmonary angiogram ruled out pulmonary but picked up incidental 8-cm right adrenal lesion, highly suspicious for phaeochromocytoma. Further imaging with CT thorax, abdomen and pelvis and raised urinary metanephrines confirmed non-metastatic phaeochromocytoma diagnosis. During admission, Doxazosin was titrated up to the maximum dose; however, blood pressure remained uncontrolled while she started to develop symptoms of bowel obstruction. CT abdomen revealed non-mechanical small bowel obstruction which confirmed paralytic ileus diagnosis. She was put on NBM and moved to ICU for IV Phentolamine infusion; however, paralytic ileus continued to deteriorate. Accordingly, she underwent urgent laparoscopic right adrenalectomy which managed to resolve paralytic ileus and allowed her to

gradually stop antihypertensive medications. In conclusion, this case sheds light on rare complications of phaeochromocytoma, including intestinal pseudo-obstruction, that should be assessed in acute presentations.

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EP1297

The efficacy of pasireotide treatment in invasive crooke's cell corticotropinoma – case report

Katarzyna Maliszewska[1], Anna Poplawska-Kita[2], Aleksandra Januszewska-Gilis[3], Przemyslaw Witek[4], Tomasz Lyson[2] & Adam Kretowski[1]
[1]Madical University of Bialystok, Department of Endocrinology, Diabetology and Internal Medicine, Bialystok, Poland; [2]Madical University of Bialystok, Department of Neurosurgery with Department of Interventional Neurology, Bialystok, Poland; [3]Jagiellonian University Medical College, Cracow, Poland, Department of Endocrinology, Cracow, Poland; [4]Warsaw Medical University, Warsaw, Poland, Department of Internal Medicine, Endocrinology and Diabetology, Warsaw, Poland

Introduction
Crooke's cell adenomas (CCA) are a rare type of pituitary neoplasm, associated with Cushing's disease. They are characterised by accumulation of perinuclear cytokeratin filaments, appearing distinctly hyaline in hematoxylin and eosin (HE) staining (Crooke's hyaline change). Due to their rarity, the management and treatment remain a challenge.
Clinical case
A 33-year-old male patient, presented sudden visual impairment, no signs of Cushing's disease were reported. The pituitary MRI revealed a 51×29×32mm macroadenoma within sella turcica, penetrating into the cavernous sinus, suprasellar region and the third ventricle with compression of the optic chiasm. Two months after the initial diagnosis, the typical hypercortisolemia symptoms (sudden weight gain, striae and hypertension) occurred. The laboratory results showed high ACTH concentrations (230pg/ml), loss of circadian cortisol rhythm, elevated urinary free cortisol excretion (UFC 675 mg/24 h), and lack of cortisol inhibition after 1 mg of dexamethasone. The patient underwent transsphenoidal surgery, the mass was partially (~50%) removed (diameters of mass 19x14x12mm in MRI) without normalisation of ACTH and UFC. After the post operation period, gradual increases of cortisol hormones and tumor mass progression were observed. After analyzing the risk associated with reoperation or possible radiation therapy, the decision was made to start with conservative treatment. Regarding the presence of functional Cushing disease, long-acting pasireotide administered once monthly was introduced, with the initial dose of 10 mg with gradual titration to 30 mg. However, the normalisation of ACTH and UFC after 6 months of treatment was not achieved. For the next 6 months osilodrostat (1 mg twice a day) was added to the therapy simultaneous with pasireotide 30 mg each month. In imaging data, a year after the pharmacology therapy, the slight progression in tumor size was detected (diameters of mass 22x15x20mm). Another attempt at transnasal resection was made, but no complete resection was achieved. Postoperatively the normalisation of UFC was observed with persistent slight increase of ACTH concentration (150pg/ml). Histologically, the tumour was described as densely granulated adenoma, Ki-67 labeling index was low; surprisingly no Crooke hyaline change was detected. Again, the therapy of pasireotide was restarted with stabilisation of the disease (UFC in normal laboratory range 54.6 mg/24 h and slight increase of ACTH concentration 135pg/ml) after one year of observation.
Conclusion
CCA is a rare pituitary adenoma that should receive significant attention. Pasireotide could be considered as a second or third line treatment in CCA. However, further studies of the effectiveness of such treatment are required.

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EP1298

Primary hyperparathyroidism secondary to parathyroid carcinoma in a 53 year-old male presenting with lassitude, constipation and bone pains: a case report

Rhoda Mae Pableo & Donnah Bless Lumanlan-Mosqueda
Brokenshire Medical Center, Internal Medicine, Davao City, Philippines

Parathyroid carcinoma is a rare (<1-5%) cause of primary hyperparathyroidism (pHPT) marked by excessive parathyroid hormone secretion leading to hypercalcemia. The prevalence rate of parathyroid carcinoma is 0.005% among all malignancies which has a slow and indolent course. A 53 year old male presented with lassitude, constipation, and bone pains which are common but non-specific symptoms. Diagnostic examination showed ionized calcium of 2.16mmol/l, nephrolithiasis, elevated creatinine and shortened QT interval. Intact PTH (iPTH) is elevated at 177.57 pg/ml with normal thyroid function tests. Hypercalcemia was managed with hydration and diuretics. Imaging revealed a hypoechoic mass posterior to the thyroid gland. Sestamibi scan showed increased tracer accumulation almost occupying the entire right lobe. Right inferior parathyroidectomy with right thyroid lobectomy was done wherein biopsy revealed parathyroid carcinoma. Post-operative iPTH showed a significant decline (>50%) from baseline at 39.91 pg/ml indicating complete removal of the abnormal hyperfunctioning parathyroid gland. Succeeding iPTH and serum calcium showed a decreasing trend alongside improving signs and symptoms. Although parathyroid carcinoma is rare, its manifestations as a result of hypercalcemia is common. Given that the best chance for treatment success is with a complete en-bloc resection, early diagnosis is imperative for treatment success and prolonged disease-free survival.

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EP1299

Unraveling the link: polycythemia and hyperparathyroidism - a case report

Sulmaaz Qamar[1] & Bernard Khoo[1,2]
[1]Royal Free Hospital, United Kingdom; [2]University College London, United Kingdom

Introduction
This case report explores the intricate relationship between polycythemia and hyperparathyroidism in a 42-year-old male, shedding light on the resolution of polycythemia following surgical intervention for PTH-dependent hypercalcemia. Despite the absence of symptomatic nephrolithiasis or renal failure, the patient's DXA scan revealed osteoporosis, prompting a deeper investigation into the complex interplay between these two conditions.
Methods
Comprehensive diagnostics, including ultrasound and SPECT scans, identified a 3.4 cm parathyroid adenoma. Initial pharmacological interventions with Colecalciferol and Cinacalcet escalated, revealing a Cinacalcet dosage of 60 mg BD. Notably, the patient remained asymptomatic, presenting an intriguing clinical paradox.
Results
The excision of the right inferior parathyroid adenoma yielded more than a resolution of hypercalcemia. Postoperatively, the patient experienced a marked normalization of blood calcium levels and the unexpected resolution of polycythemia. Histological examination confirmed a solid cystic parathyroid adenoma with no malignancy, emphasizing the unique relationship between these two conditions.
Discussion
This case challenges existing paradigms, raising whether polycythemia may be an underrecognized consequence of hyperparathyroidism. Literature suggests an association between polycythemia and parathyroid carcinoma; however, the absence of malignancy, in this case, prompts consideration of broader factors influencing the resolution of polycythemia.
Follow-up and Management
Subsequent clinic assessments three months postoperatively revealed successful recovery and resolution of pins and needles. Cinacalcet was discontinued due to the normalization of blood calcium and PTH levels. The unexpected resolution of polycythemia underscores the importance of continuous monitoring and further research into the incidence and mechanisms of this phenomenon.
Conclusion
This case highlights the successful management of PTH-dependent hypercalcemia and emphasizes the need for heightened awareness of the potential relationship between hyperparathyroidism and polycythemia. Further studies are warranted to elucidate the intricate connections between these conditions and their impact on patient outcomes.

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EP1300

Thyroid cyst infected with capnocytophaga canimorsus

Sinead Cadogan[1] & Siobhán McQuaid[1,2]
[1]The Mater Misericordiae University Hospital, Department of Endocrinology, Ireland; [2]University College Dublin, School of Medicine, Dublin, Ireland

Infected thyroid cysts are a rare complication of the thyroid gland, with haematogenous spread from a distal site of infection believed to be one mechanism of infection. We report the case of a patient who presented with an infected thyroid cyst due to Capnocytophaga canimorsus bacteraemia after sustaining a dog bite on her hand. A 37-year-old female presented to the Emergency Department with a five-day history of fevers, neck pain, and a rapidly enlarging neck swelling. The patient reported a dog bite on her right hand two days prior. Physical examination revealed temperature of 39.2°C, tachycardia, and a 3 cm tender mass in the left thyroid lobe. Laboratory investigations demonstrated leukocytosis (white blood cell count: 16.6×10^9/l) and elevated C-reactive protein (160 m g/l). Thyroid Ultrasound revealed a 3.1 cm left lobe cyst which demonstrated vascularity, and an overall multinodular appearance to the left lobe. The thyroid cyst was aspirated, and the fluid culture grew gram negative bacillus. Subsequent PCR testing confirmed this as Capnocytophaga canimorsus. The infected thyroid cyst was attributed to haematogenous spread of bacteria. Following a two week course of ceftriaxone and metronidazole, the patient's condition improved, with resolution of fever and normalisation of inflammatory markers. Capnocytophaga canimorsus is a gram-negative bacterium and an oral commensal in dogs, and occasionally causes serious infections in humans. To our knowledge, this is the first case report of an infected thyroid cyst due to capnocytophaga canimorsus.

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EP1301

Autoimmune polyglandular syndrome type 2: a clinical case of a rare combination of primary adrenal insufficiency and latent autoimmune diabetes in adults

Ilana Katsobashvili, Laura Ebanoidze, Ivan Golodnikov, Larisa Dzeranova, Ekaterina Pigarova & Tatyana Nikonova
Endocrinology Research Centre, Moscow, Russian Federation

Introduction
According to statistical data, the combination of chronic adrenal insufficiency and diabetes mellitus is the rarest among patients with autoimmune polyglandular syndrome type 2 (APS-2).
Clinical Case
In 2017, a 32-year-old patient B. with excess body weight manifested type 2 diabetes mellitus with typical clinical symptoms of carbohydrate metabolism disorder. Metformin and gliclazide were recommended. After a viral pneumonia episode with hospitalization in the intensive care unit in December 2022, the patient experienced pronounced weakness, nausea, hypotension, and weight loss. During outpatient examination for worsening general well-being, a sharp increase in ACTH and a decrease in blood cortisol were detected for the first time. In May 2023, the patient was urgently hospitalized in the endocrinology department, where primary adrenal insufficiency was diagnosed based on hormonal studies (morning blood cortisol – 94 nmol/l, ACTH – 1250 pg/ml). Hydrocortisone 10 mg in the morning/evening and fludrocortisone 0.1 mg/day were prescribed. Due to organizational difficulties, mineralocorticoid therapy was not administered. Due to decompensated carbohydrate metabolism (HbA1c - 19%), the patient was switched to basal-bolus insulin therapy (Protaphane 8 IU in the morning, 6 IU in the evening, Biosulin R 4 IU before main meals). In November 2023, during hospitalization in an endocrinological ward, considering a low C-peptide level of 0.501 ng/ml (1.1-4.4), antibodies to GAD >2000 U/ml (0-10), insulin – 6.38 U/ml (0-10), and tyrosine phosphatase <1 U/ml (0-10), latent autoimmune diabetes in adults (LADA) was confirmed in combination with other criteria (age >35 years, being on oral hypoglycemic therapy for >6 months). Hormonal studies revealed morning ACTH - 1044 pg/ml (7.2-63.3) and morning cortisol - 45.5 nmol/l (171-536). The hydrocortisone regimen was adjusted to 10 mg in the morning, 5 mg at 13:00, and 5 mg at 18:00. Data indicating mineralocorticoid deficiency were obtained: sodium - 133.7 mmol/l (136-145), potassium - 4.09 mmol/l (3.5-5.1), renin - 75.95 mU/l (2.8-39.9), and fludrocortisone 0.1 mg/day was initiated. To exclude celiac disease, antibodies to gliadin IgA were taken, yielding 2.79 U/ml (0-12). Upon admission, HbA1c was 14%, and insulin therapy was optimized: insulin degludec 100 U/ml 12 IU at 22:00, insulin aspart 6 IU before main meals, stabilizing glycemic indicators within individual target ranges.
Conclusion
The clinical manifestations of APS-2 underscore the complex nature of the interplay between autoimmune and metabolic disorders necessitating an interdisciplinary approach in the timely diagnosis and treatment of this syndrome.

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EP1302

Denosumab, immobility and calcium dysregulation

Raisa Minhas & Asjid Qureshi
Northwick Park Hospital, Diabetes & Endocrinology, London, United Kingdom

Case Summary
We report a case of a 79 yr old female with multiple co-morbidities including diabetes mellitus, hypertension, recurrent TIAs, CABG (2015), HfpEF and osteoporosis. Following treatment for the latter with Denosumab 60 mg, the patient developed hypocalcaemia (1.87 -2.13 mmol/l) with appropriately raised PTH (7.2 - 457.4 pmol/l). Her 25 hydroxy vitamin D level was 99 nmol/l. Her hypocalcaemia was managed with alfacalcidol and intravenous and then oral calcium supplements. Over a period of 4 months, these were withdrawn, and the patient maintained a normal calcium off supplements for 1 month. The patient then developed sepsis requiring prolonged admission to ITU for 33 days. During this period of her inpatient stay, she developed hypercalcemia (2.60-3.24 mmol/l) with a suppressed PTH. Her serum ACE and electrophoresis were normal. Her PET-CT scan demonstrated no evidence of malignancy. Her hypercalcaemia was suspected to be secondary to immobility and possibly rebound hypercalcemia after the discontinuation of denosumab. Treatment was with rehydration and bisphosphonates following which her calcium normalized. Immobilization is a recognized cause of hypercalcaemia. This is associated with a suppressed PTH, as in our case. Its onset is usually in 4 to 6 weeks after the precipitating injury/immobilization and calcium levels are usually no higher than 2.99 mmol/l?????. Severe hypercalcemia with levels $>$ 4.31 mmol/l, have been rarely described in the literature. Risk factors included prolonged inpatient stay (e.g. 6 months), sepsis (inflammatory cytokines accelerate osteoclastic resorption), chronic kidney disease stage 4, ITU stay, young age, spinal cord injury????. Rebound hypercacalcemia after discontinuing Denosumab has also been described in the literature. So far 6 cases have been reported amongst which 4 have been reported in pediatric population. Such cases are also associated with suppressed PTH levels, as in our case. Its onset is usually in 7 weeks to 6 months after discontinuing this drug and the severity of hypercalcaemia ranges between 2.5 to 3.79 mmol/l in adults. The mechanism may involve rebound osteoclast activity. Gradual tapering of denosumab dosage or prophylactic administration of bisphosphonates may prevent such cases. The management options for hypercaclaemia due to these two causes include hydration, bisphosphonates, corticosteroids, calcitonin, etc. Others have suggested that in severe cases, repeated use of bisphosphonates or reinjection of denosumab may be required to repress the surge of calcium released into the circulation.

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EP1303

The effect of teriparatide on bone density in osteoporotic patients with hiv infection

Eleni Palioura[1], Eleni Herolidi[1], Nikolaos Kalogeris[1], Alexandros Dermentzoglou[1], Maria Katsafyloudi[1], Alexandros Konidaris[1], Georgios Tsekes[2], Maria Chini[2] & Andromahi Vryonidou[1]
[1]Korgialenio Benakio, Hellenic Red Cross Hospital, Department of Endocrinology and Diabetes Center, Athens; [2]Korgialenio Benakio, Hellenic Red Cross Hospital, Department Infectious Diseases, Athens, Greece

Introduction
HIV infection has been associated with bone loss and increased frequency of bone fractures. The main pathogenetic mechanisms involve the direct effect of the virus and the HIV-induced inflammatory cytokines on bone metabolism, the effect of antiretroviral therapy (cART) *per se* and the frequently coexisting nutritional disorders and hypogonadism, further accelerating bone loss. Bisphosphonates remain the first-line treatment for these patients. Limited data are available for the safety and efficacy of denosumab while the effect of teriparatide is largely unknow in this population with only one case report described in literature.

Aim
To study the effectiveness and safety of teriparatide in osteoporotic patients with HIV infection.
Methods
This is a 36-month follow-up study. Subcutaneous teriparatide 20 mg was administered once daily for 24 months in three patients (two females and one male aged 68, 54 και 33 years, respectively). In two patients teriparatide was administered after vertebral fractures while on bisphosphonates therapy whereas in the third the agent was initiated after completing a 10-year treatment with risedronate. All patients received adequate calcium and vitamin D supplementation. Laboratory and imaging evaluation with DEXA of lumbar spine (L1-L4) and hip were performed before treatment initiation, at 24, and at 36 months. All patients had well controlled HIV infection (CD4 cell count >500 cells/ μl; undetectable viral load) under cART including tenofovir alafenamide.
Results
At 24 months a significant increase in BMD was observed in the lumbar spine (L2-L4) in all three patients: in the two females [percentage increase 9.4 and 18.4, respectively] and in the male [percentage increase 11.4], while a moderate increase was documented in total hip only in one female and the male [percentage increase 2.2 and 3.2, respectively]. At 36 months, thus one year since completing teriparatide treatment, two patients (68-year-old female and the male) showed further increase in bone density, especially in the lumbar spine (L2-L4) [percentage increase 11 and 3.1, respectively] and to a lesser extent in the total hip in the female [percentage increase 6.9]. CD4 cell count and viral load remained unaffected throughout the study. Additionally, none of the patients developed hypercalcemia during the treatment period, nor did they present any other biochemical or hormonal disturbances.
Conclusions
Teriparatide administration in osteoporotic patients with HIV infection, after bisphosphonate failure, seems to have a favorable impact on bone density. Further studies are needed to confirm the long-term effectiveness and safety of teriparatide in this population.

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EP1304

Efficacy and side effects of subcutaneous pasireotide alone or in combination with cabergoline in patients with cushing's disease whithout postoperative remission

Alev Selek, Nurgül Demir, Berrin Çetinarslan, Zeynep Cantürk, Emre Gezer, Mehmet Sözen, Damla Köksalan, Özlem Alkan, Saadet Acar & Fatma Öktem
kocaeli university, endocrinology, Kocaeli

Pasireotide is a second-generation, multireceptor-targeted somatostatin receptor ligand and is approved for the treatment of patients with Cushing's Didease (CD) for whom surgery has failed or is not an option. This retrospective single center study aims to report the efficacy, side effects and follow-up of the treatment with pasireotide alone or in combination with cabergoline in patients without remission after transsphenoidal surgery. Among 187 patients with CD, 15 patients, who did not achieve post operative remission and on pasireotide tretment, were enrolled to the study. Demographic data, comorbid diseases and clinical status of the patients before pasireotide treatment were shown on table 1. The mean pasireotide treatment duration was 15±13 months. UFC normalization was seen in 10 (67%) patients in 12 months, 2 patients discontinue the treatment <6 months because of drug intolerance (gastrointestinal disturbance and hypoglycemia) and 3 patients were unresponsive. Among 10 patients with normalization of UFC, 3 had remission and stopped medication after three years (2 had radiosurgery before, one not), one patient had treatment escape after 3 years and 6 of them are still on medication. New onset diabetes was seen in two cases (13%) however deterioration of glycemic control was seen in 3 (50%) of the diabetic patients. Cholelithiasis was seen in one patient. Clinical prognostic factors were also evaluated between pasireotide responsive and nonresponsive groups; all the factors were similar between groups probably due to small sample size (table 2). Pasireotide is an effective treatment in patients without surgical remission. Approximately half of the patients in our study were successfully treated with pasireotide alone or in combination with cabergoline without severe side effects. Radiosurgery is another treatment choice and pasireotide is also a good option until the effect of radiosurgery appears.

Table 1.

12 female (80%)	Mean age was 43 ±15 years
9 macroadenoma (60%)	Mean follow-up was 80 ±58 months
6 overt diabetes mellitus (40%) 5 prediabetes (33%)	Mean tumor size was 14.6 ±11.8 mm
6 2 or more operations (40%)	Mean pretreatment kortizol was 17.6 ±5.8 mg/dl
10 sterotactic radiosurgery (67%)	Mean pretreatment ACTH was 63.9 ±43 pg/ml
12 on cabergoline treatment (80%)	Mean pretreatment fold increase of urinary-free cortisol (UFC)was 2.7±1 /day (x ULN)

Table 2.

mean (±STD)	Pasireotide Responsive 10 (67%)	Pasireotide Unresponsive 5 (33%)
Age, years	14.5±3	14.8±7.6
Tumor size, mm	45.5±5.2	39.2±6
Pretreatment kortizol, mg/dl	16±14	20±10.3
Pretreatment ACTH, pg/ml	60±46	70±31
Pretreatment UFC, fold increase	2.2	3

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EP1305

Diabetes as a consequence of chronic calcifying pancreatitis: case report

Ikrame Qasdi, Hasna Ouirar, Amal Riad, Caimae Zouna, Fatima Toulali, Ghizlane Sabbar, Kaoutar Rifai, Iraqi Hinde & Mohamed Elhassan Gharbi
Ibn Sina University hospital, Endocrinology and Metabolic Diseases, rabat

Introduction
Diabetes stemming from pancreatic causes constitutes 0.5% of diabetes cases (1–2). It is defined as 'other specific types of diabetes resulting from exocrine pancreas impairment.' Through this case report, we elucidate the distinctive clinical features of chronic calcifying pancreatitis-related diabetes.
Case report
A 31-year-old male with a diabetic family history and a history of occasional alcohol consumption, is presenting with exocrine pancreatic insufficiency for the last 9 months. Characterized by diffuse abdominal pain, malabsorption-type diarrhea, concomitant onset of cardinal symptoms, and a weight loss of 14 kg over a year. Diabetes was revealed during the weight loss investigation. Clinical examination showed epigastric tenderness on palpation, capillary blood glucose at 5.9 g/l without ketonuria. Biochemically, fasting blood glucose was 2.5 g/l, eGFR at 123ml/min, HbA1c at 16.4g/dl, along with hepatic cytolysis and cholestasis. The infectious panel yielded negative results. The diagnosis of Chronic Calcifying Pancreatitis (CCP) was considered due to clinical and biological manifestations of exocrine insufficiency, weight loss, diabetes, and morphological findings. Notably, the pancreatic CT scan indicated a predominantly atrophic appearance of the entire pancreas with numerous micro and macro calcifications, along with dilation of the common bile duct and intrahepatic bile ducts, and findings consistent with calcifying pancreatitis without signs of glandular necrosis on magnetic resonance cholangiopancreatographic (MRCP). Given the indications of insulin deficiency, the patient was placed on insulin therapy using a basal-bolus strategy, and pancreatic enzyme supplementation was introduced. There were no manifestations of macroangiopathy or microangiopathy.
Discussion
Diagnosis of pancreatic diabetes is frequently delayed, with a notably higher occurrence in chronic calcifying pancreatitis. It should be considered in the presence of early signs of insulin deficiency

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EP1306

Changes in gut microbiota and arginine metabolic rates in patients with type 1 diabetes

Yelena Aghajanova[1,1], Arthur Melkonyan[1], Nina Alchujyan[2], Bayburdyan Gayane[1], Lusine Arakelyan[1], Sona Hakobyan[1], Zara Gevorgyan[1], Naira Zohrabyan[1], Margarita Hovhannisyan[2], Armine Mnatsakanyan[3] & Anna Vardanyan[1]
[1]Yerevan State Medical University, Endocrinology, Yerevan; [2]H. Bunyatyan Institute of Biochemistry NAS RA, Department of Pathological Biochemistry and Radioisotope Methods, Yerevan; [3]«Nork» Infectious Diseases Clinical Hospital, Clinical Laboratory, Yerevan

Introduction
Type 1 diabetes (T1DM) is one of the most frequent autoimmune and metabolic disorders in childhood and youth, developing due to autoimmune destruction of β-cells, which leads to an absolute insulin deficiency. Accumulating data suggest that gut microbiota (GM) may contribute to the pathogenesis of diabetes influencing the immune response, in which arginine-metabolizing enzymes are involved, particularly arginase. We examined the connection between GM and cytoplasmic and mitochondrial arginase isoforms (AI and AII respectively) in the leukocytes of patients with T1DM.

Materials/Methods
All patients were recruited at the Muratsan University Hospital, Endocrinology Department, Yerevan. Microbiota was examined in feces of participants in the clinical laboratory of «Nork» infectious diseases hospital. Fasting venous blood was taken into 3.8% sodium citrate anticoagulant, mixed with 6% dextran, and leukocytes were isolated by conventional procedures, then the leukocyte cytoplasmic and mitochondrial fractions were prepared by differential centrifugation. Arginase assay was based on the accumulation of L-ornithine produced by arginase in the reaction mixture during 1 hour incubation and determined by means ninhydrin. Measurement of the nitric oxide stable metabolites in protein-free samples was performed using Griess-Ilosvay reagent.
Results
Number of E.coli, Bifidobacterium spp., Lactobacillus spp. were drastically decreased with a concomitant increase in that of Candida albicans, and a manifestation of Staphilococcus aureus was also observed in T1DM, which may compete with the gut beneficial bacteria. E.coli plays a protector role for GM, whereas clinical cultures of C.albicans has detrimental effects causing desquamation of small fragments peptidoglycan layers of cell wall and total destruction of the cytoplasm in lactobacilli. Changes in GM were associated with 1.3 and 1.5 fold increase in the activity of cytoplasmic and mitochondrial arginase isoforms in newly-diagnosed T1DM patients and 1.6 and 1.7 fold increase in patients with duration of T1DM more than 1 year. Simultaneously, in the same groups, statistically significant decline in the number of NO metabolites was observed. Arginase is known to contribute to decreased availability of L-Arginine in the organism, and particularly to nitric oxide synthase that may cause a subsequent reduction of NOS/NO production attributed to the pathological processes associated with diabetes.
Conclusions
Quantitative and qualitative changes in the content of GM in T1DM patients were recorded, which were associated with arginine metabolism intracellular changes in immune response involved leucocytes. Arginase isoforms stimulation in cytoplasme and mitochondrias of leucocytes in T1DM patients was revealed, associated with a decrease in nitrates level, which indicates the involvement of these processes in pathogenesis of the disease.

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EP1307

Hypocalcemia revealing digeorge syndrome: case report

Mariem Cheikh, Cheibete Zakaria, Mohamed Mokhtar, Kaoutar Rifai, Iraqi Hinde & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology Department, Rabat, Morocco

Introduction
DiGeorge syndrome is a genetic abnormality caused by a microdeletion of chromosome 22. Chromosome 22q1 1.2 microdeletion was first identified in 1992 as the common genetic anomaly associated with a range of conditions previously known as DiGeorge or velocardiofacial syndrome.
Case report
A 17-year-old Moroccan male was mildly mentally challenged and had seizures from the age of 9 years. He had dysmorphic facial features, and mild tortuosity of the vessels of the retina but no hemorrhage or exudates. The clinical examination found the presence of a hydrocele, Chvostek's and and Trousseau's signs were positive. Corrected calcemia was at 68 mgl/l, Urea was at 0, 21 g/l, creatinine at 8 mg/l, albumine 45 g/l, PTH was at 8 pg/ml A CT scan of the head showed Farh syndrome. Echocardiogram showed an interventricular septal defect with no aortic arch abnormalities. The diagnosis of DiGeorge's syndrome was suspected based on mental retardation, seizures, the dysmorphic facial features and cardiac abnormalities and the biochemical findings of hypoparathyroidism and hypocalcemia.
Discussion
The overall prevalence of DiGeorge's syndrome is 1 in 5950 births. It usually presents later in childhood, often leading to hypernasal speech caused by cleft palate, submucous cleft palate, or velopharyngeal insufficiency. Both disorders share similar clinical features, such as conotruncal heart defects and mildly dysmorphic facial characteristics. Approximately 13% of patients receive a diagnosis at the age of 15 or older, with most of them being identified through familial genetic studies. In adulthood, the presence of hypocalcemia as a result of pseudohypoparathyroidism (PH) is often the primary indicator of the disorder. Adults with PH typically exhibit developmental delays, psychiatric issues, and cardiac anomalies. Additionally, there may be an increased risk of early-onset Parkinson's disease. The majority of patients experience hypocalcemia (49-80%), which can manifest at any age. Hypocalcemia is caused by PH, which is characterized by congenital parathyroid aplasia or hypoplasia
Conclusion
This case highlights the diagnostic complexity of hypocalcemia in a setting of multiple potential etiologic factors. It emphasizes the importance of considering that chromosome 22q11.2 deletion syndrome is not a rare occurrence and may manifest later in life, ought to prompt healthcare providers to request genetic testing regardless of the individual's age.

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EP1308

Thyroid replacement therapy with liquid levothyroxine as an alternative for patients with gastrointestinal absorption problems

Eduardo Torrecillas del Castillo, Mercedes Peinado Ruiz, Pablo Rodriguez de Vera, Alberto Torres Cuadro, Clara García Socorro, María Asunción Martínez Brocca & Tomás Martín Hernández
Hospital universitario virgen macarena, Sevilla, Spain

Aim
Illustrating a case series of two patients with levothyroxine malabsorption and suboptimal control of the thyroid profile who experienced a significant improvement after switching to liquid levothyroxine.
Material and Methods
Case saries of two patients who were attended in monographic thyroid pathology consultations at Virgen Macarena University Hospital.
Results
Case 1: a 46-year-old female patient who had multinodular goitre detected incidentally by CT. Her personal history included Crohn's disease, ileocecectomy in 2007. No treatment. A thyroid ultrasound was performed, showing TIRADS4 nodule, on which FNA was performed with suspected papillary carcinoma. A total thyroidectomy was performed. Postoperative control showed Thyrotropin (TSH) levels 39.30 IU/ml and free-thyroxine(FT4) levels 0.75 ng/dl. Non-specific symptoms were reported. The patient required multiple dose readjustments with difficulty in achieving optimal control, requiring up to 300 mg/day of levothyroxine, with level variations, compatible with both treatment deficit and iatrogenic hyperthyroidism. A change to liquid levothyroxine was proposed. the next follow-up visit the laboratory tests showed a thyroid profile within target range: TSH 1.46 IU/ml; FT4 1.32 ng/dl; FT3 2.44pg/ml, dose of 200 mg/day. Case2: a 32-year-old primigravida patient who was unable to adjust her thyroid replacement levels despite progressive increases in the dose of oral levothyroxine. Her personal history included a total thyroidectomy for a papillary thyroid carcinoma that showed excellent control for 10 years with oral levothyroxine 200 mg/day. She reported symptoms of nausea and vomiting from the fourth week of gestation, which had worsened the last few days, leading to a weight loss of 2 kg. She reported muscle fatigue and generalised weakness in the last month. Laboratory tests were normal. Foetal follow-up and obstetric check-ups presented within normal limits. The thyroid profile showed TSH 58 IU/ml; FT4 0.36 ng/dl. A loss of muscle strength of 4/5 was observed on physical examination. Stretch reflexes slightly elongated. No thyroid remnants on cervical ultrasound. Based on these findings and the thyroid hormone levels, a clinical assessment of hypothyroidism secondary to thyroid hormone malabsorption was made, replacing levothyroxine tablets by liquid thyroxine at a dose of 2.3 mg/kg/24h, with thyroid hormone levels returning to normal and fatigue and muscle weakness also subsiding.
Conclusions
There are a significant number of patients who do not achieve an adequate response to oral levothyroxine therapy due to problems in its absorption, with negative consequences on the patient's well-being. Liquid levothyroxine could help this group of patients achieve more stable TSH values, improving their quality of life and reducing the risk of iatrogenic hyperthyroidism.

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EP1309

Malignant pheochromocytoma unmasked by paralyzing sciatic symptoms: a case report

Hasna Ouirar, Caimae Zouna, Ikrame Qasdi, Kaoutar Elmoatamid, Fatima Toulali, Ghizlane Sabbar, Kaoutar Rifai, Iraqi Hinde & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco

Introduction
Developing in the adrenal medulla's chromaffin cells, pheochromocytoma (PC) is an infrequent tumor Illustrating the instance of a patient diagnosed with malignant adrenal pheochromocytoma (PCM) following the onset of paralyzing sciatic pain

Case
A 60-year-old patient managing hypertension with triple therapy and type 2 diabetes using metformin and insulin glargine. The patient sought emergency care due to recurrent and disabling sciatic pain progressing to paraplegia. Concurrent constitutional symptoms, significant weight loss, and anorexia prompted a lumbar spine MRI, revealing spinal cord compression with an L3 fracture, and a concurrent 88mm adrenal mass, as further confirmed by an abdominopelvic CT scan. Secretory biochemical analysis indicated a significant increase in plasma Normetanephrines, measuring 116 times the normal level, while Metanephrines remained within the normal range. An 18F-FDG PET scan performed for staging purposes confirmed the hypermetabolic adrenal mass and identified a vertebral tumor extension with comparable features to the adrenal tumor. Surgical intervention has been advised after medical preparation.
Discussion
A neuroendocrine tumor, pheochromocytoma, is an infrequent condition marked by excessive catecholamine secretion. Malignancy is noted in 10% of cases, determined by metastases in tissues lacking chromaffin cells. It has a hereditary component in 40% of cases and in order to provide the best care, a coordinated, multidisciplinary approach is imperative

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EP1310

Somatotropinoma masked by morbid obesity: a case report

Anastasia Averkina[1,2], Raisat Guseinova[1,2], Manushak Rafaelyan[1,2], Olga Vasukova[1,2], Elena Andreeva[2], Ekaterina Pigarova[2], Vilen Azizyan[2], Ekaterina Bondarenko[2], Daria Kopytina[2] & Natalia Mokrysheva[2]
[1]Endocrinology Research Center, Center for the Treatment and Prevention of Metabolic Diseases and Obesity, Moscow, Russian Federation; [2]Endocrinology Research Center, Moscow, Russian Federation

Introduction
Acromegaly can be asymptomatic for a long time and morbid obesity can mask typical clinical signs (facial disfigurement, large hands and feet) and even severe disorders, such as hypopituitarism, cardiomyopathy, respiratory dysfunction, sleep apnea, atherosclerosis, endothelial dysfunction, arthropathy, prediabetes/-diabetes, dyslipidemia and mineral dysmetabolism. Menstrual irregularity and infertility combined with headaches are among the earliest issues a patient both with acromegaly and obesity might experience. This trio could be a clue for a diagnostic search for acromegaly long before obvious clinical manifestation.
Case Report
36 years old women was referred to endocrinologist, specialised in Obesity and Metabolism, by gynecologist due to infertility, stagnation of body weight at 120 kg (BMI 43 kg/m^2, max body weight was 160 kg at the age of 23), fatigue, headaches, episodes of high blood pressure up to 140/100 mm Hg and striae on the body. There were no changes in apperence typical for acromegaly. 2 years ago, an MRI scan was performed for headaches and delayed menstrual cycle investigation and a pituitary microadenoma was suspected. Hyperprolactinemia 628 mU/l (94-557) was detected, but after a single dose of cabergoline (0.125 mg) the cycle was restored and remained regular, patient discontinued the therapy. IGF-1 level was high = 364-428 ng/ml (78-311) and suppression of GH during the OGTT was inadequate (0-30-60-90-120 min – 2.2-1.1-2.0-2.3-3.1 ng/ml). Endogenous hypercortisolism was excluded (cortisol after the 1 mg overnight dexamethasone suppression test was 19 nmol/l). Prolactin was within a normal range (470 mU/l). Neither hypopituitarism nor glucose or mineral metabolism disorders (including hyperparathyroidism) were found. A patient underwent a transsphenoidal surgery for an endo-infrasellar pituitary microadenoma (7.5×6×8.8 mm). Histology showed a neoplasm of a solid structure from cells with basophilic cytoplasm; the immunohistochemical study revealed cytoplasmic expression of CAM5.2, pronounced expression of somatotropic hormone and focal weak expression of prolactin. Patient was biochemically in remission 6 month after surgery with no signs of hypopituitarism. Restoration of ovulatory ovarian cycles and regression of adipose mass resulted in clinical improvement and the occurrence of pregnancy.
Conclusion
This case report highlights a necessity to evaluate pituitary function in patients with morbid obesity and reproductive dysfunction, especially in presence of regular headaches. The application of a described multidisciplinary approach led to the timely verification of the underlying «asymptomatic» acromegaly and enabled us to prevent the development of complications and improve patient's quality of life.

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EP1311

High levels of serum prolactin associated with antipsychotic use: Should we be concerned? About two cases

Emna Mraihi[1], Imen Rojbi[1,2], Sabrine Mekni[1,2], Sawsen Essayeh[1,2], Rihab Laamouri[1], Meriem Werfelli[1], Karima Khiari[1] & Ibtissem Ben Nacef[1,2]
[1]Charles Nicolle Hospital, Tunis, Tunisia; [2]Laboratory of renal pathology (LR00SP01), Tunis, Tunisia

Introduction
Antipsychotic-induced hyperprolactinemia is a prevalent hindering condition that is often overlooked. It is responsible for several significant consequences that alter the patients' therapeutic compliance and quality of life. It can be a debilitating condition that warrants routine assessment and careful management through well-structured protocols.
Case details
We report the case of two patients treated with antipsychotics:
-The first one was a 25-year-old female with a personal history of chronic psychosis grafted onto mental disability treated with risperidone 2 mg per day. She presented with hyperprolactinemia (serum prolactin = 277 ng/ml) associated with secondary amenorrhea and galactorrhea.
-The second female patient was 31-year-old with a personal history of schizophrenia stabilized on both clozapine 100 mg per day and amisulpride 400 mg per day presented with hyperprolactinemia (serum prolactin = 168 ng/ml) associated as well with secondary amenorrhea. Neither patient exhibited signs of tumor syndrome. We ruled out, first, any active pregnancy. Then we measured serum thyroid stimulating hormone that came back in the normal range excluding, thus, primary hypothyroidism. Both patients had no renal insufficiency Pituitary MRIs were lastly conducted to rule out prolactinomas or tumors causing the 'Stalk effect'. A bone density test was performed to evaluate the long-term effect of hyperprolactinemia on the bone mass and showed no signs of osteopenia/osteoporosis. Since drug switch or discontinuation, as well as dose reduction, were not possible we aimed for hormone replacement therapy with estrogen.
Conclusion
Antipsychotic-induced hyperprolactinemia is a widespread endocrine disorder that can typically range from 25 to 100 ng/ml. Levels above 100 ng/ml can be observed and need further evaluation to rule out lactotroph tumors. Its approaches are controversial and numerous clinical trials are still being conducted.

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EP1312

Improvement of blood pressure in patients with type 2 diabetes, labelled as metformin-intolerant when rechallenged with extended-release metformin

Agnieszka Kuzior[1], Jennifer Maria Perez-Rivero[2], Claudia Arnas-Leon[1], Alba Hernandez-Lazaro[3], Ricardo Jose de Leon-Durango[4], Borja Santana-Ojeda[4], Inmaculada Molinero Marcos[4], Carmen Acosta-Calero[5], Maria del Pino Perez-Garcia[6] & Francisco Javier Martinez Martin[1, 4]
[1]Hospitales Universitarios San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [2]Centro Salud Escaleritas, Family & Community Medicine, Las Palmas de Gran Canaria, Spain; [3]Parc Taulí University Hospital, Endocrinology & Nutrition, Sabadell, Spain; [4]University Hospital of Gran Canaria Dr. Negrín, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [5]University Hospital of Gran Canaria Dr. Negrín, Cardiology, Las Palmas de Gran Canaria, Spain; [6]Centro de Salud El Calero, Family & Community Medicine, Telde, Gran Canaria, Spain

Introduction and Objective
Extended-release metformin has much better gastrointestinal tolerability than conventional (immediate release)metformin and according to the UK NICE guidelines should be offered to patients who have gastrointestinal tolerance issues with conventional metformin. We rechallenged patients with T2DM labelled as metformin-intolerant and treated with a DPP4i with a single-pill combination (SPC) of extended release metformin and sitagliptin (1000/50 mg) in order to assess its tolerability. We retrospectively calculated the cardiovascular risk of our patients at baseline and after 3-4 months on treatment with this SPC with the SCORE2-Diabetes calculator, and assessed the changes in office blood pressure.
Design & Methods
Consecutive patients with T2DM, HbA1c >7% but < 9% and eGFR (CKD-EPI) >45 ml/min/1.73m^2 labelled as metformin-intolerant due to gastrointestinal symptoms, and treated with a DPP4i were switched to the mentioned SPC, taking 1 pill daily in the first month and afterwards 2 pills if the tolerance was good. Additional antidiabetic medication, if any, was unchanged; however, lifestyle, antihypertensive and cholesterol-lowering medication were adjusted according to

current guidelines. Tolerance data were obtained by questionnaire in the follow-up visit. Calculations were done by intention to treat.
Results
We applied the SCORE2-Diabetes in 72 patients (45 women, aged 55±8 years, 7.5±3.2 years since the diagnosis of T2DM), of which 52 tolerated 2 tablets, 8 tolerated 1 tablet and 12 did not tolerate any. After 3-4 months of treatment, systolic office blood pressure was reduced from 147.3±21.2 to 131.8±18.9 mmHg ($P<0.001$); diastolic office blood pressure was reduced from 92.8±16.3 to 81.8±15.7 mmHg ($P<0.001$). The number of patients at target (<130/80 mmHg) changed from 14 (19.1%) to 33 (48.5%), $P=0.0011$ The baseline CV risk (major event in the next 10 years) was estimated as 12.8±2.3%; 7 (10.3%) patients were classified as intermediate risk, 46 (67.6%) as high risk and 15 (22.1%) as very high risk patients. After 3-4 months of treatment the 10-year CV risk was reduced to 10.3±1.8% ($P<0.001$); 27 (39.7%) patients were classified as intermediate risk, 34 (50%) as high risk and 7 (10.3%) as very high risk patients ($P<0.001$).
Conclusions
A large majority of the patients tolerated the rechallenge; their blood pressure and cardiovascular risk were significantly reduced. These changes must be considered as multifactorial, as in most patients there were additional interventions in lifestyle, antihypertensive and cholesterol-lowering drugs.

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EP1313

Papillary thyroid microcarcinoma revealed during surgical treatment of squamous cell carcinoma of the larynx

Karimi Meryem, Hajar Azagouagh, Talbi Dounia, Rifai Kaoutar, Iraqi Hind & Mohamed Elhassan Gharbi
Ibn Sina Rabat, Endocrinology, Rabat, Morocco

Introduction
The association of thyroid carcinoma with squamous cell carcinoma of the larynx is very rare, with few clinical cases reported in the literature.
Case report
We report the case of a 63-year-old patient with no significant medical history who presented with progressive dysphonia. Fiberoptic examination revealed a budding lesion. CT scan showed a tumor process centered on the right vocal cord, with negative extension findings. The patient underwent right laryngectomy with hemithyroidectomy and right recurrent laryngeal nerve dissection. Histopathological examination revealed two foci of well-defined, non-encapsulated, 3mm each, papillary microcarcinoma of the thyroid, vesicular variant, with no metastatic lymph nodes found in the totalization and central lymph node dissection. The patient was classified as low risk of recurrence. Subsequently, the patient received radiotherapy/chemotherapy as part of the management of the squamous cell carcinoma and was started on suppressive therapy with l-thyroxine.
Discussion and Conclusion
Surgical treatment of squamous cell carcinoma of the larynx is an unusual circumstance for the discovery of thyroid cancer, most often representing a histological surprise. According to the literature, there is no well-established therapeutic protocol, but the prognosis is closely linked to upper aerodigestive tract cancer.

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EP1314

Characteristics of ferritin status in patients with NAFLD and insulin resistance

Olha Kozak, Ihor Hospodarskyy & Oksana Prokopchuk
Ternopil National Medical University, Highter nursing education and clinical immunology, Ternopil, Ukraine

Introduction
Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent pathologies in the modern world. Despite the prevalence of this pathology, it continues to be studied, with new facts and mysteries about this diagnosis emerging. One such aspect is the impact of NAFLD on serum ferritin levels.
Aim
To investigate whether NAFLD affects serum ferritin levels in patients with insulin resistance.
Materials and Methods
To explore this topic, we examined 19 patients with NAFLD and insulin resistance, who were treated at the Ternopil regional central hospital (Group 1). The control group consisted of 16 patients with NAFLD but without nsulin resistance and without pathologies that could directly affect serum ferritin levels (Group 2). All patients underwent medical examinations. For comprehensive research, we conducted general clinical analyses (complete blood count, urinalysis, biochemical blood analysis) and instrumental studies (ultrasound, elastography, ECG). Special examination methods were also performed, including analyses of serum ferritin levels. The combination of these studies allowed us to confirm NAFLD and Insulin resistance in patients of the first group and exclude it in patients of the control group.
Results
When comparing the results of the control group (2) and the examined group (1), we identified certain patterns and peculiarities. Among the patients in the control group (2), the serum ferritin level was normal in 8 patients (50%), decreased in 5 patients (31.25%), and elevated in 2 patients (12.5%). In group 1 (patients with NAFLD), the distribution of results was as follows: the serum ferritin level corresponded to the norm in 7 patients (36.8%), was decreased in 2 patients (10.52%), and was elevated in 10 patients (52.63%). Thus, comparing the percentage ratio of data between group 1 and group 2 (control group), a clear pattern of elevated serum ferritin levels in the majority of NAFLD patients with Insulin resistance was evident.
Conclusions
According to the aforementioned results, we can assert that the presence of NAFLD and Insulin resistance is one of the factors influencing the elevation of serum ferritin levels in patients. This issue requires further and deeper investigation.

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EP1315

Renal cell carcinoma, solitary fibrous tumor and papillary thyroid carcinoma: an exceptional association

Elloumi Yesmine, Mrabet Houcem ElOmma, Ayadi Younes, Ayadi Mariem, Boubaker Fadia, Lassoued Najoua, Zantour Baha, Alaya Wafa & Med Habib Sfar
Hospital of Taher Sfar

Introduction
The solitary fibrous tumor is a rare spindle cell neoplasm, originally described in the pleural cavity. However, it can occur in other locations. Multiple primary cancers are a rare entity and their incidence is described at 5.5%. We report a case associating three neoplasms: a renal cell carcinoma, a mediastinal solitary fibrous tumor and a papillary thyroid cancer.
Obervation
We report the case of a 38 year old patient with no particular medical history, who presented a cough with fever. Chest scan showed a voluminous 10 cm mass in the upper mediastinum adhering to the upper lobe of the lung along with an incidental left mediorenal mass of 9 cm extending to the hilum. The patient underwent surgery: Resection of the lung mass with an enlarged left nephrectomy. Anatomopathological examination showed a mediastinal solitary fibrous tumor and a chromophobe renal cell carcinoma. Ten years later, the patient consulted for a cervical mass. Ultrasound showed suspicious cervical adenopathies along with a right mediolobar thyroid nodule of complex appearance measuring 17*13mm graded Eutirads 4. The patient underwent a total thyroidectomy. The histological examination showed a bifocal papillary carcinoma of the right thyroid lobe. The first one measures 1.7 cm, non-encapsulated and infiltrates the peri-thyroid adipose tissue and the 2nd nodule measures 0.1 cm, non-encapsulated and non-infiltrating along with lymph nodes metastases.
Conclusion
The association between renal cell carcinoma, mediastinal solitary fibrous tumor and papillary thyroid carcinoma wasn't described before in the literature. The coexistence of several neoplasms is rare. Common genetic and environmental risk factors seem to be involved in many cases. Multiplicity itself is not necessarily a poor prognostic factor. The role of genetic study is essential to codify these different diseases into a syndromic approach.

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EP1316

Clinical case of idiopathic osteoporosis associated with pregnancy

Ilana Katsobashvili, Laura Ebanoidze, Ekaterina Pigarova, Larisa Dzeranova & Svetlana Vorotnikova
Endocrinology Research Centre, Moscow, Russian Federation

Introduction
According to published data, pregnancy-associated osteoporosis is a rare disease, the pathophysiology of which is currently not fully explored.
Clinical case
In 2014, a 27 year-old patient B. after the first childbirth, pain appeared in the lumbosacral spine, for which a course of physical therapy was carried out with a short-term positive effect. In 2016 after the second childbirth, pains increased; according to the results of further examination, severe osteoporosis was revealed. According to densitometry (DXA) - the maximum decrease in bone mineral density (BMD) according to the Z-score in L_1-L_4 до -3.7 SD; MRI visualized compression fractures of the vertebral bodies $Th_{5,\ 8,\ 10}$. Later, vitamin D deficiency was verified (8.0 ng/ml), and colecalciferol was recommended to take 6000 IU/day in combination with calcium citrate and carbonate 500 mg/day, followed by ibandronic acid 150 mg once a month. In December 2019, MRI revealed new compression fractures of the vertebral bodies (Th_6 - 60%, Th_7 - 40%, Th_{11} - 40%). In order to exclude contraindications to the prescription of anabolic therapy, a blood test for the M-gradient was performed, followed by hematologist and oncologist consultation; multiple myeloma was not found. In this connection, in 2020 Teriparatide 20 mg subcutaneously daily was initiated, after 18 months the patient was transferred to zoledronic acid infusion. During hospitalization in the endocrinology hospital in December 2023, secondary hyperparathyroidism was diagnosed due to the use of bisphosphonates and insufficient calcium intake: PTH – 76.86 pg/ml (15-65), Ca adj. – 2.1 mmol/l (2.15-2.55). Therapy with calcium carbonate + calcium lactogluconate 1000 mg/day was recommended, the dose of colecalciferol is adjusted to 3000 IU daily. According to DXA, positive dynamics were noted - BMD was within the age norm ($L_{1\text{-}4}$ -1.2 SD; in the femur and radius: -1.3 SD and -1.2 SD, respectively).
Conclusion
The described case confirms the relevance of timely identification of risk factors and emphasizes the need to develop a personalized approach to the diagnosis and treatment of osteoporosis associated with pregnancy.

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EP1317

Concomitant multiple myeloma in a patient with primary hyperparathyroidism

Anna Somogyi[1], Eszter Berta[2], Inez Lengyel[3], László Váróczy[4], Endre Nagy[2] & Miklos Bodor[2]
[1]Faculty of Medicine, University of Debrecen, Endocrinology, Debrecen, Hungary; [2]Faculty of Medicine, University of Debrecen, Department of Endocrinology, Debrecen, Hungary; [3]Doctoral School of Health Sciences, University of Debrecen, Debrecen, Hungary; [4]Faculty of Medicine, University of Debrecen, Division of Hematology, Department of Internal Medicine, Debrecen, Hungary

Introduction
Primary hyperparathyroidism (PHPT) is one of the most common causes of non-neoplastic hypercalcemia with characteristically increased or inappropriately normal plasma parathyroid hormone (PTH) levels. Hypercalcemia is also a significant feature of patients with multiple myeloma (MM), and a pathogenetic link is presumed between the two diseases, strengthened by preclinical data. Only limited number of case reports of concomitant PHPT and MM are available in the literature.
Case report
A 58-year-old male patient was referred to the Department of Endocrinology, University of Debrecen, in 2022 with fatigue and hypercalcemia. His PTH was in the normal range and a 15×7 mm lesion was depicted by ultrasound in the region of left parathyroid gland. Imaging with technetium 99m-pertechnetate/technetium 99m-MIBI subtraction scintigraphy and with single photon emission tomography affirmed the suspected localization of parathyroid adenoma, PTH level became slightly elevated. After the surgical removal of the parathyroid adenoma histology affirmed benign lesion, and hypercalcemia persisted accompanied by normal PTH (se calcium 2.95 mmol/l, PTH 2.4 pmol/l). Nuclear imaging was repeated, and the results excluded the existence of another parathyroid adenoma, therefore we started to evaluate the opportunity of a concomitant neoplasia. Hyperproteinemia was also detected, and hematology workup started which confirmed the diagnosis of first stage IgG-kappa type multiple myeloma without typical lytic bone lesions. Since there is increasing evidence that monoclonal gammopathies are more common in patients with PHPT, a search for multiple underlying causes of uncontrollable hypercalcemia should be performed.

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EP1318

Hypocalcemia revealing digeorge syndrome: case report

Zakaria Cheibete[1], Mariem Cheikh & Mohamed Elmoctar
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
DiGeorge syndrome is a genetic abnormality caused by a microdeletion of chromosome 22. Chromosome 22q1 1.2 microdeletion was first identified in 1992 as the common genetic anomaly associated with a range of conditions previously known as DiGeorge or velocardiofacial syndrome.
Case report
A 17-year-old Moroccan male was mildly mentally challenged and had seizures from the age of 9 years. He had dysmorphic facial features, and mild tortuosity of the vessels of the retina but no hemorrhage or exudates. The clinical examination found the presence of a hydrocele, Chvostek's and and Trousseau's signs were positive. Corrected calcemia was at 68 mgl/l, Urea was at 0, 21 g/l, creatinine at 8 mg/l, albumine 45 g/l, PTH was at 8 pg/ml A CT scan of the head showed Farh syndrome. Echocardiogram showed an interventricular septal defect with no aortic arch abnormalities. The diagnosis of DiGeorge's syndrome was suspected based on mental retardation, seizures, the dysmorphic facial features and cardiac abnormalities and the biochemical findings of hypoparathyroidism and hypocalcemia.
Discussion
The overall prevalence of DiGeorge's syndrome is 1 in 5950 births. It usually presents later in childhood, often leading to hypernasal speech caused by cleft palate, submucous cleft palate, or velopharyngeal insufficiency. Both disorders share similar clinical features, such as conotruncal heart defects and mildly dysmorphic facial characteristics. Approximately 13% of patients receive a diagnosis at the age of 15 or older, with most of them being identified through familial genetic studies. In adulthood, the presence of hypocalcemia as a result of pseudohypoparathyroidism (PH) is often the primary indicator of the disorder. Adults with PH typically exhibit developmental delays, psychiatric issues, and cardiac anomalies. Additionally, there may be an increased risk of early-onset Parkinson's disease. The majority of patients experience hypocalcemia (49-80%), which can manifest at any age. Hypocalcemia is caused by PH, which is characterized by congenital parathyroid aplasia or hypoplasia
Conclusion
This case highlights the diagnostic complexity of hypocalcemia in a setting of multiple potential etiologic factors. It emphasizes the importance of considering that chromosome 22q11.2 deletion syndrome is not a rare occurrence and may manifest later in life, ought to prompt healthcare providers to request genetic testing regardless of the individual's age.

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EP1319

Peculiar case of post-gastrectomy noninsulinoma pancreatogenous hypoglycemic syndrome

Saša Ilić[1], Bojana Popovic[1,2], Drasko Gostiljac[1,2], Gordana Milic[1,2], Sandra Pekic Djurdjevic[1,2], Dragana Miljic[1,2], Masa Ristic[1] & Vesna Dimitrijevic Sreckovic[1,2]
[1]Clinic for endocrinology, diabetes and metabolic diseases, University Clinical Center of Serbia, Serbia; [2]University of Belgrade - Faculty of Medicine, Beograd, Serbia

For the diagnosis of hyperinsulinemic hypoglycemia (HH), it is necessary that in symptomatic hypoglycemia in the fasting test the insulin/glucose ratio is >0.3, or that in spontaneous hypoglycemia there are C-peptide >0.6 nmol/l and insulin >3.0 mIU/ml. It is a well-known fact about the increasing frequency of hypoglycemia after bariatric surgery (estimated up to 30% of patients), mostly within the Dumping syndrome, but the frequency of occurrence of noninsulinoma pancreatogenous hypoglycemia (NIPHS) after gastrectomy is still unknown. A 55-year-old female patient was referred to an endocrinologist due to hypoglycemia with neuroglycopenia and a positive Whipple triad – minimal home-measured glycemia was 1.9 mmol/l. Malnutrition dominates among the physical findings, with a BMI of 15 kg/m^2. Namely, 4 years ago, she was operated on because of gastric carcinoma (gastrectomy, lymphadenectomy, omentectomy, and right-sided hemicolectomy have been done), and during her follow up there were no signs of recurrence of the disease and/or dissemination. During the endocrinology examination, daily hypoglycemias were in the range of 2.0-2.7 mmol/l, during which was observed significant insulinemia (24.4-50.9 mIU/l) and C-peptide (1.4-2.8 nmol/l), During 5h oral glucose tolerance test and mixed meal test, HH was recorded. Radiological diagnostics (CT, MRI) ruled out the existence of a focal lesion in the pancreas. The response of counterregulatory hormones in repeated spontaneous hypoglycemia was blunted, which is why an

insulin tolerance test was performed: cortisol 86...61...100...119...99.9 nmol/l, PRL 377...290...227...195...180 mIU/l, HGH 0.5...1.0... 2.5...0.4...0.5 mIU/l – showing hypopituitarism. MRI showed no focal changes in the sellar region, but there were two aneurysms of the internal carotid artery slightly compressing the pituitary. Throughout the examination, the patient used megestrol for appetite stimulation. After excluding megestrol, normal baseline values of stress hormones were verified, and an adequate spike of cortisol was recorded in the ACTH test. Despite compliance with the diet, HH continued. Trial therapy with fast-acting octreotide was accompanied by significant hyperglycemia, so it was replaced with diazoxide, and with a daily dose of 175 mg, a satisfactory therapeutic response was achieved. HH in gastrectomy patients is a rarity and the most of published literature is in the form of case reports. In our patient, we speculate that during the post-gastrectomy period, she developed functional gastrointestinal hormonal adaptation and secondary nesidioblastosis (NIPHS). Hypopituitarism in our patient was observed as a transient and described side effect of megestrol, but close monitoring was continued due to aneurysms in the sellar region.

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EP1320

***in vitro* study of 17-beta-estradiol effects on a renal cancer cell line**

Lucrezia Rossi, Maria Rosaria Ambrosio & Maria Chiara Zatelli
Ospedale Universitario Sant'Anna di Cona, Section of Endocrinology, Department of Medical Sciences, University of Ferrara, Ferrara, Italy, Ferrara, Italy

Introduction
Renal carcinomas (RCs) are the most common kidney cancers, and their prognosis is affected by many factors; 5-year survival rate is >90% in patients with small tumors confined to the kidney. RC makes up 2-3% of cancers in adults aged between 50 and 70 years; in particular, the incidence in men is higher than women, 66.7 vs 33.3% of the cases, respectively.
Aim
RC incidence is twice as high in men as in women. This difference could suggest that estrogens may play a role in influencing a lower RC incidence in women. The aim of this study is to evaluate the effects of 17-β-estradiol (E2) on renal cancer cell proliferation *in vitro*.
Materials and methods
Experiments were performed with the HEK293 cells, a RC cell line, transfected with the pBIND-ERα Vector, containing the gene for the estrogen receptor. Cells were incubated for 48 and 72 hours with increasing E2 concentrations and proliferation was assessed by cell counting.
Results
We found that E2 concentrations in the range 1, 5 - 100 mM (*phase 1*) were killing the cells, being 1 mM E2 the maximum tolerated concentration, with a reduction in cell viability of 33%. E2 concentrations in the range 1, 5 - 100 μM (*phase 2*) significantly reduced viable cell number by 20%.
Conclusions
In *phase 1*, RC cells were exposed to high E2 concentrations, mimicking those of a woman in the peak of childbearing age (15-45 years). Conversely, in *phase 2*, RC cells were exposed to very low doses, mimicking those of a menopausal woman and/or a man. These results suggest a potential protective role of E2 towards RC.
Disclosure of interest: None declared.

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EP1321

Possible concurrence of primary aldosteronism with cushing's disease: a case report

Diana Becheanu, Adina Mariana Ghemigian, Laura Stanescu, Bianca Bucur, Eugenyia Petrova & Andra Cocolos
Parhon Institute, Bucharest, Romania

Resistant hypertension of endocrine cause can make for a challenging diagnosis but it certainly is a very important one.
Case report
We present the case of a 65 year old male patient with a history of arterial hypertension and hypokalemia for the past 10 years, for which he was prescribed a combination of alpha and beta blockers, calcium channel blockers, angiotensin receptor blockers (ARBs), loop diuretic, and spironolactone. The lack of response to this treatment suggested a possible endocrine cause and he was admitted to our clinic for further investigation. The blood biochemistry confirmed the hypokalemia (2, 9 mmol/l) and the endocrine panel showed high normal aldosterone levels (145 pg/ml), suppressed renin (0, 96 pg/ml) with an aldosterone/renin ratio (ARR) of 15, 1 ng/dl, and normal levels of metanephrines and normetanephrines. Additionally, we tested the serum cortisol and ACTH and performed 1 mg overnight dexamethasone test and 2 mg two-day dexamethasone test with lack of suppression with a slight increase of the blood pressure after the latter. Rising the spironolactone dose did manage to normalize the potassium levels, but the blood pressure remained high. The abdominal CT scan revealed bilateral macronodular adrenal hyperplasia and the pituitary MRI a micro-adenoma thus indicating that further investigations, such as adrenal venous sampling (AVS) and inferior petrosal sinus sampling could be needed in order to establish a correct diagnosis and treatment plan.
Conclusions
When facing with a patient with severe secondary hypertension it is important to search thoroughly for the endocrine imbalance since the results can sometimes be misleading and disorders could concur.

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EP1322

Primary hyperparathyroidism meets vascular malformation: a tale of intriguing coexistence

Ait Kassi Nada[1], Kouira Hiba[2,2], Issouani Jade[2] & Guerboub Ahmed Anas[2]
[1]Mohamed V Military Hospital, Endocrinology, Morocco; [2]Mohamed V Military Hospital, Endocrinology, Rabat, Morocco

Introduction and importance
Primary hyperparathyroidism is a prevalent source of hypercalcemia, predominantly attributed to a solitary adenoma in 80-85% of cases. Progress in imaging techniques has enhanced the accurate preoperative identification and targeted removal of hyperfunctional parathyroids in primary hyperparathyroidism (PHPT). The amalgamation of imaging methods or a "dual" approach, when congruent, enhances the precision of adenoma localization. Surgery remains the sole curative intervention for pHPT. The surgical approach must be carefully chosen to ensure optimal cure while minimizing dissection and associated morbidity.
Case presentation
We report the case of a 62-year-old female with a history of well-controlled hypertension on dual therapy and a history of cholecystectomy. She was admitted for the management of primary hyperparathyroidism, biochemically confirmed with a corrected calcium level of 110 mg/l, a phosphorus level of 22 mg/l, a PTH level 3.7 times the normal range, and elevated 24-hour urine calcium. As part of the impact assessment, we identified osteoporosis. In the localization assessment, cervical ultrasound revealed a right parathyroid adenoma with a distinctive aspect involving the carotid artery. Initially, we conducted a MIBI scintigraphy, which did not reveal any abnormalities, followed by a cervicothoracic CT scan that did not show evidence of a parathyroid adenoma. *In situ* echoguided PTH measurement returned high at 1 335 000 pg/ml. A PET scan with F-choline was performed, confirming a parathyroid adenoma adjacent to the lower pole of the right thyroid lobe. Additionally, an angioscan was conducted for a more comprehensive characterization of the carotid artery, indicating a right common carotid dolichoartery.
Conclusion
Surgery stands as the optimal course of treatment for our patient; nevertheless, the presence of this vascular malformation requires a thorough evaluation of the risk-benefit profile to recommend a suitable therapeutic strategy. Our patient's case will undergo review in a multidisciplinary team meeting to formulate an optimal management plan.

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EP1323

Quality of life improvement associated with the rechallenge with extended-release metformin in patients with type 2 diabetes labelled as metformin-intolerant

Inmaculada Molinero-Marcos[1], Alba Hernandez-Lazaro[2], Ricardo Jose de Leon-Durango[1], Carlos Rios-Gomez[1], Borja Santana Ojeda[1], Agnieszka Kuzior[3], Claudia Arnas-Leon[1, 3], Jennifer Maria Perez-Rivero[4], Maria del Pino Perez-Garcia[5] & Francisco Javier Martinez Martin[1, 3]
[1]University Hospital of Gran Canaria Dr. Negrín, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [2]Parc Taulí University Hospital, Endocrinology & Nutrition, Sabadell, Spain; [3]Clinica San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [4]Centro Salud Escaleritas, Family & Community Medicine, Las Palmas de Gran

Canaria, Spain; [5]Centro de Salud El Calero, Family & Community Medicine, El Calero, Spain

Introduction and Objectives
The tolerability of extended-release metformin (XRM) is clearly superior to that of conventional metformin, with the potential to improve patient compliance, effectiveness and outcomes. Since 2005 the NICE guidelines for type 2 diabetes mellitus (T2DM) recommend its use in patients with metformin-caused gastrointestinal disturbances. XRM is recently available in Spain as a fixed combination with sitagliptin, but not in monotherapy. We assessed the efficacy and tolerability of XRM/sitagliptin in patients with T2DM previously labeled as metformin-intolerant and treated with a DPP4 inhibitor (DPP4i), and additionally analyzed the data for quality of life before and after the switch.
Patients and Methods
Consecutive patients with T2DM, HbA1c $>7\%$ and GFR (CKD-EPI) >45 ml/min/1.73m^2 labelled as metformin-intolerant due to gastrointestinal symptoms, and treated with a DPP4i were switched to the 50 mg sitagliptin plus 1000 mg XRM combination, taking 1 pill daily in the first month and afterwards 2 pills if the tolerance was good. Tolerance data were obtained by questionnaire in the follow-up visit. Quality of life was assessed by the well-validated questionnaire EuroQol-5D-3L on health-related quality of life, before the onset of treatment and again after 3-4 months on treatment. The questionnaire consists of 5 triple-answer questions (on mobility, personal care, daily activities, pain or discomfort, and anxiety or depression), and a visual analogue scale (VAS) or "thermometer" for health. All Included patients granted informed consent.
Results
69 of a total 72 patients completed the EuroQol-5D-3L before and after the switch from DPP4i to XRM/sitagliptin. The questionnaire was never administered to the patients by their prescribing physicians. The Quality of life score increased from 0.759 ± 0.121 to 0.866 ± 0.130; this change was driven mainly by the pain/discomfort score. The VAS score increased from 68.3 ± 13.8 to 82.5 ± 15.5 (both $P<0.01$). The reductions in fasting plasma glucose were 36 mg/dl with 1 pill of XRM/sitagliptin (1000/50 mg), and 44 mg/dl with 2 pills, and the reductions in HbA1c were 0.6% with 1 pill and 0.9% with 2 pills (all $P<0.01$). 51 patients (74%) tolerated 2 pills, 8 (12%) tolerated 1 tablet and 10 (14%) did not tolerate any.
Conclusions
A large majority of the patients with T2DM labelled as metformin-intolerant and treated with an DPP4i tolerated the XRM/sitagliptin combination, and their glycemic control was significantly improved The switch from DPP4i to the XRM/sitagliptn combination was associated with increased quality of life, particularly in relationship with decreased pain and discomfort.

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EP1324

Endocrine osteoporosis: report of a series of cases

Essafi Mohammed Amine[1], Aynaou Hayat[1] & Salhi Houda[2]
[1]Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition. Hassan II University Hospital Center, Fez, Morocco; [2]Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition. Hassan II University Hospital Center, Morocco

Background and aims
Endocrine osteoporosis should be uncommon in contemporary times due to improved early diagnosis of endocrinopathies. Our objective is to analyze the osteodensitometric profiles of patients under endocrinopathy care.
Methods
A cross-sectional study of patients followed for endocrinopathies at the Endocrinology Department of the Hassan II University Hospital of Fez, spanning from the beginning of January 2016 to January 2022. Exclusion criteria encompassed patients receiving treatment for inflammatory rheumatism and those under care for systemic diseases. Analysis was conducted using SPSS26 software.
Results
A total of 83 patients diagnosed with endocrinopathy underwent Bone Mineral Density (BMD) assessment. The average age was 35.77 years, and a majority were female (73.49%). Primary and secondary amenorrhea were the predominant reasons for consultation, accounting for 37.35% of cases. 15.66% of the cases exhibited normal osteodensitometry, while 84.34% displayed abnormal Bone Mineral Density (BMD), with 34.94% diagnosed with osteoporosis and 49.40% with osteopenia. The identification of BMD issues, primarily osteoporosis and osteopenia, occurred in 87.14% of cases subsequent to the detection of the endocrinopathy. Hypogonadism prevailed among endocrinopathies, accounting for 71.08% of cases. Hyperparathyroidism constituted 19.28%, endogenous hypercorticism at 6.02%, and acromegaly at 3.62%. Osteoporosis was more commonly observed in the spine, occurring in 26.3% of cases with an average T-score of -2.88 ± 0.85. In the femur, osteopenia was present in 25.6%, while osteoporosis was noted in 8.64%, with a mean T-score of -1.46 ± 1.02. All patients underwent treatment for the underlying cause of their endocrinopathy along with adopting hygienic-dietary measures. Anti-osteoporotic treatment, primarily bisphosphonates, was prescribed in 34.94%. Regarding the follow-up, only 34.94% managed to undergo a follow-up Bone Mineral Density (BMD) assessment, and in every instance, there was an enhancement observed in T-scores.
Conclusions
This study underscores the notable occurrence of osteoporosis and osteopenia among patients undergoing treatment for endocrine disorders. Consequently, it emphasizes the necessity to systematically assess bone health in any endocrinopathy that may lead to rheumatological complications. Additionally, it highlights the importance of a thorough etiological investigation, aiming to identify an underlying endocrine pathology before the onset of osteoporosis or osteopenia.

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EP1325

Special case: giant invasive macroprolactinoma complicated by cerebrospinal fluid rhinorrhea and meningoencephalitis

Gema Martinez Tames[1], Sana Abid[2], Hanene Sayadi[2], Farah Ayechi[2], Raoua Naouar[2], Ghassen Belkahla[3], Atef Ben Nsir[3], Bilel Ben Amor[2], Ekram Hajji[2], Ines Bayar[2], Héla Marmouch[2], Inès Khochteli[2], Mahdi Darmoul[3] & Gema Martinez Tames[1]
[1]Hospital Valle del Nalon, Servicio de Endocrinología y Nutrición, Spain; [2]Fattouma Bourguiba Hospital, endocrinology and internal medicine department, monastir; [3]Fattouma Bourguiba Hospital, Neurosurgery department, monastir

Introduction
Prolactinomas are the most commun secreting adenomas of the pituitary gland. They are classified according to their sizes into microprolactinomas (<10mm long axis) and macroprolactinoma ($>=10$mm long axis). According to studies its prevalence is approximately 3.5-5 for 100000 inhabitants. The diagnosis is made by the blood prolactin assay as well as the pituitary magnetic resonance imaging (MRI) which is the radiological reference exam to evaluate the dimensions of the adenoma. The severity of these tumors mainly depends on their size.
Methods
we conducted a monocenter cross-sectional analytical study including 40 patients with confirmed prolactinoma followed in the Endocrinology Diabetology and neurosurgery departments of the Fattouma Bourguiba Hospital of Monastir during the period from January 2000 to march 2022.
Results
A 30-years-old patient with no medical history was reffered to our department for exploration of a pituitary macroadenoma. The circumstances of discovery were the onset of headaches with progressive decrease of visual acuity and bilateral amputation of the visual field for which he consulted an ophtalmologist. A brain CT revealed a sellar and parasellar tumor with hormonal assessment of hyperprolactinemia at 258ng/ml. The diagnosis of macroprolactinoma was made on the basis of hyperprolactinemia confirmed twice (258 and 296 ng/ml) and the presence on pituitary MRI of a macroadenoma measuring 25*26*40mm with extrasellar extension. The patient was treated with cabergoline withe a dose up to 2 mg/week. The evolution was marked bay the regression of the tumor size on the MRI in a year but we noticed the appearance of a cerebrospinal rhinorrhea complicated by pneumococcal meningoencephalitis for which he recieved an appropriate antibiotic therapy with a good clinical and biological progress. The pituitary scan showed the presence of a sphenoidal gap with lysis of sellar turcica. After that, the patient underwent transphenoidal surgery with biopsy of the adenomatous tissue and multilayer repair of the breach. The post operative evolution was simple with rhinorrhea drying up. The pathological and immunohistochimical study showed a lactotroph pituitary adenoma. The further evolution was marked by improvment of headaches and visual disturbances with a partial tumor response and biological remission under cabergoline 1 mg/week.
Conclusion
Prolonged and regular multidisciplinary collaboration seems to be essential for optimizing the management of these patients with endocrine, ophtalmological, neurosurgical, and radiological evaluation at initial diagnosis and throughout follow-up.

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EP1326

Pasireotide induced diabetic ketoacidosis in a patient with secondary diabetes with acromegaly

Nishchil Patel[1,2] & Daniel Flanagan[1]
[1]University Hospital Plymouth NHS Trust, Endocrinology and Diabetes, Plymouth, United Kingdom; [2]University Hospital Plymouth, Endocrinology and Diabetes, Plymouth, United Kingdom

Background
We report this interesting case of worsening diabetes and diabetes ketoacidosis in a young male with acromegaly who was commenced on Pasireotide treatment.
Case Report
This 30 years gentleman was diagnosed with Acromegaly in April 2015. He underwent trans- sphenoidal surgery in January 2016 with significant residual tumour post-surgery. His IGF1 remained elevated and was unresponsive to Lanreotide. He was commenced on adjuvant therapy with Pasireotide, in early 2017 under the Novartis clinical trial. He was also found to have partial hypopituitarism, and required hydrocortisone and testosterone replacement. He was found to have elevated HbA1c- 55 mmol/mol in April 2016. He was initiated on Metformin and Sitagliptin treatment along with lifestyle and dietary advice. Two months after commencement of Pasereotide, he was admitted with an episode of severe diabetic ketoacidosis (DKA) with no other obvious precipitant. His HbA1c at the time was 75 mmol/mol. Basal bolus regime of insulin was commenced along with Metformin. His HbA1c improved over time with insulin treatment and regular diabetes team input.
Conclusion
Pasereotide is a novel multi-receptor-targeted somatostatin receptor ligand used in therapy for acromegaly. It has been associated with hyperglycemia and DKA in patient with Acromegaly and Cushing's disease. The hyperglycemia is attributed to reduced insulin secretion and incretin response. This case highlights the need for closer monitoring of HbA1c and glycaemic control in patients with acromegaly and diabetes, and more so for those on Pasireotide therapy.

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EP1327

Early gestational diabetes vs late gestational diabetes: are there any differences?

Leire Garaizabal Azkue[1], Ihintza Larrañaga Unanue[1], María Magdalena Arteaga Ossa[2], Ainhoa Etxaniz Cerezo[1], Celia Bravo Ansorena[1] & Maite Unamuno Lecuona[2]
[1]Mendaroko ospitalea, Mendaro, Spain; [2]Hospital Alto Deba - Osakidetza, Arrasate, Spain

Whether frequency of complications during pregnancy increases when gestational diabetes (GD) is diagnosed early (<24 weeks) compared to late (>24 w) is not fully define. Observational studies suggest fasting glucose values (>92 mg/dl) during the first trimester are associated with adverse perinatal outcomes.
Objectives
describe the characteristics of pregnant women with GD, the frequency of complications during pregnancy and delivery and assess the differences between early and late diagnosis of GD.
Material and methods
Retrospective study of 70 women with GD diagnosed between 2022 and 2023 in two second level hospitals. We described demographic, anthropometric and clinical data, and compared obstetric-perinatal outcomes according to whether GD was early or late.
Results
Of all women, 64.3% were non-European (North Africa 28.6%, South America 22.9% and Pakistan 10%), mean age of 34 ± 5.74 years. 42.9% had early GD. The reasons for 1st trimester screening were BMI, previous GD and age (42.8%, 31.42% and 28.6%, respectively). The mean BMI of the early GD group was 31.91 kg/m^2 vs 28.64 kg/m^2 in the late group ($P=0.003$) and 1st trimester fasting glucose and O'Sullivan score were higher in the early group (98.93 mg/dl vs 89.88 mg/dl ($P=$NS) and 197 mg/dl vs 171 mg/dl $P<0.001$). Insulin was required in 47.1% of the sample, the majority in the early group (18/30 vs 15/40 ($P=$NS)). Only 5/18 were insulinised in the 1st trimester, 15 in the 2nd and 13 in the 3rd trimester. There were differences in the need for insulin according to origin: 60% of non-European vs 24% of Europeans ($P=0.004$). Regarding delivery, 8 patients had a preterm birth: 15% on the late group vs 6.6% on the early group ($P=$NS). Of all new-borns, 9 had neonatal hypoglycaemia, without differences between clusters. Hypoglycaemia was not related to prematurity, macrosomia or small for gestational age (SGA). 37% had complications during pregnancy ($P=$NS), being pre-eclampsia/HT the most frequent (12.9%). Large for gestational age (LGA) new-borns were higher in the early GD group (26.6% vs 17.5%, $P=$NS).
Conclusions
- In our setting, early diagnosed GD does not increase the frequency of obstetric complications, although there is a higher rate of LGA new-borns. It would be necessary to assess differences according to the degree of GD control.
- Basal glycaemia in first trimester was higher in the early GD cluster. It is necessary to evaluate it as a risk factor for the development of GD.

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EP1328

Latvian health professionals' knowledge of diabetes mellitus and safe driving: a survey

Katrīna Elīna Bērziņa[1] & Ingvars Rasa[2]
[1]Rīga Stradiņs University, Faculty of Medicine, Rīga, Latvia; [2]Riga East Clinical University Hospital, Outpatient, Rīga, Latvia

Background
Hypoglycemia refers to blood glucose levels dropping below 4.0 mmol/l, which can cause dizziness and confusion in those with diabetes. In severe cases, patients may experience seizures, vision problems, and cognitive impairment. It is unsafe to drive while in this state of mind. Health professionals (HP) must possess the necessary expertise to educate patients on this matter and ensure their safety.
Aims
The current study aimed to investigate HP's endocrinologists, internists, and family physicians' understanding of diabetes mellitus (DM) and safe driving practices.
Methods
The survey was conducted from 2022 to January 2024, with a total of 140 respondents. HP in Latvia received a 17-question original, anonymous questionnaire. IBM SPSS 29.0 was used to analyze the results.
Results
HP's mean age was 48.1 ± 15.4 years. 86.4% ($n=121$) of the respondents were females. Of the respondents, 9.3% ($n=13$) were endocrinologists, and 90.7% ($n=127$) were internists or general practitioners. HP work experience ranged from 1 to 55 years. 15% ($n=21$) did not believe that DM is a risk factor for car accidents. Of those 85% ($n=119$) who believed that DM is a risk factor, 66.4% ($n=79$) educated their DM patient about safe driving. 97% ($n=136$) consider frequent and severe episodes of hypoglycaemias to be a contraindication for driving, but only 39% ($n=53$) of them had advised their DM patients not to drive. 88.6% ($n=124$) believed that not recognizing hypoglycaemia is a contra-indication for driving, but only 38.7% ($n=48$) recommended that DM patients measure their blood glucose levels before driving. Information materials on hypoglycaemia and safe driving were not available at the workplace of 80% ($n=112$) of respondents, but 62.5% ($n=70$) of them discussed the topic of diabetes and safe driving. Of the 20% ($n=28$) who had informational materials in the workplace, 82.1% ($n=23$) discussed the topic of diabetes and safe driving. Only 33.6% ($n=38$) of respondents knew that blood glucose levels below 4.0 mmol/l are unsafe for driving.
Conclusions
Less than half of health professionals educate DM patients about safe driving despite their knowledge of the increased risks associated with diabetes mellitus. Healthcare providers must receive education about DM and safe driving to inform their patients better.

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EP1329

A case of HARS2-related perrault's syndrome

Amina Al-Qaysi, Yuyu Kyaw & Janan AlAjaimi
Buckinghamshire Healthcare NHS Trust, United Kingdom

Introduction
Amenorrhea is a frequent cause of Endocrinology clinic attendances. While causes like menopause, thyroid disorders and hyperprolactinemia are common, less common aetiologies need to be considered, especially the inherited ones that could affect a patient's family. Identifying rare conditions requires constant vigilance, as well as clinical experience and the knowledge of the diagnostic criteria.
Case report
We report the case of a 39-year-old female that attended our Endocrinology clinic for secondary amenorrhea since the age of 29 years and hypergonadotropic

hypogonadism due to premature ovarian failure. Her parents are first cousins, she has also married her first cousin whose parents are distant cousins. She was diagnosed with bilateral sensorineural hearing loss at the age of five years requiring cochlear implant, and her son suffered from autistic spectrum disorder and bilateral sensorineural hearing loss at a young age as well. Perrault's Syndrome was highly suspected, and genetic testing revealed two alterations in the HARS2 gene which is linked to Perrault's syndrome. She was found to have small ovaries on ultrasound and bone densitometry revealed normal bone density. The Clinical Genetics team is arranging genetic counselling and testing for her family.
Conclusion
Perrault's syndrome is a rare condition that is inherited in an autosomal recessive pattern, resulting in ovarian dysgenesis and bilateral sensorineural hearing loss. The spectrum of this condition also includes cerebellar ataxia, motor-sensory peripheral neuropathy, and learning difficulties. The management of these cases includes the management of its manifestations, with no available treatments or gene therapy yet. Identifying carriers of autosomal recessive disorders within families is crucial for understanding the likelihood of passing on the condition to future generations.

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EP1330

Primary hyperparathyroidism related to mediastinal ectopic parathyroid adenoma: about 2 cases

Lamiae Zarraa[1], Siham Rouf[1,2] & Hanane Latrech[1,2]
[1]Endocrinology-Diabetology and Nutrition Department Chu Mohamed VI, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy Mohammed Premier University Oujda, Morocco, Oujda; [2]Morocco, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy Mohammed Premier University Oujda, Morocco, Oujda

Introduction
Primary hyperparathyroidism is a frequent endocrinopathy characterized by a disorder of phosphocalcic metabolism related to an inappropriate secretion of parathyroid hormone (PTH). Parathyroid adenoma can be located ectopically and represents a particular diagnostic and therapeutic challenge. We report 2 clinical cases of ectopic parathyroid adenoma in mediastinal location.
Observations
Case 1: A 47-year-old patient without any pathological history consulted for paresthesias associated with diffuse joint pain predominantly in the shoulders. The biological assessment revealed hypercalcemia at 146 mg/l, and hypophosphatemia with hypercalciuria at 323 mg/24h. The diagnosis of primary hyperparathyroidism was confirmed by a biointact PTH 1-84 assay at 925 pg/ml on an ectopic parathyroid adenoma located in the upper mediastinum which became intensely and heterogeneously enlarged after injection of PDC measuring 44*20 mm. This nodule insinuated itself into the later-aortic-cava. The management was first medical obtaining normocalcemia followed by surgical treatment with a low cervical approach, the postoperative course was simple and the anatomopathological study was in favor of a benign parathyroid adenoma without signs of malignancy.
Cas 2: This is a 59-year-old patient with recurrent renal lithiasis, the etiological finding revealed hypercalcemia at 120 mg/l on a primary hyperparathyroidism with a bio-intact PTH level at 414 pg/ml, and the cervical ultrasound localized a left posteroinferior parathyroid adenoma, the patient was operated and the anatomopathological study concluded to a parathyroid adenoma. Postoperatively, hyperparathormonemia with hypercalcemia was noted, hence the indication of parathyroid scintigraphy which revealed the presence of a mediastinal parathyroid adenoma, the patient refused the surgical treatment and she was put under medical treatment by calcimimetic (Mimpara) with a favorable clinical and biological evolution, especially of the calcemia.
Discussion-Conclusion
Primal hyperparathyroidism is a frequent pathology that requires a topographic diagnosis to rectify surgery when indicated. Ectopic parathyroid adenoma is a rare entity and the advent of new radiological techniques including parathyroid scintigraphy has allowed the topographic diagnosis of this entity.

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EP1331

Diabetes and depression -a cyrculus vitiosus: case report

Snjezana Popovic Pejicic[1,2], Nina Pejicic[1,2], Valentina Soldat Stankovic[1,2], Gabrijela Malesevic[1,2] & Anja Jankovic Pejicic[3]
[1]University of Banja Luka, Faculty of Medicine, Banja Luka, Bosnia and Herzegovina, Banja Luka; [2]University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina, Banja Luka, Bosnia and Herzegovina; [3]Medical University of Vienna, Wien, Austria

Introduction and aim
Depression has a strong impact on psychosocial as well as medical outcomes in patients with diabetes. Consequently, depression treatment in diabetes is also aimed at improvement of glycemic control and reduction of diabetes complications and mortality risk.. Up to now, no single treatment that consistently leads to better medical outcomes in patients with both depression and diabetes has been clearly identified.
Matherial and methods
Patient was a 61 year old male worker, married. He has low educational and socioeconomic status and has been treated for type 2 diabetes with oral antidiabetics for 10 years. The predictors of depression were longer duration of diabetes, low social support and unemployment. Due to high glycemic values in daily profile and HbA1c 9.8% for the past 3 months, intensified insulin therapy was started, but was not regularly monitored. Fifteen days before he was admitted to the Clinic for Psychiatry, University Clinical Center of the Republic of Srpska, he became irritable, overwhelming, troubled by small things, complained of malaise, loss of energy and strength. On admission the following symptoms are present psychiatric interview was done; psychological, somatic and neurological status;routine laboratory tests with the daily glycemic profile and HbA1c; EEG; psychological testing; Beck's Depression Assessment Scale showed score of 57.
Results
Because of high glycaemic levels endocrinologist was adjusted insulin and antihypertensive therapy. Psychiatric condition stabilized on applied treatment and improvement of glycoregulation. The score on Beck's scale was reduced to 12, and he was discharged with recommendations for follow ups with endocrinologists and psychiatrists. Selective serotonin reuptake inhibitors, antipsychotics in low doses, anxiolytic and psychotherapy was used. Treatment according to endocrinologist's suggestion Structured education program "Düsseldorf model" After structured education HbA1c levels decreased by 1.8% after 6 months (9, 8 to 8, 0%) and by 1.2% after 12 months, compared to initial levels (9, 8 to 8, 6%) The score on Beck's scale was reduced from 57 to 12, and patient was discharged with recommendations for follow ups with endocrinologists and psychiatrists.
Conclusion
It could be concluded that presence of depression is likely predictor of poor metabolic control of diabetes. Structured education program is efficient in improving glycaemic control in patients with type 2 diabetes. It motivates patients in achieving better glycaemia control. There is a decline in motivation after 12 months resulting in glycoregulation impairment and need for re-education at least once a year.

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EP1332

A case of combined PTH-dependent and PTH-independent hypercalcemia

Larisa Danilova, Galina Korolenko, Irina Bourko, Maxim Lushchyk & Alexei Ramanouski
Institute for Advanced Training and Retraining of Healthcare Personnel, Belarusian State Medical University, Endocrinology, Minsk, Belarus

Patient D., 74 years old, suffering from type 2 diabetes mellitus, was urgently taken to hospital No. 10 in Minsk with complaints of weakness, nausea and dry mouth. On admission glycemia was 26 mmol/l. Laboratory examinations revealed elevated levels of urea - 34.5 mmol/l, creatinine - 238.2 μmol/l, calcium - 3.12 mmol/l, extremely low levels of vitamin D - 4.8 ng/ml, high levels of parathyroid hormone - 101.3 pg/ml. The laboratory ratio of calcium and parathyroid hormone was assessed as parathyroid hormone-dependent hypercalcemia. An ultrasound examination of the thyroid and parathyroid glands did not reveal any pathological formations. No focus of high uptake of the Te99m MIBI around the parathyroid gland was also identified. Clinical diagnosis: primary hyperparathyroidism in the absence of visualization of the source of parathyroid hormone production. Severe vitamin D deficiency. Type 2 diabetes. Arterial hypertension grade 2. Nephropathy of combined origin. CKD C4 (eGFR 29.4 ml/min/1.73 m^2). She was discharged for outpatient treatment after calcium values normalized. After 3 weeks, the patient was again admitted with complaints of severe general weakness, thirst, frequent urination, nausea, vomiting and dizziness. Extremely high values of total calcium were noted – 4.26 mmol/l. The condition was regarded as the onset of a hypercalcemic crisis. Conservative therapy did not lead to normalization of serum calcium. New ultrasound examination of right parathyroid gland revealed a hypoechoic formation 21.5*7.8*11.3 mm similar to

a parathyroid adenoma, in the thickness of the left lobe - an isoechoic node measuring 12.2*14.0*18.6 mm and altered lymph nodes in the supraclavicular areas. A trephine biopsy of the cervical lymph node was performed, and sarcoid-type granulomas were identified. During surgery, the altered lower parathyroid gland on the right and the left lobe of the thyroid gland were removed. By the evening after surgery the level of calcium in serum decreased to 2.32 mmol/l; after 10 days, the level of calcium was above 3 mmol/l with a steady increase to 3.96 mmol/l, while the level of parathyroid hormone decreased. A diagnosis of sarcoidosis was made. The patient received methylprednisolone at a dose of 32 mg daily. A day after starting methylprednisolone, calcium levels gradually began to decrease. In the presented clinical case, a thorough analysis of clinical, laboratory and instrumental data revealed a rare combination of parathyroid hormone-dependent and parathyroid hormone-independent hypercalcemia. The patient was diagnosed with primary hyperparathyroidism and sarcoidosis with involvement of the mediastinal and cervical lymph nodes.

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EP1333

A case report of a patient with severe postoperative hypoparathyroidism

Marina Milotić, Daniela Fabris Vitković, Mariza Babarović-Jurišić, Aleksandra Blagonić, Manuela Ferjančić & Marina Milotic
General Hospital Pula, Endocrinology and Diabetology, Pula, Croatia

Beckgrounds and aims
The most common cause of hypoparathyroidism is postoperative, i.e., after thyroid, parathyroid, or radical neck surgery due to neoplasms, and is most often transient, whether continuous or even intermittent. The incidence of permanent hypoparathyroidism ranges from 0.8 to 3.0% in patients after total thyroidectomy. In this case report, we will present a patient with a severe form of postoperative hypoparathyroidism refractory to standard treatment regimens.
Methods
A 49-year-old patient underwent total thyroidectomy due to recurrent hyperthyroidism and diffuse goiter. Postoperatively, she received levothyroxine, cholecalciferol, and calcium carbonate. Two months after the procedure, the patient complained of tingling in her hands, feet, and face and spasms of the esophagus. Since then, lower values have been constantly observed in the findings of total and ionized Ca with immeasurably low PTH. The dose of drugs was gradually increased (cholecalciferol: 25 000 IU once a week; calcitriol: up to 4.5 mg; calcium carbonate: up to 6 g; magnesium citrate: 300–400 mg per day) with frequent applications of calcium gluconate infusion, without improvement. Since rhPTH (l-84) is not available in our country, we started with subcutaneous administration of teriparatide with a gradual increase in the dose up to 3x20 mg per day, but without improvement. After reviewing the literature, we decided to use teriparatide via an insulin pump.
Results
After the introduction of the catheter-less pump, the serum Ca values quickly normalized, and during the following 3 months, they were maintained at reference values with a stable dose of teriparatide (24 mg/24 h). On January 5 2023, the patient switched to a catheter pump, and since then, large oscillations of serum Ca have been monitored again with symptoms of hypocalcemia and the need for constant correction of the teriparatide dose. On April 28 2023, she switches again to a catheter-less pump with stabilization of the general condition and the dose of teriparatide (18 mg/24 h).
Conclusions
Although chronic postoperative hypoparathyroidism rarely occurs, in most cases it is easily resolved with the use of vitamin D and calcium supplements. In a small number of patients, it is necessary to apply replacement therapy with a parathormone analogue. In our case, the patient stabilized only after continuous use of teriparatide via an insulin pump.

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EP1334

Severe hypomagnesemia: outpatient management in endocrinology and nutrition unit

Ana María Moyano-Sánchez[1], Ángel Rebollo-Román[1], Mª Carmen Serrano Laguna[1], Alfonso Jesús Calañas Continente[1], Maria José Molina[1] & Maria Angeles Galvez Moreno[1]
[1]Hospital Universitario Reina Sofia, Endocrinology And Nutrition Unit, Córdoba, Spain

Magnesium disorders are common in clinical practice. Hypomagnesemia is seen in inherited disorders, with excessive gastrointestinal or renal losses and due to medications. Replacement of magnesium can be challenging, with oral replacement strategies being generally more effective at slowly replacing body storages and intravenous (iv) replacement being more effective at treating life-threatening and severe cases of hypomagnesemia.
Objective, material and methods
To analyze clinical history and evolution of a group of patients with severe hypomagnesemia who received treatment with iv magnesium in the Endocrinology and Nutrition day hospital center of a tertiary hospital during 2023.
Results
7 patients. 5 men. Mean age: 62.6 years. Follow-up 40.9 months. Hypomagnesemia causes: - Short intestine syndrome (5), etiology: Crohn disease (3), surgery complications (1) and radical enteritis (1). - Chronic diarrhea syndrome with Gitelman syndrome (1). - Malabsortion syndrome post bariatric surgery (1). No diagnosis of severe hypomagnesemia due to pharmacology causes. 3/7 with ileostomy. Two patients received additional treatment with iv suerotherapy weekly. One received domiciliary daily suerotherapy through PICC. 3/7 with chronic renal disease. 4/7 chronic consumers of PPIs at start of follow-up. 3/7 maintained it at the end of follow-up as part of high debit ileostomy treatment. 2/7 went to the emergency department during follow-up for neurological complications in the form of vegetative symptoms followed by distal paresthesias and dizziness. The most frequent frequency of infusion was once a week, except for one patient who received iv magnesium infusion every 4 days. As for the amount of magnesium administered, the mean was 585 mg iv per week, with a maximum of 900 mg iv per week and a minimum of 300 mg iv every 15 days. All patients received oral supplementation with magnesium, on average 745 mg/day. 5/7 received oral calcium supplementation, mean 960 mg/day. 3/7 were receiving oral potassium supplementation, mean 2400 mg/day. Magnesium levels improving during the follow-up (initial compared to last visit) [0.91 vs 1, 44 mg/dl (t -3.17 p.019)]. 3/7 treated with oral nutritional supplements because of malnutrition (GLIM criteria). No significant changes in weight and BMI during follow-up.
Conclusions
In our series, the pathology that led to treatment with iv magnesium and high-dose oral supplementation was mainly due to digestive and malabsorption causes. Close monitoring, as well as joint treatment with iv magnesium and high-dose oral supplementation, achieved significant improvements in magnesium blood levels in our sample.

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EP1335

Adipsic central diabetes insipidus as a result of neurosarcoidosis

Radmila Milosheska[1], Ivana Mickovski[1,2] & Daniela Buklioska Ilievska[2,3]
[1]General City Hospital "8th September", Endocrinology, diabetes and metabolic disease, Skopje, Macedonia; [2]Faculty of Medical Sciences, Goce Delcev University Stip, Stip, Macedonia; [3]General City Hospital "8th September", Pulmonology and Allergology, Skopje, Macedonia

Background
Sarcoidosis is a multisystemic disease, the cause of which has not yet been determined. It's characterized by the appearance of granulomas, which typically target the lungs, the lymphatic system and in rare cases, around 5-15%, changes in the nervous system are observed. Neurosarcoidosis leads to hypothalamus-pituitary axis dysfunction and the most common clinical manifestation is the onset of central diabetes insipidus.
Case report
We present the case of a 46-year-old female patient with neurosarcoidosis and changes in the hypothalamus-pituitary axis and clinical manifestation of hypopituitarism, along with a non-typical presentation of central diabetes insipidus. The diagnosis of neurosarcoidosis has not been confirmed with a biopsy due to its high risk and difficulty to access. However, according to the CT and MRI results and the clinical presentation, an intensive hormone replacement therapy was administered to reduce the clinical symptoms. What is notable about this case is the diagnosis for central diabetes insipidus, which could not be confirmed based on the clinical characteristics because of the absence of polydipsia and polyuria, as well as with the classic water deprivation test because of persistent hypernatremia, which was confirmed by excluding other potential causes of hypernatremia.
Conclusion
Neurosarcoidosis has a rich clinical presentation and is a challenge when it comes to diagnosis and treatment, particularly with patients with disorders in the hypothalamus-pituitary axis and non-typical adipsic central diabetes insipidus.
Keywords: neurosarcoidosis, central diabetes insipidus, hypernatremia

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EP1336

An uncommon cause of high gonadotropins and testosterone in a 53-year-old male

Maria Mathiopoulou, Maria Iris Romay, Anna Mavromanoli, Martin Bucher & Roger Schneiter
University Hospital of Zürich, Zürich, Switzerland

A 53-year-old male was referred to the endocrinology outpatient clinic due to elevated levels of gonadotropins and testosterone (LH 11.7 IU/l, reference range 1.7-8.6 IU/l; FSH 17.7 IU/l, reference range 1.5-12.4 IU/l; testosterone 40.9 nmol/l, reference range 6.68-25.70 nmol/l; free testosterone 712.7 pmol/l, reference range 163-473 pmol/l) noted during an annual urologic check-up. No spermiogram was performed, and testicular ultrasound showed no abnormalities. The patient reported no physical complaints other than chronic fatigue and reduced energy since experiencing an occupational burnout 2 years ago. He was not on any medications but regularly consumed Withania somnifera (Ashwagandha) and Tinospora cordifolia. These herbs are commonly used in alternative medicine to alleviate anxiety, stress, and fatigue. MRI imaging showed no signs of pituitary lesions. Despite discontinuation of the herbal remedies, gonadotropin and testosterone levels remained elevated even after 3 months. Withania somnifera contains substances such as steroid lactones, phytosterols, and alkaloids. Phytosterols, resembling cholesterol, can serve as precursors to steroid hormone synthesis. According to the Memorial Sloan Kettering Cancer Center database, Withania somnifera may increase testosterone levels for this reason, as demonstrated in a randomized, double-blind, placebo-controlled study. The cause of elevated gonadotropins remained unclear and requires further investigation. Tinospora cordifolia also contains phytosterols, but data on its effect on steroid hormone synthesis is limited to animal models. Although no definitive effect on steroid hormone synthesis has been proven, it cannot be excluded. Determining a causal relationship between drug use and observed adverse drug reactions involves intrinsic evidence (temporal relationship with drug exposure, dechallenge and rechallenge if applicable, exclusion of other causes, pathophysiological plausibility) and extrinsic evidence (well-documented comparable cases in drug information, pharmacovigilance databases, systematic clinical or epidemiological studies, and possibly case reports). In this case, a clear temporal relationship was observed between the intake of herbal remedies and elevated testosterone levels. Other likely causes were ruled out, and the pathophysiology involving phytosterols as steroid hormone precursors is plausible. The absence of intrinsic evidence is due to the lack of a positive dechallenge, as gonadotropin and testosterone levels remained high after discontinuation. However, extrinsic evidence from a randomized, double-blind, placebo-controlled study, although rare for alternative remedies, supports the conclusion that hypergonadotropic hypergonadism may be caused by Withania somnifera.

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EP1337

Sarcoidosis and hypothalamohypophyseal insufficiency: a case report

Hajar Azagouagh, Talbi Dounia, Karimi Meryem, Sebbar Ghizlane, Rifai Kaoutar, Iraqi Hind & Mohamed Elhassan Gharbi
Chu Ibn Sina, Endocrinology, Rabat

Introduction
Sarcoidosis is a multisystem inflammatory disease. Hypothalamic-pituitary involvement in sarcoidosis is rare and poorly described. We report here a case of pituitary insufficiency during sarcoidosis disease.
Observation
Patient aged 49 years, followed for systemic sarcoidosis with cutaneous, pulmonary and ocular tropism for 7 years, admitted for exploration of a severe polyuro-polydipsic syndrome with four nocturnal awakenings, questioning revealed secondary amenorrhea for 2 years, and physical examination found signs of intra- and extra-cellular dehydration. After eliminating the obvious causes of polyuro-polydypsic syndrome, namely diabetes mellitus and hypercalcemia, the diagnosis of diabetes insipidus was made in view of a low urinary osmolarity of 122 mosmol/l and a plasma osmolarity of 289 mosmol/l. A hormonal workup showed corticotropic, thyrotropic and gonadotropic insufficiency, and a hypothalamic-pituitary MRI revealed a hypothalamic sarcoid granuloma. We put the patient on a vasopressin test, and retained the diagnosis of central diabetes insipidus in view of the improvement in the polyuro-polydipsic syndrome and the increase in urinary osmolarity to 580 mosmol/24h. Therapeutically, our patient was put on hormone replacement therapy and vasopressin spray with a good clinical and biological evolution.
Discussion and conclusion
Neurosarcoidosis affects 5-26% of sarcoidosis patients. Hypothalamohypophyseal involvement is exceptional. It accounts for 0.5% of sarcoidosis cases, MRI provides diagnostic support in cases of clinical suspicion. The most common endocrine disorders are diabetes insipidus and hyperprolactinemia, thyrotropic insufficiency and, to a lesser degree, hypogonadism, hence the need to screen for hypothalamic-pituitary involvement in the presence of systemic sarcoidosis.

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EP1338

Rethinking how we classify pituitary tumours: insights from a serious case of prolactinoma

Waiel Bashari[1,2] & Azmi Mohammed[2]
[1]Addenbrooke's Hospital, Endocrinology, Cambridge, United Kingdom; [2]Sudan Pituitary Foundation, Endocrinology, Khartoum, Sudan

Prolactinomas are a common type of pituitary tumours, making up about 40% of these tumours in total, with an estimated occurrence of 40-50 people per 100, 000. They are more common in women, especially during their reproductive years, but they can affect anyone at any age. Although most prolactinomas are small and respond well to treatment, around 2-10% are aggressive, growing into nearby areas like the cavernous sinus or sphenoid bone. The World Health Organisation's 2017 guidelines classify pituitary tumours based on various factors, aiming to improve diagnosis, treatment, and research. However, these guidelines might not always capture the severity of certain tumours, as seen in our case of an aggressive prolactinoma that led to a patient's death.
Case presentation
We present a 22-year-old male who was admitted with visual bilateral field loss and was found to have a large pituitary lesion with a serum prolactin that is 65000 my/l. A working diagnosis of macroprlactinoma was made and he was treated with an escalated dose of cabergoline, with concomitant replacement of partial anterior pituitary hormone deficiency. After a few months of treatment his tumour had reduced and the vision improved, however, a phase of tumour re-growth took place with complete resistance to dopamine agonist therapy. The tumour invaded the skull base and grew outside his mouth in as short a period as 3 months. Despite efforts for maximum DA dose escalation (reaching 1-2 mg/day) and debulking surgery followed by radiotherapy, his health had deteriorated rapidly and he developed tumour infection and became unfit for chemotherapy options (e.g., temozolamide). He unfortunately succumbed to a cranial infection shortly after that. Although his tumour had not metastasised, it was treatment resistant and locally aggressive, which then led to his death. This case illustrates the need for a more nuanced approach to classifying prolactinomas, especially aggressive ones in young males. It suggests that factors like local tumour invasion should be given more standing in the classification, similar to how other cancers are evaluated (e.g., TNM classification). This could help in better understanding and treating these aggressive tumours.

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EP1339

Pediatric pituitary microadenomas: a spectrum of clinical presentations and therapeutic responses"

Noor Hamed, Nada Alaaraj, Shayma Mohamed, Fawzia Alyafei & Ashraf Soliman
Hamad General Hospital, Doha, Qatar

Pituitary microadenomas in children and adolescents are relatively rare, accounting for a small percentage of pediatric endocrine disorders. These benign tumors often present a diagnostic challenge due to their subtle and variable clinical manifestations at this young age. We present clinical and lab data of 5 children with pituitary microadenoma. Case 1: A 12-year-old female with a history of short stature and slow growth velocity was diagnosed with a small pituitary microadenoma. Despite the presence of this lesion, her growth hormone stimulation test was suboptimal, and MRI imaging showed a slightly smaller pituitary gland. Treatment with somatropin led to a significant improvement in height. Case 2: This case involves a 12-year-old female with recurrent headaches, vomiting, dizziness, blurring of vision, early menarche, and recent amenorrhea. MRI confirmed a pituitary microadenoma. She exhibited signs of hormonal imbalances, including elevated ACTH, cortisol, and prolactin levels, suggesting a complex endocrine interaction. Case 3: A 12.4-year-old girl with a history of headaches and fatigue, and a family history of hypothyroidism, was found to have central hypothyroidism and a pituitary microadenoma. Despite levothyroxine treatment, her growth velocity remained low, and her final height was significantly below the mid-parental height. Case 4: This 7-year 10-month-old girl presented with premature thelarche and pubarche. An MRI revealed a

Case	Age	Sex	Clinical Manifestations	Lab Data	MRI Data	Treatment
1	12 years	Female	Short stature, slow growth velocity	WtSDS: -2.22, HtSDS: -2.6, GV: 4 cm/year, IGF1 SDS: -1.81, GHST peak: 5.2 mcg/L	Slightly smaller pituitary gland, microadenoma (2.2 x 2 mm)	Somatropin 0.035 mg/kg/day
2	12 years	Female	Recurrent headaches, vomiting, dizziness, blurring of vision, early menarche, recent amenorrhea	BMISDS: 2.5, Advanced bone age, High HOMA IR, ACTH: 69.5pg/ml, Cortisol: 492nmol/l, Prolactin: 477mIU/L, IGF1SDS: 1.8	Normal height pituitary gland, microadenoma (4.7 x 4.9 x 5.3 mm)	Planned for GH suppression test, pelvic US, salivary cortisol
3	12.4 years	Female	Headaches, fatigability, central hypothyroidism	Low FT4: 11.7pmol/l, TSH: 2.8pmol/l, Negative thyroid autoantibodies, IGF1 SDS: -1.28, GHST peak: 6.7 mcg/L	Globular pituitary gland, microadenoma (2 x 9 x 5 mm)	Levothyroxine 50 mcg daily
4	7 years 10 months	Female	Premature thelarche, pubarche, accelerated growth	Advanced bone age, LH: 8.7 IU/L, FSH: 6.5 IU/L, Estradiol: 130 pmol/L, IGF1: 531.0 ug/L	Microadenoma (3.3 mm diameter)	GnRH analogue monthly injections
5	2.8 years	Female	Premature thelarche, accelerated growth	LH: 0.8 basal, 9 peak, FSH: 2.8 basal, 57 peak, Estradiol: 202, IGF1SDS: +3.1, Bone age: 3.5 years	Microadenoma (3.4 x 2 mm)	Triptorelin

microadenoma in the anterior lobe of the pituitary. Her case was complicated by advanced bone age and elevated hormone levels, indicating early pubertal development. She was treated with GnRH analogue injections. Case 5: A 2.8-year-old girl presented with premature thelarche and accelerated growth. Her hormonal profile and advanced bone age suggested early pubertal changes, and MRI confirmed a pituitary microadenoma. She started on triptorelin for management. Clinical and Lab data of the five cases of pituitary microadenoma

Conclusion

These cases collectively demonstrate the diverse presentations of pituitary microadenomas in pediatrics, ranging from growth disturbances to early pubertal changes. The importance of a comprehensive endocrine evaluation and individualized treatment approach in managing these patients is emphasized. The outcomes varied, reflecting the complexity of pituitary disorders in pediatric populations.

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EP1340

Features of diagnosis and treatment of fulminant hypercortisolism due to ACTH-producing pheochromocytoma: a clinical case

Laura Ebanoidze, Ekaterina Pigarova, Dmitry Beltsevich, Anastasia Sheve, Larisa Dzeranova, Ivan Sitkin, Natalya Tarbaeva, Angelina Khairieva, Michail Degtyarev & Ekaterina Bondarenko
Endocrinology Research centre, Neuroendocrinology, Moscow

Introduction

Statistical data show that in the etiological structure of ACTH-ectopic syndrome pheochromocytoma occupies one of the last places in terms of frequency of occurrence (from 2.8 to 5.6%) Its manifestations such as adrenal mass with ACTH-dependent hypercortisolism lead to significant difficulties in establishing the correct diagnosis.

Clinical Case

A patient with clinical manifestations of hypercortisolism underwent laboratory testing in October 2022: evening saliva cortisol - 220.6 nmol/l (0.5-9.65), evening serum cortisol -1548 nmol/l (64-327), 24-hour urine cortisol -12332.25 nmol/day (100-379); ACTH evening -204.1 pg/ml (2-25.5), morning -313.4 pg/ml (7.2-63.3). Brain MRI with contrast enhancement revealed a microadenoma (3×3.5 mm) in the posterior part of the adenohypophysis. A concomitant search for the source of ACTH ectopia was carried out. According to the abdomen CT: a lesion of the left adrenal gland measuring 37×30×46 mm, a malignant phenotype with a density of 42/49/69/60 HU (active/arterial/venous/delayed phases). Thebilateral selective sampling from the lower petrosal sinuses revealed the absence of thegradient of ACTH secretion (maximum on the right - 1.15; on the left - 1.10). SPECT-CT of the abdominal cavity in the left adrenal gland revealed a formation of soft tissue density measuring 39×30×49 mm, accumulating 99Tc-tectrotide, which confirmed moderately increased expression of somatostatin receptors. Thus, the data obtained supported the extrapituitary genesis of ACTH-dependent hypercortisolism due to pheochromocytoma which was confirmed by 24h-urine analysis - metanephrine - 1122.9 mg/day (25-312), normetanephrine - 1039.11 mg/day (35-445). Taking into account the rate of disease progression, a somatostatin analog (lanreotide autogel 120 mg s.c.) was administered once - without a significant decrease in ACTH secretion (from 313 pg/ml to 243 pg/ml). Ketoconazole 600 mg/day was also prescribed - no effect on 24-hour urine cortisol levels (>35.000 nmol/day). Treatment for complications of hypercortisolism was also initiated. Due to profound hypokalemia (up to 1.9 mmol/l), spironolactone 300 mg/day + kalium chloride 1200 mg were added to therapy. In view of newly diagnosed diabetes due to hypercortisolism, insulin therapy was initiated according. In November 2022 left-side adrenalectomy was performed with preliminary preparation of the α-adrenergic blocker doxazosin with dose escalation to 4 mg/day. Morphological examination revealed pheochromocytoma; immunohistochemistry verified intense expression of chromogranin A and ACTH by pheochromocytoma cells.

Conclusion

Considering the rarity of the described pathology, correct diagnostic tactics make it possible to reliably establish a diagnosis and provide timely medical care before the development of life-threatening cortisol- and adrenaline-mediated complications.

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EP1341

Autoimmune polyendocrinopathy type 2 associated with celiac disease: a case report

Hajar Azagouagh[1], Karimi Meryem[1], Talbi Dounia[1], Sebbar Ghizlane[1], Rifai Kaoutar[2], Iraqi Hind[1] & Mohamed Elhassan Gharbi[1]
[1]Chu Ibn Sina, Endocrinology, Rabat; [2]Chu Ibn Sina, Endocrinology, Rabat

Introduction

Autoimmune polyendocrinopathies (AEP) are rare diseases defined by the presence of at least two endocrine deficiencies linked to an autoimmune mechanism, sometimes with an associated non-endocrine autoimmune disease. Autoimmune polyendocrinopathy type 2 is a more common syndrome, appearing mainly in adults.

Observation

We report the case of a 27-year-old patient, admitted for management of acute inaugural adrenal decompensation, with a history of celiac disease since childhood on a gluten-free diet. Clinically, the patient presented with vomiting and abdominal pain, evolving in a context of altered general condition and melanoderma with slate patches on the inner sides of the cheeks. A blood ionogram showed hyperkalemia at 6.4 mmol/l with hyponatremia at 111mmol/l. We started the patient on hydrocortisone hemisuccinate with intravenous rehydration. Biological investigations revealed low 8-hour plasma cortisol with high ACTH, high anti-21 hydroxylase antibodies, high anti-TPO antibodies with normal TSH, and glycated hemoglobin at 6.3% with positive anti-GAD antibodies. The diagnosis of type 2 AEP was accepted. Treatment consisted of hormone replacement for adrenal insufficiency, with strict monitoring of blood glucose levels and patient education.

Discussion and conclusion

AEP-II combines several autoimmune pathologies, including Addison's disease and autoimmune thyroid disease (Schmidt's syndrome) and/or type 1 diabetes (Carpenter's syndrome). Adrenal insufficiency is the initial manifestation in 50% of AEP-II cases, appearing at the same time as diabetes or thyroid damage in 20% of cases, and occurring after the other manifestations in 30% of cases. Other endocrine components of the syndrome may include primary ovarian failure, rarely testicular failure, and autoimmune hypophysitis. Non-endocrine autoimmune manifestations are polymorphous, dominated by Biermer's disease, vitiligo, celiac disease, rheumatoid arthritis and inflammatory bowel disease. The age of onset of AEP-II varies widely, from childhood to late adulthood, usually between 20 and 40. Celiac disease has become one of the most common diseases in the world. It may be part of a multiple autoimmune disorder. This makes it necessary to screen celiac patients for other autoimmune diseases, in particular Addison's disease.

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EP1342

Mayer-rokitansky-kuster-hauser syndrome: a cause of primary amenorrhea not to be ignored !

Talbi Dounia, Qasdi Ikrame & Guerboub Ahmed Anas
Mohammed V Military Hospital, endocrinology, Morocco

Introduction
Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a rare congenital cause of primary amenorrhea, characterized by aplasia of the vagina with or without concurrent uterine and/or cervical aplasia. MRKH syndrome has a heavy psychological impact, and requires multidisciplinary management.
Case Report
A 17-year-old female patient presented for exploration of a primary amenorrhea. Her medical history was significant for recurrent urinary tract infections. Her physical exam was notable for Tanner stage IV pubic hair and Tanner stage V breast development, normal external female genitalia. The hormonal profile was normal with estradiol at 137 pg/ml and the karyotype was 46, XX. A pelvic magnetic resonance imaging revealed an aplastic, blind-ending vaginal canal without an identifiable cervix or uterus. Bilateral ovaries were visualized with normal morphology. The rectum, urinary bladder, kidneys were normal in appearance.
Discussion and Conclusion
Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is characterized by a physiological development of the secondary sexual characters and by a normal female karyotype 46 XX, but with a congenital aplasia of the uterus and of two/third superior parts of upper vagina. MRKH syndrome is divided into two subtypes: type I and the less-frequent type II (MURCS). 2D/3D ultrasound (US) remains the first-line examination for diagnosing this syndrome, but MRI is more sesitive and specific, and remains the gold standard for accurate diagnosis, with a view to optimal management. The etiology of MRKH, unfortunately, remains unclear. The majority of cases appear to be sporadic; however, rising accounts of familial cases with an autosomal dominant mode of inheritance complicated by an incomplete penetrance and variable expressivity are noted in the literature. In cases involving type II MURCS, disturbances during gastrulation can affect the migration and differentiation of the mesoderm, leading to defects involving the paraxial mesoderm (cervical vertebrae), intermediate mesoderm (urogenital structures), and lateral plate mesoderm (limb defects). Treatment for MRKH depends on your goals and symptoms. There are surgical and nonsurgical treatment options, including vaginoplasty, vaginal dilation and a uterine transplant requiring multidisciplinary management.

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EP1343

Ovarian steroid cell tumor: a case report

Mohamed Elmoctar, Mariem Cheikh, Cheibete Zakaria, Rifai Kaoutar, Hinde Iraqi & Mohamedlhassan Gharbi
Ibn Sina Hôpital, Endocrinology, Rabat, Morocco

Introduction
Ovarian steroid cell tumors are very rare, and are endowed with steroid-secreting capacity. Most often, they are virilizing. Ovarian steroid cell tumours NOS, even if are rare, should be considered in any case of hyperandrogenism and excluded if elevated androgens levels are present. Our case illustrates this exceptional entity.
Case report
A 47-year-old female presented with virilism associated with severe hirsutism, frontotemporal baldness and muscular and clitoral hypertrophy. Biological work-up revealed an increase in androgens (total testosteronemia 12.75 ng/ml), with no associated hypercorticism. Pelvic MRI showed a suspicious left ovarian mass classified as ORADS5 The patient underwent left adnexectomy. Anatomopathological examination concluded that the ovarian stroma was a steroid cell tumour. Post-operative management was straightforward and the patient was placed under observation.
Discussion and conclusion
Steroid cell tumors are defined as ovarian neoplasms composed of cells secreting steroid hormones and represent less than 0.1% of ovarian tumors.... They generally occur in adults, with an average age at diagnosis of 47. In 50% of cases, they are virilizing tumors. They may be non-secreting, causing hyperestrogenism or, more rarely, Cushing's syndrome. They are generally benign, but the potential for malignancy is not negligible, given well-defined histological criteria. Good ovarian imaging is essential in the assessment of hyperandrogenism without associated adrenal abnormalities. Treatment is usually surgical. Complementary therapies are required once malignancy has been confirmed.

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EP1344

Causal relationship between rheumatoid arthritis and hypothyroid state in young females in iodine deficiency area

Diyora Kurambaeva[1], Zulaykho Shamansurova[1,2] & Maftunakhon Burkhanova[3]
[1]Central Asian University Medical School, Endocrinology, Tashkent, Uzbekistan; [2]Institute of Biophysics and Biochemistry at the NUUz, Metabolomics, Tashkent, Uzbekistan; [3]Queen's University, Department of Health Sciences, Kingston, Canada

Introduction
In hypothyroidism bone turnover and osteoclastic resorption will be reduced which also aggravates Rheumatoid arthritis (RA) symptoms. In the literature shown data about relationship between RA and thyroid dysfunction. We aimed to discuss some possible causes and triggers that interplay in both conditions based on data from the literature.
Material and methods
Data analysis was done using the systematic search performed in PubMed, MEDLINE, Scopus, Web of Science database of the articles published during the past 5 years related to RA and thyroid disorders. Main factors to consider were age, gender, cortisol, TSH, T4, T3, anti-TPO.
Results
Combined data from 250 patients with RA were checked for thyroid dysfunction and anti-TPO positivity. Thyroid dysfunction were found in 84 (33.9%), in which 60 (24.2%) cases have prior history of thyroid diseases. Anti-TPO was positive in 77 (32.0%) cases. The frequency of AITD was 52 (21.5%) in cases. The autoimmune Hashimoto's thyroiditis was 2.77 times more common in RA patients than in those without RA. It was reported that occurrence of thyroid pathology in Rheumatoid Arthritis patients is 34%, while specifically the range of Hashimoto's Thyroiditis is 13, 5%. 75% of RA patients were women from 20-39 years and the incidence of hypothyroidism in this group were 3.6 times greater than men had. Tumor necrosis factor-α and interleukin-6, that involved in inflammatory process in RA can exacerbate the dyslipidemia in hypothyroidism. Inflammation leads to deteriorated lipid profiles and low HDL levels. Interestingly, antithyroglobulin antibodies were found in synovial fluid of 34 from 54 patients with Rheumatoid Arthritis. Steroid therapy can lead to hypothyroid state, increasing TSH and inhibiting T4 to T3 conversion. Endocrine changes in young women (puberty, pregnancy, childbirth, and abortion) considered as a risk factors.
Conclusion
Understanding the link between RA and thyroid dysfunction will be helpful in primary prevention, early detection, management, and diminishing further complications of these interconnected diseases in patients at risk. RA patients should be screened for thyroid diseases. Patients with thyroid diseases with increasing of thyroid autoantibody level, in particular Hashimoto's thyroiditis should be screened for other autoimmune conditions, such as RA.

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EP1345

Third nerve palsy spontaneously resolved in diabetic patient

Imen Zone[1], Aida Jallouli[1], Mona Rekik[1], Meriem Sahli[1], Faten Haj Kacem Akid[2], Nabila Mejdoub[3] & Trigui Amira[1]
[1]Habib Bourguiba Hospital., Department of Ophtalmology, Tunisia; [2]Hedi Chaker Hospital, Department of Endocrinology, Tunisia; [3]Hedi Chaker Hospital, Department of Ophtalmology, Tunisia

Introduction
We report a case of pupil sparing third nerve palsy caused by diabetes.
Case Presentation
A 68-year-old woman consulted for acute left upper lid ptosis appeared since 2 days ago. The patient complained of blurred vision and periorbital pain. No history of head trauma or infection was reported. The patient has been diagnosed with type II diabetes mellitus and arterial hypertension since 15 years. Ophthalmological examination revealed complete left ptosis, reactive pupillary reflex with deficient elevation, and adduction. The best-corrected visual acuity was 4/10 in both eyes. Anterior segment examination revealed bilateral cataract. Fundus examination didn't show any signs of diabetic retinopathy. Neurological examination was normal. Brain magnetic imaging was unremarkable without intracranial mass lesions and acute infarction. Blood analyses showed hyperglycemia (320 mg/dl) and elevated glycated hemoglobin (11.7%) without other anomalies. A complete recovery of ptosis was achieved after 3 weeks of blood sugar control with control of other cardiovascular risk factors The diagnosis of diabetic third nerve palsy was made.
Discussion
Diabetic third nerve palsy is the most frequent complication of nerve palsy in diabetic patients. The incidence of nerve palsy increases with the duration of the disease, uncontrolled glucose levels and age of the patient. The main etiology is microvascular cranial nerve palsy with high vascular risk factors such as smoking, hypertension, hypercholesterolemia. Third nerve palsy is frequently incomplete with ptosis, divergence of the affected eye, and paralysis eye movements such as adduction, elevation, and lowering without pupil involvement. Full recovery generally takes place at 6 months of follow up. Recurrences of third nerve palsy or other ocular motor nerve is possible.

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EP1346

An uncommon manifestation of a common problem

Muhammad Shoaib Zaidi[1,2]
[1]King Saud University Medical City, Internal medicine, Riyadh, Saudi Arabia; [2]King Saud University Medical City, Internal Medicine, Riyadh, Saudi Arabia

Background
The commonest etiology for the chronic kidney disease and end-stage renal disease, universally, is diabetes. Although, the histology of the kidney is the gold standard for diagnosing diabetic kidney disease, but in common practice it's usually diagnosed clinically and through laboratory testing.
Clinical Case
43 yrs old Saudi house-wife was admitted on the 7th of February, 2024 with 5 months history of progressive pitting pedal edema, facial puffiness, followed by dyspnea (NYHA-III), orthopnea, paroxysmal nocturnal dyspnea and frothy urine for 1 month, prior to the admission. She had a past medical history of long-term Type 2 diabetes and Chronic liver disease (HBV+). Systemic review-weight gain and anorexia. Family history unremarkable. No allergies or addictions. She also developed acute diarrhea during the admission. On evaluation, the patient was found to have the following issues: 1-Diabetic kidney disease (anasarca with moderate ascites+, hypoalbuminemia [S.albumin 26 (39.7-49.4 g/l)], S. Creatinine 140(45-84umol/l), Albuminuria (Albumin/Creatinine-2541(0-30 mg/g), CBC (Hb% 95(12-16 g/l, MCV 86.6fl, TLC and PLTs normal), HbA1c 8.7%, US abdomen (normal liver, spleen, portal vein & kidneys, moderate ascites and right pleural effusion), ascitic tap (serum-ascitic albumin gradient 0.8 g/l) and renal biopsy showed Class III DM nephropathy (classification 2010), with secondary focal segmental glomerulosclerosis 2- Right renal vein thrombosis with poor right renal perfusion (US proven) 3- Clostridium-difficile colitis (toxin+on stool testing. Other important investigations- Hepatitis B core and e Abs +, HBV PCR 159 IU/ml, Auto-immune workup negative. Serum immune electrophoresis-polyclonal gammopathy, Transthoracic Echo-mild concentric left ventricular hypertrophy with normal LV systolic function, moderate pericardial and left pleural effusions, US pelvis-anterior sub-serosal fibroid (2.7 × 2.9 cms)
Results
The patient was managed with moderate protein intake, diuretics, oxygen, fluid restriction, therapeutic abdominal paracentesis, apixaban,, angiotensin receptor and calcium channel blockers, atorvastatin, dapagliflozin, linagliptin and basal-bolus insulin. Her condition got stabilized and was advised follow-ups in the nephrology, hepatology and gynecology clinics.
Conclusions
Our case taught us that one should never assume the heavy proteinuria in diabetes to be related to diabetic nephropathy, until the secondary causes have been excluded. The value of the tissue biopsy in arriving at the precise diagnosis, cannot be overemphasized.

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EP1347

Frequency of major clinical syndromes in patients with drug-induced liver injury

Oksana Prokopchuk[1,2], Svitlana Danchak[1,2], Ihor Hospodarskyy[1,2], Olha Kozak[1,2] & Nadiia Gavryliuk[1,2]
[1]Ukraine, Ternopil, Ternopil; [2]I. Horbachevsky Ternopil National Medical University

Drug-induced liver injury (DILI) today is a global problem in modern gastroenterology and is increasingly common worldwide, demanding focused attention and in-depth study, particularly in terms of recognizing the major clinical syndromes. These often complicate the course of DILI and as a result, its correction.
Objective
To investigate the frequency of major clinical syndromes in patients with DILI during chemotherapy with normal and excess body weight.
Materials and methods.
A total of 123 patients with DILI without signs of cirrhosis and concomitant liver and biliary tract pathology, aged 35 to 79 years, were examined. The control group consisted of 20 practically healthy individuals.
Results
Evaluating subjective manifestations, it was noted that the asthenovegetative syndrome was present in 45.2% ($n=56$) of patients who complained of general weakness and rapid fatigue, significantly affecting work capacity. Patients complained of a bitter taste in the oral cavity, changes in dietary behavior in response to changes in appetite, periodic nausea, and a feeling of bloating in the abdomen, which manifested as dyspeptic syndrome in 25.8% ($n=32$), the latter had a reliable connection with the asthenovegetative syndrome ($r=0.65$, $P<0.05$). During the objective examination, an increase in liver size was detected in 51.2% ($n=63$) of patients, while the feeling of heaviness in the right hypochondrium was felt by 28.5% ($n=35$) of patients ($r=0.62$; $P<0.05$). An increase in blood pressure was diagnosed in 25.2% ($n=31$) of patients, and arterial hypertension had a reliable dependence on the asthenovegetative syndrome ($r=0.64$; $P<0.05$), hepatomegaly ($r=0.57$; $P<0.05$), and the feeling of heaviness in the right hypochondrium ($r=0.92$; $P<0.05$). Additionally, high normal blood pressure was found in 16.35% ($n=20$) of patients, and in turn, indicators corresponding to the criteria for stage I hypertension were found in 8.94% ($n=11$) of those examined.
Conclusions
In patients with DILI during chemotherapy with normal and excess body weight, the presence of asthenovegetative and dyspeptic syndromes, a feeling of heaviness in the right hypochondrium, hepatomegaly, and increased blood pressure were detected, which should be taken into account when choosing treatment tactics.

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EP1348

Mild hypercalcemia and osteoporosis in a patient with breast cancer: case report

Magdalena Matejkova Behanova[1], Petr Libansky[2], Kateřina Personová[3], Josef Vcelak[4], Kristyna Procykova[4] & Petr Vlcek[5]
[1]Motol University Hospital Prague, Department of Nuclear Medicine and Endocrinology, Prague, Czech Republic; [2]Motol University Hospital, 3rd Department of Surgery, Prague, Czech Republic; [3]Motol University Hospital, Department of Nuclear Medicine and Endocrinology,, Prague, Czech Republic; [4]Institute of Endocrinology, Czech Republic; [5]Fn Motol, Czech Republic

Introduction
The most common causes of hypercalcemia are primary hyperparathyroidism and malignancy. Malignancy-related hypercalcemia occurs in approximately

(Abstract EP1348)
Table 1.

	Sept2020	Jul2021	Jan2022	Aug2022	Feb2023	Aug2023	Feb2024
Ca	2.74	2.72	2.70	2.75	2.93	2.62	2.65
correctedCa	2.61	2.69	2.59	2.68	2.84	2.47	2.54
P	0.72	0.61	0.64	0.66	0.66	0.67	0.79
PTH	10.21	7.23	8.56	8.56	6.45		7.36
Vitamin D	52.2	69.7	57.6		62.7		67.9

20% - 30% of all cancer patients during their clinical course and mainly affects patients with solid tumors such as breast carcinoma.
Case Report
57 yrs old woman was referred for hypercalcemia and osteoporosis. Laboratory: calcium 2.8 mmol/l (normal range 2.15 - 2.55) calculated ionized calcium 1.41 mmol/l (normal 0.9 – 1.3), PTH 8.2 pmol/l (normal 1.3 - 7.6), normal renal function, no symptoms of hypercalcemia. Osteoporosis was diagnosed in routine screening by decreased density in lumbar spine (0, 700 g/cm^2, T score – 3.2), no compressive fractures. She was managed with ibandronate 150 mg monthly and we continued with differential diagnosis of hypercalcemia. We found hypercalciuria: urine calcium 16.7 mmol/24 hours, urine calcium/creatinine 1.4 (normal 0.25-0.55), CCCR (calcium creatinine clearance ratio) 0, 04. Vitamin D supplementation was added to ibandronate. The ongoing laboratory monitoring is in the table. During the follow-up the patients was diagnosed with breast cancer. PTH was only slightly elevated and malignancy could be a possible cause of hypercalcemia in this case. She underwent oncological treatment: surgery 11/2020, chemotherapy 1-5/2021, radiotherapy 5-7/2021 and anti-oestrogen therapy from 5/2021. The final diagnosis: 30 mm invasive (no special type) breast carcinoma with one micrometastasis in one sentinel lymph node, no distant metastasis. Remission of the breast cancer has been documented after the treatment. The hypercalcemia persisted until we noticed the normalization of calcium levels during the last two visits to our clinic.
Conclusion
This case represents mild hypercalcemia in patient with osteoporosis and breast cancer. The diagnosis of osteoporosis and hypercalcemia was prior of the cancer diagnosis. Hypercalcemia of malignancy should be considered in cases without known malignancy. The calcium level normalised during more than 2 years after completed oncological treatment and documented remission. Bisphoshonates were indicated for osteoporosis and also probably helped maintain calcium levels.
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EP1349

Abnormal thyroid function tests in a patient with history of breast cancer taking tamoxifen

Sama Gitti
Al-Kindy College of Medicine, University of Baghdad, Internal Medicine, Iraq

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EP1350

Association of parkinson's disease in a patient with graves' disease

Faizan Sandhu[1] & Muhammad Tahir Chohan[2]
[1]University Hospital of North Durham, General internal medicine, Durham, United Kingdom; [2]University Hospital of North Durham, Diabetes and Endocrinology, Durham, United Kingdom

Introduction
Parkinson's disease is considered as a second most common neurodegenerative disorder but rarely associated with the Graves' disease.
Case report
A 44-year-old female diagnosed as Graves' disease having classical features of hyperthyroidism i.e. tremors of hands, palpitations, weight loss despite of good appetite and biochemical evidence of thyroid function tests (TFTs) i.e. raised free T4, low TSH and positive antibodies. She was given carbimazole for twelve months and then stopped with a warning of disease relapse. She remained symptomatic and treatment free for about one and a half year, then reported back with similar presentation and investigations were in favour of hyperthyroidism. She was offered a radioactive iodine treatment but given a risk to her child, she opted for a medical treatment. After having carbimazole for the next two years, she had a radioactive iodine treatment which resulted in the hypothyroidism, therefore, started on levothyroxine. Her levothyroxine was titrated and despite of her tremors, the rest of her symptoms subsided. Hence, she was given a trial of propranolol. She presented back to the clinic with tiredness and tremors. The TFTs showed TSH 19.14, fT4 23.3 (slightly above then normal). It showed that either there is an issue with the intermittent compliance or it could be there is interference antibodies. It was decided to repeat her TFTs using different assay.
Management
There were no changes made with regards to her medications. In the meantime, she was referred to the movement disorder team and found to have tremors which, at that time, were more obvious in the left arm along with a degree of some stiffness and bradykinesia. Therefore, DaT scan, copper and autoimmune studies were arranged. The results of her DaT scan consistent with idiopathic Parkinson's disease. She was then reviewed by the Neurologist and started on anti-Parkinson's medications and she noticed a significant symptomatic improvement.
Conclusion/learning points
Parkinson's disease is a rare condition in young age group but, it should be considered in patients having non-resolving tremors, who had radioactive treatment for Graves' disease and biochemically hypothyroid.

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EP1351

Graves' orbitopathy: Ocular manifestations and management

Imen Zone[1], Aida Jallouli[2], Faten Haj Kacem Akid[3], Nabila Rekik[3] & Trigui Amira[2]
[1]Habib Bourguiba Hospital., Department of ophtalmology; [2]Habib Bourguiba Hospital., Department of Ophtalmology, Tunisia; [3]Hedi Chaker Hospital, Department of Endocrinology, Tunisia

Introduction
Graves' orbitopathy is an inflammatory autoimmune disorder. It is the most common extrathyroidal manifestation of Graves' disease and it is the leading cause of proptosis in adults. We report 3 cases of Graves' orbitopathy in order to detail ocular manifestations and protocol management in this disease.
Observation 1
A 63-year-old woman was referred for left conjunctival redness. The best-corrected visual acuity was 10/10 in the right eye and 6/10 in the left eye. Examination showed von Graves' sign, bilateral proptosis, and eyelid retraction. Slit lamp examination revealed left conjunctival hyperemia and superficial punctuate keratitis. Elevated levels of thyroid hormones and the presence of anti-TSH receptor antibodies confirm the diagnosis of moderate Graves' orbitopathy.
Observation 2
A 52-year-old woman presented with orbital pain with eye movement. Ophthalmological examination revealed bilateral proptosis mainly affecting the left eye, restriction of eye movements, left relative afferent pupillary defect and high left intra-ocular pressure. Brain MRI showed bilateral orbital involvement extraocular muscle enlargement and left optic nerve sheath infiltration. The diagnosis of severe Graves' orbitopathy with dysthroid optic neuropathy was established. The patient received 500 mg intravenous methylprednisolone /week for 6 weeks with a good response.
Observation 3
A 16-year-old woman with a history of Grave's disease since 2 months was referred for bilateral eyelid swelling. Ophthalmological examination revealed best-corrected visual acuity of 8/10, ophthalmoplegia, bilateral conjunctival hyperemia with swelling of caruncle. The patient was treated with corticosteroids 60 mg/day with complete restoration of the eye motility.
Discussion
The most common clinical signs of Graves' orbitopathy are proptosis, upper eyelid retraction, oculomotor disorders, and ocular inflammatory signs such as conjunctival hyperemia, and caruncle swelling. Optic neuropathy and corneal ulceration are the most vision-threatening complications. Clinical examination allows assessing the activity and severity of the disease on the basis of predefined scores. Computerized tomographic and magnetic resonance imaging are both useful in establishing the diagnosis and in evaluating the severity of orbital damage. The management of moderate and severe Graves'orbitopathy is based on local treatment and intravenous glucocorticosteroids. Immunosuppression therapy is administered in cases of resistance to corticosteroids.

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EP1352

Researching of the relationship between the numberof t regulatory cells and serum arachidonic acid level in autoimmune thyroiditis patients

Eylem Cagiltay[1], Cengiz Bukrek[2], Kırkık Duygu[3] & Fatih Hacımustafaoğlu[4]
[1]Memorial Hospital, Endocrinology and Metabolic Diseases, Istanbul, Turkey; [2]Sultan 2. Abdulhamid Han Training and Research Hospital, Endocrinology and Metabolic Diseases, Istanbul, Turkey; [3]Health Sciences University, Biology, Istanbul, Turkey; [4]Health Sciences University, Biochemistry Department, Istanbul, Turkey

Objective
Autoimmune Thyroid Disease (AITD) is a common disease, accounting for 1-4% of the overall episode. Regulatory T Cells are a substructure of CD4 + T cells that have received great attention for their role in maintaining tolerance by suppressing the growth response and preventing autoimmune diseases. Arachidonic Acid is found in cell membrane phospholipids and is the lipid mediator affected by the inactivation of bacteria. We aimed to determine the change in Regulatory T Cell and Arachidonic Acid levels in Autoimmune Thyroiditis patients compared to healthy controls.
Materials and Methods
The scope of the study was conducted at S.B.Ü. between 01.04.2023 and 01.04.2024. Patients and healthy volunteers who applied to the Internal Medicine and Endocrinology Polyclinics of Sultan Abdülhamid Han Training and Research Hospital were recruited. A total of 42 people, 12 men and 30 women, aged between 21 and 76, participated in the study. 13 of them are in the healthy control group, 14 in the Hashimoto Thyroiditis group and 15 in the Graves' Disease group. Peripheral blood samples were taken and Human Arachidonic Acid and Human T-Cell Immune Regulator 1 Elisa Kits were tested in these samples and measured at the level.
Results
There was no significant difference in serum Treg levels between Hashimoto's Thyroiditis, Graves' patients and the control group ($P=0.884$, $P=0.765$, $P=0.663$, respectively). Arachidonic Acid levels were found to be higher in Hashimoto Thyroiditis and Graves patients than in the control group, but were not found to be statistically significant ($P=0.081$, $P=0.369$, $P=0.844$, respectively). Anti-TPO, Anti-Thyroglobin and TRAB were examined separately in the Healthy, Hashimoto's Thyroiditis and Graves' Disease groups for comparison purposes between individuals with high and normal arachidonic acid levels, and no significant results were found.
Conclusion
In this study, in Autoimmune Thyroiditis Patients; It was observed that there was no statistically significant difference in the amount of T Regulatory Cells and Arachidonic Acid in serum. More studies are needed to clarify the contradictory results in the literature regarding the amount and function of Arachidonic Acid and Treg Cells, and to develop genetic data that predict AITD and diagnostic tests that can measure the functions of Treg Cells.

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