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Abstracts

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Mission statement: To advance the scientific basis of human pathology by the publication (encouragement and dissemination) of high quality research (including molecular and translational studies) and thereby contribute to patient care. Manuscripts of original studies reinforcing the evidence base of modern diagnostic pathology, using immunocytochemical, molecular and ultrastructural techniques, will be welcomed. In addition, papers on critical evaluation of diagnostic criteria but also broadsheets and guidelines with a solid evidence base will be considered. Consideration will also be given to reports of work in other fields relevant to the understanding of human pathology as well as manuscripts on the application of new methods and techniques in pathology. Submission of purely experimental articles is discouraged but manuscripts on experimental work applicable to diagnostic pathology are welcomed. Biomarker studies are welcomed but need to abide by strict rules (e.g. REMARK) of adequate sample size and relevant marker choice. Single marker studies on limited patient series without validated application will as a rule not be considered. Case reports will only be considered when they provide substantial new information with an impact on understanding disease or diagnostic practice.

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OFP-02	Oral Free Paper Session Digestive Diseases Pathology – Liver/Pancreas
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OFP-04	Oral Free Paper Session Digestive Diseases Pathology – GI
OFP-05	Oral Free Paper Session Joint Session: Pulmonary Pathology / Nephropathology
OFP-06	Oral Free Paper Session Joint Session: IT in Pathology / Other Topics (Pathology in Favour of Developing Countries / Cardiovascular Pathology / History of Pathology / Autopsy Pathology)
OFP-07	Oral Free Paper Session Joint Session: Soft Tissue and Bone Pathology / Infectious Diseases Pathology
OFP-08	Oral Free Paper Session Joint Session: Neuropathology / Ophthalmic Pathology
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Abstracts

30th European Congress of Pathology

Oral Free Paper Sessions

Sunday, 9 September 2018, 08:30 - 12:00, Room A2
OFP-01 | Joint Session: Molecular Pathology / Haematopathology

OFP-01-001
Microfluidic-based automated multiplex immunophenotyping and imaging
B. Pelz*, D. Migliozzi, G. Cappi, D. Dupouy, M. Gijs
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Background & Objective: The tumour microenvironment plays a vital role in cancer development. Multiplex immunostainings allow studying the interaction of different cell types in the tumour microenvironment using a single tissue slide. The objective is to develop a fully automated microscope integrated method for rapid 10-plex fluorescent immunostaining and imaging of tissue sections.
Method: FFPE tonsil sections underwent manual dewaxing and antigen retrieval step. All subsequent steps of staining, antibody elution and imaging were automated on the microscope integrated microfluidic device. A single tissue section was stained sequentially for CD3, CD4, CD8, CD20, CD56, CD68, FOXP3, PD-1, PD-L1 and CK with mouse or rabbit primary antibody and corresponding Alexa Fluor labelled secondary antibody. The section was imaged after each staining step and subsequently eluted before staining the next marker.
Results: Our microscope integrated microfluidic system allowed automated 10-plex staining with conventional primary and fluorescently labelled secondary antibodies in less than five hours, including image acquisition steps. Protocol optimization resulted in a high signal to background noise ratio for each marker, while fully eluting antibodies from the previous staining step.
Conclusion: With the microscope integrated microfluidic system, it is possible to perform fast multiplex stainings including image acquisition without removing the tissue slide. Moreover, due to the sequential nature of the system it would be easily possible to further increase the number of markers in the multiplex staining. We believe that this technique greatly facilitates the execution of high-plex stainings and thereby the discovery of novel tumour-microenvironment interactions.

OFP-01-002
The potential biomarker HR23b regulates sensitivity towards histone deacetylase inhibitors (HDACi) via the NGFR death receptor pathway
S. Wagener*, M. A. Ihle, C. Alidousty, C. Heydt, J. Fassunke, S. Merkelbach-Bruse, R. Büttner
*University Hospital Cologne, Institute of Pathology, Germany

Background & Objective: Deregulation of histone deacetylases (HDACs) plays an important role in tumourigenesis and progression. Restoring a regular acetylation profile by HDAC inhibitors (HDACi) is a promising therapeutic approach. Human Rad Homolog B (HR23b), has been identified as a predictive biomarker of HDACi sensitivity in haematological and hepatocellular tumours. We showed previously that HDACi also exhibit antiproliferative and pro-apoptotic effects in sarcomas in dependence of HR23b expression. We therefore aim to elucidate the regulatory relationship between HR23b expression and sensitivity towards HDACi.
Method: A stable knockout of HR23b was generated in a malignant peripheral nerve sheath tumour (MPNST) cell line (ST-8814) using CRISPR /Cas9-technology. An efficient knockout was verified both, on DNA- and expression level. Its influence on proliferation and apoptosis was measured with the ApoTox ™ Glo assay. HDACi vorinostat was adminstered at IC50 concentration to wildtype and HR23bKO cells. Afterwards expression analysis of important signaling pathways was performed with the nCounter PanCancer Pathways panel on a NanoString platform.
Results: qPCR and Western Blot analysis confirmed a stable knockout of HR23b in ST-8814 cells. HR23b dependent sensitivity towards HDACi is mediated by apoptosis induction via the NGFR death receptor pathway. In contrast, HR23b loss reduces apoptosis induction and shifts response to TLR2-regulated autophagy.
Conclusion: Understanding the key pathways by which HDAC inhibitors affect tumour growth plays a major role for future therapeutic approaches. In particular, the importance of HR23b as a predictive biomarker should help to select patients who may benefit from HDACi therapy.

OFP-01-003
Patient-derived colorectal cancer explants retain the histological and molecular key features of their primary counterparts
S. Mata*, S. Abreu, R. Fonseca, B. Filipe, S. Morgado, I. Francisco, M. Mesquita, T. Franchi Mendes, C. Albuquerque, P. Chaves, E. R. Boghaert, V. E. Santo, I. Rosa, C. Brito
*IPOLFG, Anatomia Patológica, Lisboa, Portugal

Background & Objective: Colorectal cancer (CRC) 5-year overall survival is 64.9%. Chemotherapy responses are limited. In order to improve clinical outcomes, reliable models predictive of drug response are needed. Patient derived explants (PDE) are ex-vivo cultures that can overcome representability limitations of other models.
Method: Our aim is to develop PDEs from CRC samples dissociated and placed in a dynamic system; evaluate their viability by metabolic and morphologic evaluations; characterize their phenotype (architecture, senescent phenotype, stroma cellularity, inflammatory cells); and assess PDE representation of the primary tumour (gland formation, p53 and mismatch repair proteins, microsatellite instability, KRAS exon2 and BRAFV600E mutations).
Results: Eleven adenocarcinomas were successfully cultured. All PDEs retained their originals' glandular architecture. There was viable tumour

for at least 28 days (~46(28-87 days)) and for most of the cases (N=7/11) viable stroma was evident as long as neoplastic cells were present. PDEs (N=10/11) lost architectural complexity and stroma cellularity at the first evaluation (days 7-11), but less significantly thereafter. Tumour cells progressively acquired a senescent phenotype. PDEs (N=10/11) replicate the tumours' immunohistochemical and genetic features. KRAS mutated clones seem to be positively selected in culture (N=3/5). For one PDE, KRAS status and p53 staining were consistently different from the primary counterpart since the starting point.
Conclusion: PDE is an efficient method to culture CRC. Overall the key pathological features of the primary tumours are retained over time, supporting their use in drug predictive assays. Divergent results may be due to intratumoural heterogeneity and optimization in tumour collection should improve PDE representation of the tumour.

OFP-01-004
A study of gene expression profiling in gastric adenocarcinoma: comparison between Epstein-Barr-Virus positive and microsatellite unstable tumours

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Background & Objective: Different molecular classifications have been proposed for gastric cancer (GC), trying to decipher its molecular heterogeneity. Epstein-Barr virus positive (EBV+) and microsatellite unstable (MSI-high) GCs are well-recognized molecular subgroups. The Singapore-Duke group classification is based on gene expression data and identified three GCs subtypes, with implications for response to therapy: mesenchymal, proliferative and metabolic [doi:10.1053/j.gastro.2013.05.010]. In this study we aimed at exploring and comparing RNA expression profiling of EBV+ and MSI-high GCs.
Method: Fifteen EBV+ and 27 MSI-high GCs were selected by RNA in situ hybridization for EBV and PCR/fragment analysis for MSI, respectively. RNA expression profiling was performed using the NanoString nCounter platform, analysing 474 genes, previously published [doi:10.1136/esmoopen-2015-000009] and additional 21 genes, associated with immune response. We searched for differentially expressed genes (FDR<0.05) between the EBV+ and MSI-high molecular groups (nSolver Analysis Software).
Results: EBV+ GCs showed up-regulation of genes related to immune response (T-cell activation, IFNγ/TNFα pathways, proinflammatory cytokines/chemokines) and degradation of extra-cellular matrix. Gene expression data of a subset of EBV+ GCs fitted into the mesenchymal subtype (30 out of 31 genes, 96.8%). In contrast, MSI-high GCs showed enrichment of genes related to cell division, cell cycle and mitotic activity and, accordingly, could be classified as GCs belonging to the proliferative subtype (27 out of 34 genes, 79.4%).
Conclusion: The search for EBV infection and MSI-high status might aid on the stratification of GC into molecular subtypes with clinical relevance. We demonstrated the differential transcriptional profile between EBV+ and MSI-high GCs, which have putative therapeutic implications.

OFP-01-005
Epigenetic changes in DAXX and/or ATRX negative pancreatic neuro-endocrine tumours

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Background & Objective: MEN1, DAXX and ATRX are the most commonly mutated genes in Pancreatic Neuroendocrine Tumours (PanNETs). Interestingly all these genes are involved in epigenetic regulation. DAXX and ATRX mutations correlate with loss of protein and predict for poor patient outcome. DAXX and ATRX participate in the chromatin structure organization as well as in regulating DNA methylation (DNAme) while MEN1 recruits MLL1 (mixed lineage complex) which plays a crucial role in chromatin remodelling. We hypothesized that MEN1 mutations and DAXX/ATRX loss induce epigenetic changes which mediate PanNET progression. We aim to describe epigenetic profiles of MEN1 mutated and DAXX/ATRX negative PanNETs and to identify specific epigenetically regulated pathways that contribute to tumour development.
Method: We analysed genome wide DNAme profiles (Illumina 450K) in 55 PanNETs. miRNA expression (800 miRNA) in a subset of 24 PanNETs and the expression of a panel of 398 potentially epigenetically regulated genes (Nanostring) on 48 matching primary tumours.
Results: We found that MEN1 mutated and DAXX/ATRX negative tumours showed a specific methylation profile for 3078 genomic regions, including 393 differentially methylated promoters. Thirtyone miRNAs were differentially expressed in DAXX/ATRX negative vs. DAXX/ATRX positive tumours. We integrated these data with publically available RNAseq data. Based on these analyses we identified 398 genes for which the expression was assessed and validated.
Conclusion: Our results strongly support the hypothesis that DAXX/ATRX loss and MEN1 mutation in PanNETs result in consistent dysregulation of DNAme, accompanied by expression changes in genes and miRNAs.

OFP-01-006
Can routine gene mutation profiles help favor a specific tumour origin?

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Background & Objective: Gene mutation profiles can be extracted from routinely used Next Generation Sequencing (NGS). However, can they be used as a complementary tool to favor a tumour origin over another?
Method: 503 quality-controlled cases were routinely sequenced on the Illumina Miseq, using the Truseq Amplicon Cancer Panel (48 genes), at the Jules Bordet Institute. For each case, we retrieved clinical data, pathology results, molecular quality control scores and detailed DNA variants. We then used a multinomial logistic regression test with a p-value threshold of 0.01 for more power.
Results: From a total of 72076 DNA variants, only 2548 (3.5%) were exonic quality-controlled modifying non-polymorphism variants, reported in COSMIC as pathogenic. That averaged 5 mutations per case. Cases were mainly colorectal cancers (40.0%), lung cancers (27.2%) and melanomas (10.5%). Genes favoring lung over colorectal cancer had low sensitivity (3.6-12.4%) and high specificity (97.0-99.0%): NPM1, EGFR, ABL1 and VHL. APC was the only high sensitivity/specificity gene (43.3%/89.1%) favoring colorectal over lung cancer, compared to PTEN (9.5%/90.5%) and PDGFRA (4.5%/95.6%). Analysis of melanoma and colorectal cancer yielded higher sensitivity (39.6-58.2%) and lower specificity (81.1-94.5%) genes: NRAS and BRAF favoring melanoma, and APC and TP53 favoring colorectal cancer.
Conclusion: Lung cancer and colorectal cancer were distinguished by few low sensitivity/high specificity mutated genes, with the exception of APC. Genes distinguishing between melanoma and colorectal cancer had higher sensitivity but slightly lower specificity (NRAS, BRAF, APC and TP53). Bearing in mind these limitations, NGS can be considered complementary to the gold standard microscopic examination for tumour origin identification.

OFP-01-007
STARTRK-2 basket trial for TRK, ROS1 and ALK fusions in cancer patients treated in a single institution

A. Tysarowski*, M. Wagrodzki, K. Seliga, A. Szumera-Cieckiewicz, J. H. Christiansen, S. J. Potts, M. Kotarska-Puerto, J. A. Siedlecki, M. Prochorec-Sobieszek
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Background & Objective: The STARTRK-2 (Studies of Tumour Alterations Responsive to Targeting Receptor Kinases) trial is a potentially registration-enabling Phase 2 global basket trial of the investigational tyrosine kinase inhibitor compound entrectinib in patients with solid tumours harboring TRK, ROS1, or ALK gene fusions. Phase 1 studies of entrectinib reported a 79% Overall Rate of Response across multiple histology types in patients with gene fusions who were naive to inhibitors of these targets, received an efficacious dose, and had extracranial disease. In general patients harboring these gene fusions account for <3% of cancer population; however, they have been seen in over 40 histologies, including gastrointestinal, lung, head & neck, and sarcoma. In this presentation, we report on the occurrence of TRK, ROS1, and ALK fusions in patients treated in Cancer Center Institute of Oncology.
Method: The occurrence of TRK, ROS1, and ALK gene fusions in solid tumours was studied in FFPE specimens from 645 patients. We used 2-step diagnostic test. At first, the IHC screening was performed using a pan-receptor tyrosine kinase cocktail of antibodies targeting those proteins, secondly an RNA-based anchored multiplex-PCR next generation sequencing (NGS) assay was performed in IHC positive specimens.
Results: The 221 out of 645 clinical specimens screened by IHC were positive and further analyzed by NGS. The presence of gene fusions was confirmed in 17 (2,6%) of them.
Conclusion: The two-step testing approach is an effective strategy to identify patient populations with low prevalence of molecular alterations and can be included into standard clinical practice.

OFP-01-008

Epitranscriptomics in testicular germ-cell tumours: the value of m6A and related proteins for tumour subtyping and prognostication

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Background & Objective: Epitranscriptomics is a growing new field in Science. RNA modifications, such as N-6-methyladenosine(m6A), play a role in various biological processes but their role in cancer remains largely unexplored. We aimed to assess the value of these epimarkers in a cohort of Testicular Germ Cell Tumours (TGCTs).
Method: In silico analysis (TCGA database) showed altered expression of the writer KIAA1429 and reader YTHDF3 in 51% and 48% of TGCTs, hence they were chosen for further validation. Formalin-fixed paraffin-embedded (FFPE) tissues from 122 TGCT patients (2005-2016) were included. RNA extraction, cDNA synthesis and real-time qPCR (Taqman assay) for KIAA1429 and YTHDF3 was performed. Immunohistochemistry for KIAA1429, YTHDF3 and m6A was performed and staining intensity assessed.
Results: There were significant differences in KIAA1429/YTHDF3 mRNA expression levels among tumour subtypes, with Seminomas (SEs) exhibiting higher levels than Non-Seminomatous tumours (NSTs) ($p<0.01$, $p<0.01$). KIAA1429 showed the best performance, discriminating SEvsNST with AUC=0.85(sensitivity 77.3%, specificity 81.1%, PPV 71.6%, NPV 85.3%, Accuracy 79.7%). Stage I patients had higher YTHDF3 expression($p=0.04$). A moderate correlation was found between expression levels of KIAA1429 and YTHDF3(correlation coefficient 0.44). Immunohistochemistry reproduced transcript findings, with patients showing strong KIAA1429 immunoexpression exhibiting higher mRNA expression levels($p<0.001$). KIAA1429 immunostaining also discriminated SEvsNST($p<0.01$). Patients with strong m6A immunoexpression showed significantly higher KIAA1429 mRNA expression levels and stronger KIAA1429 immunostaining ($p<0.001$, $p<0.01$), indicating an association between the writer and the established RNA modification (m6A). KIAA1429/YTHDF3 were differentially expressed among individual TGCT components, both at mRNA and immunohistochemistry levels.
Conclusion: We confirmed that m6A and related proteins are differentially expressed among TGCT subtypes and might serve as useful biomarkers for diagnosis and prognosis.

OFP-01-009

Monitoring leukemic mutations using ultrasensitive IBSAFE digital droplet analysis predicts relapse of acute myeloid leukemia

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Background & Objective: Optimal management of patients with acute myeloid leukemia (AML), a dismal disease with poor prognosis, depends on accurate monitoring of minimal residual disease (MRD), which predicts outcome and affect treatment decisions. Current MRD methods either suffers from limited sensitivity or can only be applied on leukemias carrying the targeted mutation. We developed an innovative digital droplet PCR technique, IBSAFE, that enables an improved limit of detection down to 0.001% mutant allele frequency (MAF). Given that even patients with negative multicolor flow cytometry (MFC)-MRD results (<0.1%) often have poor prognosis, we set out to analyze AML patients using IBSAFE to investigate if this method could predict the outcome.
Method: 10 relapsing and 4 non-relapsing AML patients were retrospectively tested for MRD with IBSAFE in bone marrow aspirates taken at several follow-up time points. First, the mutational profile was determined at diagnosis and relapse by next generation sequencing (NGS). Mutations for MRD monitoring were selected with priority towards mutations in recurrently mutated genes.
Results: For all relapsing patients, IBSAFE was able to track early recurrence of leukemic clones. At most follow-up time points, residual leukemia was apparent with IBSAFE, but absent with MFC-MRD. For the non-relapsing patients, some mutations were detected during follow-up, but the levels gradually declined in response to different therapeutic strategies.
Conclusion: We demonstrate that our IBSAFE method can track early recurrence of leukemic clones, with possible applications in clinical routine AML-MRD analyses. The advantage as compared to other MRD methods is the high sensitivity and applicability on virtually all AML patients.

OFP-01-010

Burkitt-like lymphoma with 11q aberration: clinico-pathological and genetic characterisation

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Background & Objective: Burkitt-like lymphoma with 11q aberration (BLL-11q) is a new provisional category in the 2016 WHO classification. Due to the few published cases it is still controversial if it should be upgraded to a definitive entity. Here we performed a complete study of BLL-11q aiming to improve its knowledge.
Method: A total of 60 cases diagnosed of BL or atypical BL in patients ≤40 years were included. Clinico-pathological and genetical data (immunohistochemical and FISH) were recorded. Copy number (CN) analysis and Target Next Generation Sequencing (NGS) mutational status (including ID3, CCND3, TCF3, MYC and ETS1 genes) were performed in the subset of BLL-11q cases identified.
Results: Ten cases lack MYC translocations and present 11q aberration by FISH. Seven were male and the mean age at diagnosis was 16 years (8-37). The presentation was nodal in 8 cases. All patients received chemotherapy and are alive without disease after 25 months of follow-up. Histologically, all of them mimicked BL but with greater cellular pleomorphism. One case was positive for BCL2 and 3/8 were negative for

LMO2. CN array confirmed the presence of alteration of the 11q arm with different patterns in all cases (Range 2-15, Mean alterations 6.85). Most recurrently mutated genes in the 9 cases analysed by target sequencing NGS analysis were MYC, BTG2 and ETS1. Any case harboured mutations in ID3, CCND3 or TCF3.
Conclusion: In our series nodal involvement is frequent in BLL-11q cases and the prognosis is good. 11q alteration pattern is wider than previously described and BL-related mutations are not present.

OFP-01-011
Three cases of Epstein-Barr virus-positive plasmacytoma in immunocompetent patients: a diagnostic dilemma
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Background & Objective: By literature review, plasmacytomas arising in immunocompetent patients are rarely associated with Epstein-Barr virus (EBV) infection. EBV-positive plasmacytoma may cause a diagnostic dilemma as it may morphologically and phenotypically overlap with a clinically aggressive plasmablastic lymphoma (PBL).
Method: Three cases of EBV-positive plasmacytoma in immunocompetent status were retrospectively reviewed in this study followed at the Affiliated Hospital of Nanjing University, Nanjing Drum Tower Hospital between January 2008 and March 2018 (two cases of extramedullary plasmacytomas, one case of solitary plasmacytoma of bone). We summarized the available ancillary studies including pre-existing H&E-stained tissue sections, immunohistochemistry, in situ hybridization, molecular analysis, radiological findings and laboratory results upon diagnosis.
Results: Microscopically, these tumours were characterized by proliferation of mature differentiated plasma cells in a diffuse and sheet pattern, which were diffusely positive for EBV encoded RNA (EBER) by in situ hybridization. The neoplastic plasma cells were positive for CD138 and CD38 while Ki67 proliferation index ranges from 2%-20%. The plasma cells were clonal and exhibit light chain restriction on immunohistochemical staining for kappa and lambda light chains. All the three patients were alive with no evidence of disease at last follow up.
Conclusion: EBV-positive plasmacytomas in immunocompetent patients can have a lot of morphological and phenotypical overlaps with PBL. Comprehensive clinical findings, morphological and phenotypical investigation may contribute to a specific diagnosis.

OFP-01-012
Assessment of CD34-positive blasts in bone marrow core biopsy: inter-observer agreement study
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Background & Objective: A value of immunohistochemistry (IHC) in the assessment of CD34+ cells in the bone marrow biopsy (BMBx) is well established. Various protocols for the IHC protocols, different cutoff points for the readout of stained slides, and various statistical methods for analysis of readout results were published. Our study specifically addressed one component of this method, namely inter-observer agreement in percent of CD34-positive cells consistent with blasts. This study was performed by the working group of the International Council for Standardization in Haematology (ICSH).
Method: 110 CD34 IHC slides were included with equal representation of cases in the following diagnostic groups: <5%, 6-9%, 10-19%, and ≥20%. Eight expert haematopathologists were asked to determine the percent of CD34+ cells.
Results: Several different methods were applied for the readout of CD34 IHC slides. Although there was a significant correlation between all observers (Kendall W=0.441), Kappa-value was mostly poor and varied from 0.174 to 0.557. SD and CV of each individual samples were not dependent on the CD34 counts. Congruency of CD34 diagnostic group assignment was: all in one for 11%, all in 2 for 68%, all in 3 for 31%, and all in four for 2%.
Conclusion: Experienced haematopathologists use different methods for readout of CD34 IHC slides and showed poor kappa for classifying patients into different diagnostic groups. These results call for harmonized, evidence-based methods for the readout of CD34 IHC slides as well as for reassessment how the CD34 IHC readouts should be used in the work up of haematological malignancies (e.g. MDS).

OFP-01-013
Pyrosequencing analysis of KRAS, NRAS and BRAF in pancreatic adenocarcinoma, PanIN precursor lesions and normal pancreatic tissue
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Background & Objective: Pancreatic cancer has a high mortality rate and forms the 7th cause of cancer deaths. Histologically, 90% of pancreatic tumours are pancreatic ductal adenocarcinoma (PDAC). Conventional PDAC mainly originates from pancreatic intraepithelial neoplasia (PanIN) and results from accumulation of genetic alterations. The aim of this study was to analyze the genetic status of KRAS, NRAS and BRAF on a series of normal pancreatic tissue, PanIN and PDAC.
Method: We analyzed mutation status of codons 12, 13, 59, 60, 117 and 146 of KRAS and NRAS; and codon 600 of BRAF; using pyrosequencing via a Pyromark Q24 in 25 normal pancreatic tissues, 25 pancreatic intraductal neoplasia (PanIN), and 39 PDAC. These samples were prepared using an enrichment method via 4 mm punch macrodissection of formalin-fixed paraffin-embedded (FFPE) tissues.
Results: There was a statistically significant progressive increment ($p < 0.001$) in the percentage of mutated cases through normal pancreas (8%), PanIN-1A (28.6%), PanIN-1B (33.3%), PanIN-2 (60%), and PanIN-3 (85.7%) to PDAC (94.8%). These mutations were arising in codons 12 and 61 of KRAS and in codon 600 of BRAF. Most frequent mutations were G12D (46%), G12A (23%), and G12V (18%) of KRAS. No mutations were found in codons 13, 59, 117, and 146 of KRAS or in codons 12, 13, 59, 61, 117, and 146 of NRAS.
Conclusion: Our study supports the model progression of PanIN to PDAC. We found a slight difference in predominant mutation subtypes; which suggest an ethnic role in pancreatic carcinogenesis. Further studies on larger Tunisian series should be performed to confirm our results.

OFP-01-014
Detection of NAB2-STAT6 gene fusions in solitary fibrous tumour by targeted RNA-seq
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Background & Objective: Solitary fibrous tumour (SFT) is a rare mesenchymal neoplasm presenting three pathologic variants: typical (TSFT), malignant (MSFT) and dedifferentiated (DDSFT), the latter with a worse prognosis. An intrachromosomal fusion between NAB2 and STAT6 is the defining driving event. These genes lye adjacent in the genome hindering FISH analyses, but nuclear STAT6 expression is consistently detected by IHC. We evaluated targeted RNA-seq performance in detecting NAB2-STAT6 fusions and investigated the association between fusion and histological variants.

Method: We used Archer™ FusionPlex™ Sarcoma Panel for fusion transcripts detection in a series of 56 SFT comprising 22 TSFT, 31 MSFT and 3 DDSFT. IHC for STAT6 expression was performed in a subset of 25 cases. Molecular findings were correlated with pathological features.
Results: STAT6 nuclear staining was observed in 22 cases and SFT fusion transcripts were identified in 21 cases, thus achieving 95% sensitivity for detection of SFTs predicted by IHQ. No fusion transcripts were detected in two IHC negative samples, but SS18-SSX6 fusion (pathognomonic of synovial sarcoma) was identified in the remaining IHC negative case. The most frequent fusion variants in the whole series (n=56) were NAB2ex6-NAB2ex16 (18 cases) and NAB2ex4-STAT6ex2 (16 cases). Any correlation was found between fusion variants and histopathology. Interestingly, no fusion was detected in 2 out of 3 DDSFT.
Conclusion: Targeted RNA-seq detects with high accuracy different variants of NAB2-STAT6 fusion which are not related to different histology. Targeted RNA-seq could be useful when SFT diagnosis is uncertain and may prevent misdiagnosis of other mesenchymal tumours expressing STAT6 protein.

OFP-01-015

Intravascular large B-cell lymphoma (IVLBCL) – a case presenting with anemia, thrombocytopenia and a two-year history of a difficult to classify tremor

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Background & Objective: Intravascular large B-cell lymphoma (IVLBCL) is a rare aggressive entity with a broad spectrum of clinical symptoms
Method: We present a case of 72-year old female with a 2-week history of physical decline. She further reported on an increasing tremor which started to develop two years before. Laboratory testing revealed a normochromic normocytic anemia with Hb of 8.2 g/dl, thrombocytopenia with 47,000/µl and elevated LDH of 1018 U/l. A bone marrow aspirate was unremarkable. The CT scan showed a splenomegaly. Since a haematologic malignancy was suspected the spleen was removed for diagnostic reasons. The 1020 g splenectomy specimen showed a pronounced extension of the red pulp with moderate siderosis. In the adjacent soft tissue an atypical lymphoid infiltrate composed of large- and medium-sized tumour cells located mainly in small sized vessels was noted. Immunohistochemical characterization revealed a CD20+, CD79a+, PAX5+, MUM1+, CD5+, IgM+, bcl2+, bcl6+, CD10–, CD30–, CD23–, Cyclin D1– phenotype and a Mib1 proliferation index of greater than 95 percent, thus the diagnosis of IVLBCL was made.
Results: A six-cycle chemotherapy consisting of vincristine, prednisolone, cyclophosphamide and doxorubicin in a reversed CHOP regimen combined with eight-cycles of Rituximab was administered. During the first cycle of chemotherapy the patient recovered, the Hb returned to normal and the tremor improved and finally dissolved.
Conclusion: A complete neurological assessment performed 3 months after completion of the chemotherapy was unremarkable. The most recent follow-up, 2.5 years after diagnosis, did not show signs of a relapse and the patient reported well-being.

Sunday, 9 September 2018, 17:15 - 19:15, Room A3
OFP-02 | Digestive Diseases Pathology - Liver / Pancreas

OFP-02-001

Long-term survivors of pancreatic cancer exhibit a potent anti-tumoural immune response

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Background & Objective: Tumour microenvironment (TME), especially immune cells, modulate cancer progression and pose promising novel therapeutic targets. However, their influence on tumour characteristics and clinical outcomes in pancreatic ductal adenocarcinoma (PDAC), a neoplasm considered highly immunosuppressive, is ill defined.
Method: Three well-characterized PDAC-cohorts, surgically resected with curative intent and composed of long-term survivors (LTS, n=30, overall survival (OS) >60 months), medium-term survivors (MTS, n=40, OS 12-60 months), and short-term survivors (STS, n=40, OS 3-12 months), were included. An integrative tumour analysis was carried out by immunophenotyping (CD3, CD4, CD8, CD20, Foxp3, dendritic cells, iNOs, CD163, RHAMM, MHC1, PD-L1) and next-generation sequencing. Results were correlated with clinico-pathologic characteristics, including tumour budding.
Results: The TME of LTS exhibited numerous CD3+, CD4+ and CD8+ T-cells, and CD20+ B-cells with frequent presence of tertiary lymphoid tissue (TLT), was enriched with iNOS+ M1-macrophages and dendritic cells, and scarce of Foxp3+ Tregs, and CD163+ M2-macrophages. Moreover, LTS displayed no PD-L1 expression, were less frequently RHAMM-positive, and showed the highest MHC1 positivity. STS presented an immunosuppressive TME, rich in Foxp3+ Tregs and CD163+ M2-macrophages, and poor in T- and B-cells, while MTS lied in-between. On genomic level, LTS displayed low mutation frequency in common cancer genes, with significantly less CDKN2A and SMAD4 alterations, and were characterized by significantly lower tumour budding.
Conclusion: Different immune host responses correlate with different molecular and morphological tumour characteristics, affecting cancer progression in PDAC. A combination of tumour-related and host-related microenvironmental features confers a significant survival advantage in PDAC-patients.

OFP-02-002

Critical role of the ECM-molecule Tenascin C for the viability of activated pancreatic stellate cells in pancreatic ductal adenocarcinoma

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Background & Objective: Pancreatic ductal adenocarcinoma (PDAC) possibly develops from acinar-to-ductal metaplasia (ADM) and is accompanied by an abundant fibrotic reaction rich in extracellular matrix (ECM) molecules. Activated pancreatic stellate cells (aPSC) secrete a variety of signalling and ECM molecules, including Tenascin C (Tnc), thereby modulating tumour microenvironment and promoting epithelial to mesenchymal transition (EMT). Here, we aim at investigating the relevance of Tnc in epithelial-stromal interaction in a PDAC mouse model.
Method: PSC isolated from wildtype and Tnc-knock-out (Tnc-/-) mice were compared concerning their activation status (α-SMA, fibronectin) and EMT promoting cytokines (IL-6, TGF-β) by qPCR. Cancer cells isolated from p48Cretg/+;LSL-KrasG12D/+;p53flox/flox(KPC);Tnc+/+ and KPC;Tnc-/- mice were tested for proliferation and adhesion. Expression levels of ADM markers (Mist1, Ptf1a, Sox9, Ck19) were analysed in pancreatic tissue of KPC and KPC;Tnc-/- mice by qPCR. 3D co-cultures of aPSC from Tnc-proficient and deficient mice with Tnc+/+ cancer cells were established and viability was measured.
Results: Tnc+/+ and Tnc-/- aPSC did not show difference in their activation status or cytokine expression. Moreover, no differences were found regarding proliferation and adhesion of isolated cancer cells or expression of ADM markers in pancreas tissue of KPC;Tnc+/+ and KPC;Tnc-/- mice. Remarkably, in 3D co-cultures,

Tnc-/- aPSC displayed significantly increased viability compared to Tnc+/+ aPSC (p = 0.04).
Conclusion: In conclusion, Tnc influences the viability of aPSC in a PDAC-like in vitro scenario, suggesting a pivotal role of this protein in a relevant biologic feature of aPSC in vivo.

OFP-02-003
Morphology and immunohistochemistry predict two unique basal molecular subtypes in pancreatic ductal adenocarcinoma
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Background & Objective: Recently, transcriptional analyses have identified several distinct molecular subtypes. However, to date, a morphological analysis of these molecular subtypes has not been performed. Herein, we investigated specific morphological features and immunophenotype associated with distinct molecular subtypes of PDAC.
Method: We profiled gene expression of 79 primary PDAC specimens from University Health Network (UHN) using RNA sequencing. Gene expression data was deconvoluted using non-negative matrix factorization (NMF), to distinguish tumour and stromal gene expression signatures, resulting in 2 molecular subtypes (basal and classical). The histology of all cases were reviewed and IHC panel incorporating genes enriched in the different subtypes were performed (Basal= CK5, p63, p40, CK14; classical= MUC5AC). IHC was quantified based on proportion of positive tumour cells and scored as 0%, <25% 25-49%, 50-75% and >75%.
Results: Classical subtype (N=59; 75%) uniformly showed a glandular morphology. The basal subtype (N=20; 25%) displayed an array specific histological patterns present in >40% tumour. All basal tumours showed staining in 3/> basal markers and can could be further subdivided into 2 groups based on the % of staining (Group 1=<50% in <3 basal IHC; Group 2= >50% in 3/> basal IHC). Interestingly, this group also showed CK14 selectively staining the leading edge cells, suggesting a potential role for "collective invasion" in PDAC. All classical cases were negative for basal markers and showed variable staining of MUC5AC.
Conclusion: This is the first study to correlate morphology and immunohistochemistry to specific molecular subtypes of PDAC. Additionally, we have identified 2 distinct basal molecular subtypes. However, presently the clinical significance of these subgroups is not known.

OFP-02-004
Keratin 7 expression in hepatic cholestatic diseases
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Background & Objective: We aimed to evaluate keratin 7 (K7) immunohistochemical expression in cholestatic liver disease of variable aetiology in relation to bile duct loss, fibrosis stage, bilirubinostasis and serum biochemistry.
Method: K7 expression was assessed and semiquantified in liver biopsies from 103 patients [males 41%/females 59%, mean age ±SD 53±16 years] with bile duct obstruction/destruction (BDO/D) (58%) [partial 55/60 (91%), complete 5(9%)] or parenchymal cholestasis (P-CH) (42%) [acute hepatitis-AH 19(44.2%), pure/mixed cholestasis (P/M-CH) 24(55.8%)].
Results: K7 expression was detected in hepatocytes in 87/103 (84.5%) cases. It was more frequent in BDO/D-CH [55/60 (91.7%) vs P-CH 32/43 (74.4%), p=0.026] with no statistical difference among the subgroups of each category, including zonal distribution pattern with the exception of zone 1 extensive positivity in P/M-CH (6/24, 25%) vs AH (0/19) p=0.027. It also correlated with bile duct loss (p=0.0046) with more extensive zone 1 expression in 15/38 cases (39.5%) vs 8/65 (12.3%) with intact bile ducts (p=0.003). There was no correlation with fibrosis stage or bilirubinostasis besides more frequent panzonal K7 expression in severe bilirubinostasis (56.3%) compared to mild/moderate (25%). K7 expression was negatively correlated with lower levels of direct bilirubin (p=0.047), AST(p<0.001) and ALT(p=0.012), while there was a positive correlation trend with γGT values (p=0.074) but no correlation with ALP.
Conclusion: K7 hepatocyte expression is a sensitive cholestatic marker almost constantly present in cholestatic liver diseases. It predominates in BDO/D showing a strong association with bile duct loss. K7 expression does not reflect the severity of liver biochemical profile indicating differences in pathogenetic mechanisms.

OFP-02-005
Necroptosis is associated with a better survival in intrahepatic cholangiocarcinoma
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Background & Objective: Intrahepatic cholangiocarcinoma (iCC) has a poor prognosis and few therapeutic options. Necroptosis is a programmed cell-death pathway, which depends on several signaling proteins among which the Receptor-interacting Protein Kinase-3 (RIPK3) activates the necroptosis executioner Mixed Lineage Kinase domain-like (MLKL). In turn, RIPK3 may be activated by RIPK1. By the assessment of the necroptotic pathway protein expression, triggering the necroptosis could be very important in cancer treatment. The expression of RIPK3, MLKL and RIPK1 has not yet been investigated in iCC; therefore, the aim of this study was to assess their immunohistochemical expression and their relationship with patient survival in a cohort of iCC.
Method: RIPK3, MLKL and RIPK1 expression was assessed in 61 paraffin-embedded samples obtained from resected iCC patients. Immunostaining was semi-quantitatively scored by a four-tier scale based on the percentage of positive cancer cells as follows: 0 = <5%, 1+ = 5-30%, 2+ = 31-60%, and 3+ = >60%.
Results: The highest percentage (3+) of RIPK3 was found in 52.4% of cases, MLKL in 41% and RIPK1 in 23.8% and it was associated with a significant decrease of perineural invasion and lymph nodes metastasis (the latter was related only to RIPK3). A diffuse expression of RIPK3 and RIPK1 was related to an improvement of the overall (p=0.01 and p=0.02, respectively) and disease-free (p= 0.01 and p= 0.02, respectively) survival.
Conclusion: Overexpression of RIPK3 and RIPK1 is related to a better prognosis in iCC, which opens the way to new therapeutic options.

OFP-02-006
Lysyl oxidase-like protein 2 in cholangiopathies
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Background & Objective: The lysyl oxidase-like protein 2 (LOXL2) promotes stabilization of the extracellular matrix, cell growth and cell mobility. We aimed to (i) identify stimuli of LOXL2 in cholangiopathies, (ii) characterize the effects of LOXL2 on biliary epithelial cells' (BECs) barrier function, (iii) compare LOXL2 expression in PSC, PBC, and disease controls, and (iv) to determine LOXL2 expression and cellular sources in 4 mouse models for cholangiopathies.
Method: Murine BECs were challenged with triggers of cellular senescence, hypoxia, Abcb4-/- mouse bile and chenodeoxycholic acid (CDCA) and investigated for LOXL2, SNAIL1 and E-cadherin expression and transepithelial electrical resistance (TEER) with and without LOX-inhibition. In vivo, LOXL2 expression was studied in PSC livers, and controls and mouse models. We compared LOXL2 serum levels in PSC, SSC, PBC patients, and controls.
Results: Cellular senescence, hypoxia, Abcb4-/- bile and CDCA induced LOXL2 and SNAIL1 expression, repressed E-cadherin expression, and significantly reduced TEER in BECs. All of the pathological changes could be recovered via pharmacological LOX-inhibition. Mouse models showed induced LOXL2 expression in the portal region and in association with ductular reaction. LOXL2 serum levels were significantly elevated in patients with cholangiopathies. In PSC, LOXL2 expression was located to periductal onion skin-type fibrosis, ductular reaction, Kupffer cells, and fibrotic septa. In PSC, LOXL2 overexpression was paralleled by E-cadherin loss in BECs from medium-sized bile ducts.
Conclusion: Reactive BECs produce LOXL2, resulting in increased tight junction permeability, which can be ameliorated by pharmacological LOX-inhibition in vitro. Reactive BECs, portal myofibroblasts, and Kupffer cells are the main sources of LOXL2 in cholangiopathies.

OFP-02-008

Hepatocyte transporters expression in hepatocellular adenoma subtypes and focal nodular hyperplasia helps to understand their imaging at Gd-EOB-DTPA magnetic resonance imaging

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Background & Objective: GdEOBDTPA enhanced magnetic resonance imaging (MRI) has simplified the diagnosis of focal nodular hyperplasia (FNH) vs. hepatocellular adenoma (HCA) (91% specificity, 92% sensitivity), but the ability of this technique to clearly distinguish the different HCA subtypes is more controversial. Aim of this study was to investigate the expression of hepatocyte transporters (HTs) (OATP2/8, MRP2, MRP3) involved in GdEOBDTPA pharmacodynamics in a large series of FNH and subtyped HCA.
Method: We semiquantitatively scored the immunohistochemical expression of OATP2/8, MRP2 and MRP3 in resected FNH (n=40) and HCA (n=54). From the results of this first step of our study, we further validated our working hypothesis in a supplementary set of FNH (n=7) and HCA (n=10) with GdEOBDTPA imaging data.
Results: All FNH showed consistent expression of all three HTs. HNF1a-inactivated-HCA (H-HCA, n=24) and inflammatory HCA (I-HCA, n=15) subtypes were characterized by a loss of OATP2/8 expression, predictive of no uptake of GdEOBDTPA, as opposed to beta-catenin-activated-HCA (B-HCA, n=11) and HCA with malignant transformation (n=4) ($p<0.01$). The latter entity also showed an overexpression of MRP3 ($p<0.01$), predictive of a faster efflux of GdEOBDTPA. At imaging, on the validation set, FNH and HCA uptake of GdEOBDTPA was congruent with tissue expression of HTs, with H-HCA and I-HCA showing no GdEOBDTPA uptake, by contrast to B-HCA and FNH.
Conclusion: Tissue expression of HTs in FNH and HCA subtypes correlates with hepatocyte GdEOBDTPA uptake at MRI. GdEOBDTPA uptake pattern helps in distinguishing H-HCA and I-HCA lacking typical features at nonhepatospecific MRI from B-HCA and HCA with malignant transformation.

OFP-02-009

Pre-operative diagnosis of pancreatic cystic lesions: value of molecular analysis of cytologic samples

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Background & Objective: The spectrum of pancreatic cystic lesions ranges from benign to malignant lesions. Cytology is increasingly performed, but results are often inconclusive. Molecular testing of cytologic samples could possible increase pre-operative diagnostic accuracy. The aims of this study were to evaluate the diagnostic accuracy of pre-operative cytology and to assess the value of molecular analysis.
Method: 52 surgically resected pancreatic lesions with pre-operative cytology were analyzed retrospectively. 15/52 cases (28.8%) were excluded, as lesions were non-cystic (10/52; 19.2%) or had biliary origin (5/52; 9.6%) at final diagnosis. Molecular analyses (DNA cytometry/FISH/GNAS sequencing/NGS panel sequencing) were performed in 14/37 cases (37.8%).
Results: At final diagnosis, 28/37 cases (75.7%) were intraductal papillary mucinous neoplasms (IPMN). Additionally, two pancreatic ductal adenocarcinomas, one intraductal tubulopapillary neoplasm, one solid pseudopapillary neoplasm, one mucinous cystic neoplasm, one serous cyst adenoma, one pyloric gland adenoma, one non-neoplastic cyst and one inflammatory pseudocyst were found. Correct diagnosis was possible by cytology alone in 18/37 cases (48.6%). Indication for surgery was correct in 30/37 cases (81.1%). Molecular analysis helped establish a correct diagnosis or indication for further treatment in 9/14 cases without certainly positive cytologic diagnosis (64.3%). In 17/37 cases (46%), (further) molecular analysis could have supported 'suspicious'/'equivocal' cytological diagnosis or confirmed neoplasia in cytologically negative diagnosis.
Conclusion: Our preliminary results underline the need to increase pre-operative diagnostic accuracy in pancreatic cystic lesions, which can potentially be achieved by molecular analysis. However, this needs to be confirmed in a prospective larger cohort.

OFP-02-010

ROS1, ALK, MET and HER2 rearrangements and or amplifications in a series of biliary tract carcinomas

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Background & Objective: Biliary tract carcinomas (BTC) are aggressive carcinomas associated with a poor prognosis and no alternative treatment but surgery. In this context, it is urgent to find targetable molecular alterations.

Method: Using a fluorescent in situ hybridization assay, we retrospectively evaluated the frequencies of ROS1, ALK, MET and HER2 rearrangements and or amplifications in a series of 138 BTC (62 intrahepatic cholangiocarcinomas (CC), 29 hilar CC, 15 common bile duct CC, 32 gallbladder adenocarcinomas). ROS1, ALK, MET and HER2 immunostaining was performed together.
Results: We detected HER2 amplifications in 2% (1/62) of intrahepatic CC and in 16% (5/32) of gallbladder adenocarcinomas. Anti-HER2 immunostaining was strongly positive in these 6 cases. We detected 1 MET amplification in the whole series. This case was an intrahepatic CC and was associated with a strong anti-MET immunostaining. We did not detect any other targetable molecular alterations using our panel of probes against ROS1, ALK, MET, HER2. Particularly, hilar and common bile duct CC showed no targetable molecular alteration. We observed several chromosomic alterations suggestive of chromosomal instability in 12% of BTC. Interestingly, 5 cases (all intrahepatic CC) harbored a centromeric alpha-sequences amplification.
Conclusion: HER2 amplifications are recurrent molecular alterations in BTC and seem to be more frequent in gallbladder adenocarcinomas. Immunostaining seems to be performant to detect these cases in routine practice. MET amplifications seem to be rare events. Nevertheless, due to a low rate of targetable molecular events detected in this series, we could not perform any survival analysis and this would require a larger series.

OFP-02-011
Evaluation of necroptosis related genes RIPK1, RIPK3 and MLKL-p immunogenicity in hepatocellular carcinoma
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Background & Objective: Necroptosis is a form of programmed necrosis. When necroptosis occurring in cancer, dispersed tumoural elements may contribute to boost the immune response. Receptor-interacting protein kinases 1 and 3 (RIPK1 and RIPK3) and the mixed-lineage kinase domain-like protein (MLKL) are the main elements composing the subcellular pathway that realizes necroptosis. Aim of this study was to assess expression of RIPK1, RIPK3 and phosphorylated MLKL in a cohort of HCC patients and their correlation with infiltrating CD8+ T-cells and clinical follow-up data.
Method: RIPK1, RIPK3 and MLKL-p expression was assessed with immunohistochemistry (IHC) in 83 FFPE samples of resected HCC patients. Expression was evaluated on a 4-tired scale. Tumoural and peritumoural infiltrating CD8+ T cells were automatically assessed on digitized sections. Co-localization of necroptotic factors was verified by multiplex imaging. Wilcoxon Rank Sum test and survival analysis were applied to: 1) compare the correlation between RIPK1, RIPK3, MLKL-p and their combination with T cell-infiltration; 2) evaluate the prognostic impact of these necroptotic kinases in HCC. Results were compared with those obtained from computational analysis of RNA-seq data in 373 HCC patients from TCGA.
Results: RIPK1, RIPK3 and MLKL-p expression are significantly associated with tumoural but not peritumoural CD8+ T-cells infiltration (p-values < 6e-05 and > 0.4, respectively). By combining the IHC scores of the three kinases, the strength of the association with tumour infiltrating CD8+ T-cell increases (p-value 2.6e-09). Results are confirmed by TCGA RNAseq data.
Conclusion: Necroptosis occurs in a subsets of HCC patients and it is correlated to the entity of infiltrating CD8+ T-cells.

OFP-02-012
Immunohistochemical staining patterns of the PDAC stroma and their prognostic implications
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Background & Objective: Our aim is to evaluate the relationship between stromal markers (Galectin-1, SMA, Collagen Type IV) and histopathological parameters of pancreatic ductal adenocarcinoma (PDAC), to investigate the role of these parameters in predicting the prognosis, and to show their relationship with response to therapy, if any.
Method: 76 consecutive resections diagnosed as PDAC, were immunostained with SMA, Collagen Type IV and Galectin-1 antibodies. Statistical analysis was performed over the semiquantitative results of immunhistochemistry (IHC).
Results: Mean survival was 17.9 months (1,6-75 months). M/F = 48/28. Male gender, high grade, and surgical margin positivity were independent poor prognostic factors. There was a significant correlation between high SMA expression, and presence of angioinvasion (p= 0.006). High Galectin-1 immunreactivity had an effect over survival independent of the N stage (p= 0.035). Although not statistically significant, Collagen Type IV high-reactive cases were found to have better prognosis (HR= 0.595), independent of the pathological stage.
Conclusion: This is the first microscopy-based study to show relationship between Collagen Type IV and PDAC. Collagen Type IV can also be included in the study objectives during antiangiogenic and antistromal treatments are being developed. SMA IHC might be helpful in determining the risk of angioinvasion and capacity of systemic spread. Unlike the literature, we showed high stromal Galectin-1 expression is a good prognostic factor independent of the pathological stage. Our findings suggest, the stroma is trying to limit the spread of the tumour.

Sunday, 9 September 2018, 17:15 - 19:15, Barria
OFP-03 | Dermatopathology

OFP-03-001
25 kgy radio-sterilised human skin graft shows effective skin regeneration in nude mice
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Background & Objective: There has been a growing interest in radiosterilized skin grafting, especially in extensive and deep burns. Our purpose was to evaluate the histoarchitecture of the human skin graft irradiated during the tissue repair process in NUDE mice.
Method: Nude mice received skin grafts irradiated with dose at 25 kGy and 50 kGy and non-irradiated, submitted to euthanasia on the 3rd, 7th and 21st days after surgery. Morphometric evaluation was performed to quantify keratinocytes, fibroblasts, defense cells and blood vessels. Expression of human type I collagen, mouse type I and III collagen, identified by immunofluorescence and histomorphometry.
Results: Histological results showed that irradiated human skin has influence on cell growth. At 25 kGy, on the 3rd there was an increase in fibroblasts (41.53±8.81vs21.68±4.90) and inflammatory cells respectively on 3rd and 7th (115.8±16.73vs11.17±6.56 and 144.1±19.15vs70.17±23.62) in relation to non-irradiated; on the 21st the keratinocytes increased in relation to the non-irradiated (260.9±69.46vs138.0±40.12) and 50 kGy (260.9 ±69.46vs0.0). On 21st, the three groups presented incorporation of the human graft, being 25 kGy better to skin regeneration with lower inclusion of the human collagen I (6.31±4.34vs43.20±18.78) and greater mouse collagen III (34.60±10.28vs22.48±10.66) in relation to non-irradiated.

Conclusion: This study showed that the group irradiated at 25 kGy presented greater cell proliferation and better regeneration, suggesting that this dose is probably more indicated for skin grafting, providing faster and more effective healing.

OFP-03-002

The lupus band test, an uncomplimentary diagnostic tool in the diagnosis of lupus erythematosus

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Background & Objective: The lupus band test (LBT) using Direct Immunofluorescence (DIF) is routinely used in the diagnosis of lupus erythematosus (LE) at Cork University Hospital, Cork. However, low positive LBT rates and poor concordance with histological diagnoses have warranted a review of the sensitivity of the LBT in the diagnosis of LE. We undertook a large case study to evaluate the efficacy of the LBT in the diagnosis of LE.
Method: From 2011 to 2017, all cases of DIF requested for the investigation of LE were retrieved and reviewed with key aspects recorded: lupus band test result; DIF detected antibodies; and diagnosis on histology. All skin biopsies sent for DIF had a corresponding skin biopsy sent for histology.
Results: 258 of 947 requests made for DIF were requested for LE. 24 (9.4%) had a positive lupus band test. 16(66.7%) of these cases showed IgG and IgM antibody distribution at the basement membrane zone. This was discordant with histology, as 102 (39.8%) cases were diagnosed with LE on histology, with only 19 of these cases having a positive LBT. The sensitivity and specificity of the LBT was 18.3% and 96.75% respectively.
Conclusion: This study has established that the LBT is not a sensitive diagnostic test in the diagnosis of LE. It is appreciated that DIF is a useful diagnostic tool however it would be a more prudent and cost effective to use DIF when an additional diagnostic tool is required to rule out LE. A case study of this size has not been reported before.

OFP-03-003

PTEN hamartoma of soft tissue: presentation of two cases and a literature review

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Background & Objective: PTEN gene was isolated and cloned in 1997 and germline mutations have been identified in Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome, Proteus syndrome and Proteus-like syndrome. Since then, a variety of vascular anomalies have been reported in these patients. In 2012 a vascular lesion with a distinctive histopathologic feature was described and named phosphatase and tensin homolog (PTEN) hamartoma of soft tissue (PHOST).
Method: We present two cases diagnosed with PHOST in Hospital Universitario La Paz between 2012 and 2018. A 31-year-old female with Cowden syndrome (R233 de novo mutation of PTEN gene) with a lesion in the upper extremity and an 11-year-old male with a lesion in the lower extremity who is being studied for PTEN mutation.
Results: In both patients the lesions of the extremities had the same histopathologic characteristics and were composed of a variable admixture of adipose tissue, abnormal vessels, dense and myxoid fibrous tissue. The tissues appeared mature without cytologic atypia, necrosis or mitosis. The vascular component consisted of thick and thin walled dilated veins and of medium-sized tortuous arteries with smooth muscle hyperplasia. Nerves with periaxonal spindled cell proliferation resulting in onion bulb formation and lymphoid aggregates were observed.
Conclusion: In 2014 PHOST has been included in the International Society for the Study of Vascular Anomalies Classification. It is important to recognize it and the diagnoses should prompt a clinical evaluation and genetic testing for a PTEN mutation. To the best of our knowledge only one case has been published since the original report in 2012.

OFP-03-004

Clinical and molecular heterogeneity in DNA repair diseases predisposing to accelerated ageing: example of Xeroderma Pigmentosum and Cockayne syndrome

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Background & Objective: Xeroderma pigmentosum (XP) and Cockayne syndrome (CS) are rare autosomal recessive disorders that affect DNA repair system (NER). Clinical and genetic heterogeneity within these pathologies makes genotype-phenotype correlation very difficult. Indeed, the XP is characterised by UV-induced skin dyspigmentation, sunburn, cancers, skin photo-ageing and in some patients, neurological degeneration. However, the CS is characterised by progressive neurological disorder, a progeroid appearance, microcephaly, severe psychomotor delay, and intracranial calcifications. The combined (XP/CS) phenotype, is characterized by severe growth defects, cognitive disability, premature aging, dwarfism, in addition to XP disease. Here we investigate 4 patients with severe clinical phenotype of CS and 2 patients with atypical mild XP phenotype.
Method: Blood were collected and DNA extracted. We carried out mutational analysis through Sanger and target gene sequencing.
Results: We identified a recurrent mutation (p. Tyr200LysfsX12) in ERCC8 gene in patients carrying typical characteristics of CS. This mutation seems to be specific to North African patients. Regarding XP patients, in two siblings, a homozygous variant p. L778P was found in ERCC5 gene, these are the first XPG patients reported in North Africa also.
Conclusion: This study extended the mutation spectrum of rare DNA repair diseases such as XP and CS. Defects in ERCC5 gene remain a paradigm in DNA repair diseases. Indeed, mutations in this gene could result in phenotypes that range from mild XP form to the most severe combined form of XP/CS. Both XPG and XP/CS are models for premature ageing studies, especially for immune system senescence and skin ageing investigations.

OFP-03-005

Is microsatellite-instability a prognostic factor in melanoma patients treated with immune-checkpoint inhibitors?

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Background & Objective: To investigate the prevalence of mismatch repair (MMR) deficiency and its correlation with treatment response (TR) and mortality in melanoma patients treated with immune checkpoint-inhibitors.
Method: In this retrospective study we investigated patients who received pembrolizumab, nivolumab or ipilimumab between 2012 - 2015 with melanoma cTNM stage III unresectable (n=1) or IV (n=21). Loss of MMR enzymes MLH1, MSH2, MSH6 and PMS2 was evaluated immunohistochemically. Five melanomas were further tested for microsatellite instability (MSI) and loss of heterozygosity (LOH) using the Promega-MSI-Analysis-System. Samples were classified as MMR deficient only if MSI was confirmed by PCR. TR was measured three and six months after therapy initiation using the immune related response criteria (irRC). Statistical testing regarding correlation of MMR deficiency and

LOH status with TR and overall survival was performed using Fisher's-exact-test and log-rank-test.
Results: None of the 22 patients showed MSI confirmed by PCR. LOH at the marker locus Penta D was detected in 2 of 5 patients (40%). No significant correlation between LOH-status with TR after 3 ($p>0.05$) and 6 ($p>0.05$) months was found. LOH-status had no impact on overall survival ($p>0.05$).
Conclusion: Our pilot study demonstrates that MMR deficiency was suspected immunohistochemically in a few cases but could not be confirmed by MSI testing. LOH was detected in 2 patients, but no correlation with TR or overall survival could be observed.

OFP-03-006
eIF6 is overexpressed in melanoma of the skin and might be a novel therapeutic target
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Background & Objective: Malignant melanoma (MM) of the skin ranges among the most frequently diagnosed cancer entities. Aim of this study was to determine which eIF subunits are involved in tumourigenesis of melanocytic skin neoplasms and melanoma progression. Therefore, eIF expression in MM was compared to corresponding normal skin tissue and benign naevi.
Method: The immunohistochemical evaluation included 62 patients: 13 MM (primary and recidive) and 49 benign naevi at the Medical University of Graz, Austria. Age at removal of lesion, location, histopathological diagnosis, congenital pattern for naevi, BRAF status for MM and time to recurrence were recorded. For eIF expression, tissue was stained for eIF2α, eIF3p110, eIF3H, eIF4E, eIF4H, eIF5 and eIF6. Based on the IHC results, siRNA knockdown of eIF6 was performed in two metastatic and two non-metastatic MM cell lines and evaluated for cell viability, apoptosis and migration.
Results: Our results demonstrated that in MM of the skin compared to naevi, eIF2α ($p=0.013$) and eIF6 ($p=0.034$) were significantly overexpressed. Based on these results, siRNA knockdown for eIF6 was performed in vitro. Successful eIF6 knockdown was confirmed in all cell lines using qRT-PCR. The siRNA mediated knockdown of eIF6 reduced cell viability in all analysed cell lines. Reduction of cell viability was more prominent in the metastatic cell lines than in the non-metastatic ones. Cell migration was only impaired in the metastatic cell lines upon siRNA treatment.
Conclusion: Our preliminary data reveal an important role for eIF6 in the carcinogenesis of MM and a potential novel target for new anti-cancer drugs in MM therapy.

OFP-03-008
Increased SMAD7 expression is associated with tumour aggressiveness and independently predicts poor survival in cutaneous melanoma patients
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Background & Objective: SMAD7 is a key inhibitor of transforming growth factor-β signaling and its involvement in cancer development and progression has been identified in a number of tumour types. The aim was to characterize SMAD7 expression and clarify its clinical significance in skin melanoma.
Method: SMAD7 expression was evaluated by means of immunohistochemistry in formalin-fixed paraffin-embedded tissues of 205 cutaneous melanoma primary tumours. The results were correlated with classical clinicopathological characteristics, including patient survival.
Results: SMAD7 was expressed in melanoma cells, at least weakly, of virtually all tumours (204/205 cases) and the pattern was almost exclusively nuclear. Increased SMAD7 reactivity was most commonly observed in nodular melanomas and coincided with other features of aggressive tumour phenotype, including greater tumour thickness, higher mitotic rate and the presence of ulceration. According to Kaplan-Meier analysis, enhanced SMAD7 expression was correlated with considerably shorter melanoma-specific survival and recurrence-free survival. Prognostic significance of SMAD7 expression was confirmed after adjustment for Breslow thickness, pN status and the intensity of tumour-infiltrating lymphocytes in a multivariable analysis.
Conclusion: Our results indicate that SMAD7, a marker of aggressive tumour behavior and adverse clinical outcomes, plays an important role in melanoma progression. Targeting SMAD7 for therapeutic purposes in cutaneous melanoma merits further investigations.

OFP-03-009
Digital pathology versus light microscopy in evaluation of malignant melanoma
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Background & Objective: Malignant melanoma is not the most common skin neoplasm, but it is responsible for the vast majority of skin cancer deaths. Assessment of prognostic factors such as mitotic rate, tumour thickness and surgical margins is crucial for the therapy process. The aim of the study was to compare traditional and digital method in evaluation of histopathological parameters that are prognostically important in malignant melanoma.
Method: We examined 41 cases of malignant melanoma of the skin, diagnosed in 2001-2005. The histopathological slides were scanned and analysed with regard to features such as tumour thickness, mitotic rate per 1 square millimetre and the shortest surgical margin. Scanned slide images were evaluated using the available precise measuring tools. The results were compared with the interpretation of the features in traditional light microscopy.
Results: The use of precise digital measuring instruments caused changes in pT stage in 15% of cases. Mitotic rate was different in as much as 50% of cases: lowered in 20 cases and increased in 2 cases. Minimal changes concerned surgical margins, which varied averagely by 0,11 mm.
Conclusion: The diagnostics of malignant melanoma of the skin basing on the digital images of the scanned slides allows more precise and reproducible method to evaluate the parameters that are prognostically important.

OFP-03-010
Re-excision benign perineural epithelial infiltrates: a pitfall in the assessment of residual carcinoma
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Background & Objective: Carcinomatous perineural invasion is a sign of aggressive tumour behavior and poor prognosis. Nonetheless, diagnosing perineural invasion can be complicated by benign mimics. Among these, one occurs in re-excision skin specimens and represents perineural infiltration by benign epithelial cells without any perineural spread beyond the previous biopsy site or residual malignant tumour adjacently, possibly explained by reactive eccrine duct regeneration into perineural spaces or displacement of the overlying epidermis.
Method: We present the case of a 66 year old man having undergone an excision and subsequent re-excisions for the treatment of a retroauricular tumour in a three-month interval.

Results: Histologic examination of the first excision specimen revealed a squamous cell carcinoma, grade 2, completely excised with close deep margins. The second surgical intervention revealed an incidental superficial basal cell carcinoma, completely excised and no residual squamous cell carcinoma. The third intervention revealed skin ulceration and small nerve fascicles cuffed by epithelial cells with morphology similar to the perilesional regenerated adnexal epithelium, some located right under the regenerative epidermis suggestive of a continuous lesion. Careful examination of the whole tissue submitted showed no residual tumour cells and permitted establishing the final diagnosis of benign perineural epithelial infiltrates.
Conclusion: Re-excision skin specimens may show benign perineural epithelial infiltrates, mimicking carcinomatous perineural invasion. These have to be carefully evaluated in order to avoid misdiagnosis and unnecessary additional treatment.

OFP-03-011
Hypoxic gene signature of primary and metastatic melanoma cell lines: focusing on HIF1-beta and NDRG-1
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Background & Objective: Hypoxia is an important microenvironmental factor significantly affecting tumour proliferation and progression. The importance of hypoxia is not well known in oncogenesis of malignant melanoma.
Method: The mRNA expression levels of hypoxic genes in primary and metastatic melanoma cell lines and in primary cell line at experimental hypoxia conditions were evaluated by using real-time PCR. Depend on experimental data, we focused on two gene/protein, Hypoxia-inducible Factor-1 Beta (HIF-1β) and N-Myc Downstream Regulated 1 (NDRG1). The protein expression levels of two proteins were investigated by immunohistochemistry methods, in 16 primary and metastatic melanomas, 10 intradermal nevi, and commercial tissue array comprised of 208 cores, including 192 primary and metastatic malignant melanomas.
Results: The real-time PCR study showed that hypoxic gene expression signature was different between metastatic and primary cell lines. Hypoxic experimental conditions significantly affect hypoxic gene expression signature. In immunohistochemical study, NDRG-1 expression was found to be lower in primary cutaneous melanoma compared to intradermal nevi (p=0.001). In contrast, the cytoplasmic expression of HIF-1β was higher in primary cutaneous melanoma than in intradermal nevi (p=0.001). We also detected medium/strong significant correlations between studied two proteins in the study groups.
Conclusion: This study may show that hypoxic response consists of closely related proteins in more complex pathways. These findings will shed light to hypoxic processes in melanoma and unlock "Pandora's box" for development of new therapeutic strategies.

Monday, 10 September 2018, 08:30 - 12:00, Room A1
OFP-04 | Digestive Diseases Pathology - GI

OFP-04-001
The consensus molecular subtypes (CMS) and tumour budding: a study on 1525 patients
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Background & Objective: In colorectal cancer (CRC), tumour budding is recognized as an important prognostic factor. The molecular profile of tumour buds is consistent with (partial) epithelial-mesenchymal transition and stemness, similarly described in the "mesenchymal" Consensus Molecular Subtype (CMS4), representing a particularly poor prognostic subgroup. Here, we determine the association of tumour budding with CMS classification and prognosis.
Method: The AMC-AJCCII-90 series (n=76, stage II) was evaluated for peritumoural budding on H&E slides. The LUMC (n=470, stage I-IV), CAIRO (n=484, mCRC) and CAIRO2 (n=475, mCRC) cohorts were investigated for intratumoural budding using pan-cytokeratin-stained tissue microarrays. Budding was scored as a count/area, then classified as <5 or ≥ 5 buds. For all patients, CMS classifications were available (gene-expression/immunohistochemistry-based classifiers).
Results: High (≥5) budding predicted worse outcome in multivariate analysis in AMC-AJCCII-90 (p=0.018), LUMC (p<0.0001), and CAIRO (p=0.03), and in univariate analysis in CAIRO2 (p=0.042). Tumour budding counts were significantly higher in CMS4 mesenchymal tumours compared to epithelial CMS2/3 cancers (p<0.01, all), and associated with KRAS/BRAF mutations (p<0.01, all).
Conclusion: Tumour budding is an adverse prognostic factor across all CRC stages and associated with the mesenchymal CMS4 phenotype. KRAS/BRAF mutations are strongly correlated with tumour budding suggesting its involvement in regulation of this phenotype.

OFP-04-002
Assessing the stability of pathologist diagnostic rate over seven years in a cohort of 38,813 colorectal polyp specimens and implications for histomorphology and statistical process control / next generation quality
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Background & Objective: The objective of this work was to understand the stability of diagnostic bias in colorectal polyps, focused on high grade dysplasia (HGD) and villous morphology (TVA|VA), and how this may impact the utility of statistical process control|next generation quality (SPC|NGQ) for histomorphologic diagnoses.
Method: All colorectal polyp specimens (CRPS) for 2011-2017 in a region were categorized using a previously validated hierarchical free text string matching algorithm. Pathologist diagnostic rates (PDRs) were assessed (1) longitudinally for each pathologist in yearly intervals with control charts (CCs), and with (2) logistic regression (LR).
Results: The study period included 64,115 CRPS. Fifteen pathologists each interpreted >150 CRPS/year in all years and together read 38,813 (range 1335 to 3644). Yearly PDRs compared to each pathologist's overall PDR showed CC drift/outliers (P<0.05|P<0.001) in HGD (9|2 of 105 pathologists x PDR years), and TVA|VA (24|10 of 105). Few pathologists accounted for many of the P<0.05 outliers; two pathologists accounted for four of the HGD outliers and three pathologists for 15 in TVA|VA. LR confirmed, in the 27 pathologists reading >600 CRPS each (total 52,760 CRPS), that predictors for HGD and TVA|VA included pathologist, clinician, year (all P<0.0001), and hospital (P=0.01).
Conclusion: Pathologists have a mix of (1) drift in their yearly PDRs (that exceeds that expected due to sampling), and (2) PDR stability. The substantial PDR stability supports the hypothesis that histomorphology is amendable to calibration via SPC|NGQ and expert review. Adoption of SPC|NGQ would probably allow pathologists to deliver more uniformity and greater healthcare value, and result in better patient outcomes.

OFP-04-003

Does tumour budding contribute to the molecular classification of colorectal carcinoma?

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Background & Objective: The mesenchymal subgroup (CMS4) of the colorectal cancer (CRC) consensus molecular classification is the most aggressive subtype, showing upregulation of genes implicated in epithelial-to-mesenchymal transition (EMT). Tumour budding (TB) represents the histological picture of cells having undergone at least partial EMT. In the base of this knowledge, we aimed to explore the influence of TB in the expression of genes and microRNAs (miRNAs) implicated in EMT and to assess their value as survival predictor factors.
Method: We retrospectively analyzed tumour budding grade in 125 consecutive diagnosed formalin fixed paraffin-embedded (FFPE) colectomy specimens in all stages. The expression analysis of miR200a, miR200b, miR200c, ZEB1 and ZEB2 was made through Quantitative real time-PCR (qRT-PCR) from samples of two different areas: the tumour center and the invasion front with the higher concentration of buds.
Results: We found a significant overexpression of ZEB and a significant reduction of miRNAs in TB areas compared with the center of the tumour. Only the under expression of miR200c and miR200a measured in the TB areas showed a significant correlation with survival. In multivariate analysis of cases in clinical stage I to III, miR200c under expression in TB areas was an adverse tumour-specific survival factor (HR: 0.12, CI 95% 0.03-0.81, p=0.02) independent of clinical stage.
Conclusion: The molecular expression profile in TB areas define a worse prognosis subgroup of cases, suggesting the contribution of these areas to the CMS4 molecular classification. These results highlight the importance of including TB areas in samples for biomarkers evaluation.

OFP-04-004

Tumour budding versus T-cell infiltrates in colorectal cancer: can opposite forces be united?

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Background & Objective: Tumour budding and T-cell infiltrates are well-established prognostic factors in colorectal cancer (CRC), but their value in combination has only rarely been investigated. Here, we examine tumour buds and T-cell infiltrates in CRC each alone and together as a budding/T-cell score (BTS).
Method: This study was performed on a multi-punch tissue microarray containing material from 394 patients with Stage I-IV CRC. Areas from tumour center, front and microenviroment were stained for Pancytokeratin/CD3, Pancytokeratin/CD8 and Pancytokeratin/CD45RO. Tumour buds were scored manually and T-cell infiltrates digitally. Tumour buds, T-cell counts as well as combined BTS were associated with clinicopathological features and overall survival (OS).
Results: Out of the T-cell markers, CD8 and CD3 were markedly superior to CD45RO for predicting clinicopathological features and OS. A higher combined BTS score (Buds/CD8) performed slightly better than budding or CD8/CD3 alone in predicting nodal metastases ($p<0.0001$, OR 1.466, 95%CI: 1.115-1.928). Out of all scores (budding, T-cells and BTS), only higher BTS (Buds/CD3) was significantly associated with poorer OS on multivariate analysis ($p=0.012$, HR 1.218, 95%CI: 1.044-1.419).
Conclusion: Although CD8+/CD3+ T-cells are strongly predictive of tumour biology in CRC, we found a combined BTS to be stronger in predicting survival and certain features with high clinical relevance, such as nodal metastases, in comparison to budding or T-cells alone. Further studies combining the assessment of T-cell infiltrates and tumour budding as markers of opposite forces are necessary to optimize risk assessment of CRC.

OFP-04-005

Profiling lymphocyte and macrophage infiltration in association with tumour budding to personalise stage II colorectal cancer prognosis

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Background & Objective: A growing awareness exists that the tumour microenvironment (TME) contributes to cancer progression. Reporting infiltrating immune cells and tumour buds (TBs) within the TME, has been shown to correlate with clinical outcome. Traditionally these are studied in isolation of each other. The aim of this study is to evaluate the prognostic significance of their association and interaction in patients with stage II colorectal cancer disease (CRC).
Method: Multiplexed immunofluorescence and automated image analysis were used for the quantification of CD3+, CD8+ lymphocytes; CD68+, CD163+ macrophages and TBs, across whole slide images (n=114). Machine learning algorithms were used for feature selection and prognostic risk model development.
Results: A higher number of TBs was correlated with advanced pT stage ($P = 0.004$). A higher number of CD3+ cells at the invasive margin was correlated with a lower number of TBs ($P = 0.03$). A higher ratio of CD68+/CD163+ cells at the tumour core was associated with a higher number of TBs ($P < 0.0001$). A novel prognostic signature, derived from integrating TBs, lymphocytes and their spatial relationship reported a cohort stratification ($P < 0.0001$) which outperformed the clinical gold standard of pT stage ($P = 0.003$).
Conclusion: This study provides evidence that the interaction between lymphocytes and TBs holds prognostic significance in stage II CRC and the combination of these features shows a prognostic significance, which exceeds that of each in isolation.

OFP-04-006

Morphological assessment of immune checkpoint expression in colorectal adenocarcinoma

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Background & Objective: 40% of patients with mismatch repair-deficient (MSI) tumours benefit from immunotherapy. The establishment of predictors of treatment response and the understanding of the immunomodulation have become a priority. In colorectal cancer, cytotoxic T cells density and location predict better outcome. However, immune checkpoint expression has been shown to be associated to worse prognosis, independently of tumour staging in MSI tumours, challenging the anti-tumoural cytotoxic T cells response in this subset of highly immunogenic colon tumours. Therefore, the purpose of this study is to assess the morphological immune profile counterpart of the transcriptomic analysis, by density and location of known immune key players, taking into account the molecular subtypes of colorectal cancer and the immunecheckpoints.
Method: A well studied population-based series of 399 colon cancers (184 MSI tumours and 215 tumours without microsatellites instability (MSS)), operated on between 2004 and 2013, is investigated. Tissue microarray (TMA) samples have been collected from the tumour centre

(IT), the invasive front (IF) and normal tissue (NT) away from tumour. They were immunostained with cytotoxic and immune modulators antibodies. A software dedicated to TMA morphometric analysis with virtual slides was developped, allowing to study the density of the immunostained cells.
Results: As expected, a significant increase of CD3+ T lymphocytes, cytotoxic T lymphocytes CD8+, Granzyme B+ , memory lymphocytes CD45RO+ is evidenced in MSI colorectal cancer compared to MSS and associated with an increase expression of immunecheck points (PD-L1, PD1, LAG-3) and immune modulators (IDO1).
Conclusion: The next step is to investigate the prognosis impact of these markers and a potential immunoscoring relevance.

OFP-04-007
E-learning for determining the tumour-stroma ratio (TSR) as addition in routine diagnostic pathology; the UNITED study
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Background & Objective: The UNITED study (Uniform Noting for International application of the Tumour-stroma ratio as Easy Diagnostic tool) was designed to prepare implementation of the tumour-stroma ratio (TSR) in routine diagnostic pathology. For standardization and to reach consensus an E-learning was developed. TSR is a practical and fast assessment, to distinguish within stage II-III colon cancer (CC) patients, who will likely benefit of adjuvant therapy and who will not.
Method: The online training starts with an instruction movie available via www.watchstroma.com. The E-learning (developed in PathXL) consists of a training and test set, each with 40 CC cases. It is an online tool using digitalised Haematoxylin & Eosin stained sections. To evaluate the reproducibility of TSR scores, inter- and intra-observer agreements will be calculated. After completion of the E-learning, committed pathologists will participate in the prospective study measuring TSR in 1500 patients CC stage II and III.
Results: At this moment colorectal cancer pathologists from more than 10 European countries and 15 centres agreed to participate in the UNITED study. It takes about 45 minutes to complete a set. Eight pathologists tested the E-learning with inter-observer agreements (Kappa-score) between 0.6 and 0.81. The E-learning has become recently available. Based on preliminary results we expect all data to be ready to present at the congress.
Conclusion: Training by using an E-learning tool can result in a highly consistent and standardized method. This has an important effect on the strength of the UNITED prospective trial. Ultimately, this trial will lead to a new biomarker for selecting patients for adjuvant treatment.

OFP-04-009
MicroRNAs as markers of epithelial-mesenchymal transition in colorectal cancerogenesis
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Background & Objective: MicroRNAs are small, noncoding RNAs that regulate gene expression by posttranscriptional regulation of target genes. miR-200 family (miR-200a/b/c, miR-141, miR-429) has been shown experimentally to regulate epithelial-mesenchymal transition (EMT) in various physiologic and pathologic conditions, including cancer. As EMT is the postulated mechanism of carcinoma development and progression, we analysed the expression of these microRNAs in colorectal cancerogenesis.
Method: We analysed the expression of miR-200 family using quantitative real-time polymerase chain reaction. Forty cases of formalin-fixed paraffin-embedded tissue were included (10 adenomas, 10 malignant adenomas/early carcinomas, 10 cases of carcinoma without nodal metastases and 10 cases of carcinoma with nodal metastases). Cases of carcinoma included both tumour tissue as well as corresponding normal mucosa.
Results: We found down-regulation of the miR-200a/c, miR-141 and miR-429 in carcinoma with nodal metastases compared to carcinoma without nodal metastases. Moreover, miR-200b/c showed up-regulation in malignant adenoma/early carcinoma compared to adenoma and carcinoma with and without nodal metastases. miR-429 showed up-regulation in malignant adenoma/early carcinoma and carcinoma without nodal metastases compared to adenoma.
Conclusion: Down-regulation of the miR-200 family in colorectal carcinoma with lymph node metastases compared to carcinoma without lymph node metastases strongly supports the postulated role of EMT in carcinoma progression and metastasizing. However, our finding of up-regulation of miR-200b/c and miR-429 in malignant adenoma/early carcinoma is not consistent with the postulated role of EMT in the progression of adenoma to malignant adenoma.

OFP-04-010
Somatic copy number alterations as a biomarker of recurrence in stage II colon cancer patients
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Background & Objective: Stage II colon cancer (CC) holds a major therapeutic challenge since adjuvant chemotherapy is not systematically indicated. However, up to 15% of stage II CC patients show recurrence within 5 years after surgery. This is partially due to the fact that lymph node staging is not sensitive enough and the lack of molecular biomarkers able to predict relapse. We aimed to identify genomic imbalances associated with the increased risk of recurrence in stage II CC.
Method: Here we analyzed 84 stage II (pT3-T4, N0) CC using SNP-arrays and fluorescence in situ hybridization (FISH) to identify copy number alterations (CNAs). We also collected pathological risk factors data, microsatellite instability status, CDX2 expression, tumour infiltrating lymphocytes and microenvironment components.
Results: Our data showed that tumours of patients with recurrence have a greater amount of CNAs. Moreover, our results suggest several candidate genomic regions to discern patients at risk of recurrence, such as the loss of 6q22.31 and 17q24, the gain of 13q, and copy-neutral LOH at 17p13. The single-cell based analysis of FISH signals showed increased levels of intratumour heterogeneity in primary tumours with higher rates of chromosome instability ($P<0.0002$). Additionally, patients with relapse showed higher number of subclonal cell populations involving chromosome13 gains than those without recurrence (median of 4.56 vs 3.88).
Conclusion: Intratumour heterogeneity mediated by the increased levels of genomic instability and acquisition of genomic imbalances might be associated with the risk of recurrence in stage II CC.

OFP-04-011
Tumour budding in gastric carcinomas: a promising indicator of prognosis
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Background & Objective: Tumour budding frequently observed in carcinomas of the gastrointestinal tract. The aim of this study to investigate tumour budding in gastric carcinomas.
Method: Study compromised 95 patients with the diagnosis of gastric cancer between 2011-2018. All patients who underwent curative total or subtotal gastric resection with regional lymph node dissection. Data

collected for analysis including age and gender of the patients, resection type, localization, size, histologic differentiation, and presence of lymphovascular invasion, perineural invasion, tumour budding, and lymph node status. The mean follow-up of the patients was 21,6±20,6 months.

Results: The mean age of the patients was 64,3±11,6 (range, 35-86 years), while the male to female ratio was 59/36. The mean size of the tumours was 5,8±3,5 cm (range 0,5-19 cm). Among 95 patients, 59 had adenocarcinomas, 31 had poorly cohesive carcinomas, and 5 had mucinous adenocarcinomas. Tumour budding found correlated with the tumour type, perineural invasion, peritumoural desmoplasia and patient survival in this study. We found a relationship between increased peritumoural desmoplasia and tumour budding. Lymphovascular invasion, as an independent prognostic parameter, found to be related to patient survival ($p=0.01$). In this study group, we didn't find a relation between the lymph node metastasis and tumour budding. Although tumour budding was found lesser in poorly cohesive carcinomas than adenocarcinomas ($p<0.05$), tumour budding reduced the overall 1-year and 3-year survival rates of poorly cohesive carcinomas from 40% to 22% and, 9% to 0% ($p=0.03$).

Conclusion: Tumour budding may be used as a parameter of tumour aggressiveness and as an indicator of unfavorable outcome.

OFP-04-012

Traditional serrated adenomas do not always prefer the colorectum

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Background & Objective: Traditional serrated adenomas (TSAs) outside the colorectum are quite rare and are believed to be aggressive lesions requiring total excision of the polyp to rule out the possibility of dysplasia or invasive neoplasia. In this study, we aimed to identify the immunophenotipic characteristics of upper GI TSAs and relate them to the serrated neoplastic sequence.

Method: A total of 12 TSAs located outside the colorectum were recruited and analyzed using an immunohistochemical panel including CK7,CK20, CDX2, B-Catenin, MUC2, MUC6, MUC5AC, P53, Ki67, MLH1, MSH2, MSH6, PMS2. Differential expressions of the antibodies were correlated with the characteristic and neoplastic features of this entity.

Results: Of 12 TSAs, 7 were located in the small intestine where two had invasive carcinoma, two showed low or high grade dysplasia while 5 were gastric TSAs among which one had invasive, two had intramucosal carcinoma and one had low grade dysplasia. Dysplastic and/ or neoplastic areas showed diffuse positivity with Ki67 and p53 and showed membranous Beta-catenin staining. Gastric differentiation was observed focally in 10 polyps with MUC5AC and MUC6 expressions whereas, 9 polyps showed focal MUC2 positivity. While all showed diffuse positivity with CK20 and CDX2, only 9 had focal CK7 positivity. Two (one gastric, one small intestine) TSAs were MSI.

Conclusion: Pathologists should be aware of unusual localization of TSAs and evaluate such cases with great care using immunohistochemistry in order to identify the aggressive potential of these polyps which is highly likely.

OFP-04-013

Radial asymmetry of histologic reflux findings at the gastro-oesophageal junction: greater sensitivity and better clinical correlation at the lesser curvature

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Background & Objective: The significance of histologic diagnosis of gastro-oesophageal reflux disease (GORD) is controversial. In the prospective Central European multicentre histoGERD trial, we investigated whether conflicting data in the literature are related to the site of biopsy sampling.

Method: Seven hundred and seventy-six individuals (410 females and 366 males, median age 54 years) participated in the study. Biopsy material was systematically sampled from above and below the gastro-oesophageal junction and analysed separately for the lesser and greater curvatures. Acute reflux-associated changes of the oesophageal squamous epithelium were assessed according to the Esohisto consensus guidelines.

Results: At the lesser curvature, 175 (22.6%) individuals had severe reflux-associated changes, compared with 115 (14.8%) at the greater curvature ($p=0.0002$). In all, biopsies from the lesser curvature had a higher sensitivity (84.6% vs. 72.7%) and specificity (93.2% vs 91.6%) for the detection of microscopic oesophagitis. Cardiac mucosa (54.8% vs. 47.6%, $p=0.0052$) and intestinal metaplasia (13.9% [sensitivity 81.2%] vs. 7.1% [sensitivity 41.2%], $p<0.0001$) were also more frequently observed at the lesser curvature, and biopsies obtained from this site showed a better correlation with patients' symptoms and the endoscopic diagnosis of oesophagitis.

Conclusion: Histologic findings of GORD are not uniformly distributed at the gastro-oesophageal junction. Biopsies taken at the lesser curvature show a higher sensitivity for the diagnosis of microscopic oesophagitis. This applies to both (acute) inflammation-related changes of the squamous epithelium and their (chronic) consequences, such as cardiac and intestinal metaplasia.

OFP-04-014

Involvement patterns in inflammatory bowel disease: differences between initial and follow-up biopsies

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Background & Objective: The diagnosis of inflammatory bowel disease (IBD) requires multiple site colon biopsies including terminal ileum (TI). Therapy might have an effect in the involvement pattern of these sites by the disease. We examined the initial and follow-up biopsies of IBD patients in order to determine the involvement patterns in Crohn's disease (CD) and Ulcerative colitis (UC).

Method: A total of 268 IBD patients with multiple biopsies obtained from TI and five colonic segments were evaluated for activity (cryptitis, crypt abscesses, ulceration) and chronicity (crypt distortion, mucin depletion, pyloric/paneth cell metaplasia) in all localizations. Comparisons were committed using Chi-square test.

Results: There were 167 UC (62.3%), and 101 CD (37.7%) patients with a male predominance in the UC group (59.9% vs. 43.6%, $p<0.01$). Among the cases with follow-up biopsies (68.3%) the majority were UC (73.1% vs 60.4%, $p<0.05$). TI and right colon involvements were more frequent in CD both in initial and follow-up biopsies (85% and 73.8% for TI, $p<0.01$; 37.5% and 37.7% for right colon, respectively, $p<0.05$). Pancolitis was higher in UC in both biopsies (60% and 33.6%, $p<0.01$) than CD. No difference was observed in CD between the initial and follow-up biopsies in contrast to UC which showed more left colon involvement in follow-up biopsies (62.3%, $p<0.01$). In UC, disease activity was correlated in TI and right colon ($p<0.05$, Phi=0.174).

Conclusion: Follow-up biopsies of pancolitic UC presented with either right or more commonly left colon involvement reflecting the effect of medical treatment while no such difference was observed in CD.

OFP-04-015

Pathogenesis of fibrosis in Crohn's disease

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Background & Objective: Fibrosis is an important complication of Crohn's disease (CD). It is believed to result from tissue damage due to chronic inflammation and impaired wound healing and is characterised by proliferation of myofibroblasts and excessive deposition of extracellular matrix proteins. Despite significant morbidity, pathogenesis of fibrosis including origin of myofibroblasts is poorly understood.
Method: We analyzed resection specimens from 30 patients with CD. Normal mucosa from resection specimens of colorectal carcinoma was used for comparison. Samples were stained with Trichrome Masson and immunohistochemically for smooth muscle actin (SMA), CD34 and stem cell markers ALDH1, CD44, Oct4 and SOX2.
Results: In normal colon, we found numerous CD34+ ALDH1+ CD44+ spindle cells in the submucosa and subserosa, particularly around blood vessels. In CD, fibrosis highlighted by Trichrome Masson was found in the submucosa and subserosa, together with proliferation of SMA+ myofibroblasts and disappearance of perivascular spindle cells.
Conclusion: 1. Hot spots for fibrosis in CD are submucosa and subserosa. 2. Fibrosis in CD is characterised by proliferation of myofibroblasts and disappearance of perivascular spindle cells (pericytes/fibroblasts). 3. Distribution of pericytes/fibroblasts in the normal bowel wall, and their disappearance in fibrosis, in parallel with the appearance of myofibroblasts suggest that pericytes/fibroblasts are the source of myofibroblasts in CD. 4. These cells expressed stem cell markers, further supporting their postulated role as origin of myofibroblasts. 5. Pathogenesis of fibrosis in CD is thus comparable to fibrosis/scar formation in other organs, in which perivascular cells (fibroblasts/pericytes) have emerged as origin of myofibroblasts.

Monday, 10 September 2018, 08:30 - 12:00, Room A2
OFP-05 | Joint Session: Pulmonary Pathology / Nephropathology

OFP-05-001

Light chain proximal tubulopathy in the spectrum of B-cell dyscrasia induced renal disease

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Background & Objective: B-cell dyscrasia can cause a multitude of renal pathologies even when sometimes diagnostic criteria for multiple myeloma (MM) or B-cell Non-Hodgkin lymphoma (BNHL) are not fulfilled. Therefore, the term of "monoclonal gammopathy of renal significance (MGRS)" was coined. The aim of this study was to assess the role of light-chain proximal tubulopathy (LCPT) in the context of LC-induced renal diseases.
Method: A consecutive cohort of 320 renal specimens was collected including cases with a history of MM, BNHL, MG or monoclonal immunoglobulin (Ig)/LC induced nephropathy. Special attention was paid to immunohistochemical LC restriction in proximal tubules and/or intracytoplasmic crystals as hallmarks of LCPT.
Results: LCPT was a frequent finding observed in about a quarter of analyzed specimens. In nearly three quarters it was associated with another LC-induced disease, especially LC-Cast-nephropathy (Cast-NP). A subgroup of LCPT (11.4%) was not associated with significant acute tubular injury (ATI) and showed better renal function than the remaining LCPT cases. After exclusion of cases with concurrent Cast-NP, LCPT was not associated with inferior renal function at diagnosis compared to non-LCPT cases.
Conclusion: In summary, LCPT is frequent in the context of renal disease in B-cell dyscrasia and associates with Cast-NP. This might indicate that it is in many instances a consequence of a high monoclonal plasmacell burden as usually found in Cast-NP. Together with the fact that a subgroup of LCPT is not associated with significant ATI these findings imply that in part LCPT is a tubular trafficking-phenomenon rather than an independent disease entity.

OFP-05-002

An integrative approach for the assessment of peritubular capillaritis extent and score in microvascular inflammation – association with transplant glomerulopathy and graft loss

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Background & Objective: In active antibody-mediated kidney allograft rejection (ABMR) the microvascular inflammation score (MVI), a positive C4d staining or gene transcripts of endothelial damage are currently seen as surrogates of HLA antibody-antigen interaction as they are strong predictors of TX-glomerulopathy (TG) and TX-loss. We recently observed the association of diffuse extent of peritubular capillaritis (ptc - inflammation in >50% of cortical peritubular capillaries) with increased risk of TX-loss and higher DSA-values. We tested the suitability of this pattern as additional surrogate of ongoing HLA-antibody interaction.
Method: We retrospectively reevaluated 616 patients for ptc morphology, TG in all biopsies (n= 1619) and death-censored TX-loss. We assessed more precisely our cases with a Ptc score=1, diffuse ptc extent and no glomerulitis (ptc1diffuse, n=26), currently not diagnostic for ABMR.
Results: Positive C4d and MVI-scores≥2 were found in 11 and 19% of the samples, TG in 13% of the patients. Including ptc1diffuse in the group of MVI≥2 significantly increased the AUC for TG (0.602, p=0.008) compared to the current MVI≥2 (0.560, p=0.12). After adjustment for confounders (C4d or cellular rejection), ptc1diffuse remained independently associated with TG [OR 3.89, p=0.008]. Patients with ptc1diffuse had significantly worse TX-survival than patients with MVI≥2 and <2 (42 vs.59 vs.70%, p=0.002).
Conclusion: Our integrated approach for ptc morphology, including the distribution of ptc (diffuse ptc) in the assessment of MVI, was better than current recommendations for the prediction of TG and subsequent TX-loss risk. It highlights a risk population currently not identified as such.

OFP-05-003

Molecular assessment of C4d positive renal transplant biopsies without evidence of rejection

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Background & Objective: Immunohistochemical staining for C4d in peritubular capillaries is part of the definition of antibody-mediated rejection (AbMR) in the Banff Classification for Allograft Pathology. However, the clinical significance of C4d-positive biopsies without other evidence of rejection (C4d+ WER) is unknown. Our aim was to investigate the molecular significance of C4d positivity in such biopsies.
Method: RNA was extracted from formalin-fixed paraffin-embedded renal transplant biopsies (n=157) and gene expression analysis of 35 AbMR-associated transcripts was carried out using the NanoString nCounter system.
Results: AbMR-associated transcripts were significantly increased in samples with AbMR or suspicious for AbMR. A subgroup of 17/35

transcripts that best distinguished AbMR from C4d negative biopsies without evidence of rejection (C4d-WER) was used to study C4d+ WER samples. Most of the C4d+WER biopsies clustered with non-rejection biopsies in a heat map with hierarchical clustering. The 17 transcripts showed no differential expression between C4d- and C4d+ WER biopsies from both ABO incompatible and ABO compatible transplants. The geometric mean of the 17 transcripts was used to assign the C4d+WER patients a high- or low-risk score for AbMR. Follow-up biopsies showed AbMR within 1 year of the initial biopsy in 5/7 high-risk patients but only 2/46 low-risk patients. Logistic regression identified transcript risk group as a predictor of future AbMR, whereas factors including C4d score, DSA status, ABO status, number of transplants and time post transplant of biopsy were not.
Conclusion: Gene expression analysis in samples showing C4d positivity without evidence of rejection has the potential to identify patients at risk of imminent AbMR.

OFP-05-004

Thrombotic microangiopathy (TMA) in a cross-sectional study of native and transplanted kidneys: morphological, immunohistochemical and ultrastructural characterisation

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Background & Objective: Thrombotic microangiopathy (TMA) is a rare severe pathology defined as microvascular endothelial injury, thrombosis, thrombocytopenia and MAHA, often affecting the kidneys. Since TMA may manifest without thrombi, diagnosing TMA in kidney biopsies is demanding.
Method: Accepted morphological criteria were analyzed in archival routine paraffin sections of 225 TMA cases.
Results: TMA patients' (female 45%) age ranged from 4 to 81 years. 45% of TMA cases occured in kidney transplants (KTx), 53% of these had rejection (cellular 7%, humoral 34%, mixed 12%). Thrombi were identified in 71% of KTx TMA cases (glomerular 41%, arteriolar 40%, arteries 25%) compared to 67% of native kidneys (glomerular 38%, arteriolar 53%, arteries 41%). Most useful histological TMA criteria were fragmented red blood cells (glomerular 65%, arterioles/arteries 67%), fibrillar appearance of mesangium (66%), endothelial swelling (glomeruli 68%, arterioles 67%), thickened capillary walls (66%), collapse of capillary tuft (92%) and arterial intimal mucoid edema (arteries 78%, arterioles 47%). Detailed ultrastructural comparison between TMA combined with humoral rejection and humoral rejection alone could not define any differences between these two groups. Grouping of clinically well-characterized patients regarding the underlying cause for TMA showed differences between morphological criteria comparing genetically verified atypical HUS (e.g. arteriolar/hilar involvement), humoral transplant rejection and toxic injury (e.g. gemcitabine revealed more glomerular and overall thrombi). Stains for thrombomodulin, heparanase-2, CD34, and glycocalyx did not seem to mirror these morphological differences hitherto.
Conclusion: Certain morphological criteria vary in their diagnostic value and show differences between causes of TMA. Morphologically and ultrastructurally, humoral rejection shares numerous similarities with TMA.

OFP-05-005

Precisely quantified B-cell infiltration in whole slide images (WSI) correlates with borderline, cellular and combined rejection in a cross-sectional study of transplanted kidneys

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Background & Objective: Digital morphological approaches may facilitate the characterization of immune cell-mediated renal tissue injury in transplanted kidneys as precise quantification and localization of immune cells by eye is challenging.
Method: A total of 766 renal allograft biopsies, including both biopsies for clinical cause (57.8%) and biopsies from the Hannover Protocol Biopsy Program, were stained in an automated manner (Ventana) for B-cells using a monoclonal CD20 antibody, scanned (Leica), and subsequently analyzed for immunopositively stained area (%/region of interest) using a pixel-based digital approach (Definiens Tissue Studio). Results were evaluated separately for cortex, medulla, and extrarenal tissue.
Results: B-cell abundances in the biopsies (40.8% from females; age ranging from 2-78 years) differed significantly between patients with vs. without rejection (according to Banff criteria) and showed highest means ($p \leq 0.05$) in cellular rejection (no rejection: cortex 0.33%, medulla 0.14% ; borderline: cortex 0.65%, medulla 0.12%; cellular rejection: cortex 1.26%, medulla 0.35%; humoral rejection: cortex 0.33%, medulla 0.14%; combined rejection: cortex 0.67%, medulla 0.10%). Positive correlations ($p \leq 0.05$) for cortical B-cell densities were also obtained for fibrosis grades according to Banff category 5 and Banff coding for i, t, ti, v, ptc, ci and ct.
Conclusion: Cortical and medullary B-cell densities rather display high values in cellular (including borderline and combined rejection) than in humoral rejection. Associations with clinical data and long-term allograft outcome are currently under investigation.

OFP-05-006

Kidney biopsy codes for pathologists: towards a generally applicable terminology and coding system

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Background & Objective: Kidney biopsy registries benefit research, teaching and policy-making using larger biopsy series. However, these registries are mainly using locally developed classifications with corresponding codes for registration of pathology diagnoses, and classification rules are not always provided. As classes often have not been mapped to an underlying terminology system, the different systems hamper or even prohibit comparison, exchange or accumulation of data. Consequently, there is a great need for a more standardized, universally applicable terminology and interoperable coding. Therefore we started the project "Kidney Biopsy Codes (KBC)", aiming to provide a complete and structured set of terms and codes applicable to every non-neoplastic kidney biopsy by any nephropathologist, nephropathology unit or kidney biopsy registry.
Method: The project will be carried out in 5 work packages (WP), from April 2018 to mid 2019. WP1 investigates the current status of existing registries, current coding of renal biopsy diagnoses as well as analysis of strengths and weaknesses in international coding systems. WP2 designs principles for the new KBC system. WP3 addresses the technical design and generates the KBC as such. WP4 addresses review and improvement of the KBC by stakeholders. WP5 establishes structures crucial for maintenance and further development of the KBC. Cooperation with existing systems and organizations will be actively pursued.
Results: Results will be published in the scientific literature.
Conclusion: The KBC project has recently started, aiming to provide a comprehensive, generally applicable, interoperable and easy-to-update coding structure for recording of kidney biopsy diagnoses by pathologists.

OFP-05-007

The more the micropapillary pattern in stage I lung adenocarcinoma, the worse the prognosis - a retrospective study on digitalised slides

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Background & Objective: Although the majority of lung adenocarcinomas show mixed pattern, only the predominant component is taken into account according to the novel classification. We evaluated the proportion of different patterns and their impact on overall survival (OS) and disease-free survival (DFS).
Method: Patterns were recorded according to predominance and their proportions were rated and calculated by objective area measuring on digitalized, annotated slides of resected stage I lung adenocarcinomas. Spearman-rank correlation, Kaplan-Meier models and the log rank test were used for statistical evaluation.
Results: 243 stage I adenocarcinoma were included. Lepidic pattern is more frequent in tumours without recurrence (20% vs. 8%), and lepidic predominant tumours have favourable prognosis (OS: 90.5%, DFS: 89.4%), but proportions above 25% are not associated with improving outcome. Solid and micropapillary patterns are more frequent in patients with recurrence (48% vs. 5% and 13% vs. 4%) and predominance of each one is associated with unfavourable prognosis (OS: 64.1%, DFS: 56.3% and OS: 28.1%, DFS: 28.1%, respectively). Above 25%, a growing proportion of solid or micropapillary pattern is not associated with worsening prognosis. In contrast, tumours having micropapillary pattern as secondly predominant, form a different intermediate group (OS: 51.1%, DFS 57.8%).
Conclusion: Our study was based on measured area of each growth pattern on all available slides digitalized. This is the most precise way of determining the size of each component from the material available. We propose using predominant and secondly predominant patterns for prognostic purposes, particularly in tumours having solid or micropapillary patterns.

OFP-05-008

Genetic MET alterations in non-small cell lung cancer: biologic differences and analogies

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Background & Objective: Non-small cell lung cancer (NSCLC) is one of the most common cancers and a leading cause of cancer-related deaths. The characterization of its genetic alterations, including MET aberrations, has drastically changed treatment options and overall survival. Aim of the study was to assess biological differences in the genomic background between MET amplifications and mutations.
Method: A subset of treatment-naïve NSCLC cases with either a MET high-level amplification (n=17) or MET exon 14 skipping mutation (n=17) was analyzed using next generation sequencing, gene amplification/translocation FISH-analysis, copy number variation analysis and MET-protein expression analysis.
Results: The MET-mutant cohort was represented predominantly by never-smokers, older female patients (p<0,001) showing recurrent MDM2 (n=6), CDK4 (n=3) and HMGA2 (n=3) amplifications. No other driver mutations were detected. Conversely, the MET-amplified group, represented smoker, younger male patients, harbored pathogenic KRAS mutations (n=3) and a higher frequency of TP53 mutations (p=0,016). Interestingly MET amplifications occurred more frequently as subclonal event, whereas MET mutations were present at high allele frequencies. High copy number variation burden was reported in both groups. MET-immunohistochemistry was demonstrated to be a reliable screening method for amplifications, but not suitable for mutations.
Conclusion: MET-mutant and MET-amplified cases differ significantly: the MET-mutant cohort harbored no co-occurring driver mutations, supporting the hypothesis that MET mutations may represent a strong oncogenic driver. Conversely, MET amplifications seem to occur primarily subclonally, in the background of other genetic driver events. Therefore, MET amplifications should always be interpreted in the context of the genetic tumour background, in particular when considering MET inhibition treatment options.

OFP-05-009

The expression and prognostic value of somatostatin receptor 1-5 in pulmonary carcinoid tumours

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Background & Objective: Pulmonary carcinoids (PC) belong to neuroendocrine tumours that often overexpress somatostatin receptors (SSTR). This overexpression provides a molecular basis for tumour imaging and therapeutic interventions with somatostatin analogs (SSA). The aim of this study was to evaluate SSTR1, SSTR2, SSTR3, SSTR4, and SSTR5 distribution in a large set of PCs as well as to investigate if the expression associates with clinicopathological parameters and patient outcome.
Method: Histological samples (n=164) from consecutive PC patients treated surgically between 1990 and 2013 were retrieved through the Helsinki Biobank and the Auria Biobank. Clinical records were retrospectively reviewed. Tissue specimens were re-evaluated according to the World Health Organization 2015 classification, processed into tissue microarray format and stained immunohistochemically with Ki-67 and SSTR1-5.
Results: Based on re-evaluation, 77% (n=126) of the tumours were typical carcinoids (TC) and 23% (n=38) atypical carcinoids (AC). Expression of SSTR1, SSTR2, SSTR3, SSTR4, and SSTR5 was detected in 52%, 86%, 55%, 15%, and 32% of the tumours, respectively. All SSTRs expressed membranous staining. SSTR expression was associated with tumour proliferation, metastatic potential, and patient outcome.
Conclusion: We showed that PC tumours express SSTRs immunohistochemically which provides a rationale for the imaging and treatment of these tumours with somatostatin analogs. As SSTR expression associates with tumour proliferation, metastatic potential, and patient outcome, these receptors may offer also a possibility for individualized prognosis estimation.

OFP-05-010

Nuclear RAD51 protein is associated with tumour-infiltrating lymphocytes (TILs) and survival outcomes in non-small cell lung cancer patients, treated with neoadjuvant chemo-/radiotherapy

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Background & Objective: The effect of DNA repair on the tumour microenvironment is not well studied. We aimed to analyse the relationship between the expression of nuclear RAD51 protein and tumour infiltrating lymphocytes (TILs) chemotherapy-naive versus chemotherapy-pretreated patients non –small cell lung cancer (NSCLC).
Method: The training set included 96 patients from the University Hospital Olomouc, Czech Republic, from which 20 patients were treated with platinum-based neoadjuvant chemotherapy. The validation set included 1109 patients from the University Hospital, Zurich, Switzerland, from which 126 were treated with neoadjuvant platinum-based chemotherapy and/or radiotherapy. TMA sections from training and validation sets were staind with antibodies against RAD51, CD8, CD68 and PD-L1. TILs were assesed in matched H&E slides.

Results: The loss of nuclear RAD51 protein was associated with increased number of TILs in patients treated with neoadjuvant chemo-/radiotherapy in both training (r=-0.388, p=0.001) and validation (r=-0.292, p=0.011) sets. In addition, nuclear RAD51 positivity (Hscore>0.2) and decreased numbers of TILs (dichotomised for median) was associated with poor overall and disease-free survivals (p<0.05)
Conclusion: The present results suggest low RAD51 expression to be a surrogate marker for a high tumour mutational burden in patients with NSCLC receiving neoadjuvant treatment. RAD51 expression should further be assessed as a potential biomarker for the treatment with PD-(L)1 targeting monocloncal antibodies.

OFP-05-011
Spread through air spaces (STAS) is a predictor of poor outcome in pulmonary carcinoids
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Background & Objective: Spread through air spaces (STAS) is a recently recognized prognostic factor for pulmonary adenocarcinomas and squamous cell carcinomas. Pulmonary neuroendocrine neoplasms (NEN) include lesions having variable morphology and a heterogeneous clinical behavior, with few factors predicting the outcome, therefore the aim was exploring the presence and potential prognostic role of STAS.
Method: A retrospective series of 260 surgically resected NENs, including 230 carcinoids and 30 control high-grade small and large-cell NE carcinomas, was reviewed. STAS was defined by the presence of neoplastic nests or single cells in air spaces beyond the tumour edge. In selected lung cancer cases, c-MET expression, an invasive growth and poor prognosis marker, was evaluated.
Results: Clinico-pathological parameters and survival were correlated by univariate and multivariate analyses. STAS was identified in 32.7% of NENs (85/260) and 26.9% of carcinoids (62/230). STAS increased with increase of tumour grade, occurring in 20.5% typical carcinoids, 42% atypical carcinoids, 71% large-cell and 88% small-cell carcinomas. STAS presence in carcinoids was significantly correlated with patients' sex, age, angioinvasion and nodal status. STAS was associated to a shorter time to progression and overall survival in the whole series, and with survival within the atypical carcinoid subgroup. A stronger c-MET expression was observed in carcinoids rather than high-grade carcinomas, including reactivity in peripheral tumour cells and STAS.
Conclusion: In conclusion, STAS is of prognostic relevance also in pulmonary neuroendocrine neoplasms, being a significant predictor of poor survival in carcinoids, including the atypical forms, that currently have the most unpredictable outcome.

OFP-05-012
Transbronchial cryobiopsy: a single-center experience
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Background & Objective: Transbronchial cryobiopsy (TBC) is establishing itself as a diagnostic tool for diffuse parenchymal lung diseases (DPLD) with a higher diagnostic yield than a classic transbronchial biopsy (TBB) and fewer peri- and post procedural complications than an open surgical lung biopsy. Our goal was to present our experience with this procedure and demonstrate its value in the diagnostic workup of DPLDs.
Method: We analyzed 50 cryobiopsies performed between 2016 and 2018 at our clinic in the workup of 50 patients aged from 46 to 80 (mean 67 years) with a clinically suspicious DPLD. In 19 cases the clinical suspicion was hypersensitivity pneumonitis (HSP), in 8 lung involvement in connective tissue diseases (CTD), in 9 idiopathic pulmonary fibrosis (IPF), in the remaining 14 cases the working diagnoses were various. We compared the histological findings in TBBs with the histological findings after TBCs.
Results: 45 TBCs were diagnostic, 3 non-diagnostic and 2 suboptimal. UIP was the most common pattern, 14 cases, followed by 11 cases of NSIP, 9 HSP, 2 obliterative bronchiolitis, 2 bronchiolitis, 2 unclassified fibrosis, 1 NSIP with features suggesting a CTD, 1 PLCH and 1 peribronchiolar fibrosis. In 36 cases a TBBs was performed before TBC. In 33 cases the findings were non-diagnostic. In 3 cases a possible DPLDs was suggested.
Conclusion: TBCs have a higher diagnostic yield than TBBs for DPLDs. We would recommend this procedure as a replacement for TBBs for the diagnosis of DPLDs.

OFP-05-013
Impact of tumour budding, cell nest size and spread through airspaces in pulmonary squamous cell carcinoma
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Background & Objective: Tumour budding is a well-established independent prognostic factor in various cancer types (e.g. colorectal). Recently, grading systems that utilize tumour budding and other morphological parameters have been proposed as prognostic factors in pulmonary squamous cell carcinoma (pSQCC).
Method: We analysed a cohort of 354 primarily resected pSQCCs (2000-2013) (UICC 2017 stage I n=108, II n=117, III n=119, IV n=10). The parameters cell nest size, tumour budding (≤4 tumour cells; assessment following the recommendations of the International Tumour Budding Consensus Conference (ITBCC)), spread through airspaces (STAS), and desmoplasia were evaluated. Morphological findings were correlated with clinical and survival data.
Results: Low tumour budding (0-4 buds) was observed in 41%, intermediate (5-9 buds) in 30%, and high (≥10 buds) in 29% of cases (mean bud count=9, max=102). Cell nests of <1, 1-4, 5-15, >15 cells were present in 68%, 20%, 5%, 7%, respectively. We detected STAS in 32% of cases, desmoplasia in 68%. Tumour budding strongly correlated with tumour size, T-/ N- and UICC stage, assessed using HE and Pancytokeratin stained slides, and in continuous as well as categorized values (p<0.005). Tumour budding was a significant prognostic parameter for overall, disease specific and progression free survival (all p<0.005). Cell nest size and STAS showed no prognostic value.
Conclusion: The histomorphological parameter tumour budding provides an accurate prognostic stratification in pSQCC. Application of the scoring system recommended by the ITBCC is suitable for the evaluation of tumour budding in pSQCC.

OFP-05-014
Testing of ROS1-positive tumours by IHC displays a FISH-positive subgroup which might not benefit form recently approved drug therapy
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Background & Objective: Non-small cell lung cancer (NSCLC), still having a high mortality rate, show in many cases define genetic alterations, whereas rearrangements of the ROS proto-oncogene 1 (ROS1) gene occur in 1-2 %. Crizotinib, an inhibitor of ROS1-kinase activity, has been recently approved by the FDA for advanced stages of ROS1-positive NSCLC. Current gold standard for detecting ROS1-gene-rearrangements is by fluorescence-in-situ-hybridization (FISH), either by presenting a break-apart-pattern or by displaying one or more isolated-green-signals. But the last mentioned subset of ROS1-positive-cases seems not to benefit from the therapy. Therefore we wanted to further characterize this subgroup.

Method: ROS1-positive formalin-fixed, paraffin embedded (FFPE) tumour-samples, 10 with the classic break-apart-pattern and 10 with isolated-green-signals, were reevaluated by FISH (ZytoLight ® SPEC ROS1 Dual Color Break Apart Probe, Zytovision) and analyzed regarding ROS1-protein expression by immunohistochemistry (IHC) (D4D6®,Cell Signaling).
Results: 100% of the cases with break-apart-pattern show a detectable protein expression (either weak, moderate or strong). But in 80% of the cases with isolated-green-signals no protein expression was detectable and only 20% presented a weak or moderate staining.
Conclusion: Our results indicate that ROS1-positive tumours presenting isolated-green-signals in FISH seldom seem be able to produce a stable protein expression detectable by IHC. This could be the reason why most patients of this subgroup does not benefit form a Crizotinib-therapy, as in most cases the drug target is simply not present. But further investigations need to be done to understand the biology of this subgroup.

OFP-05-015
Focal adhesion ILK-PINCH-PARVIN complex interacts with KRAS signaling in human lung adenocarcinoma
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Background & Objective: The ternary complex of integrin-linked kinase (ILK), PINCH, and PARVIN (IPP complex) interacts with the cytoplasmic tail of beta integrins coupling cues from the extracellular matrix to the actin cytoskeleton. The IPP complex is known to be critically implicated in human cancer. Recent data from pancreatic cancer suggest a link between ILK and oncogenic KRAS. This study aimed to elucidate potential IPP-KRAS interaction in lung adenocarcinoma.
Method: IPP levels were evaluated by western blotting, qPCR and immunofluorescence (IF) in a panel of lung cancer cell lines with various KRAS levels (shKRAS, overexpressed KRAS) and mutational status (wt, mut) were evaluated. Levels of KRAS and downstream targets (pERK, pAKT) were also examined upon ILK inhibition. Effect of ILK targeting on cell proliferation of wtKRAS, mutKRAS and shKRAS lung cancer cell lines was examined by MTT assay. Expression of IPP complex was evaluated in human primary lung adenocarcinoma tissue samples and mouse lung tissue upon KRAS-driven lung carcinogenesis.
Results: IPP complex is downregulated in shKRAS lung cancer cell lines. ILK inhibition more effectively suppresses mutKRAS lung cancer cell proliferation. IPP components and EMT markers are overexpressed in human lung cancer tissue and their expression correlates significantly with aggressive clinicopathological parameters and poor prognostic outcome. IPP is also overexpressed in lung lesions from KRASG12D (lsl) mice examined.
Conclusion: These results suggest that there is a KRAS-IPP feedback loop in lung cancer enhancing oncogenic KRAS and IPP signaling with significant clinical relevance.

Monday, 10 September 2018, 08:30 - 12:00, Room B1
OFP-06 | Joint Session: IT in Pathology / Other Topics (Pathology in Favour of Developing Countries / Cardiovascular Pathology / History of Pathology / Autopsy Pathology)

OFP-06-001
Digitalisation of diagnostic histopathology slides: a comparative study and internal survey on perception toward the digital future
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Background & Objective: In this project, we performed a comparative analysis of four slide scanners with the aim of better identifying our institute's needs. Second, we investigate our pathologists' standpoint towards digital pathology.
Method: Two slide sets were used: 1) dayload approx. 1600 slides, 2) 34 slides including special stains, immunohistochemistry and cytological samples. Compared were file size, scan time, tissue recognition, image quality, re-scan rate, number of interruptions during batch scanning, and handling. A survey was sent to pathologists and residents encompassing questions about previous experiences, perceived advantages/disadvantages, machine-/deep-learning, attitude toward digital diagnostics.
Results: At 40x, the difference between smallest and largest file size was 4.5x. Major differences in scanning times were observed, reaching 1-minute difference between the longest and shortest. Only two scanners successfully scanned the full dayload without interruption. Re-scan rates were 9-19%, failure in tissue recognition ranged from 2.8-6.3%. Image quality and diagnostic confidence was considered high at 40x only. 75% of pathologists imagined working digitally but 50% anticipate problems with standardization. Image analysis is seen as an important benefit.
Conclusion: Each scanner has advantages and disadvantages and their proper fit into routine will be individual to an institute. In general, our pathologists are open to the digital future

OFP-06-002
Recognising molecular subtypes of colon cancer from virtual slides
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Background & Objective: Recent efforts in stratification of colon cancer (CC) patient population led to the identification of four consensus molecular subtypes (CMSs), representing the common denominator of several independently-developed molecular taxonomies. The current predictor of CMSs requires profiling hundreds of genes which clearly is not applicable in routine clinical practice. The goal of the current investigation was to establish image-based classifiers for CMSs that could operate independently and provide predictions for the most probable subtype.
Method: A set of n=200 virtual slides representing H&E sections of CC tumours and the accompanying whole-genome expression profiles were used for training CMS predictors. An independent set of n=100 virtual slides were used as validation set. For image feature extraction, we used deep convolutional neural networks trained on low magnification images (10x). A hierarchical decision system based on support vector machines with radial basis function kernels was trained and validated.
Results: The system identified a number of image features related to tumour architectural patterns that were preferentially enriched in one or several of the CMSs. The non-linear classifier built on these features achieved a good overall performance in predicting the CMSs (accuracy 0.85, 95% CI=(0.76, 0.91) on the validation set)
Conclusion: The virtual slides bear information that may be mined for building surrogate biomarkers for molecular subtypes of CC. Such system may operate autonomously and provide early indications of the most probable CMS.

OFP-06-003
A word mining approach to select immune-oncological biomarkers
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Background & Objective: The selection process of biomarkers is challenging in the era of high-throughput and multiplex techniques, because of the excessive amount of published data, and the given complexity of cancer in general - leading to either time consuming literature search, or a lack of representativeness of a given set of

biomarkers. However, using automatic text mining techniques from the field of artificial intelligence, one may augment a preliminary set of biomarkers which are manually selected by medical experts. Together, we applied an evidence-based method to generate a marker set for immune-oncological purpose.
Method: First, a large-scale dataset of 50.000 abstracts of highly cited publications from the field of immune-oncology was generated using a set of topic related search terms. Second, a chain of text extraction processing, and filtering methods were used to automatically compute a relevance-sorted list of biomarkers from this dataset. To validate these markers, we sought to investigate the expression of these markers among three common cancer types, including lung adenocarcinoma, lung squamous cell carcinoma, as well as malignant melanoma from the TCGA database for correlation with mutational burden, and estimated immune cell infiltrates.
Results: The analysis revealed a set of about 250 markers of interest, that were ranked according to our approach, and correlated to immune-cell infiltration, as well as mutational burden in the common cancer types.
Conclusion: Together, these findings underscore that empirical word mining approaches can shed light on to biomarkers that have been described in function-/ and or biological relevance in the literature, but may have been neglected previously in the field of cancer research.

OFP-06-004
The results of the quantitative evaluation of Ki67 by the open and commercial software for automatic image analysis in invasive breast carcinomas

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Background & Objective: Evaluation of the index of proliferative activity of Ki67 (LI Ki67) is variable between the researchers and is characterized by insufficient reproducibility. The method of digital image analysis makes it possible to improve the reproducibility and accuracy of the index estimation to create single recommendations. There are both commercial software products for image analysis, and freely distributed. For our research, we chose QuantCell software (module NQ) from 3D Histech and freeware QuPath software (module CD).
Method: We selected 100 cases of invasive breast carcinomas, G2-G3, which were retrospectively analyzed by an expert to assess the Ki67. Slides were scanned and the scans were analyzed in tumour zones with an area of 1 mm2.
Results: The CD and NQ modules did not differ significantly ($p = 0.1$). Analysis of the data of the CD module and the visual evaluation of the pathologist showed no difference ($p = 0.5$). We compared modules CD / NQ - ICC was 0.92 CI 95%, [0.86; 0.95] and CD / pathologist - 0.85 CI 95%, [0.73; 0.91]. Coefficient of correlation Spearman was 0.96, $p < 0.001$ for CD / NQ, and 0.9, $p < 0.001$ CD / pathologist.
Conclusion: The of LI Ki67 values obtained by the CD module of freeware software showed a strong correlation with the commercial software of NQ module, as well as the pathologist. Free software QuPath can serve as a tool for increasing the reproducibility of the Ki67 proliferative activity index and compete with commercial software for image analysis.

OFP-06-005
Development and implementation of a novel affordable telepathology approach for developing countries

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Background & Objective: Telepathology has been posited as a means of bolstering diagnosis delivery in developing nations. Digital divide and high costs for digital imaging technologies prevent the diffusion of telepathology in Low&Middle-Income Countries. A novel low-cost method for slides digitization and remote diagnosis-based con the innovative telemedicine platform WaidX has been implemented at Balbala Hospital, Djibouti, aimed to: enable real-time sharing of virtual slides to guide diagnostics decision making, conference calling for learning&training of local health workers, generation of a database for clinical data that serves as a departmental registry and as tool for future research use.
Method: The initiative was funded by APOF NGO. The telepathology system is comprised of a redundant WaidX physical core, one Olympus CX23 microscope equipped with a low-cost CCD camera, a HP PC equipped with Microvisioneer applications to support slides digitization and sharing. WaidX VoIP and Webex were used to establish the teleconference.
Results: The first telepathology interaction among Djibouti, Italy, San Marino and Germany occurred on March 26th, 2018. Demonstration of manual scanning revealed ease of use. Virtual slides were easily shared without compromise of the image resolution. Conference call quality was high. This conference has opened a series of remote training sessions devoted to immunohistochemistry, lead by APOF specialists.
Conclusion: Telepathology is feasible with excellent voice quality, slides sharing capability and real-time diagnostics. The database is under construction. We are developing a new affordable model for learning, training and collaboration in surgical pathology using WaidX, to enable rapid knowledge and technology transfer for a more equitable access to high-quality cancer care worldwide.

OFP-06-006
"Copper pennies in the tropics": chromoblastomycosis, a diagnosis not to be forgotten on tropical pathology

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Background & Objective: Chromoblastomycosis, a deep mycotic infectious condition, resulted from traumatic injury and inoculation of dematiaceous fungi is a slow-course disease, predominantly reported in rural areas with tropical or subtropical climate, in some instances associated with malignancy. Its diagnosis is simple, direct and feasible once accounted.
Method: A 62-year-old male complained about a slowly-growing, firstly painless, thigh lesion. On presentation to the dermatology clinics, exhibited an extensive ulcerated and verrucous thigh lesion, on which an incisive biopsy was performed.
Results: Histopathologic examination of the biopsy revealed an extensive ulcerative process, with marked acanthosis, pseudoephiteliomatous hyperplasia and superficial granulomas, on which usual dark-coloured sclerotic bodies were evidenced without the need for further special stains. No significant atypia or other infectious agents were detected.
Conclusion: Chromoblastomycosis is a feasible and direct diagnosis when accounted as a differential, no special stain is needed for direct observation of its pathognomonic sclerotic (Medlar) bodies, reported in up to 92.5% of cases. A highly suspicious differential should warrant its diagnosis in a slow-course kin lesion, ulcerated, with acanthotic, granulomatous, multinucleated giant cell from a tropical or subtropical climate country-originated patient, as Central and South America (Brazil, Uruguay), India, Sri Lanka, Madagascar. Histopathological exam should be granted to all suspicious lesions, including during treatment, in order to exclude malignancy-associated disease (squamous cell carcinoma), as

previously reported, allowing for specific treatment and follow-up on one of the most difficult deep fungal diseases to eradicate.

OFP-06-007

NK cells in endomyocardial biopsies from cardiac allografts: detection, quantification, and precise localisation using multiplex immunofluorescence

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Background & Objective: Among the complex cellular interplay engaged in cardiac rejection, recent transcriptomic analysis of endomyocardial biopsies (EMB) has detected NK cell transcripts in the setting of antibody-mediated rejection (AMR). The precise in situ detection of NK cells in EMB supporting this molecular signature remains to be done.
Method: FFPE sections from 51 EMB [10 without rejection (NOR), 21 with acute cellular rejection (ACR) and 20 with AMR] were analyzed with anti-NKp46 antibody by immunoperoxidase. To ascertain the precise intravascular or extravascular location of NK cells and their relationship with T lymphocytes and macrophages, multiplex immunofluorescence labeling kit Opal™ (PerkinElmer) was used with anti-NKp46, CD3, CD163 and CD34 antibodies for NK cells, T lymphocytes, macrophages and endothelial cells respectively. Computerized quantification and compartmentalization of all immune cells was performed with inForm® software (PerkinElmer).
Results: The density of NK cells was very low in NOR EMB (mean ± SEM: 0.44 ± 0.23/mm2) and significantly increased in AMR and ACR (12.32 ± 2.94 vs. 19.61 ± 6.77 respectively, $p<0.0001$). Both DAB and multiplex immunofluorescence labelings demonstrated a differential compartmentalization of NK cells in ACR vs. AMR: in ACR, most of NK cells were extravascular ($p<0.05$), whereas they were prominently intravascular in AMR ($p<0.05$). Multiplex immunofluorescence labeling showed that NK cells took part to graft inflammation during rejection together with T-lymphocytes and macrophages.
Conclusion: NK cells are recruited in both ACR and AMR. Their compartmentalization differs between ACR and AMR. NK cells colocalize with T lymphocytes and macrophages and appear as a cell type engaged in cardiac rejection.

OFP-06-008

Development of fibrosis in cardiac allografts: a comparative single-centre study of two consecutive decades

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Background & Objective: The use of mechanical circulatory support as bridge-to-transplant is growing due to limited donor availability. It is uncertain whether development of cardiac fibrosis in heart transplant allografts is influenced by previous mechanical circulatory support. This is particularly important, because cardiac fibrosis is causative for progressive deterioration of cardiac function.
Method: We compared levels of fibrosis in consecutive right ventricular endomyocardial biopsies harvested over two calendar years separated by a decade from which fibrosis data were available (n= 101 in 2001 versus n= 248 in 2011). Gender, age of both recipient and donor at time of transplantation and time after transplantation were considered, before the patients were subdivided into distinct groups by use of mechanical circulatory support.
Results: Overall fibrosis levels differed only insignificantly (non-MCS group 9.2% vs 6.0% MCS group in 2001; non-MCS group 8.8% vs MCS group 5.9% in 2011). But significant differences in scar levels were found between decades, which were increasing in the MCS group ($p<0.001$, 14.9% in 2001 vs 18.4% in 2011 and decreasing in the non MCS-group 22% in 2001 vs 15.3% in 2011).
Conclusion: No relevant variation in fibrosis, but in scar levels in endomyocardial right ventricular biopsies in the two different consecutive decades could be demonstrated. Given similar donor age, difference in scar levels may be viewed as consequence of longer support times on MCS during the last decade and differences in underlying pathology of heart failure. Our findings merit further investigations.

OFP-06-009

Toll-like receptors 2 and 9 type in diagnostics of myocarditis

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Background & Objective: To study the expression of toll-like receptors (TLR) 2 and 9 in the myocardium and to evaluate their possible diagnostic and prognostic role in patients with chronic myocarditis.
Method: Myocardial samples were taken from 23 patients with different forms of non-coronary myocardial damage (myocardial right ventricular biopsy, n = 21; autopsy material, n = 2). According to the presence of myocarditis sampleas were divided into group I with dilation cardiomyopathy and myocarditis (10 patients) and group II without myocarditis (13 patients). Histological and immunohistochemical (IHC) study of the myocardium were performed (vimentin, desmin, c-kit, Ki-67 and TLR2 and TLR9). PCR of blood samples and myocardium was made to detect herpes viruses and parvovirus B19.
Results: Active borderline lymphocytic myocarditis was diagnosed in all patients in group I and in 6 patients in group II, the viral genes were detected in the myocardium in 15 patients, including 5 without morphological signs of myocarditis. We found significant correlation only in TLR2 and TLR9 expression and the presence of morphological signs of active myocarditis. With borderline myocarditis, expression of TLR2 and TLR9 was lower than without myocarditis, which may reflect death depletion of cardiomyocytes in the late stages of the disease. The relationship between the expression of desmin and the persistence of viruses, as well as c-kit with the degree of myocardial dysfunction and cardiosclerosis.
Conclusion: TLR2 and TLR9 expression in the myocardium may be used as IHC markers of active myocarditis. The expression of these markers may reflect genetic predisposition to the myocarditis development and may be used as a key to potential target of therapy.

OFP-06-010

Histological and paleogenetic analyses of two pre-Columbian mummies

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Background & Objective: Several pre-Columbian mummies are preserved in the Museum of Anthropology of the University of Florence. These bodies were brought from South America to Italy in the second half of the 19th century. We studied the natural mummies of two adults dated back between 1410 and 1530.
Method: Complete autopsies, histological and genetic analyses were performed.
Results: Histopathological study on the tissue specimens of the lungs of the first mummy showed numerous alveoli, in large fibrous stroma, areas of pulmonary anthracosis and a massive presence of alveolar exudate compatible with the diagnosis of bronchopneumonia. The other corpse presented a marked megavisceral syndrome characterized by megacolon, megaoesophagus and cardiomegaly.

Amastigotes of Trypanosoma cruzi were clearly detected in the myocardial fibers. DNA was extracted and the shotgun metagenomic sequencing showed bacterial and fungal taxa that may resemble both the thanatomicrobiome and extant human gut microbiomes. Bacterial groups present in the mummies included the Bacillales, Enterobacteriales and, especially, the Clostridiales; it is feasible to hypothesize that these individuals were exposed to these pathogens by the ingestion of contaminated food and water. Furthermore, we detected the presence of sequences of Trypanosoma cruzi, Leishmania donovani and antibiotic-resistance genes.
Conclusion: The presence of antibiotic-resistance genes clearly indicates that these genes pre-date therapeutic use of these compounds and that they are not necessarily associated to a selective pressure of antibiotics use. Studies on the ancient microbiome represent an opportunity to better understand microbe-host interactions, the membership and ecology of microbes, the evolution of commensal and pathogenic microorganisms and their impact in health and disease.

OFP-06-011
Photography in pathology: history of medicine, art and science
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Background & Objective: Photography in Pathology is an important instrument that has great value to represent macroscopic and histological findings and to write academic or scientific publications. We decided to rescue, inventory and reclassify an invaluable photo collection held in our pathology department.
Method: A review of a photographic collection that belongs to the beginning of the 20th century was carried out. It has approximately 10.900 glass negatives of different sizes (8000 of 9 x 12 cm and 2900 of 13cm x 18cm) (gelatin silver bromide), with their paper copy (silver gelatin), 3000 glass slides (lantern slides) (size: 9 x 12 cm) an epidiascope (slide projector) and an antique album with photographs
Results: Up to this moment 6188 glass negatives have been analyzed (5148 of 9 x 12 cm and 1040 of 9 x 12 cm) and then grouped in different categories. Among them it is possible to mention: dermatological, cardiovascular, gynaecological, urological disease, etc. This collection showed macroscopic, microscopic, radiographic and clinical images from multiple medical specialties. We found several examples of diseases, some of them scourges of the past and among others we can quote: Hansen disease, measles, bubonic plague, smallpox, tuberculosis, and antrax. We could not make any review of the lantern slides
Conclusion: We believe these findings have great historical value, allowing us to access images of diseases that belong to the end of the 19th century, some of which have been eradicated. We do not find registered publications that report the existence of an archive of medical images of such magnitude

OFP-06-012
No autopsy, no diagnosis
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Background & Objective: The complexity and risks of brain biopsy requires, in the majority of neoplastic cases, establish the possible infiltration of the Central Nervous System (CNS) through radiological studies. We present two autopsy studies with unexpected results.
Method: The first case corresponds to a woman diagnosed of lung adenocarcinoma in transbronchial biopsy and the second one to a man with a diagnosis of follicular lymphoma in a lymph node biopsy. In both cases , the radiological study of the CNS considered the neoplastic infiltration and were treated accordingly. At the time of death, protocolized autopsies were performed with CNS samples fixed in Fine-Fix . Tissue samples submited to the service of microbiology, where they were studied by technology of Real Time PCR looking for infectious agents.
Results: The histological findings showed inflammation and necrosis withouth evidence of tumour . Nocardia and toxoplasma DNA were detected respectively, the groccot stain evidenced nocardia structures in the first case.
Conclusion: The infections diseases can mimicking neoplastic processes with important clinical repercutions and their diagnosis is crucial for correct treatment of patients . Without autopsy , these infections would not have been diagnosed, which supposed clinical pathological discrepancies type II according to the Goldman scale, revaluing the autopsy as hospital quality control.

OFP-06-013
Cardiac metastases: two cases from the emergency clinic
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Background & Objective: Metastases in the heart are not rare, however, their diagnosis is a serious issue, especially in the elderly, when heart failure is explained by age-related issues.
Method: In 2017, we diagnosed two cases of metastases in the heart.
Results: First case: a 79-years-old patient with cardiooesophageal cancer, died in the clinic with an increasing heart failure. An autopsy revealed a tumour in the lower third of the oesophagus, which spread to the cardiac compartment of the stomach, diaphragm, pericardium, epicardium, and myocardium of a right ventricle. Histologically, the tumour included glandular structures with foci of massive necrosis. Extensive intramural metastases were found in the myocardium. Second case: a 90-year old patient K. was admitted to the hospital in a severe condition. In the course of a clinical examination, a tumour was discovered in the parietal lobe on the right hemisphere (1.6x2.5 cm) and a pigmented lesion on the right foot of the patient (5x3 cm). The patient's condition has progressively worsened, and on the fourth day, the patient died of heart failure. The autopsy revealed, isolated cardiac metastasis in the right atrium and left ventricle. Moreover, there were multiple brain metastases (up to 1.5 cm) in both hemispheres. A histological examination allowed to diagnose melanoma and distant metastases in brain and heart.
Conclusion: Metastatic heart disease in both cases was diagnosed postmortem as a result of the autopsy, while medical documents did not provide an explanation for progressing heart failure. The histological study allowed to reveal the tumour's origin.

OFP-06-014
Clinico-pathological discrepancies in the diagnosis of causes of death in adults in Mozambique
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Background & Objective: Autopsies have an important role in the quality control of clinical diagnoses and treatment. Clinical errors are likely to be more frequent in settings with limited available diagnostic techniques. In this study, we aimed to assess the accuracy of clinical diagnoses in a quaternary hospital in sub-Saharan Africa by comparing them with the postmortem findings, and to identify potential risk factors for misdiagnoses.
Method: Clinical records and autopsy findings from a series of 112 adults, excluding maternal deaths, occurring at the Maputo Central Hospital, Mozambique (n=112) during 2013-2015 period were reviewed.

Discrepancies between clinical and autopsy diagnoses were evaluated using a modified version of Goldman and Battle classification and all major clinical errors were analyzed.
Results: A major diagnostic discrepancy was detected in 64(57%) cases. Major clinical errors were particularly frequent in deaths secondary to infectious diseases (55/80[69%] major discrepancies). Major clinico-pathological discrepancies were identified in 11/11(100%) infections caused by toxoplasma,9/11(82%) invasive fungal infections, 9/12(75%) sepsis,15/23(65%) tuberculosis,3/4(75%) meningitis, and 7/13(56%) pneumonias. The percentage of major discrepancies in HIV-positive patients(48/73, 66%) was higher than in HIV-negative patients(17/39,44%)(p=0.0282, Fisher's exact test).
Conclusion: Major clinico-pathological discrepancies were frequent in this series of adults in sub-Saharan Africa. Increasing clinical awareness of the impact of infectious diseases and the introduction of a few, simple, diagnostic tests could significantly improve the recognition of common and life-threatening infections, and thus reduce the mortality associated with these diseases. The high frequency of clinico-pathological discrepancies questions the validity of mortality reports based on clinical data or verbal autopsies.

OFP-06-015
Epidemiological characteristics and anatopathological aspects of deaths caused by Chikungunya fever in a specific region

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Background & Objective: The arboviruses are a global public health problem, causing epidemics with severe and atypical cases, with both joint and neurological impairments and deaths. In Fortaleza, Brazil, there is a co-circulation of Dengue (DENV) and Chikungunya (CHIKV) viruses, making the clinical management of such cases difficult, due to the similarity of signs and symptoms and to the limited laboratory support. Many deaths have post-mortem laboratory confirmation in obtained during necropsies performed by the Death Verification Service.
Method: We describe the clinical-epidemiological and anatomopathological characteristics of deaths by Chikungunya Fever in Fortaleza, Brazil, acquired from the Mortality Information System (MIS) and from the death records of the Country Health Department.
Results: 60,563 cases of Chikungunya Fever were reported, from these, 144 deaths were confirmed by the Arboviruses Mortality Investigation Committee; 22 necropsies of suspected deaths were held; two developed Guillain-Barre syndrome, three showed encephalitis; 19 with IgM reagent, two with positive immunohistochemical; three tested positive for DENV. Necropsies showed acute pulmonary edema (5/22), Lymphocytic encephalitis (2/22), lymphocytic myocarditis (2/22), steatosis and necrosis of hepatocytes (3/22).
Conclusion: Faced with the challenge to accurately report a death caused by Chikungunya, it becomes necessary to disclose the anatomopathological aspects found in necropsies, link them to the clinical findings as well as to alert the professionals about the risks and to create protocols that targeting reducing mortality.

Monday, 10 September 2018, 14:45 - 16:45, Room A2
OFP-07 | Joint Session: Soft Tissue and Bone Pathology / Infectious Diseases Pathology

OFP-07-001
A novel, low-grade paediatric soft tissue neoplasm defined by BRAF mutation

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Background & Objective: We describe two distinctive cases of a low-grade paediatric soft tissue neoplasm with clinical, immunophenotypic, and molecular features we believe are yet undescribed in the medical literature.
Method: We reviewed findings from clinical, radiologic, and histopathologic evaluations, as well as targeted ampliseq-based NGS of cancer-related genes.
Results: Two males, aged 11 months and 3 months, presented with plaque-like ulcerative soft tissue masses over the midline cervicothoracic and lumbar spines. Both masses infiltrated deeply, one involving the cervical and thoracic cord, extending into the retroperitoneum, the second into the lumbar epidural space. Histopathologic examination revealed both tumours to be centred in the deep dermis with extension through subcutaneous adipose to deep paraspinal soft tissues and into the epidural space. Neoplastic cells were small, monomorphous spindle cells with fibroblastic morphology and patchy lipomatous metaplasia, lacking cytologic atypia or mitotic activity. By immunohistochemistry, lesional cells were diffusely positivity for CD34 and negative for S100 and EMA. PDGFB rearrangements were absent by FISH. Sequencing revealed BRAF V600E mutations in both, one with a concomitant TP53 mutation, the other with APC mutation. Neither showed progression at 15 years or 6 months despite incomplete excisions.
Conclusion: These tumours express a distinct pathological and molecular profile with features raising a differential diagnosis of diffuse neurofibroma, lipofibromatosis, dermatofibrosarcoma protuberans, and tumours in the fibroblastic connective tissue nevus/fibrous hamartoma of infancy group. The BRAF mutations, combined with infiltration of deep axial and spinal cord structures and bland fibroblastic morphology are distinctive, though the congenital presentation and indolent course suggest a hamartomatous/connective tissue nevus-like lesion.

OFP-07-002
CD31 expression determines redox status and chemoresistance in human angiosarcomas

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Background & Objective: Angiosarcomas (AS) are soft tissue sarcomas with endothelial differentiation and vasoformative capacity. Most AS show strong constitutive expression of the endothelial adhesion receptor CD31/PECAM-1 pointing to an important role of this molecule. However, the biological function of CD31 in AS is unknown.
Method: The expression levels of CD31 in AS cells and its effects on cell viability, colony formation and chemoresistance was evaluated in human AS clinical samples and in cell lines through isolation of CD31high and CD31low cell subsets. The redox-regulatory CD31 function linked to YAP signaling was determined using a CD31 blocking antibody and siRNA approach and was further validated in CD31-knockout endothelial cells.
Results: We found that most AS contain a small CD31low cell population. CD31low cells had lost part of their endothelial properties, were more tumourigenic and chemoresistant than CD31high cells due to more efficient reactive oxygen species (ROS) detoxification. Active downregulation of CD31 resulted in loss of endothelial tube formation, nuclear accumulation of YAP, and YAP-dependent induction of antioxidative enzymes. Addition of pazopanib, a known enhancer of proteasomal YAP degradation re-sensitized CD31low cells for doxorubicin resulting in growth suppression and induction of apoptosis.
Conclusion: Human AS contain a small aggressive CD31low population that have lost part of their endothelial differentiation programs and are more resistant against oxidative stress and DNA damage due to intensified YAP signaling. Our finding that the addition of YAP inhibitors can re-sensitize CD31low cells towards doxorubicin may aid in the rational development of novel combination therapies to treat AS.

OFP-07-003

Strategies of cytokines' response under septic shock

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Background & Objective: We suppose that the mosaic releasing of inflammatory mediators, known as compartmentalization, is associated with prevalence of various stages of the cell stress in whole organism. These stages are: hyperergic (cell resistant to alteration, high level of cytokines' response) and depressive (cell tolerance, lower concentration of cytokines). The dominance of one of these stages is underlying the appropriate phase of systemic inflammation (SI). These stages are characterized by microcirculation disorders and organ dysfunctions, especially under septic shock.
Method: Rates of IL-6, IL-8, IL-10, TNFα, and CRP in the plasma were measured by the immunochemiluminometric closed system Immulite (Siemens Medical Solutions Diagnostics, USA). Groups of patients were the following: septic shock (SS) under acute sepsis (SS-AS) on the 1–2th days after admission at ICU, n=14, mean age – 54.9±16.4 years, lethality – 71.43%; SS under tertiary peritonitis, long and sub-acute sepsis (SS-SAS) (more, than 14 days after diagnosed), n=17, age – 50.2±5.6 yrs., lethality – 94.12%. Control group (donors), n=50, age – 34.1±10.4yrs.
Results: All of five studied indicators of SI in patients with SS were exceeding the control. Concentrations of cytokines in the blood of patients with SS-AS were significantly ($P<0.05$) increased as compared to the ones in SS-SAS. The levels of CRP in the groups were not significantly different.
Conclusion: Two variants of cytokines' response in septic shock are associated with dominant stage of cell stress: hyperergic in SS-AS and depressive in SS-SAS.

OFP-07-004

Upstream regulation of Wnt pathway in bone and soft tissue tumours - diagnostic and therapeutic implications

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Background & Objective: Aberrant Wnt signaling is found in both developmental diseases and cancer. Studies have shown that Wnt signaling plays a critical role in normal bone development. Aberrant signaling has been also implicated in the tumourigenesis of osteosarcoma and other sarcomas. We have developed a novel antibody, YJ5 against Wntless (WLS), a Wnt signaling pathway protein regulating Wnt secretion, which can be used to screen different tumours as potential candidates for treatment with an upstream Wnt (PORCN) inhibitor drug - ETC159. The objective of this study is to: 1) investigate if osteosarcoma (OS) and synovial sarcoma (SS) samples demonstrate aberrant Wnt signaling including elevated WLS levels 2) investigate if these tumours respond to treatment with ETC-159, a novel upstream Wnt inhibitor.
Method: YJ5 expression was analyzed in over 130 cases benign and malignant bone tumours and over 15 cases of synovial sarcoma. ETC159 was used to treat OS cell line (e.g. SJSA-1) (in-vivo) and two human SS cell lines (in-vitro). Response to treatment was analysed.
Results: 1) YJ5 was strongly expressed in synovial sarcoma, osteosarcoma, osteoblastic tumours and chondroblastoma. It was variably expressed in other tumours. 2) Treated OS samples demonstrated increased tumour necrosis (30-60 percent increase across all samples $p<0.005$). Treated SS samples show marked or significant inhibitory effect on downstream Wnt signalling proteins.
Conclusion: YJ5 antibody is a potential biomarker for identifying tumours with increased Wnt secretion that may be responsive to upstream Wnt inhibitors. ETC159 has a significant effect on tumour necrosis in osteosarcoma and inhibitory effect in synovial sarcoma.

OFP-07-005

Loss of RB gene (Monosomy 13) in the diagnosis of spindle cell lipoma, myofibroblastoma and cellular angiofibroma in unusual locations

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Background & Objective: Spindle cell lipomas are characteristically located in the neck and upper back of adults, mammary type myofibroblastomas are frequently present in the breast and lower genital tract whereas cellular angiofibroma almost exclusively arises in lower genital tract region. Diagnostic confusion can result when these tumours present in unusual locations and show variant histologic features.
Method: In this poster, we present a case of highly myxoid spindle cell lipoma in the thigh of a 25-year-old female. This tumour could be mistaken for myxoid well differentiated liposarcoma or myxoid liposarcoma. The second case is that of a mammary type myofibroblastoma of the groin in a 44-year-old male. The high cellularity together with CD34 and Desmin co-expression could lead to misinterpretation and inappropriate treatment. The third case is a cellular angiofibroma arising from right femoral hernia sac in a 47-year-old female.
Results: All cases show loss of the RB gene (Monosomy 13) by using the fluorescence in situ hybridization technique. This finding coupled with careful histologic examination and proper utilization of an immunohistochemical panel, lead to correct diagnosis in all cases.
Conclusion: We have found identification of the loss of (Monosomy 13) very useful in confirming the diagnosis of spindle cell lipomas, myofibroblastomas and cellular angiofibroma especially in unusual locations.

OFP-07-006

Retinoblastoma-1 (Rb1) protein expression in smooth muscle tumours of soft tissue and female genital tract

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Background & Objective: Smooth muscle neoplasms (SMN) represent one of the largest subgroups of mesenchymal tumours. Their biological subtyping into benign (leiomyoma), malignant (leiomyosarcoma) and neoplasms with equivocal features (SMN of unknown malignant potential/STUMP) can be challenging, especially in the female genital tract. Rb1 expression in non-selected SMN across the biological spectrum of these lesions has not been sufficiently studied to date. We investigated whether loss of Rb1 is a potential marker to distinguish leiomyosarcomas from benign leiomyomas.
Method: Rb1 expression was assessed in SMN using immunohistochemistry (inlcuding 2 uterine and 23 extra-uterine leiomyosarcomas, 580 conventional uterine leiomyomas on tissue microarrays, 18 fumarate hydratase (FH) deficient uterine leiomyomas and one STUMP).
Results: 23 leiomyosarcomas showed complete loss of Rb1 (92.0 %). Out of 206 LM of the TMA cohort, 205 showed variable low, frequently hardly recognizable expression of Rb1 (99.5 %). Only one case had strong Rb1 expression. No complete loss within the 206 LM was observed. All FH-deficient LMs harboured variable low Rb1 pattern (similar to conventional leiomyomas) but no complete loss.
Conclusion: Rb1 loss is observed in most unequivocal LMS, suggesting a role as a potential marker to assess malignant potential of smooth muscle tumours. However, we also found variable low expression of Rb1 that frequently seemed close to loss in almost all benign smooth muscle tumours, hardly distinguishable from complete loss. Hence, Rb1 seems to be no adequate marker to reliably separate benign from malignant smooth muscle tumours in daily routine diagnostics. The genetic basis of the reduced Rb1 pattern in benign uterine LMs needs to be further explored.

OFP-07-007

Experience in differential diagnosis of Ewing sarcoma and Ewing-like sarcoma by targeted RNA-seq

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Background & Objective: Ewing sarcoma family of tumours (ESFT) are characterized by a canonical fusion involving EWSR1 gene in most of cases, and FLI1 as the most common partner. Ewing-like tumours (ELT) morphologically resemble ESFT but show a different clinical behavior and distinct chromosomal alterations involving CIC or BCOR genes. Therefore, differential diagnosis of ESFT and ELT upon histopathology and FISH can be challenging. Here we explored the potential of targeted RNA-seq as an ancillary technique to improve diagnostic precision.
Method: 28 cases with morphology suggestive of ESFT or ELT were FISH-probed to detect EWSR1 translocations (break apart probe). These 28 cases and 7 additional cases were studied with Archer™ FusionPlex™ Sarcoma Panel.
Results: FISH EWSR1 rearrangement was detected in 18 cases. Targeted RNA-seq identified different EWSR1-FLI1 transcripts in 17 cases, and EWSR1-NAFTC2 fusion in a single case, thus achieving 100% sensitivity. Ten cases were EWSR1 FISH negative, and targeted RNA-seq identified 3 cases expressing EWSR1-ERG, 3 cases with CIC-DUX4, 2 cases with BCOR-CCNB3, one case with EWSR1-FLI1, and one case without any fusion call. All cases without EWSR1 FISH data showed fusions consistent with a previously rendered morphologic diagnosis (ESFT or ELT).
Conclusion: Targeted RNA-seq outscores EWSR1 FISH determinations overcoming common pitfalls such us low performance in detecting EWSR1-ERG. Moreover, the RNA-seq panel simultaneously detects ELT gene fusions, circumventing singleplex FISH probing. We propose a diagnostic algorithm for differential diagnosis of ESFT and ELT in which negative EWSR1 FISH determinations are followed by an RNA-seq targeted panel assess.

OFP-07-008

Broad spectrum pathogen detection (bacteria and fungi) by NGS is a novel measure for tissue based infectious disease diagnostics

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Background & Objective: Diagnosis of infectious diseases is a common task in molecular pathology, but standard microbiological methods frequently fail to reveal causative pathogens. Microbial 16S rRNA gene and fungal ITS (internal transcribed spacer) sequencing by NGS has recently emerged as a versatile tool for research but can also be utilized for infectious disease diagnostics in molecular pathology.
Method: Variable regions of the bacterial 16S rRNA gene and the fungal ITS regions were amplified by PCR and sequencing was performed on Ion PGM or S5XL using the 400bp workflow. Data analysis included error correction, clustering and annotation using open source Qiime 1.8 software to facilitate microbial identification.
Results: In a four-year period we have investigated over 300 clinical cases in which classical microbiological methods failed to reveal causative pathogens. This method is especially effective in diagnosis of infectious diseases of solid organs (e.g. heart, brain, lung, liver) wherein a high percentage of atypical pathogens including rare diseases like tularemia, atypical cardiac valve endocarditis (whipple's disease) and polymicrobial infections could be revealed. Detection rates were very high in liver (95%) and heart (70%) specimens. In contrast, agents of putative bone and joint infections were only rarely detected, possibly due to the low bacterial load in these infections being at a level of background bacterial contamination emerging from the environment or specimen workup, sporadic contamination of reagents at the suppliers and trace amounts of bacterial DNA in enzyme cocktails.
Conclusion: Bacterial 16S rRNA gene and fungal ITS analysis is a powerful diagnostic tool for unculturable, fastidious pathogens and should be applied if classical microbiology failed to reveal causative agents in histologically suspected infectious diseases.

OFP-07-009

TERT promoter mutation and HER2 gene amplification in malignant peripheral nerve sheath tumours: is there a molecular signature playing role in malignant transformation?

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Background & Objective: Benign and malignant (MPNST) peripheral nerve sheath tumours may occur sporadically or related to neurofibromatosis (NF). Unless the mechanisms of tumourogenesis NF related cases are better understood, still remained unclear in sporadic cases. We aimed to investigate genetic route of tumour in both individuals with NF-1 and sporadic ones to open a way for targeted therapies in the future.
Method: We investigated the role of HER2 with Dual ISH DNA Probe Cocktail test; BRAF (exon 15) and TERT promoter mutation frequency with Sanger sequencing method in respectively 25 sporadic neurofibroma, 25 neurofibromatosis type-1 (NF-1) related neurofibromas and 25 MPNST cases from two institutes.
Results: We identified TERT promoter mutation only in one sporadic MPNST (% 4) and no BRAF mutation in any case. There were gene amplification of Her2 in 10/25 (% 40) MPNST cases. No mutations or gene amplification detected in neurofibromas (sporadic or NF-1 related) ($p<0,001$)
Conclusion: MPNSTs are sarcomas with poor prognosis and limited treatment options. TERT gene have been demonstrated to be absent in benign tumours and normal subjects, implicating their potentially critical roles in human carcinogenesis. Epidermal growth factor receptor (EGFR) may play a putative role in MPNST pathogenesis and be targeted for therapeutic purposes. There are very few studies assessing BRAF and TERT promoter mutations and increasing Her2 gene dosage in patients with MPNST and there is no enough data in literature to determine a molecular signature plays key role in malign transformation both sporadic and NF-1 related cases.

OFP-07-010

Mutation analysis in H3F3A and H3F3B genes in giant cell tumour of bone and chondroblastoma

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Background & Objective: Giant cell tumour of bone (GCT) represents approximately 5% of primary bone tumours and about 20% of benign bone lesions. The frequency of the other tumour- chondroblastoma (CHB) is significantly lower and the tumour is identified in about 1% of primary bone lesions. In both tumours giant cells are present and differential diagnosis of both of them is challenging. It has been observed that, in contrary to other bones tumour, specific mutations in genes H3F3A (p.Gly34Trp and p.Gly34Leu) and H3F3B (p.Lys36Met) encoding histone H3.3 are present in GCT and CHB, respectively. The aim of the study was to evaluate the usefulness of H3F3A and H3F3 B genes genotyping in the diagnosis and differentiation of GCT and CHB bone tumours.
Method: The occurrence of p.Gly34Trp, p.Gly34Leu mutations in H3F3A and p.Gly34Trp in H3F3B was studied using Sanger sequencing in FFPE specimens from 106 tumours (classified according to standard radiological and pathological criteria as GCT- 99 cases and CHB-7 cases).

Results: In 98/99 (99%) of GCT cases H3F3A mutations were present, with predominance of p.Gly34Trp (97 cases) vs p.Gly34Leu (1 case). In 7/7 (100%) cases of CHB the p.Lys36Met mutation in H3F3B was present.
Conclusion: Our observations further confirm the data, previously reported by others, that mutations in genes H3F3A and H3F3B are present in GCT and CHB, respectively. Therefore, molecular analysis is an effective, fast and valuable step in differential diagnostics of those tumours.

OFP-07-011
Evaluation of CD4 (helper T-lymphocytes) and CD8 (cytotoxic T-lymphocytes) in cervical epithelium and stroma of HIV-positive patients
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Background & Objective: In HIV+ patients, a compromised CD4+ T cell function has been described as the inducer for HPV-associated cancer occurrence. Our aim was to evaluate the distribution of CD4 (Helper T Lymphocytes) and CD8 (Cytotoxic T Lymphocytes) in cervical epithelium and stroma of HIV+ patients with Intra-Epithelial Squamous Lesions (SIL).
Method: Thirty-eight histological specimens of 21 HIV+ patients (24 Low Grade SIL and 14 High Grade SIL) were studied by immunohistochemistry to CD4 and CD8 (Ventana, Roche Diagnostics). Scoring of immune stained positive lymphocytes were counted in five randomly selected high power fields at 40X magnification and the counts were averaged. CD4+ and CD8+ positive cells were recorded as: score 1 (1-25 cells), score 2 (26-50 cells), and score 3 (≥51 cells), in the tumour and the stroma, separately. Results were analysed by Chi-Square test and Fisher's exact test, using Graph Pad Prism 6 (statistical significance for $p<0.05$).
Results: No significant differences were observed for the presence of CD4 + cells in epithelium and stroma, between women with HSIL and LSIL. As for CD8+ cells, the HSIL group presented significant higher scores in epithelium ($p=0.011$). In stroma, when considering the scores 1 and 2 together versus score 3, women with HSIL also presented significantly higher scores for CD8+ cells ($p=0.027$).
Conclusion: Our results support that alterations in T lymphocytes are present in the cervix of HIV+ patients with SIL. A higher density of CD8+ cells in the stroma of HSIL may indicate a more antigenic stimulation of these lesions in the interaction with stroma.

Monday, 10 September 2018, 17:15 - 19:15, Room A2
OFP-08 | Joint Session: Neuropathology / Ophthalmic Pathology

OFP-08-001
Implementation of methylation array-based classification of paediatric central nervous system tumours in routine diagnostic pathology
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Background & Objective: For the sake of diagnostic accuracy, the current guidelines emphasize on the integration of molecular and histological features of central nervous system (CNS) tumours. Recent reports have revealed that such integration could be achieved by methylation arrays. The methylation array-based classification of paediatric CNS tumours was implemented at the Swedish Childhood Tumour Biobank as part of the quality assessment. The results provide a level of objectivity to include methylation profiling in routine diagnostic pathology.
Method: The DNA was extracted and analyzed by 450K/EPICS array hybridization. Automated reports are then generated using the classifier at MolecularNeuropathology.org. Finally, the histopathological and classifier diagnoses are reviewed and integrated. The samples included 42 paediatric CNS tumours: glial, neuronal, embryonal, tumours of nerves, germ cell, meningioma and mesenchymal tumours.
Results: Out of 42 samples, 32 (76.2%) were matched (score>0.9) with the classifier (Version 11b4). The matching outcomes were (i) confirmation of the histopathological diagnosis in 30 cases (93.8%); (ii) new diagnosis in 2 cases; and (iii) misleading results no cases. The two cases were re-evaluated resulting in correction of histopathological diagnosis in one case while the other case was not improper histopathological diagnosis but a new entity that is not recognized yet by the WHO classification of CNS tumours.
Conclusion: Implementation of the technique in routine diagnostic practice is not complicated, and highly useful. Classifier's diagnoses are according to the 2016 WHO. Profiling the methylome is robust, reproducible, needs representative samples, and most of the mismatching scores (<0.9) was due to lack of reference cases.

OFP-08-002
Atypical meningiomas: Which histopathological features correlate with recurrence risk?
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Background & Objective: Atypical meningiomas are currently defined by: 1) at least three "minor atypical criteria"; or 2) mitotic count equal or higher than 4 mitoses per 10 HPF (high mitotic index); or 3) brain invasion. 5-year disease free survival (DFS) of patients with atypical meningioma is around 50%. Due to their heterogeneous behavior, the post-surgical treatment of atypical meningiomas is controversial. Although radiotherapy could be effective in reducing recurrence risk, adverse effects could be spared in patients who would not develop recurrences. This study aims to investigate which histopathological features may significantly predict recurrence risk of atypical meningiomas.
Method: We reviewed the histological slides and clinical data of 58 atypical meningiomas in our archive between 2005 and 2014. By applying strict definitions for minor criteria, 14 cases were excluded. Thus, we investigated the correlation between histopathological features and recurrence or disease-free survival (DFS) in 44 atypical meningiomas.
Results: meningiomas classified as atypical only on the presence of minor criteria had low recurrence risk. Brain invasion, high mitotic index and sheeting were significantly associated with recurrence (P= 0,004; P= 0,029; P= 0,007). However, the co-presence of sheeting and high mitotic index, with or without brain invasion, had the highest ability to identify recurring meningiomas (P= 0,0001) (sensitivity: 90,6%; specificity: 83,3%).
Conclusion: Our results suggest to re-consider classification of meningiomas as atypical based only on minor atypical criteria. The co-occurrence of sheeting and high mitotic count, with or without brain invasion, may be useful to identify high risk cases which may benefit from adjuvant treatments.

OFP-08-003
Alternative BRAF-activating mutation in pleomorphic xanthoastrocytomas
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Background & Objective: Pleomorphic xanthoastrocytoma (PXA) is a rare low-grade glial tumour, commonly affecting children and young adults, with a 80% 5-year survival; few cases show anaplastic features (WHO grade-III) and had a worse prognosis (30% 5-year survival). Molecular characterization indicates frequent BRAFV600E mutation (up to 70%), whereas other genetic alterations, like BRAF and RAF1 fusions, were rarely reported. In a small cohort of patients with PXA, we performed a sequencing analysis of target genes in order to investigate the presence and frequency of druggable mutations.
Method: The mutational status of BRAF exon 15, FGFR1 exons 12 and 14, TERT promoter, codons R132-IDH1 and R172-IDH2, was evaluated

among 13 PXA surgical cases (8 WHO grade-II, and 5 grade-III) by Sanger sequencing. In one patient both the primary tumour (PXA grade-II) and recurrent (PXA grade-III) were examined.
Results: BRAFV600E mutation was detected in 5 cases (38%) (3 grade-II and 2 grade-III) and BRAFT599_V600insT in 3 cases (23%) (2 grade-II and 1 grade-III). Interestingly, one of BRAFT599_V600insT was identified in the recurrent PXA grade-III but not in the primary grade-II tumour. Two PXA grade-III (15%) showed C228T TERT promoter mutation and a BRAF wild-type genotype. No IDH1, IDH2 and FGFR1 mutation were identified.
Conclusion: Our study indicated that BRAFT599_V600insT has a high frequency in PXA. Since it shows similar behavior of V600E mutation, it could be considered as therapeutic target by BRAF and MEK-inhibitors. TERT promoter mutation seems related to anaplastic phenotype, but further studies are needed to establish its prognostic significance.

OFP-08-004
Frequency of actionable molecular drivers in lung cancer patients with CNS metastases

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Background & Objective: Brain metastases are frequently in lung cancer patients. Treatment options are limited, and detailed information about the frequency of molecular alterations representing potential treatment targets is crucial.
Method: We have analyzed a consecutive series of 133 patients (86 male, 47 female) with lung cancer metastases to the central nervous system. Biopsy material was characterized by fluorescence in situ hybridization (FISH) to detect alterations (EML4/ALK, MET, FGFR, ROS, RET) and EGFR (exon 18-21) using the COBAS system. Overexpression of ALK was detected by immunohistochemistry (Ventana).
Results: ALK expression was detected in 8/133 tumours (6%). Among 117 tumours with suitable material for EML4/ALK FISH, the translocation was found in 3 cases (2.56%). MET amplification was detected in 37/127 cases (29.1%). RET amplification was detected in 2/106 cases (1.9%). ROS amplification was seen in 1/104 cases (0.9%). FGFR1 amplification was detected in 6/92 cases (6.5%). EGFR mutations were detected in 7 of 132 patients studied (5.3%). Comparing alterations of EGFR and EML4/ALK with the primary tumour in 20 patients, one patient had an EM4/ALK translocation in the primary tumour which was not detectable in the CNS metastasis, while the remaining alterations were similar (concordance rate 95%).
Conclusion: Lung cancer metastases are characterized by a high frequency of MET amplifications. EML4/ALK translocation and EGFR mutation rates are within the expected frequencies known from primary tumours. There seems to be a high concordance between primary and CNS metastatic tumour. Detailed molecular characterization of CNS metastases is essential to offer additional treatment options to the patients.

OFP-08-005
Primary gliosarcoma with IDH1 mutation and codeletion of 1p and 19q

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Background & Objective: In the 2016 WHO classification of tumours of the central nervous system, gliosarcoma is a variant of isocitrate dehydrogenase (IDH)-wildtype glioblastoma with a 5-year survival rate of less than 10%. Although mention is made of gliosarcoma arising in oligodendroglioma ("oligosarcoma"), IDH-mutant and 1p/19q-codeleted gliosarcoma is not a codified entity. We present a case of primary gliosarcoma with IDH1 mutation and 1p/19q codeletion.
Method: In 2010, a 38-year-old male presented with a right frontal lobe brain tumour. Excision showed a gliosarcoma with morphologically malignant astrocytic and spindle cell sarcomatous components. O[6]-methylguanine-DNA methyltransferase (MGMT) promoter was methylated. He was treated with adjuvant temozolomide and radiotherapy. Tumour recurrence was detected 7 years later on follow-up neuroimaging. Re-excision in 2017 showed a recurrent high-grade glioma with astrocytic morphology. No sarcomatous or oligodendroglial component was seen in the recurrent tumour. R132H mutation-specific IDH1 was positive in the recurrent tumour and in the gliomatous and sarcomatous components of the original tumour. Fluorescence in situ hybridisation performed on the recurrent tumour showed a combined deletion of 1p36 and 19q13. No confirmation of whole-arm deletions of 1p/19q was available. Review of the original tumour showed focal areas resembling oligodendroglioma.
Results: This primary gliosarcoma with IDH mutation, 1p/19q codeletion and foci resembling oligodendroglioma, suggests that rarely, primary gliosarcoma may share the genotype and phenotype of an oligodendroglial tumour, with prolonged patient survival.
Conclusion: The current classification categorises gliosarcoma as a variant of IDH-wildtype glioblastoma with similarly dismal prognosis. However, gliosarcoma may be biologically more heterogeneous, with "oligosarcoma" possibly being less aggressive.

OFP-08-006
Morphological and immune histochemical alterations of astrocyte neuroglia of epiphysis under conditions of long-term influence of heavy metals salts on the organism

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Background & Objective: It was studied the morphological and immune histochemical alterations of the glial component of the epiphysis under conditions of long-term influence of heavy metal salts in the experiment.
Method: The experiment was conducted on 24 rats aged 5-6 months (1 control and 1 experimental group). For 90 days animals received drinking water, saturated with a combination of heavy metals salts: zinc, copper, iron, manganese, lead and chromium. It was applied a common method of histological examination. Immune histochemical diagnosis of the Ki-67 proliferation marker was performed using rabbit monoclonal antibodies.
Results: Heavy metals salts cause morphological and immune histochemical alterations in all structural components of the epiphysis. Significant vascular enlargement with a violation of the rheological properties of the blood and the formation of blood stasis, the aggregation of erythrocytes, the sludge phenomenon, rare diapedesic hemorrhages. In the subcapsular zone, an explicit reactive astrocyte glial reaction is observed. Especially active proliferators are formed around the vessels of medium diameter in the peripheral regions of the gland. The evaluation of the expression level of the Ki - 67 proteins revealed its moderate proliferative activity in astrocytes of peripheral regions (35-40%).
Conclusion: The long-term effect on the body of rats of heavy metal salts causes local reactive astrocyte gliosis in the epiphysis of rats, which may be explained by the neuro protective properties of astrocytes in response to the action of the stressor agent.

OFP-08-007
Craniopharyngiomas: 20-year-period evaluation study

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Background & Objective: Craniopharyngioma is a rare histologically benign brain tumour with potential malignant clinical course because of the high propensity of recurrence, deriving from the remnants of Rathe's

pouch, presenting as solid mass and partly as fluid-filled cyst. There are two main histological subtypes: adamantinous and papillary. The aim of this study is to evaluate statistical features of this tumour in the Republic of Macedonia.
Method: This is a 20-year-period retrospective evaluation study (1998-2018) of 40 craniopharyngioma cases operated in the University Neurosurgery Clinic, diagnosed at the Institute of Pathology, Medical Faculty-UKIM, Skopje, Macedonia on paraffin-embedded section slides routinely stained with H&E. Statistica for Windows 7 was used.
Results: From total 4929 cases of benign and malignant brain tumours, craniopharyngioma comprise 40 cases (0,81%); 25(62,5%) males (37,9 ±17,8 years), 15(37,5%) females (34,0±25,4 years), age 3 to 68 years; most common localization: sellar region - 11(27.5%), cerebrum – 8(20%). Adamantinous - 27(67,5%) cases, papillary 13(32,5%) cases. Age group distribution: the most cases - 7(17,5%) in 0-9, 40-49, 60-69 years groups; least cases – 3(7,5%) in 20-29 years group. Nine (22,5%) of 40 patients have had recurrent tumour (first 1-3 years). Adamantinous was diagnosed in 14(51.85%) males and 13(48.15%) females; papillary in 11(84.62%) males and 2(15.38%) females. There is significant statistical difference between age groups and craniopharyngioma subtypes (Kruskal-Wallis ANOVA: H = 14,86; p = 0,0274).
Conclusion: We found association and correlation between gender, age and histological subtype. Papillary craniopharyngioma appears more frequently in males and adamantinous was most prevalent in younger patients.

OFP-08-008
PD-L1 expression of medulloblastoma
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Background & Objective: Medulloblastoma is the most common central nervous system embryonal tumour. Treatment protocols include surgery with the goal of gross total excision if possible, craniospinal radiation therapy, and adjuvant chemotherapy. Patient who do survive often experience significant neurologic impairment due to unavoidable side effects of cytotoxic therapy. Immunotherapy can be another option to kill cancer cells and has less side effects compared to other treatment protocols. The aim of the present study was to examine the expression of PD-L1 in medulloblastoma, and to predict immunotherapy response.
Method: 50 cases were included in this study. We analyzed immunohistochemical PD-L1 (clone SP142) expression in all cases. We used tonsil as a positive control.
Results: We couldn't detect PD-L1 expression in any of our cases.
Conclusion: Our result suggests that medulloblastomas won't have any benefit from treatment strategies with PD1/PD-L1 blockers.

OFP-08-009
Demographic and pathological characteristics of medulloblastoma: single center experience
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Background & Objective: Brain tumours are still under investigation in terms of prognostic factors. Some tumours have newly discovered molecular alterations. For medulloblastoma there is both histological and molecular classification in WHO classification of tumours of the central nervous system revised 4th edition. Although molecular classification has increasing clinical utility, histopathological classification has also been retained, due to its clinical utility when molecular analysis is limited or not feasible.
Method: We reviewed 50 medulloblastoma cases in our institution between the years 2008 and 2018 and collected their data about gender, age, histology, metastasis status, resection procedure and survival status.
Results: The median patient age at diagnosis was 4. Male to female ratio was 1,45. Tumours were located in the cerebellar parenchyma or grew into the fourth ventricle in 49 patients. One case had tumour in thoracic spine. 14 patients underwent gross total resection while others underwent subtotal resection or biopsy. 35 patients have been followed up in our center and 18 of them had progression free survival. 9 of them died and 8 of them had recurrent tumour or leptomeningeal spread although they received chemoradiotherapy. 41 cases were histologically classic subtype and 6 cases were desmoplastic/nodular, 2 cases are largecell / anaplastic and one case was medulloblastoma with extensive nodularity.
Conclusion: Current surgical approaches and therapy regimens increase the progression free and overall survival rates. Although newly described molecular parameters can be helpful for prediction of prognosis and development of new therapy strategies, histopathology maintains its importance.

OFP-08-010
Expanding on WHO guideline compliant molecular testing of central nervous system tumours by low density whole genome sequencing
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Background & Objective: Classification of CNS gliomas has been revised with current WHO guidelines incorporating several molecular features. Current guideline compliant molecular testing incorporates NGS panel sequencing, methylation screening and copy number variation (CNV) measurement. MPLA, qPCR and analysis of NGS amplicon sequencing depth are established methods to detect 1p19q codeletion in CNS tumours. However, these methods summarily fail to detect CNVs in other regions. We have introduced low density whole genome sequencing as a diagnostic routine tool for comprehensive mapping of all CNV events.
Method: Tumour DNA was processed using the Ion Torrent Fragment Library Kit and sequenced on Ion Proton to yield approximately 1-2 million reads. Data were analyzed with the open source R package „CNAnorm".
Results: In two years we have analysed 95 gliomas and demonstrate that beside 1p19q codeletion, typical gains and losses of chromosomes indicate the histological WHO grade. Additionally, in high grade gliomas also histologically low-grade tumour areas carry the high-grade copy number alterations. Furthermore, prediction of time to recurrence with CNV alterations is superior to histological WHO grade.
Conclusion: Low density whole genome sequencing is a versatile method to detect CNVs in gliomas and supports WHO grading. It provides clinically relevant information and can be used to predict recurrence free survival.

OFP-08-011
Comprehensive diagnosis and monitoring of uveal melanoma with gene panel analysis, low density whole genome sequencing and digital droplet PCR
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Background & Objective: Uveal melanoma is the most common malign tumour originating from the eye with an incidence of 400-500 patients per million. Molecular features include mutations in several genes as well as losses and gains of specific chromosome arms. Molecular diagnosis of uveal Melanoma is hampered by difficult sample extraction and low tumour volumes for diagnostic purposes. While local tumour control after radiotherapy is high (80-95%), about 45% of patients develop metastatic disease.

Method: We have established a NGS Panel to analyze mutations in nine genes by Ion Torrent NGS. Additionally, copy number variation is detected by low density whole genome sequencing. Digital droplet PCR (QX200) utilizing primers for the very common GNAQ and GNA11 mutations have been established and validated for liquid biopsy analysis.
Results: Since introduction of the method to routine diagnostics we have investigated 28 cases of uveal melanoma. Tumour tissue was collected by vitrectomy using biopsy forceps. NGS analysis revealed specific genetic aberrations in 28/28 tumours (100%). Mutational spectrum was in concordance with literature (GNAQ 46%, GNA11 39%, BAP1 36%, EIF1AX 32%). CNV analysis revealed frequent loss of chromosome 3 (46%), gain of chromosome arm 8q (25%) and other common aberrations. After initial diagnosis plasma samples were collected at 3 months intervals. Digital droplet PCR liquid biopsy analysis was performed in select cases with suspected metastases. Circulating tumour DNA was only detected in one case with clinically manifest progression to metastatic disease.
Conclusion: Combined analysis of mutations and copy number aberrations from uveal melanoma is possible even with little available tumour material and is important for clinical risk management and proper treatment monitoring.

OFP-08-012
MicroRNA in conjunctival melanocytic lesions
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Background & Objective: The management and stringent follow up for conjunctival melanocytic neoplasia emphasizes the need for early identification of aggressive lesions. Therefore, differences in microRNA expression between benign and malignant conjunctival lesions were studied.
Method: The microRNA profiles from FFPE samples of six conjunctival nevi and twenty conjunctival melanomas with or without metastasis were determined using the Taqman Low Density Array (TLDA) approach (377 miRNA targets plus controls). The minimal follow up for the non-metastatic lesions was 10 years. Amplification data were processed using the Cloud App (ThermoFisher Scientific) and analysed using QbasePlus (Biogazelle N.V., Zwijnaarde, Belgium). The benign lesions were compared with the malignant lesions and the metastatic lesions to the non-metastatic lesions. Both supervised and unsupervised clustering was performed. The differentiating microRNAs were verified using single assay qRT-PCR and validated using an independent cohort consisting of sixteen nevi and twenty melanomas.
Results: The data did not identify significant difference in miRNA levels between the conjunctival melanomas with or without metastases. In contrast, seven miRNAs were significantly different between conjunctival nevi compared to melanoma. Using single assay qRT-PCR, these results could be reproduced for five miRNAs. Validation of these miRNAs in an independent cohort of nevi and melanomas confirmed the significance (Fold Change>4, P<0.004, corrected for multiple testing). The area under the Receiver Operator Curve for each of these miRNA was over 0.85.
Conclusion: We, for the first time, demonstrate existence of prognostic microRNAs for conjunctiva melanocytic lesions, possible of interest for further development and clinical implementation.

Tuesday, 11 September 2018, 08:30 - 12:00, Room A4
OFP-09 | Breast Pathology

OFP-09-001
What is the ideal Ki67 hot spot definition in breast cancer?
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Background & Objective: Tumour proliferation is one of the hallmarks of cancer. The proliferation associated nuclear marker Ki67, a predictive and prognostic biomarker in breast cancer, is used to guide clinical decisions concerning adjuvant chemotherapy. However, the international recommendations for Ki67 are controversial due to the lack of standardization and there is no international consensus regarding Ki67 cut offs and hot spot definitions. The aim of this study is therefore to define the Ki67 hot spot using a machine learning approach for digital image analysis with correlation to prognostic value.
Method: In this study, two Swedish breast cancer cohorts (n=897) with scanned whole slide images of parallel sections with invasive tumour were stained with haematoxylin-eosin, pancytokeratin (CKMNF116) and Ki67 and analysed using a digital image analysis software from Visiopharm A/S. Image analysis was performed on aligned pancytokeratin and Ki67 images for accurate tumour identification. Clinicopathological data was included as well as outcome data for one of the cohorts.
Results: We used a machine learning approach with unsupervised learning to define Ki67 hot spots in breast tumours. Hot spots were identified as specified area with highest ratio of positive Ki67 compared to unstained pancytokeratin-positive tumour cells. Our results show significant variations in Ki67-index depending on number of included tumour cells, hot spot size, shape and location.
Conclusion: Identification of a hot spot definition based on maximal prognostic value has significant clinical implications and has the potential to affect guidelines for proliferation-assessment in breast cancer.

OFP-09-002
Intraoperative diagnosis of breast cancer sentinel lymph nodes by scrape cytology: diagnostic accuracy and cost-effectiveness
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Background & Objective: The intraoperative (IO) analysis of sentinel lymph node (SN) in breast cancer surgery relies on time and resource-consuming procedures for Pathology Departments. We analyze the diagnosis´efectiveness of a rapid and cost-saving IO cytology method.
Method: A retrospective study was performed with IO analysis of 1013 SNs from 606 patients obtained between 2010-2017. Cytological IO diagnosis was used after scraping all surfaces from the sectioned nodes, smearing onto glass slides and staining with Diff-Quick®. Frozen section was analyzed only when tumour metastasis was cytologically suspected. Cost estimation of the alternative worldwide-used molecular OSNA technique was applied to our work load.
Results: The prevalence of macrometastases in SNs was 9,9% (100/1013). There were no false positive cases and diagnostic accuracy was 98,4%. In 13/606 patients (2,1%) the method failed to detect macrometastes (false negative) and a second surgical procedure was needed for axillary dissection, (average of 1,6 cases/year). The approximate time spent in the IO diagnosis by this method was 15 minutes per node. No molecular analysis (OSNA) was performed, with an estimated annual cost saving of 150.000€/year.
Conclusion: Although a pathologist-dependent technique, the IO analysis of SN by scrape cytology in Pathology Departments reaches an excellent diagnostic accuracy with very low false negative rate and no false positive diagnoses. Besides being a safe and rapid technique, its use represents an important cost reduction when compared to molecular analysis, particularly with the recent consensus to spare axillary dissection in women with less than 3 nodes with metastatic disease.

OFP-09-003

Somatostatin receptor expression in neuroendocrine breast cancer

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Background & Objective: Neuroendocrine breast cancer (NEBC) is a group of rare tumours which could benefit from therapy approaches targeting the somatostatin receptor (SSTR). In particular, SSTR2A and SSTR5 are potential targets given their relatively consistently increased expression in gastrointestinal and pancreatic primary and metastatic neuroendocrine tumours. Currently, there are no studies describing the expression of SSTRs in NEBC. The purpose of our study was to characterize the immunohistochemical expression of SSTR2A and SSTR5 in NEBC.
Method: A retrospective series of 31 NEBC cases was analyzed, and SSTR2A and SSTR5 immunohistochemistry performed.
Results: The mean age of our population was 67 years (sd=15). Median tumour diameter was 21 mm, and the median histological grade was 2. SSTR2A showed weak positivity in 11 cases (35%), mild positivity in 6 cases (19%) and strong positivity in 5 cases (16%). Nine cases were negative for SSTR2A (29%). SSTR5 showed weak positivity in 16 cases (52%), mild positivity in 6 cases (19%), while no cases showed strong positivity. Nine cases were negative for SSTR5 (29%).
Conclusion: To our knowledge this is the first description of SSTR expression in BCNF. In our series, SSTR2A and SSTR5 were consistently expressed in BCNF. Most cases showed weak expression. These results need to be further validated in a larger series including metastatic disease, in order to provide possible therapeutic targets for patients with advanced disease.

OFP-09-004

Elastic stains in the evaluation of DCIS with comedo necrosis in breast cancers

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Background & Objective: As concerns the microscopic morphology of ductal carcinoma in situ (DCIS), neoplastic cells are surrounded by both a myoepithelial cell layer and a basement membrane as expected from the outer structure of ducts and lobules. However, in some cases it is impossible to state whether the structures involved by the disease are ducts or lobules.
Method: All anatomic structures involved by DCIS displaying comedo necrosis (seen on both haematoxylin and eosin stained and orcein stained slides) were identified as representing ducts, likely ducts, unclassifiable structures, likely acini or acini on the basis of their distribution and resemblance to normal anatomic structures. All structures were then rated as having a circumferential elastic layer (as normal ducts), a partial elastic layer around more or less than half of the periphery or having no peripheral elastic layer at all (as normal acini).
Results: Altogether 1220 anatomic structures were classified from 27 slides of 21 patients. Structures classified as ducts or likely ducts were likely to have an elastic coating, whereas acini and likely acini had no such coating. Unclassifiable structures were generally devoid of an elastic layer. Structures (and cases) that were likely to represent neoductgenesis as proposed by Zhou et al (Int J Breast Cancer 2014;2014:581706.) were generally unclassifiable and devoid of outer elastic layer.
Conclusion: Many duct-like structures in DCIS with comedo necrosis are devoid of elastic layer typical of normal ducts, suggesting that these structures are abnormal despite conservation of the myoepithelium and the basement membrane.

OFP-09-005

Transcriptional profiling of endocrine resistant versus sensitive breast cancer uncovers gene expression programmes associated with therapeutic response

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Background & Objective: The majority of breast tumours express the oestrogen receptor alfa (ER) and responds to adjuvant endocrine therapy. Endocrine therapy blocks or down-regulates ER and in turn causes inhibition of cancer cell proliferation and reduces risk of metastasis. Still, many patients do not respond to endocrine therapy in the adjuvant setting and even more metastatic patients will progress to an endocrine refractory state. No method exists to accurately predict therapeutic response but would be highly desired in the clinical situation. The overall purpose of this study was to analyse gene expression of ER-positive tumours from endocrine therapy resistant patients versus sensitive patients with the aim to identify gene expression signatures corresponding to therapeutic sensitivity and resistance.
Method: The cohort comprised 22 cases with consecutive relapses (ER+ primary tumours receiving adjuvant endocrine therapy, with ER+ breast cancer relapse during ongoing therapy) and 44 matched controls (ER+ primary tumours of patients with good outcome on adjuvant endocrine therapy), retrospectively identified through the Karolinska University Laboratory pathology LIS-system. From all retrieved tumours RNA was extracted and analysis by Affymetrix gene array was performed.
Results: We identified unique gene expression patterns in the endocrine resistant tumours. Furthermore, endocrine resistance was associated with specific transcriptional biological programs. A second validation cohort is now designed with ongoing analysis to confirm the findings.
Conclusion: Our data indicates that endocrine resistance in primary breast cancer is associated with unique transcriptional profiles that can be further utilized as therapy predictive biomarkers.

OFP-09-006

High reproducibility in Ki67 assessment in luminal breast cancers enabled by French recommendations and digital image analysis

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Background & Objective: Luminal breast carcinomas express hormone receptors and show variable aggressiveness potential and response to adjuvant chemotherapy. A proliferation marker, Ki67, is useful to categorize these lesions but the reproducibility of its assessment is controversial. The French association of quality insurance in pathology (AFAQAP) published guidelines for Ki67 counting in breast cancers taking into account intra-tumour heterogeneity. Our objective was to study the performances of digital image analysis (DIA) using these recommendations and to compare the results to the Prosigna® molecular signature.
Method: In this prospective and multicentric study, 200 invasive breast carcinomas, ER and/or PR positive, Her2 negative, stage T1/T2, N-, were included. Ki67 (MIB1) staining and the Prosigna® molecular signature were centralized. Ki67 labelling index was assessed by manual counting according to the AFAQAP recommendations by one pathologist and with DIA by two pathologists.
Results: Interobserver reproducibility of DIA was r=0.93 [IC95 0.89-0.95, p<2.2e-16]. Intraobserver reproducibility between manual counting and DIA was r=0.87 [IC95 0.83-0.90, p<2.2e-16]. Using a cutoff of 20%, manual and DIA counting properly assigned 80% and 76% of tumours to the luminal A and B categories defined by Prosigna®. Counting time per 100 cells was 34% quicker with DIA than manually (14 vs. 21 seconds).
Conclusion: The AFAQAP recommendations for Ki67 counting achieved an excellent interobserver reproducibility with DIA, including

heterogeneously stained tumours. There was a good correlation between Ki67 and the Prosigna® molecular signature. These recommendations are applicable to DIA, which reduces counting time.

OFP-09-007

Tumour-infiltrating lymphocytes in triple-negative breast cancer correlate with morphology, Bcl2 expression, proliferative activity and menopausal status

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Background & Objective: Triple-negative breast carcinomas (TNBCs) are morphologically a heterogeneous group of breast carcinomas with no or minimal estrogen/progesterone hormone receptor HER2 expression. In this study, we characterized the types and intensity of tumour infiltrating lymphocytes (TILs) in TNBCs obtained from mastectomies and correlated the results with tumour morphology and other clinicopathological parameters.
Method: We re-examined the samples of 3,544 breast cancers (2007-2017) and selected 413 TNBCs of which 61 were of those without neoadjuvant therapy. The type and intensity of lymphocyte infiltration was correlated with morphological features including spindle cell or apocrine metaplasia, tumour grade, lymph node involvement, relapse of disease, Bcl-2 expression status, proliferative activity measured by Ki67 expression, age and menopausal status.
Results: The majority of samples were invasive carcinomas NST with medullary features according to WHO classification 2012, with central necrosis/fibrosis, tendency to spindle cell and/or apocrine metaplastic differentiation and extensive lymphocytic infiltration. We found a tendency to positive correlation between the quantity of surrounding TILs and tumour size as well as statistically significant ($p<0.05$) positive correlation with tumour grade, proliferative activity, Bcl-2 expression and menopausal status. We also found an association of Bcl-2 over-expression and metastatic potential with apocrine tumour transformation. No correlation between TILs and other clinicopathological parameters was revealed.
Conclusion: The intensity of TILs considered together with specific morphological and expression features of TNBC may predict clinical outcome.

OFP-09-008

SOX10 expression in invasive ductal carcinomas of the breast and benign breast tissue

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Background & Objective: SOX10 immunohistochemical (IHC) staining is used to identify tumours of neural crest origin, including melanocytic neoplasms and has been identified in myoepithelial cells of the breast and in a subset of invasive mammary carcinomas. The aim of this study was to characterize the SOX10 IHC staining in invasive ductal carcinomas according to molecular subtype, as well as in benign breast tissue.
Method: Forty cases of invasive ductal carcinoma of the breast were retrieved. Ten cases of each of the following molecular subgroups were selected: luminal A, luminal B, HER2-enriched, and triple negative subtypes. Whole tissue sections from each case were stained with mouse monoclonal antibody against SOX10. SOX10 staining was assessed within the invasive carcinoma, and when available, DCIS and benign breast tissue.
Results: Six (60%) of 10 triple-negative tumours were SOX10+ compared to 1 (3%) of 30 carcinomas of other molecular subtypes ($p = 0.0003$). All but one of the positive tumours showed at least moderate expression in at least 40% of tumour cells. All 7 cases SOX10+ carcinomas were grade 3 tumours ($p = 0.01$). Of the 13 cases with DCIS available for assessment, 1 (8%) showed positive SOX10 expression. All 22 cases with normal breast tissues available for assessment showed patchy SOX10 expression in both myoepithelial and luminal cells. SOX10 showed incomplete myoepithelial staining compared to other myoepithelial markers.
Conclusion: The triple-negative subtype of invasive ductal carcinomas shows a high rate of SOX10-positivity. SOX10 IHC cannot reliably differentiate between high-grade triple negative carcinomas, melanomas, and myoepithelial tumours in the breast.

OFP-09-010

Comparative analysis of human epidermal growth factor receptor 2 (HER2) testing in breast cancer according to 2007 and 2013 American Society of Clinical Oncology / College of American Pathologist guideline recommendations (ASCO/CAP)

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Background & Objective: Accurate determination of HER2 status is critical for optimal treatment of breast cancer. Our objetive was to study the effect of the 2013 updates to the 2007 ASCO/CAP recommendations for HER2 testing in breast cancer.
Method: Patient cases with HER2 studies were selected during two 12-month periods (2012 and 2015). The number of tests performed, type of specimen, proportion of HER2-positive and equivocal cases, and number of repeat tests on subsequent excisional specimens were examined and compared.
Results: Although the number of samples tested increased between 2012 and 2015 (378 v 540) , HER2 positivity remained constant (14.1% v 14.8%). The number of repeat tests for immunohistochemistry (IHC) within 6 months increased (2% v 7%). Determination on percutaneous biopsies was also increased (46,8% v 80.42%). Tumours categorized as negative (0 - 1+) on IHC decreased from 72% to 68 %. Tumours categorized as equivocal (2+) increased (14,8% v 29,7%).
Conclusion: Our findings indicate that the 2013 updates guidelines did not affect the overall HER2-positivity rate. The proportion of tests and repeat tests performed increased, as did the number of patient cases categorized as HER2 IHC equivocal (2+). There is a shift towards the use of core biopsy for HER2 testing.

OFP-09-011

Doxycycline pre-operatively in early breast cancer

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Background & Objective: Cancer stem cells (CSCs) have been implicated in disease recurrence, metastatic spread and poor patient survival in multiple tumours, breast cancer (BC) included. CSCs selectively overexpress key mitochondrial-related proteins and inhibition of mitochondrial function may represent a new potential approach for the eradication of CSCs. Because mitochondria evolved from bacteria, many classes of FDA-approved antibiotics, including doxycycline, actually target mitochondria. Our study aimed to determine whether short-term pre-operative treatment with oral doxycycline results in reduction of CSCs in early BC patients.
Method: Doxycycline was administered orally for 14 days before surgery for a daily dose of 200 mg. Immunohistochemical analysis on formalin-fixed paraffin-embedded samples from 15 patients, of which 9 were treated with doxycycline and 6 controls (no treatment), was performed with known biomarkers of stemness (CD44, CD24, ALDH1), mitochondrial mass (TOMM20), cell proliferation (ki67, p27), apoptosis (cleaved caspase-3) and neoangiogenesis (CD31). For each patient, the analysis was performed both on pre-operative specimens (core-biopsies) and

surgical specimens. Changes from baseline to post-treatment were assessed with MedCalc 12 (unpaired T-test).
Results: Post-doxycycline tumour samples demonstrated a statistically significant decrease in the stemness marker CD44 (p-value < 0.005), when compared to pre-doxycycline samples. In contrast, markers of mitochodrial mass, proliferation, apoptosis and neoangiogenesis were similar between the two groups.
Conclusion: The decrease of CD44 expression is consistent with preclinical experiments and suggests that doxycycline can selectively eradicate CSCs in BC patients in vivo. Future studies (with larger numbers of patients) will be conducted to validate these promising pilot studies.

OFP-09-012

Tumour infiltrating lymphocytes (TILs) among multiregional metastases in metastatic breast cancers

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Background & Objective: Tumour heterogeneity affects the progression of breast cancer. TILs have been studied in primary tumours, but few is known about their patterns in metastases. Our objective has been to study the tumour immune microenvironment in multiple organs affected by breast cancer.
Method: We included 10 patients with breast cancer in whom a clinical autopsy was performed. Their primary tumours(N=3) and multiple metastatic foci(N=99) were collected. The immunohistochemical expression of 5 markers (MA) was evaluated: CD3, CD4, CD8, CD45RO, FOXP3. The Kruskal-Wallis test (ANOVA) and the method of comparison by pairs were used through the Dunn test.
Results: The levels of the MA were evaluated in brain, liver, lung, ovary and other organs and in 3 primary tumours. Marker variation was seen by affected organ for metastasis of CD8, CD3, CD4, CD45RO ($p<0.05$), but not for FOXP3 ($p=0.68$). In organ comparisons, lung samples had a higher expression of several MA than brain samples (CD8, CD3 and CD45R0, $p<0.05$). In the intra-patient evaluation it was possible to observe differentiated patterns of the TILs according to the location of the neoplastic cells (more in lung vs other organs). Differences were seen in the expression of CD45RO between ER+/HER2- and ER+/HER2+. Patients with ER+/HER2- presented higher values of CD45RO compared to the ER+/HER2 + patient group($p=0.008$).
Conclusion: The tumour immune microenvironment within the same patient and in different organs is heterogeneous. This finding could explain why multiple metastases escape differently from the host immune system.

OFP-09-013

Internal radiation exposure from radioactive seeds for pathology staff, an unexplored aspect?

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Background & Objective: Localization of breast lesions using seeds containing radioactive iodine-125 is performed for almost 20 years. Iodine-125 is encapsulated in a titanium shell, eliminating the possibility of internal radiation exposure. Literature demonstrates that the titanium shell remains intact during surgical resection. However, in the pathology laboratory occasionally a seed is damaged. Hypothetically, processing weakens the shell. Ingestion of iodine-125 from one seed may cause a radiation dose over 100 times annual exposure limits. In our experience, radiation safety concerning iodine-125 in pathology laboratories requires more attention. This study aimed at investigating the effect of processing steps in the pathology laboratory and embedment in human tissue and minimizing staff radiation risks through process optimization.
Method: Used and new seeds were exposed to the regular processes of cutting up surgical specimens, processing to paraffin blocks and sectioning of tissue blocks. Effects on the seeds were investigated by energy-dispersive X-ray spectroscopy. Staff radiation exposure and possible procedural improvements were assessed in each step.
Results: Neither exposure to chemicals applied nor embedment in tissue altered the thickness or composition of titanium. Improvements to the process included accurate accounting for radioactive seeds, individual storage of seeds and improved documentation for tissue supplied by the surgeon. After optimizing the protocol, no additional radiation incidents were observed. Awareness of radiation safety among staff increased.
Conclusion: Iodine-125 seeds are not fully resistant to mechanical handling in the pathology laboratory. Optimizing procedures reduces the chances of dissecting radioactive seeds and improves radiation safety in the pathology laboratory.

OFP-09-014

"Oncomining" breast: findings of NGS analysis in carcinomas and applicability in needle biopsies

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Background & Objective: With the implementation of NGS-based techniques in routine diagnostics, tumours are currently not only classified on the basis of their histology, but also on their profile of genomic alterations. In this context, targeted-gene sequencing can be of great value to offer the best possible treatment. We report our experience with Oncomine Solid Tumour DNA Kit®, a test covering hotspots of 22 frequent mutated genes in cancer, in a small cohort of invasive breast carcinoma, mostly in small needle biopsies
Method: Oncomine Solid Tumour DNA Kit® was performed in the PGM platform in 34 formalin-fixed paraffin-embedded tissue samples of invasive breast carcinoma (14 estrogen receptor positive [ER+], 16 triple negative [TN], 1 HER2-enriched, 2 unclassified). Relevant clinical and pathological information was collected for each case. Mutation status was examined with respect to clinical, pathologic, and immunohistochemical parameters.
Results: TP53 was the most prevalent mutated gene (33%), followed by PIK3CA (24%). Non-luminal (TN, Her2-enriched) cases displayed significantly more mutations per case than ER+ cases (p=0,0384). Mutations in TP53 as well as in receptors tyrosin kinase EGFR and MET were significantly associated with TN subtype (p=0,0084; p=0,0068). Interestingly, the 4 cases with MET mutations had coincidental mutations in TP53. A luminal B case immunohistochemically negative for Her2 showed an activating actionable mutation in ERBB2 by NGS that was used for treatment.
Conclusion: NGS analysis with the Oncomine test is feasible in breast needle biopsies and has the potential for detecting relevant genetic events for patient management by offering personalized therapeutic options.

OFP-09-015

Papillary breast lesions: concordance study between core needle biopsy and surgical specimen diagnosis. Are we overtreating patients?

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Background & Objective: Papillary breast lesions represent a heterogeneous group with similar morphological characteristics but distinct biological behavior. The categorization of papillary lesions remains one of the most challenging topics in breast pathology. Aim: to determine the concordance rate between core needle biopsy (CNB) and surgical

specimen diagnoses of papillary breast lesions in a nineteen-year period (2000-2018).
Method: Papillary lesions diagnosed in CNB (n=152) and respective surgical specimens, when available, were retrieved from our Pathology Department database and reviewed.
Results: Papillary lesions in CNBs were classified as: B2-benign (n=63;41,4%), B3-uncertain malignant potential (n=67;44,1%) and B5-malignant (n=22;14.5%). In B2 group, 18/63(28.6%) lesions were excised and diagnosed as: papillomas (n=17;94.4%); papilloma with DCIS (n=1; 5.6%). In B5 group, all excised lesions were classified as malignant: papillary DCIS (n=8); encapsulated papillary carcinoma (n=6); solid papillary carcinoma (n=3); mixed invasive carcinoma (n=2); NST carcinoma with solid papillary areas (n=2); papillary carcinoma (n=1). In B3 group, 58/67(86.6%) lesions were excised, and 40 (69%) were classified as benign: papilloma (n=32); papilloma with atypical hyperplasia (n=7); complex sclerosing lesion (n=1). The remaining B3 lesions 18/58(31%) were classified as malignant: papillary DCIS (n=10); encapsulated papillary carcinoma (n=6); solid papillary carcinoma (n=1); mixed invasive carcinoma (n=1). Size tended to be smaller in benign compared to malignant lesions (median diameter:16mm and 34.5mm, respectively).
Conclusion: The concordance rate between the diagnoses in CNB and surgical specimens is high in benign and malignant lesions (94.4% and 100%, respectively). The high rate of benign lesions in the B3 group (69%) raises the possibility of overtreatment in some cases and should be taken into consideration whenever discussing treatment options.

Tuesday, 11 September 2018, 08:30 - 12:00, Room B1
OFP-10 | Gynaecological Pathology

OFP-10-001
Genotype and phenotype of POLE mutated endometrial cancer
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Background & Objective: Since the TCGA publication in 2013 endometrial carcinoma with POLE mutations are of interest as they are typically ultra-mutated and highly immunogenic. Previous studies with limited patient numbers additionally showed an excellent outcome. The aim of our study was to substantially increase the number of POLE mutated tumours and to correlate it with clinicopathologic parameters and outcome.
Method: The cohort was combined from the University Hospital of Bern, Switzerland (N=255) and the Karolinska Institute, Sweden (N= 349). Clinical data include preoperative patient characteristics, therapies, histology, and follow-up. To identify POLE exonuclease domain mutations, genomic DNA was isolated from FFPE tumour tissue and transferred to standard Sanger Sequencing of the exons 9-14.
Results: Pathogenic POLE mutations were identified in 54 of 599 analyzable tumours (9%). The mutations were located on exons 9,12,13, and 14. POLE mutated tumours occurred at younger age (61.3 yrs vs 66.6 yrs; p=0.001), showed more lymphovascular space invasion (LVSI) and more aneuploid tumours. Clinically, no significances were found for BMI, family history of cancer or medication. Histologically, no differences in FIGO stage, tumour type or grade were evident. POLE mutated tumours showed a slightly better progression free and disease specific survival, however these differences were not significant (log rank p= 0.322 and p= 0.988).
Conclusion: Our findings indicate that the role of POLE mutations in the prognosis of endometrial cancer still needs more clarification. Possibly more factors such as additional mutations or total mutational burden might be needed to define the differences of prognostication in POLE mutated endometrial carcinoma.

OFP-10-002
Time series analysis of TP53 gene mutations in recurrent vulvar cancer
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Background & Objective: The impact of TP53 gene mutations in the clinical course of vulvar squamous cell carcinomas (SCC) is unclear. In is unknown which role TP53 gene mutations play for recurrent vulvar SCC and if the TP53 gene mutational status influences disease-free intervals.
Method: To document the course of TP53 mutations in recurrent HPV-negative SCC arising in inflammatory vulvar dermatoses the full coding sequence of the TP53 gene was analyzed in DNA extracted from archival tissues of primary and recurrent SCC of 21 women and correlated with disease-free survival.
Results: 6/21 patients with a p53 wild-type SCC had the first recurrence after a median of 62 months (range 14-144). 3 SCC recurred as p53 wild-type and 3 harbored TP53 mutations. 15/21 primary SCC with TP53 mutations recurred after 42 months (range 12-108). The primary SCC harbored TP53 point mutations (n=10), frame shift (n=4) and stopgain mutations (n=1). 13/15 recurrent SCCs carried again TP53 mutations: 5 with identical mutations, 8 with different, more complex TP53 mutations. The p53 mutational status in the recurrence changed in 5/21 patients after 5-7 years disease-free intervals. Patients with multiple recurrences had increasingly shorter disease-free intervals with identical TP53 mutations.
Conclusion: In summary SCCs with and without TP53 mutations recurred, but patients with p53 wild-type SCCs had longer disease-free intervals. TP53 mutations showed higher complexity in recurrences indicating increased genetic instability. True clonal recurrences with identical mutations were rare. These observations suggest that TP53 mutational status may affect oncological outcome in HPV-vulvar SCC and may assist in therapy planning and as a prognostic marker.

OFP-10-003
P16 immunostaining and HPV detection are reliable tools to differentiate squamous cell carcinoma of the cervix metastatic to the lung and primary pulmonary squamous cell carcinoma
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Background & Objective: Squamous cell carcinoma (SCC) of the cervix is virtually always associated with persistent high-risk human papillomavirus (HR-HPV) infection. When women with primary cervical SCC develop squamous lung lesions, distinguishing a metastatic lesion from a second primary is challenging. We aimed to assess the usefulness of p16 and HPV in the differential diagnosis between primary pulmonary SCC and metastatic lung SCC originating from the cervix.
Method: We retrospectively reviewed a cohort of primary pulmonary SCCs (n=22), lung metastases from cervix SCC (n=25) and paired cervical primaries (n=14) diagnosed at IPO-Porto (1986–2018). P16 immunostaining and HPV genotyping were performed. Statistical analysis was done to compare groups.
Results: P16 was diffusely positive(block-like) in 21 metastases and one primary pulmonary SCC (84%vs.5%, p<0.001); multifocal in two metastases and six primaries (8%vs.27%) and negative in two metastases and 15 primaries (8%vs.68%). HPV DNA was detected in 14 lung metastases and in none of primary pulmonary SCCs (67%vs.0%, p<0.001). In 7 metastases HPV testing was inconclusive due to poor/insufficient material. Sensitivity/specificity were: 84%(CI:64-96)/96%(CI:77-100) for p16 immunohistochemistry (positivity threshold: block-like staining), 67%(CI:43-85)/100%(CI:84-100) for HPV detection and 88%(CI:69-98)/96%(CI:77-100) for combined p16/HPV. Most HPV-positive tumours displayed p16 block-like positivity (13/14, 93%). HPV

genotypes identified in metastases included HPV16 (57%), HPV18 (14%), HPV39 (14%), HPV59 (7%) and concomitant HPV18/HPV31 (7%). Metastases and corresponding primary cervical SCCs were concordant both for p16 (n=14) immunostaining and HR-HPV (n=5).
Conclusion: P16 and HPV testing are sensitive and specific markers to differentiate primary pulmonary SCC from metastatic SCC originating from the cervix and should be considered for routine diagnosis.

OFP-10-004
Should we continue to report cytopathic effects of HPV infection without dysplasia in cervical biopsies?
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Background & Objective: According to current terminology, lesions previously described as koilocytosis without atypia, condylomas and CIN1 should all be designated as LSILs. However, given the high false-positive rate of histology for prediction of HPV infection, many pathologists continue to descriptively report koilocytosis per se. We aimed to determine the diagnostic frequency of koilocytosis without dysplasia in our current practice and review the clinicopathological features of these patients.
Method: We retrospectively reviewed all cervical biopsy reports from 2012 to 2017 (IPO-Porto, n=951), and identified those reporting koilocytosis without dysplasia. Patients' clinical files were reviewed to retrieve HPV testing and previous cytology results, colposcopic findings, treatment and follow-up.
Results: We identified 93(10%) reports consistent with koilocytosis without dysplasia, corresponding to 82 patients. Mean patient age was 41y(range:21-75), four were under 25y. Globally, 69% cases were positive for high-risk HPV, but considering only patients without previous HPV testing, this decreases to 43%. Cytology results included: 25(31%) NILM, 25(31%) ASC-US, 23(29%) LSIL, 6(8%) ASC-H, 1(1%) HSIL. Colposcopy identified transformation zone not fully visible in 39% of patients and abnormal (minor/major) findings in 64%. Thirteen patients (16%) were submitted to cone biopsy, due to persistent LSIL(n=3), cytohistological discrepancy(n=3), progression to HSIL(n=2) and inadequate colposcopy(n=6).
Conclusion: Reporting histologic changes consistent with HPV instead of LSIL, reflects the expected level of uncertainty due to difficulties in distinguishing them from normal or reactive changes. Previous knowledge of HPV testing results seems to influence pathology reporting. Overdiagnosis of HPV changes in cervical biopsies may result in increased health care costs and unnecessary surgical procedures.

OFP-10-005
Systematic histology review of 1318 cases of gestational trophoblastic disease (GTD) referred to a tertiary referral centre in one-year period (2011)
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Background & Objective: In the UK, clinical care for patients with GTD has been centralized since 1973. There are 3 centres for central review of these cases providing specialist care and centralised review of all cases with HM. This study was designed to look at the diagnostic pattern of cases referred with diagnosis of Hydatiform moles (HM) and gestational trophoblastic neoplasm (GTN) to Charing Cross Hospital, London in year 2011 and the role of referent pathologist in refining the diagnosis.
Method: All the cases of GTD referred from 1st January to 31st December 2011 were retrieved from our electronic data base. The diagnosis imparted on systematic review by one of the two specialist pathologists was compared to the referral diagnosis.
Results: A total of 1269 cases were referred with diagnosis of HM in the uterine cavity. Review confirmed HM in 849 (66.9%) cases; 420 (33.1%) cases were overcalled as HM. 1 of the 9 cases referred as non- molar miscarriage turned out to be a partial hydatiform mole. Of the 11 tubal ectopics that were submitted as likely molar, none showed evidence of HM. Of 38 cases referred with a diagnosis of GTN, 16 were confirmed as gestational trophoblastic tumours, 11 were placental site nodules (PSN/APSN) and 11 diagnosed as non-gestational tumours.
Conclusion: Nearly a third of cases were overcalled as HM. Common mimics included aneuploidy, placental mesenchymal dysplasia, Digynic triploid, hydropic abortion and early miscarriage. Tubal ectopics with exaggerated appearing trophoblast remains the most common pitfall.

OFP-10-006
Association of tumour morphology with mismatch-repair protein status in endometrial cancers: a single unit experience
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Background & Objective: The aim of the study was to analyze the clinicopathological characteristics of endometrial cancers (EC) focusing on those correlated with DNA mismatch repair (MMR) alterations.
Method: 106 cases of EC have been collected between 2015 and 2017. For each case we reported: histotype, tumour grade, isthmus involvement, pattern of invasion, tumour-infiltrating lymphocytes (TILs), lymphovascular invasion (LVI), myometrial invasion, lymph node metastases, endometriosis, tubaric lesions. Immunohistochemical evaluation of the MMR proteins (hMLH1, hPMS2, hMSH2, hMSH6) and microsatellite instability (MSI) analysis were performed.
Results: 23/106 (21%) cases showed immunohistochemical alteration of MMR proteins: 7 (33.3%) cases lost hMLH1 with MLH1 promoter hypermethylation, 16 (66.7%) EC had a loss of hMSH2 and/or hMSH6 and 13 (81.2%) of these had a familiar neoplastic history. 11 (68%) MSH2-MSH6 deficient EC were endometrioid, 4 (25%) showed prominent ambiguous features and 1 was a serous carcinoma. MELF pattern of myoinvasion was identified in 9 cases. TILs was >40/10HPF in 5 cases. 2 cases of tubaric lesions (1 case of STIC - Serous Tubal Intraepithelial Carcinoma -, 1 case of SCOUT - Secretory Cell Outgrowth -) were found. 5 (21.7%) EC cases had lymph node metastases (all with diffuse LVI and 4 (80%) with MELF). A statistically significant association between loss of MMR-IHC and EC with ambiguous features and/or MELF pattern of invasion was found ($p<0.05$).
Conclusion: The MMR-deficient EC showed more frequent ambiguous features, TILs and MELF pattern of myoinvasion. Morphological features along with IHC-MMR enhance the detection of EC patients at risk of Lynch syndrome.

OFP-10-007
Hedgehog pathway expression in high grade serous carcinoma of the ovary and clinical implications
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Background & Objective: Ovarian cancer is the fifth leading cause of death from cancer among women. A pathway of interest is Hedgehog (HH) signalling pathway, whose aberrant activation has been reported in ovarian cancer. We determined the prevalence of HH pathway activation in high-grade serous ovarian cancer (HGSOvCa) by immunohistochemistry and in cell lines.

Method: Formalin-fixed paraffin embedded blocks were obtained for a cohort of 56 patients and immunohistochemical staining performed for HH pathway components GLI1, PTCH1 and SHH. Expression of the HH pathway components was correlated to clinical outcomes. Ovarian cancer cell lines were tested.
Results: All cases had a high or moderate expression of GLi1 and greater than 90% of patients had either high or moderate expression of PTCH and SHH. Patients with high expression of HH pathway components had more disease recurrence. The risk of disease recurrence was significantly increased in those with high SHH expression ($p = 0.0121$). Patients with high SHH ligand expression in their primary tumour had significantly reduced 5-year survival. Western blotting analysis demonstrated an increase in GLI1 and SHH protein expression in six ovarian cancer cell lines compared to the immortalised normal ovarian epithelial cell strain, OCE-1 indicating aberrant HH activation. Expression of both HH pathway components was decreased following treatment with HH inhibitors.
Conclusion: *Hedgehog pathway is aberrantly activated in HGSOvCa and over expression of HH components increases the risk of disease recurrence *Over-expression of SHH ligand is associated with a poor survival outcome following primary treatment *Hedgehog pathway components are overexpressed in ovarian cancer cell lines and are downregulated with Hedgehog inhibitors.

OFP-10-008
BCOR rearranged endometrial stromal sarcoma (ESS). A clinico-pathological study of four cases

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Background & Objective: A new translocation involving BCOR have been recently described in ESS. The literature covering this entity mainly consisted so far in small case series focused on molecular genetics and pathology. There is therefore a needing for a more precise clinical and pathological description of this entity to allow a more precise approach to patients. The aim of this study is to provide a detailed clinico-pathological description of BCOR rearranged ESS (BRESS).
Method: This study was approved by Institutional Ethics Committee. All the BRESS diagnosed at Fondazione IRCCS Istituto Nazionale dei Tumouri, Milan, Italy were included. All slides were reviewed; morphology, immunohistochemistry, AJCC Staging Group, treatment and follow-up were evaluated and recorded.
Results: Four patients full-filled the inclusion criteria (median age, 43 y). Most cases (3/4) presented with advanced stages. Surgical approach was hysteroannessectomy in all cases. Tongue like projections, lymphovascular involvement, spindle cell fascicular appearance and cytological atypia were demonstrated in all specimens. Collagen plaques were found in 3/4 cases, a myxoid microcystic pattern was found in half of the cases. All cases were strongly positive for BCL1 and CD10. Smooth muscle antigens, oestrogen and progesterone receptors were mostly negative. All patients underwent neoadjuvant or adjuvant Epirubicin + Ifosfamide. Case #1 did Gemcitabine + Docetaxel at progression. The final follow-up ranged from 7 to 13 months (median Follow-up, 9 mo). Two patients were with No Evidence of Disease after multimodal therapy. The remaining two patients are Alive With Disease.
Conclusion: BRESS is an aggressive disease presenting at advanced stage, managed with multimodal therapy.

OFP-10-009
Primary neuroectodermal tumours of the ovary: a clinico-pathologic study of 10 cases

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Background & Objective: Primary Neuroectodermal Tumours (PNETs) of the ovary are rare monophasic teratomas composed exclusively or almost exclusively of neuroectodermal tissue. Approximately 100 cases of ovarian PNETs have been reported in the literature. The aim of this study was to investigate the morphologic features, clinical manifestations and prognosis of 10 cases of PNETs of the ovary.
Method: 10 ovarian PNETs diagnosed between 2000 and 2017 were collected from the surgical pathology files of the Hospital de Oncología, CMN SXXI IMSS.
Results: Patients ages ranged from 14 to 46 years (median, 28 years). The main clinical manifestations were irregular vaginal bleeding (5 patients), pelvic mass (8 patients), and lower abdominal pain (7 patients). The CA-125 levels of 5 patients were elevated. Eleven patients underwent surgical resection, and four patients underwent preoperative and/or postoperative combination chemotherapy. The tumours, which varied from cystic to solid, range from 8 to 24 cm (average, 15 cm) in diameter. Morphologic features of central nervous system tumours were seen: 5 ependymomas, 4 medulloblastomas, and one glioblastoma. By immunohistochemistry all cases expressed at least one marker of neuronal differentiation (synaptophysin, CD56, and chromogranin, GFAP was positive in 6 cases). The follow-up of all patients was available and ranged from 8 to 128 months. Six patients died of disease, 3 experienced recurrences and one is alive with disease.
Conclusion: PNETs of the ovary are rare monophasic teratomas, they mainly involve young women during their reproductive age, therefore, accurate diagnosis followed by multimodal treatment should be taken into consideration for fertility preservation.

OFP-10-010
Napsin and AMACR are superior to HNF1B in distinguishing between mesonephric carcinoma and clear cell carcinomas of the gynaecologic tract

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Background & Objective: Mesonephric carcinoma is a rare, non-HPV associated, gynaecologic neoplasm commonly mistaken for clear cell carcinoma. Both mesonephric carcinomas and clear cell carcinomas are negative for estrogen receptor (ER) and p16. HNF1B, a marker for clear cell carcinoma, has also been found to also be positive in a subset of mesonephric carcinomas. However, other more recent markers for clear cell carcinoma, such as Napsin and AMACR, have not yet been studied in mesonephric carcinomas.
Method: We assessed the immunohistochemical expression of HNF1B, Napsin, AMACR and ER in a series of 13 mesonephric carcinomas (5 uterine corpus, 5 cervical, 1 ovarian, 1 broad ligament, 1 vaginal; on whole sections) and 55 clear cell carcinomas (5 cervical, 50 uterine; on tissue microarrays). Any intensity staining in >1% of cells was considered positive.
Results: HNF1B expression was seen in 3/9 (33%) of mesonephric carcinomas and 50/55 (91%) of clear cell carcinomas. ER expression was seen in 3/13 (23%) mesonephric carcinomas and 6/55 (11%) clear cell carcinomas. Napsin expression was seen in 2/11 (18%) of mesonephric carcinomas, which was focal and present in only 1% of cells in both cases. Napsin expression was seen in 42/55 (76%) of clear cell carcinomas, which was more likely to be diffuse (average: 50% of cells). AMACR expression was seen in 1/11 (9%) of mesonephric carcinomas, which was again present in only 1% of cells.
Conclusion: Napsin and AMACR appear to be superior to HNF1B in distinguishing between mesonephric carcinomas and clear cell carcinomas of the female genital tract.

OFP-10-011

Transformation of ovarian low-grade serous carcinoma to high-grade carcinoma: a rare phenomenon and report of 4 cases

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Background & Objective: The transformation of ovarian low-grade serous carcinoma (LGSC) to high-grade carcinoma is exceedingly rare (with only 6 cases in the literature) and the molecular events behind the transformation are unknown. Our objective was to evaluate p53, BRAF and WT1 immunohistochemistry in 4 cases of LGSC with high-grade transformation, in order to better understand the underlying molecular events.
Method: We identified 4 cases where LGSC showed high-grade transformation. H&E slides were reviewed and immunohistochemistry was performed. p53 was scored as wild-type, null or overexpressed. BRAF and WT1 were scored as positive or negative.
Results: Two cases with a high-grade carcinoma arising from LGSC, showed positive WT1 and negative BRAF in both the low-grade and high-grade components. p53 was wildtype in the low-grade area of both cases. In the high-grade area of case 1, p53 was wild-type and in case 2, p53 was null. In case 3, the LGSC component was p53 wildtype but the transformed carcinosarcomatous component was p53 overexpressed. Again, BRAF was negative and WT1 was positive in both components. In case 4, LGSC transformed to an undifferentiated carcinoma (immunohistochemical stains were not available).
Conclusion: Transformation from LGSC to high grade carcinoma is rare, with only 4 cases occurring over 20 years at our institution. Acquisition of abnormal p53 was observed in 2 of 3 cases. No cases displayed abnormal BRAF. Targeted DNA sequencing is being performed with results to follow.

OFP-10-012

Evaluation of mismatch repair (MMR) protein expression with correlation of germline mutation analysis for Lynch syndrome screening in endometrial cancers in Turkish women; preliminary results

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Background & Objective: Universal screening for Lynch syndrome has been recommended for all endometrial carcinoma cases. Our aim is to investigate the incidence of MMR protein expression loss in a series of endometrial carcinomas; which can reflect Lynch syndrome (LS).
Method: We performed MLH1, MSH2, MSH6 and PMS2 immunohistochemistry (IHC) in 227 endometrial tumours operated between 2008-2018 followed by MLH-1 methylation testing when appropriate. MMR deficient cases were further sent to genetic analysis.
Results: 40 out of 227 (17.6%) cases displayed MLH1&PMS2 loss, 9 (3.9%) MSH2&MSH6 loss, 1 (0.4%) MSH6 loss and 5 (2.2%) PMS2 loss. 6 (15%) of MLH1 deficient cases were unmethylated. Overall a total of 21 (9.5%) cases were unmethylated MMR deficient and directed to genetic testing. 36.1% of these cases were nonendometrioid tumours. 3 patients had a history of colon cancer, synchronous colon cancer and synchronous ovarian cancer respectively. Concomitance and history of other cancers were associated with MMR deficient status (p=0.0001). Germline testing was performed in 5 cases until now and in 80% (n:4) Lynch syndrome was confirmed.
Conclusion: In our study, MMR immunohistochemistry and MLH1 methylation analysis together seems to be efficient for selecting patients to direct genetic surveillance and the preliminary results showed high correlation with germline testing. Therefore we suggest use of universal IHC screening for all endometrial carcinoma cases.

OFP-10-013

Does HPV16 status influence outcome in HPV positive cervical carcinomas?

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Background & Objective: HPV is an established cause of cervical cancer. In oral\cranogenital carcinomas HPV status possesses prognostic value, where HPV16 has a more favourable prognosis attributed to better treatment response. We compared HPV16 with other genotypes for disease-free survival (DFS) in HPV-associated cervical cancer.
Method: A retrospective cohort study evaluated 212 cervical carcinomas and analysed 159 cases after excluding HPV-negative carcinomas (n=20), multiple HPV infection (n=16), unknown HPV type (n=3) and persistent disease after initial treatment (n=14). LiPA25 was used for HPV-detection. Kaplan-Meier estimator and Cox regression were used.
Results: Median age was 50 years (range:26-87); 82% were squamous-cell carcinoma; FIGO stage was ≤IB1 in 37%, IB2-IIB2 in 40%, ≥III in 23%, unknown in 1%; 16% had lymph node metastases; 65% were HPV16-positive. Initial treatment comprised radiotherapy (RT, 64%) surgery (50%) and chemotherapy (9%). Median follow-up was 67 months. Overall 5-year DFS was 60% (65% in HPV16 and 49% in other genotypes group). HPV16 was associated with a significant 39% reduction in the hazard of relapse/death in univariate analysis (HR=0.61,95%CI0.38-0.98, p=0.04) and a non-significant 30% reduction when controlling for FIGO stage, lymph node metastasis and RT (adjusted HR=0.70, 95%CI 0.42-1.17, p=0.17). RT was independently associated with DFS (p=0.02) but without increased benefit in HPV16-driven cancers.
Conclusion: HPV16 was associated with an improvement of DFS although not significant when controlling for stage, lymph node metastasis and RT. We also found no evidence that HPV16 genotype predicts a better disease control in RT-treated patients.

OFP-10-014

BRCA and ovarian cancer: a morphological, immunohistochemical and genetic study of high grade serous carcinoma and tubal precursors

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Background & Objective: Solid-pseudoendometrioid-transitional (SET) variant of high grade serous carcinomas (HGSC) has been recently described in BRCA 1/2 mutated patients. The association between SET-HGSC and Serous tubal intraepithelial carcinoma (STIC) is still unclear. The aim of the study was to investigate the correlation between BRCA mutational status and HGSC morphology, tubal lesions, immunohistochemical (IHC) profile and tumour infiltrating lymphocytes (TILs).
Method: 27 consecutive patients with HGSC (patient mean age 52.5 years) were collected from 2015 to 2017. Tumour histological patterns were evaluated on H&E sections. HGSC diagnosis was confirmed by p53/WT1 IHC status, histological assessment of SCOUT (Secretory Cell Outgrowth), STIL (Serous Tubal Intraepithelial Lesion) and STIC was performed using a double Bcl2/p53 IHC staining. Intratumoural TILs (iTILs) were counted semi-quantitatively as reported in literature. BRCA mutational status was tested both on blood and tissue samples.
Results: 9 out of 27 (33.3%) patients carried a BRCA mutation, amongst them 7 (77.8%) were known pathological variants and 2 (22.2%) were variants of uncertain significance (VUS). SET morphology (≥50% solid-pseudoendometrioid-transitional) statistically tended towards BRCA+ patients compared to BRCA- group (p=0.06), while BRCA status became statistically irrelevant when VUS patients were excluded from BRCA mutated group. SET morphology resulted strongly associated with increased iTILs (p=0.0005). Furthermore, SET-HGSC showed a lower association with STIC compared to classic morphology (p=0.02).

Conclusion: SET-HGSC showed a statistically significant association with increased iTILs. STIC was significantly more frequent in HGSC with classic morphology. However, no histological features were significantly associated with BRCA mutational status in our series.

OFP-10-015

Human papillomavirus typing of cases showing atypical squamous cells of undetermined significance in pap tests in Israel

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Background & Objective: The types of HPV associated with development of uterine cervix dysplasia, carcinoma and genital warts are well characterized. Our aim was to study the distribution of HPV types in Israel among patients diagnosed as ASC-US in Pap test.
Method: HPV typing was performed in 209 cervical ThinPrep samples diagnosed as ASC-US using Master Diagnostics HPV Direct Flow CHIP on the eBRID automated system. This PCR amplification and reverse dot blot hybridization-based method identifies 36 types of HPV (18 high risk, 18 low risk) and the presence of unspecified HPV genotype (using a universal HPV probe detecting L1 consensus region).
Results: The median patient age in our cohort is 33 years (range 20-60 years, average 34.1 years). HPV typing showed no infection in 93 patients (44.5%), high risk HPV in 58 patients (27.8%), both high and low risk HPV in 17 patients (8.1%), low risk HPV in 27 patients (12.9%) and unspecified HPV in 13 patients (6.2%). In one case HPV typing failed. The relative prevalence we found for each of the 36 types is presented and shows differences from the traditional accepted distribution (e.g high prevalence of types 53, 66 and 42).
Conclusion: The relative prevalence of the HPV types we found in our cohort of ASC-US diagnosed patients deviates from the accepted distribution in the literature. The type of epithelial abnormality (LSIL & HSIL vs USC-US), method of HPV detection, geography as well as HPV vaccination may all contribute to these differences.

Tuesday, 11 September 2018, 17:15 - 19:15, Auditorium
OFP-11 | Cytopathology

OFP-11-001

Conisation rates in HPV-positive women after screening cotest with 2-3 year follow-up

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Background & Objective: Primary high-risk HPV (hr-HPV) screening yields a large number of positive tests needing follow-up (FU). For the sake of not missing high-grade lesions (CIN2+), we may be at risk for overtreatment. The aim of this study is to analyze the rate of cervical conization (CC) after a positive HPV test in a screening cotest study.
Method: Following positive HPV baseline results from a cotest screening of 5053 women, they were advised to undergo colposcopy. Depending on biopsy results, they were managed according to EU guidelines. Cytology was performed with ThinPrep® and HPV-mRNA detected by APTIMA®. CC of women with biopsy-proven CIN2+ lesions was issued. After a 2-3 year FU period, conization rate and histological review of samples was analyzed.
Results: The prevalence of hrHPV was 9% (454 cases), 299 samples with normal cytology and 155 with ASCUS+. A CIN2+ lesion was diagnosed in 90 of 272 (33,1%) hrHPV-positive women biopsied and was more common in women with HPV and cytology abnormalities (59,5% vs 21,3%). Conization was performed in 73 of them (26,8% of biopsied women) after FU, increasing from 22,2% (60/270) at baseline. Upon review, 6 cases were considered overtreated (2,2% of patients at FU) , reclassifying CIN2 biopsies.
Conclusion: CIN2+ lesions were treated by CC in 22,2% of hrHPV-positive women biopsied who underwent screening with cotest. This rate increase to 26,8% after 2-3 year FU. Histological overinterpretation of CIN lesions prompted conization in 2,2% of these patients. Caution to avoid overtreatment is advised after primary hrHPV testing.

OFP-11-002

Pitfalls in the diagnosis of anaplastic large cell lymphoma in cytology

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Background & Objective: Anaplastic large cell lymphoma (ALCL) is CD30 positive T-cell neoplasm which includes two morphologically indistinguishable subtypes ALK+ and ALK– ALCL. In fine needle aspiration biopsy (FNAB) samples it is sometimes difficult to differentiate between ALCL and other types of lymphomas with anaplastic features.
Method: We reviewed 48 cases that were initially diagnosed as ALCL or suspicious for ALCL from FNAB samples between 2008 and 2017.
Results: 26 out of 48 cases were confirmed as ALCL by histology, in 10 cases histological examination was either not performed or was inconclusive due to inadequate or necrotic samples and in eight cases different type of lymphoma was diagnosed: peripheral T-cell lymphoma NOS (PTCL NOS) in two, Hodgkin lymphoma (HL) in three cases and one case of diffuse large B-cell lymphoma (DLBCL), ALK-positive large B-cell lymphoma and angioimmunoblastic T-cell lymphoma (AITL). In cases of PTCL NOS and AITL cytological diagnosis was based on many anaplastic cells similar as present in other ALCL cases, which expressed CD30 and T-cell markers. In one case of HL we only had morphology, in two other cases CD15 was negative and T-cell markers were not performed. In DLBCL case anaplastic cells were CD30 positive and on flow cytometry we could not prove monoclonality of B cells. The case of ALK-positive large B-cell lymphoma was missed because of inadequate immunostains.
Conclusion: Most cases of ALCL could reliably be diagnosed from FNAB samples if material is adequate for additional immunocytochemical and flow cytometric studies. The main issue remains differentiation from other CD30 positive T-cell lymphomas with anaplastic morphology.

OFP-11-004

Cytomorphological and fluorescent immunocytochemical diagnosis of effusions from the abdominal cavity on biochips using telemedicine technologies

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Background & Objective: The study is conducted to evaluate the possibilities and advantages of using fluorescent immunocytochemical techniques (FICC) of effluent liquids on biochips, and the possibility of remote result interpretation.
Method: 98 ascites fluids were studied cytologically and with FICC on biochips, including the further use of telemedicine technologies. Biochip is a high-tech medical product that is a glass preparation divided in cells and containing MA: Ber-Ep4, CA-125, SK7, CK20 conjugated with fluorochrome AlexaFluor488. The study included: traditional cytological study on liquid preparations, FICC biochip study, on-line consultation of biochip reaction images. Used equipment: Cytospin-3 cytocentrifuge, Bioscan001S scanner, Zeiss Axio imager Z2 fluorescence microscope. The control was made by the traditional ICC.
Results: 98 samples were cytologically examined: specific exudate was diagnosed in 41 cases, exudate with reactive changes in mesothelium – 23

cases, presumptive diagnosis of metastatic effusion - 34 cases. Subsequent FICC confirmed traditional cytology and supplemented the metastatic exudate group to 63 samples, and the reactive ones up to 35 samples. The reaction with the MA group in 90.5% of the samples allowed to localize the primary source. Time for a single biochip study is 60 minutes. Result comparability with the traditional ICC was 91%.
Conclusion: FICC study on the biochip is a reliable and fast method for diagnosing the nature of exudate fluids, which is comparable in accuracy with traditional ICC differential diagnosis of the tumour process. This biochip advantage is the availability at the medical institutions, where there is no full cytological laboratory.

OFP-11-005
Pancreatic endoscopic ultrasound-guided fine needle aspiration cytology: its importance in clinical practice over a period of 10 years
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Background & Objective: Pancreatic Endoscopic Ultrasound-Guided Fine Needle Aspiration Cytology (EUS-FNAC) is a well-established, minimally invasive, safe and cost-effective diagnostic procedure, leading to accurate diagnoses. We aimed to analyze the importance of Pancreatic EUS-FNAC, in the diagnosis of pancreatic lesions at our institution, over a period of 10 years.
Method: All pathology reports and clinical data were retrieved from the files, over a period of 10 years. The EUS-FNA and Cytology protocols, as well as the percentage of non-diagnostic cytologies and the diagnoses, were analyzed.
Results: Over a period of 10 years, 653 Pancreatic EUS-FNAC were performed at our hospital by the same gastroenterologist using 19G, 22G or 25 G needles, in the presence of a cytotechnologist. Smears (an average of 3 Giemsa+ 3 Papanicolaou) and a cell-block (for Haematoxylin-Eosin stain, immunocytochemistry and molecular biology techniques), were performed. FNACs were read by 2 pathologists. There were 94.2% diagnostic cytologies. Forty-eight percent (48.4%) of the cytologies were positive for malignancy. 82.5% had a specific diagnosis of which the main groups were: adenocarcinoma (n=255), serous cysts (n= 66), neuroendocrine tumours (n= 44), mucinous tumours (n=40), and metastatic lesions (n=16). In the group of patients with a EUS-FNAC specific diagnosis, this was accepted as the final diagnosis for the management of patients by the Multidisciplinary Team Meeting with no further invasive diagnostic procedures.
Conclusion: At our institution, pancreatic EUS-FNAC has proven to have a high accuracy for the diagnosis of pancreatic lesions and be an important tool in the management of these patients.

OFP-11-006
False negative results in thyroid fine needle aspiration cytology
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Background & Objective: Thyroid fine needle aspiration (FNA) has a reported false negative rate (FN) lower than 3%. We aimed to estimate the FN of thyroid FNA in our institution and to understand its causes.
Method: Between 2012 and 2016, 8160 thyroid FNAs were performed, the vast majority (95%) with ultrasound (US) guidance. Of these, 4900 (60%) were diagnosed as benign, from which 659 were submitted to surgery. A histologic diagnosis of malignancy was made in 10 (1.5% FN). These cases were then reviewed.
Results: The patients (6 men, 4 women) were between 18-72 years old. Nodules ranged from 38-95 mm. The US risk of malignancy was reappreciated in 7 patients (low in 6, intermediate in 1 - ATA 2015). The diagnosis of hyperplastic/colloid nodule was maintained in 8 cases and 2 were reclassified as follicular lesions of undetermined significance. Histologically, 7 cases were reclassified as NIFTP, and the remaining as follicular variant PTC (PTCFV). Macrofollicular/cystic areas, focal or diffuse, and a heterogeneous distribution of typical PTC nuclei were found in all tumours. Clinical follow-up was available for 7 patients (from 9-24 months). Only one did not remain free of disease; he developed lung and bone metastasis that regressed after radioactive iodine therapy.
Conclusion: The FN in our institution is according to the literature. All cases were nodules >35mm, diagnosed as NIFTP or PTCFV. The US risk of malignancy did not contribute to identify these cases. Macrofollicular/cystic areas rich in colloid and heterogeneous distribution of typical PTC nuclei are potential pitfalls for the occurrence of FN.

OFP-11-007
Evaluation of a biomarker panel for the diagnosis of cavity effusions
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Background & Objective: Laboratory investigation of cavity fluids involves the combined evaluation of biochemical, immunological, microbiological, molecular and cytological parameters. However, routine laboratory exams do not always clarify the etiology of an effusion, stimulating the research for new biomarkers for this purpose. This aim of this study was to evaluate the performance of a hybrid panel of biomarkers in the diagnosis of the main diseases affecting pleura and/or peritoneum.
Method: Peritoneal and pleural fluids samples from 120 patients were evaluated for: NGAL (neutrophil gelatinase), VEGF-A (vascular endothelial growth factor A), PD-L1/B7-H1 (death-binding pathway), CEA (carcinoembryonic antigen), TREM-1 (trigger receptor expressed in myeloid cells type 1) and IFNγ (gamma-interferon) by Luminex®; CALP (Calprotectin) by ELISA, and ADA (adenosine deaminase) by enzymatic deamination.
Results: For malignant effusion diagnosis, CEA and NGAL presented superior performance than VEGF-A, PD-L1 and CALP. A CEA-NGAL-VEGF-A association improved sensitivity (82.0%) and accuracy (79.2%). For parapneumonic pleural effusion (PPE) and bacterial peritonitis (SBP), NGAL presented the best performance with sensitivity (57.1%), specificity (84.7%), NPV (84.7%) and accuracy (80.0%), higher than TREM-1 and CALP. A NGAL-TREM-1 association improved sensitivity (75.0%). For the diagnosis of pleural tuberculosis, γINF and ADA presented excellent specificity and NPV (93.3% and 98%, respectively) and accuracies (~93%). ADA associated to γINF-ADA showed sensitivity of 100%.
Conclusion: ADA, γINF, NGAL, CEA and VEGF-A were useful in discriminating tuberculosis and malignant etiology. However, for PPE and SBP, the used panel did not demonstrate diagnostic advantages over classic parameters DHL, pH and glucose.

OFP-11-008
Performance of the UroVysion® FISH assay for the diagnosis of malignant effusions using two cutoff strategies
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Background & Objective: The cytological examination of cavity fluids has limited sensitivity in the diagnosis of malignancy. Aneuploidy, which is commonly observed in neoplastic cells, could potentially be used as an ancillary diagnostic tool. The aim of this study was to evaluate the detection of aneuploid cells in cavitary effusion samples using the fluorescence in situ hybridization (FISH) assay UroVysion® with some adaptations and two different cutoff strategies.

Method: Seventy samples of pleural or peritoneal fluid with positive (n=40), negative (n=15) or suspicious (n=15) oncotic cytology were subjected to FISH assay with the multitarget UroVysion® kit, which is composed of probes that hybridize to the centromeric region of chromosomes 3, 7 and 17 and to the locus 9p21. FISH performance was evaluated using two different cutoffs: 1) the manufacturer's cutoff (M-FISH) and 2) a proposed cutoff (P-FISH).
Results: Using M-FISH, the diagnostic sensitivity was 57.1%, specificity 87.5% and accuracy 60.0%; with P-FISH, the sensitivity was 87.3%, specificity 71.4% and accuracy 85.7%. When combined to cytology, the sensitivity, specificity and accuracy were 88.0%, 83.3% and 87.8%, respectively. Malignant cells presented a predominance of chromosomal gains.
Conclusion: The UroVysion® test using the P-FISH cutoff was effective in demonstrating aneuploid cells in all malignant effusions, confirming the diagnosis of malignancy even in cases with suspicious cytology.

OFP-11-009

Insulinoma-associated protein 1 (INSM1) is a sensitive and specific marker for lung neuroendocrine tumours in cytologic and surgical specimens

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Background & Objective: Insulinoma-associated protein 1 (INSM1) is a potential immunohistochemical (IHC) marker for neuroendocrine differentiation with reported superior sensitivity and specificity. In this study, we performed INSM1 staining in cytology cell blocks (CB) and tested its performance in large cohorts, which has previously not been done.
Method: Small cell (SCLC, 10 cases) and large cell neuroendocrine carcinoma (LCNEC, 9 cases), typical and atypical carcinoid (12 and 11 cases), squamous cell carcinoma (SQ, 10 cases) and adenocarcinoma (ADCa, 12 cases) CB from 2007-2018 were retrieved along with 430 ADCa, 58 SQ, 17 large cell carcinoma (LCC), 24 non-small cell lung carcinoma (NSCLC) surgical cases. INSM1 (SantaCruz Biotech.) IHC was graded as 1+, 2+ or 3+. For CB, 2+ and 3+ were considered positive, whereas for resections, 1+ and higher in >5% of cells was considered positive.
Results: Nuclear INSM1 was seen in carcinoids (typical 12/12 (100%) and atypical 11/11 (100%)), 8/10 (80%) SCLC and (7/9) 78% LCNEC in CB, but not in AdCa and SQ cases. In resections, INSM1 was seen in carcinoids (typical 17/18 (94.4%); atypical 14/15 (93.5%), 11/11 (100%) SCLC and 10/12 (83.3%) LCNEC. AdCa 6/424 (1.4%), SQ 1/58 (1.7%), LCC 3/17 (21.4%) and NSCLC 1/24 (4.4%) showed INSM1 expression. INSM1 sensitivity and specificity in cytology and surgical cases were 90.5% and 100%, and 92.9% and 97.9%, respectively.
Conclusion: This large cohort further establishes the high sensitivity and specificity of INSM1 in pulmonary neuroendocrine tumours, in both cytologic and surgical specimens, which outperforms existing neuroendocrine markers.

OFP-11-010

Comparison of SurePath and GluCyte LBC platforms in detecting CIN2+ among ASC-US cytology patients using biomarkers

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Background & Objective: To assess and compare the predictability of ASC-US cytology by SurePath (BD) and CellSolutions LBC platforms in relations to MCM/Top2A (ProEx C, BD), HPV E6E7 mRNA (Proofer, NorChip) and HPV DNA (HC II, Qiagen) in identifying CIN2+.
Method: Study population consisted of patients referred for colposcopy in 5 of the 10 Canadian provinces as part of the TPAPT (Transient Persistent And Persistent Transforming) study. Cytology sample from each patient was collected in SurePath medium and processed per manufacturer's instructions and read. From the residual SurePath sample, a GluCyte slide was likewise processed and read. SurePath samples were tested for MCM/Top2A, HPV E6/E7 mRNA, and HPV DNA. Histology confirmed CIN2+ served as the disease end point. Binary logistic regression models were performed to examine the usefulness of biomarker profiles for each of the LBC platforms.
Results: 13.8% (251/1821) and 20.8% (69/331) patients were identified as having ASC-US cytology by SurePath and GluCyte platforms, respectively. The frequency of CIN 2+ in SurePath and GluCyte cohorts were 22.3% (56/251) and 17.4% (12/69). Logistic regression analysis showed no statistically significant difference between the odds ratio in each model between the two platforms.
Conclusion: Our findings show that combining biomarkers are useful in identifying high grade dysplasia in patients with ASC-US cytology. No statistically significant difference was found between the odds ratio in each model between the two LBC platforms.

OFP-11-011

Causes of discordance between cytology and histology in pancreatic lesions

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Background & Objective: This audit assessed the diagnostic performance of FNA in diagnosis of benign and malignant conditions of the pancreas in our department during 2013-16. We aimed to ascertain the proportion of discordant cases, and review these to determine if results alter diagnostic accuracy.
Method: All pancreatic FNA cytology specimens performed in our department during 2013-16 with corresponding subsequent surgical specimens were identified. For each case the reported cytological category was recorded (C1 – inadequate, C2 – benign, C3 – atypical; mucinous lesions, endocrine lesions C4 – suspicious for malignancy, C5 – malignant). The final surgical diagnosis was recorded. Discordant cases (benign histology vs C4/C5 cytology or malignant histology vs C2/C3 cytology) were retrieved from archives and reviewed by a cytopathologist blinded to the previous results. The cytological categories on review were compared to those originally reported.
Results: A total of 75 cytology specimens with corresponding surgical specimens were identified. A total of 17 cases (22.6%) were discordant. Slides were retrieved for all except three cases which were not available for review. Six out of 14 reviewed cases were confirmed to be correctly categorised (42.8%); the discordance being due to non-representative sampling. Of the remaining eight cases (57.2%), two were interpreted as inadequate (C1) while six were given a different cytological category on review which was at most one tier above or below the original cytological diagnosis.
Conclusion: Review of discordant cases confirms that sampling errors and inadequacy are the main causes of discordance. Discussion at MDT meetings allows avoidance of pitfalls associated with pancreatic cytology.

OFP-11-012

Assessing the healthcare provider factor and anatomical site in 4,381 thoracic lymph node fine needle aspirations using funnel plots/ control charts and logistic regression

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Background & Objective: Thoracic lymph node fine needle aspiration (TLNFNA) is a common procedure; however, variation by healthcare provider (HCP) and anatomical site (AS) is not routinely assessed.

Method: All cytology reports for endobronchial ultrasound (EBUS)/endoscopic ultrasound (EUS) TLNFNA specimens (4,381) were retrieved from a thoracic surgery centre for July 2012-June 2017 and classified by a hierarchical free text string match algorithm (HFTSMA) into 50 diagnostic categories (Dx), four mutually exclusive diagnostic groups (benign(BEN)|suspicious(SUSP)|malignant(MAL)|insufficient(INS)), and 23 AS. Pathologist and submitting physician/surgeon (PSPS) bias was assessed using logistic regression (LR) and funnel plots|control charts (FP|CC) centred on the group median (diagnostic/capture) rate (GMR).
Results: The HFTSMA could assign an AS and Dx in ~98% cases and the coding was accurate ~97% of time in 500 audited specimens. Eleven pathologists and six SPS were involved in >150 specimens each (range 169to1115). Overall, the TLNFNAs were BEN|SUSP|MAL|INS in 40%|6%|26%|27% of specimens. Percent MAL (number of samples) varied by station; 7|4R|4L|2R|10R|11R|11L were respectively 22%(1488), 30%(1256), 25%(476), 39%(282), 27%(254), 27%(227), 37%(138). The number of pathologist outliers (P<0.05andP<0.001) of 11 from the GMR for BEN|SUSP|MAL|INS was 4and2|2and2|1and0|0and0 respectively. Submitting physicians/surgeons (SPS) outliers (P<0.05andP<0.001) of 6 for BEN|SUSP|MAL|INS was 1and1|1and0|2and1|3and3 respectively. SPS INS rate was dependent on AS. LR confirmed the FP|CC findings.
Conclusion: The HCP and AS are significant predictors of TLNFNA pathology. If HCP bias is demonstrated, it is essential to review the reports and assess for confounders. Data was provided to interested HCPs to assist in practice self-assessment and quality improvement.

Tuesday, 11 September 2018, 17:15 - 19:15, Room A3
OFP-12 | Paediatric and Perinatal Pathology

OFP-12-001
Morphological diagnostics of Takayasu arteritis in infants
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Background & Objective: Takayasu arteritis is extremely rare in the child population. The clinical diagnosis of Takayasu arteritis in infants presents serious difficulties, and the diagnosis is rarely established during life. The aim of the study is to analyze the case of Takayasu arteritis in an infant which was not diagnosed during life.
Method: We reported an autopsy case of Takayasu arteritis occurring in a 14-week-old infant male who died on the 7th day after admission to the children's hospital
Results: An autopsy revealed left toes dry gangrene; rupture of an ascending aortic aneurysm. The histological study of aorta demonstrated round cell infiltration surrounding vasa vasorum and in the adventitia. The most severe changes were found in aortic media, which manifested itself as diffuse inflammatory infiltration and as large foci of the destruction of elastic fibers. In the aortic media, there was a proliferation of dense fibrous connective tissue, the formation of fibrous plaques. Those fibrous plaques were located in the ascending aorta, in the aortic arch, and in the descending aorta. In addition, pronounced circular cell infiltration was detected in the aortic valve and in coronary artery walls.
Conclusion: The features of the case include a rupture of the aorta and pericardial tamponade. The severity of the child's condition can be explained by the onset of aortic dissection due to large foci of elastolysis. In this case, in addition to the divergence between clinical and morphological diagnoses, we observed an overdiagnosis (sepsis and thromboembolism of the pulmonary artery), while these conditions were not confirmed by morphological examination.

OFP-12-002
Primitive mesenchymal myxoid tumour of infancy (PMMTI), a potentially highly aggressive neoplasm in infants
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Background & Objective: Primitive myxoid mesenchymal tumour of infancy (PMMTI) is a recently, described tumour with a primitive spindle/round cell morphology. BCOR internal tandem duplication is a recurrent genetic alteration shared by PMMTI and a subset of undifferentiated sarcoma (UND). In this study, we focus on UND/PMMTI with BCOR ITD to further define their clinicopathologic features.
Method: Surgical pathology and consultation files at University of Padova from 1995 to 2018 were searched for cases diagnosed as PMMTI or UND with BCOR-ITD demonstrated by FISH or RT-PCR. Clinico-pathologic features were obtained through evaluation of the medical records.
Results: 17 BCOR-ITD UND/PMMTI in the first year of life, enrolled in EpSSG or RMS 96 protocols had a M/F ratio of 8/9. Sites included head (33%), paraspinal (33%), extremities (17%) and retroperitoneum (17%). Eleven PMMTI showed round to spindle cells with prominent myxoid stroma, 6 UND were composed of round cells with minimal stroma. At last follow-up (range 2-16yr): 3 PMMTI died of disease (DOD), 1 alive in progression, 3 (2 with initial diagnosis of CIF) in remission, after relapses in 2 and metastasis in one. All 5 UND DOD with distant metastases. Five cases were recent or lost to follow up.
Conclusion: BCOR-UND are highly aggressive sarcomas with poor prognosis in 100% of cases. PMMTI, especially those morphologically resembling infantile fibrosarcoma have a better prognosis with survival in 43%, suggesting that spindle cell/CIF like morphology can define a subset of PMMTI with good prognosis.

OFP-12-003
Structural basis of complications in pregnancy using the donor egg in surrogate maternity
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Background & Objective: Placenta pathology study in surrogate maternity may reveal predictors of pregnancy complications, and thus help to develop criteria for the selection of surrogate mothers and donor blastocysts To study the structural basics for the development of pregnancy complications in surrogate maternity.
Method: Morphological study of the placenta from 206 surrogate mothers and 193 multiparous females (after IVF with own oocytes) (comparison group).
Results: Placentas in the surrogate maternity group showed extensive pseudoinfarctions, the relative immaturity of the villous tree, the increase in the number of perivillous fibrinoid, and the fibrinoid reaction of decidual tissue. Chronic villites and deciduites of unclear etiology were more often detected in the form of focal lymphohistiocytic infiltration in the villi stroma and in decidual tissue. Conclusion: The complications development in surrogate maternity are due to the failure of tolerance formation in the mother-fetus system, which manifests itself in early pregnancy by the violation of trophoblast invasion, the lack of proper spiral arteries remodeling. Surrogate mothers more often developed preeclampsia (8.5%), premature detachment of the normally positioned placenta (4.7%), hypotonic bleeding (6.1%), tight attachment of the placenta (6.6%), delayed parts of the placenta (6.6%), premature birth (23.0%) (p <0.05).
Conclusion: These processes form the substrate for the development of utero-placental insufficiency, as well as pre-eclampsia, as the most frequent complication in the surrogate maternity group. The high incidence of villites and deciduites of unclear etiology and a significant increase in the number of fibrinoids also indicate the presence of immunopathological processes.

OFP-12-004

Salivary gland neoplasms in paediatric population. Retrospective analysis of 21 cases (2000-2018) and correlation with literature

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Background & Objective: Salivary gland tumours are infrequent, representing less than 3% of head and neck neoplasms. Only 5% of them occur in children. Most of these tumours are benign, being pleomorphic adenoma (PA) the prime diagnostic. Mucoepidermoid carcinoma (MEC) is the most common malignant tumour.
Method: We collect the casuistry from 2000 to 2018 at HUVH obtaining 21 cases.
Results: Of the 21 cases, 11 (52,4%) were girls and 10 (47,6%) were boys, and the average age was 12,7y. Primary lesions account for 18 (85,7%) and 3 were secondary infiltrations (14,3%). Within the primary lesions, benign tumours represent 61,1%, being all of them PA. Malignant neoplasms represent 38,9% and comprise 5 MEC (27,8%) and 2 acinic cell carcinoma (ACC)(11,1%). Secondary lesions correspond to Hodgkin lymphoma, granulocytic sarcoma and non-Langerhans cell histiocytosis. In our series, most affected salivary gland was parotid gland (13), followed by submandibular gland (5) and palate (3). Previous fine needle aspiration (FNA) was performed in 10 cases. In 8/10 the diagnosis was concordant (6PA, 1MEC, 1ACC), being the diagnostic sensibility of 80%. In the other 2 cases, both MEC, the cytologic study suggested this entity.
Conclusion: The casuistry of our center concurs with the data found in literature, although there is few series published. Malignant neoplasms in salivary gland are more frequent in paediatric population than in adults in absolute value. Previous cytologic diagnostic in salivary gland tumours in children has a high sensibility in our series and it helped to guide the diagnosis and treatment.

OFP-12-005

Identifiable stillbirth risk factors in a province. Eleven-year register

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Background & Objective: Stillbirth definition varies through countries but the commonest used one is the WHO system. In Spain, fetal deaths are officially certified from 28 weeks of gestation or if the fetus weight 500 gr or more. Nevertheless, autopsies are performed from 22 weeks in most of the centers. Our objective is to identify risk factors associated with intrauterine fetal death in our medium.
Method: We reviewed fetal autopsies from 22 weeks or 500gr or more from the five hospitals in our province that performed autopsies between the periods 2006-2016. We analysed the risk factors previously identified at the literature: maternal infections (toxoplasma, rubeola, cytomegalovirus or Herpes), AIDS, Hepatitis, mother age, parity multiple gestation, gestation week, fetal gender, intrauterine growth restriction (IGR) according to image techniques or IGR according to autopsy examination.
Results: We analysed 210 cases. Three cases of infections were detected (2 Chagas disease and one toxoplasmosis). Mother age range was 15-44 (mean: 31,3). There was 62 cases under 30 years, 111 cases between 30 and 35 years, and 37 cases above 35 years. A 47% of mothers never gave birth before, 25% were in their second gestation, and 28,2% have more than three gestations; Less than 9% of cases were classified as IGR. 53% were female 45,5% males and 1,5% undetermined.
Conclusion: Our results differs with those already published in our country. There were few cases in mothers with infections. We found a predominance of female foetuses, a predominance of primigravidas, low rates of IGR and a higher prevalence in young mothers.

OFP-12-006

Perinatal causes of death in a province. An 11 years multicentric retrospective longitudinal study

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Background & Objective: Perinatal causes of death shows a huge variety among different countries and across timeline. There is still not a unified system of classification for stillbirth and perinatal deaths. Autopsy is the gold standard method to define causes of death. Our objective is to describe the causes of death in our province.
Method: We reviewed fetal autopsies from 28 weeks or 500gr or more from the five hospitals in our province (the reference hospital and district ones). We classified causes of death according to the RElevan Cause Of DEath (RECODE) system. Other variables were registered such infections, mother age, parity, gestation week, and intrauterine growth restriction.
Results: 143 autopsies were found that accomplished the mentioned criteria. We observed differences in causes of death between the different hospitals. Unclassified death rate was 34% in general. Amniotic fluid pathologies were predominant in the reference hospital and placental pathologies in the district ones. Mother age also showed differences, being higher in the district hospitals. Only three cases of infections were detected (2 Chagas dissease and one toxoplasmosis).
Conclusion: Having a system of classification it is important to analyse causes of death. It is also important to improve maternal obstetrics care. A centralize analysis that analyse and compare causes among hospital can aid to identify risks, problems and peculiarities.

OFP-12-007

Paediatric soft tissue sarcomas / borderline tumours: a series of 27 cases

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Background & Objective: Paediatric soft tissue sarcomas/ borderline tumours (STS) are part of a heterogeneous group of tumours originating from embryonic mesodermal tissues during the process of differentiation into various mesenchymal tissue components of the human body. These tumours constitute 6% to 8% of all cancers in children less than 15 years of age. Of all the soft tissue sarcomas in this age group, approximately 50% to 60% are rhabdomyosarcoma (RMS), whereas the remainder are non-RMS soft tissue sarcomas, a designation that includes a variety of rarer soft tissue tumours including fibrosarcomas, synovial sarcomas, the extraosseous Ewing's family of tumours, malignant peripheral nerve sheath tumours (MPNSTs) and inflammatory myofibroblastic tumour.
Method: We review all cases of paediatric STS from 2014 to 2018, at Centro Hospital e Universitário de Coimbra
Results: We found 27 cases: 9 females (33%), 18 males (66%), with a mean age of 7.1- years-old; 2 cases were less than one year old. RMS was the most common STS with 9 cases (33%), followed by synovial sarcoma with 5 cases (18,5%), MPNST with 4 (14,8%) and fibromatosis with 3 (11,1%). Genetic studies were performed. Correlation with imaging studies and follow-up were evaluated.

Conclusion: According to data published in literature, RMS are the most common sarcoma in the paediatric population. The imaging characteristics often are nonspecific, and the diagnosis consists of putting together the clinical, imaging and pathologic findings.

OFP-12-008

The significance of cell foetal DNA (cffDNA) and DAI-receptors (DLM-1/ZBP1) (DNA-dependent activator of IFN-regulatory factors) expression in preeclampsia

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Background & Objective: Preeclampsia is a serious pregnancy-related disorder of unknown etiology. The aim was to identify cell free fetal DNA (cffDNA) level in maternal blood and evaluate the expression of DAI-receptors in DNA-mediated activation of innate immune responses in placental tissue in cases of early-(EPE) and late-(LPE) onset preeclampsia.
Method: The concentration of cffDNA was determined by quantifying hypermethylated RASSF1A sequences using PCR method at 11-14, 24-26, 30-32 gestation weeks (wg) in 10 women with uncomplicated pregnancy and 10 PE (5-EPE, 5-LPE). By immunohistochemistry was performed on the paraffin-embedded slices of placental samples using DAI primary polyclonal antibodies (1:1000;Thermo Fisher Scientific; Ventana,Roche). The 4 placental samples up to 33 wg (early control-EC) were used as a control for EPE, 3 samples after 34 wg for LPE (late control-LC).
Results: The intensity of immunohistochemical reaction was estimated by means of program NIS-Elements. Compare to uncomplicated pregnancy cffDNA level was higher in PE (287.1±130.7 versus 893.6±539.3, 391.5±142.3 versus 1050.3±435.1, 663.2±314.7 versus 2341.7 ±2031.0GE/ml at 11-14, 24-26, 30-32 wg; $p<0.05$). DAI-receptors expression was higher in EPE group than in EC (0.145±0.019 and 0.086 ±0.013 respectively; $p=0.006$) and no differences in LPE compared to LC($p>0.05$).
Conclusion: Increased cffDNA level in maternal blood may be the pro-inflammatory activity trigger and probably leading to preeclampsia

OFP-12-009

Retrospective evaluation of central nervous system defects in foetal autopsies and comparison with prenatal diagnosis

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Background & Objective: Central nervous system defects (CNSD) are the most common group of malformations detected prenatally and account for substantial proportion of all congenital abnormalities. Poor timing of sonographic evaluation, rather than poor sensitivity, can be an important factor in failing to detect abnormalities. This study pretends to demonstrate CNSD and evaluate concordance between prenatal diagnosis and postmortem findings (PD/PF).
Method: Retrospective review of 1372 autopsies of fetuses performed at Centro Hospitalar e Universitário de Coimbra between 2005-2016. For evaluation of CNSD were established nine categories for classification prenatal ultrasound/magnetic resonance imaging and autopsy findings and posterior correlation.
Results: One hundred and eighty fetuses were included in this study, 84 males, 92 females and 4 undefined sex foetus. The mean maternal age was 30,53 years-old (range 15 - 45) and gestational age 20,72 weeks (range 11 – 36). The most common pathologies were myelomeningocele/Arnold-Chiari II (35,4%), midline anomalies (21,9%), anencephaly/encephaloceles (20,2%) and holoprosencephaly (9%). Excluding 24 cases without ultrasound description or non-CNSD and with severe fetal maceration, there was good agreement between prenatal diagnosis and postmortem findings, with K=0.9832 (95% Confidence Interval, 0.9601-1, $p<0,0005$).
Conclusion: CNSD encompass a heterogeneous group of congenital anomalies that may be isolated or appear as part of a genetic syndrome. As well as data published in literature, neural tube defects is the most common group of anomalies, followed by midline defects. The agreement between PD/PF in fetuses with CNSD is good despite the broad spectrum of defects, some of them difficult to evaluate imagiologically.

OFP-12-010

Expression of the Nkx-2.2 and FasL in human placentas with foetal trisomy 21

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Background & Objective: Molecular pathogenesis of trisomy 21 (Down syndrome) is still incompletely understood. The biological mechanisms, including Nkx-2.2 and FasL expression, belong to potential influencing factors. The aims of this study were to compare Nkx-2.2 and FasL expressions in placentas with normal and trisomic karyotype and to associate differentially expressed Nkx-2.2 and FasL with concrete biological pathways.
Method: The placentas were collected from two groups of patients: Group A – placentas from fetuses of gestation 19-20 weeks with trisomy 21 (10 placentas); Group B – placentas from fetuses of gestation 19-20 weeks without any congenital defects and abnormal karyotype (20 placentas). Nkx-2.2 and FasL expression was studied immunohistochemically with use of mouse monoclonal antibody to Nkx-2.2 (Anti-Nkx2.2 antibody, Abcam), FasL (Diagnostic BioSystems, 1:75) and further morphometric analyses with the program ImageJ.
Results: The expression of Nkx-2.2 in placentas Group A was not found. The expression of Nkx-2.2 was found in placentas Group B. The area expression of Nkx-2.2 in endothelial cells of vessels of villi has made 0,41±0,14%. The area expression of FasL in endothelial cells of vessels of villi in placentas Group A has made 1,22±0,77%, in placentas Group B – 4,43±0,79% ($p<0,05$).
Conclusion: Thus, we were not found expression of Nkx-2.2 in placentas from fetuses with trisomy 21. The expression of FasL was the highest in placentas from fetuses without any congenital defects and abnormal karyotype.

Tuesday, 11 September 2018, 17:15 - 19:15, Room A4
OFP-13 | Uropathology

OFP-13-001

The depth of tumour invasion is superior to 8thAJCC/UICC staging system to predict patients' outcome in radical cystectomy. A proposal for a new staging system

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Background & Objective: AJCC/UICC staging system is the golden standard to predict the outcome. However, not a few studies report that pT staging (pT2 vs. pT3) may not be a prognostic factor. Also, pathological criteria of distinction between pT2 and pT3 are variable among pathologists.
Method: We retrospectively evaluated 117 bladder cancer patients who underwent radical cystectomy and reviewed the all HE slides. No patients received neoadjuvant chemotherapy. The depth of tumour invasion (DTI) was measured from normal urothelium to the deepest invaded lesion. Data on the patients' age, DTI (1.0 mm < vs. >1.0 mm), pT stage,

WHO1973 grade, and lymph node status were analyzed. Fine & Gray and multivariate Cox proportional hazard regression models were developed to predict progression-free survival (PFS), cancer-specific survival (CSS), and overall survival (OS).
Results: The median age of the patients was 71 years (35–87 years). The median follow-up period was 32 months (range 1–247 months). Pathological characteristics were as follows: Median DTI 10.80mm (range 2.57 - 37.14mm), pT (pT2:pT3=38:79)、1973 WHO grading (G2:G3=28:89). In the multivariate analysis, depth of tumour invasion was significantly associated with PFS (p = .019), CSS (p = .011) and OS (p = .017). Lymph node status was significantly associated with CSS (p = .0168). pT staging was not associated with PFS (p = .786), CSS (p = .894) and OS (p = .337).
Conclusion: DTI is a more useful prognostic factor for PFS, CSS, and OS in bladder cancer than those of the AJCC/UICC pT system.

OFP-13-002
Three-dimensional analysis of clinical prostate cancer samples
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Background & Objective: The Gleason Score (GS) is one of the most important parameters for clinical decision-making in prostate cancer (PCa), existing of individual growth patterns. The objective of this study was to elucidate on the underlying three-dimensional (3D) architecture of clinical PCa growth patterns.
Method: Formalin fixed, paraffin embedded tissues (n=46) were fluorescently stained with antibodies CK8-18 and CK5, and optically cleared in benzyl alcohol: benzyl benzoate. Imaging up to 700 micron depth was done with an SP_5 confocal microscope.
Results: The basic 3D architecture of most PCa samples consisted of tubules with branching and connections. While branching occurred sporadically in GG3 PCa, frequent and adjacent connections characterized fused GG4. GG3 formed a 3D morphologic continuum with ill-formed GG4 and cord-pattern GG5 with gradual decreasing tubule and lumen diameter, with concomitantly increased branching. Glomeruloid GG4 structures were represented by one-sided intraluminal proliferations in tumour tubules often being present at branching points. On the other hand, cribriform GG4 and solid GG5 formed a continuum of large epithelial proliferations characterized by loss of stromal contact by the majority of tumour cells. The frequency and size of inter-epithelial lumens in these proliferations decreased from cribriform to solid growth.
Conclusion: Three-dimensional reconstruction of clinical PCa reveals two fundamentally different growth patterns: 1) Gleason grade 3, ill-formed GG4, fused GG4 and cord-pattern GG5 form a 3D tubular morphologic continuum, 2) cribriform GG4 and solid GG5 both are non-tubular proliferations, while glomeruloid GG4 represents an intermediate between both basic structures.

OFP-13-003
Relationship of E-cadherin, beta-Catenin, CD44 and Bcl-2 expression with different gene fusion subsets of prostate cancer and PTEN status
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Background & Objective: In ERG+ prostate cancer (PrCa), we reported that combined ERG expression and Prostein and PTEN loss (3-hit) is associated with high grade and stage and shorter PSA progression-free survival. We have investigated the relationship of these genes with E-cadherin, β-Catenin, CD44 and Bcl-2, as markers of epithelial-mesenchymal transition (EMT), stemness and apoptosis regulation in a series of PrCa.
Method: An immunohistochemical study of all these molecules was performed in a TMA series with 220 radical prostatectomies (Parc de Salut MAR Biobank, MARBiobanc, Barcelona, Spain).
Results: Bcl-2 expression was found in 44.7% ERG+ versus (vs) 26.7% ERG- cases (p=0.015). CD44 was positive in 68.2% ERG- (wild type) vs 52.2% ERG+ PrCa (p=0.044). E-cadherin loss was found in 45.3% PCa cases with Prostein loss and in 13.6% Prostein wild type (wt) cases (p<0.0001). β-Catenin was lost in 38.4% cases with Prostein loss vs 24.6% Prostein wt cases (p=0.042). E-cadherin loss was found in 35.6% PCa with PTEN loss vs 17.3% PTEN wt cases (p=0.0035). Finally, E-cadherin loss was detected in 71.4% cases with the 3-hit compared to 13.4% non-3-hit cases (p<0.0001).
Conclusion: ERG- cases are associated with stemness and ERG+ cases, with inhibition of apoptosis. EMT-related features are more frequent in the ERG+ subset of PCa with loss of Prostein and PTEN. All these findings mark relevant steps in the progression of PCa.

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OFP-13-004
Incidence of penile squamous-cell carcinoma and its relation with the Human papillomavirus: a 10-year review of cases at a university hospital
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Background & Objective: According to current publications, 30 - 40 % of all Penile Squamous-cell carcinoma (SCC) are related to concomitant infection with Human Papillomavirus (HPV) whose predominant genotype is the high-risk HPV. Objective: Determine the incidence of Penile SCC in our institution during the last decade (2008-2017), its relation to HPV infection and correlation with the histologic subtype, stage and anatomical location.
Method: Retrospective and descriptive study. 44 patients diagnosed with Penile SCC at Hospital Universitario Central de Asturias (HUCA) from 2008 to 2017 have been included in this study. Anatomical location, histologic subtype and pathological stage have been determined for every case. Immunohistochemical stains have been realized of p16, pan-HPV and high-risk-HPV.
Results: The average age of the 44 cases was 68 years old. 77 % (34) presented Conventional Penile SCC, 13.6 % (4) presented Warty SCC and 4.5 % (2) Papillary SCC. 43 % (19) of the cases showed HPV infection. 67% (13) of penile SCCs related to HPV infection were at stages I-II. 79 % (15) of the HPV-associated carcinoma corresponded to conventional penile SCC, and these latter represented only 49 % of all conventional penile SCC (34).
Conclusion: Only 43 % of all cases with penile SCC studied presented relation with HPV infection. Most of HPV-associated Penile SCC were at stages I-II. The most common histological subtype was conventional Penile SCC followed by warty SCC. Our data are correlated with global tendency.

OFP-13-005
FH deficient renal cell carcinoma and FH deficient-like renal cell carcinoma: morphologic comparative study of 23 genetically tested cases
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Background & Objective: Recent publications dealing with aggressive renal carcinomas associated with HLRCC syndrome expanded

the morphologic spectrum of the renal tumours associated FH gene abnormalities, emphasizing the presence of papillary, tubulary or mixed architecture, eosinophilic cells and red macronucleoli with perinucleolar halos.
Method: Architecture, cytology, presence of prominent nucleoli and perinucleolar clearing were analyzed in 13 FH deficient renal cell carcinomas (FHRCC) with proved FH mutation/LOH and 10 FH deficient-like renal cell carcinomas (FHLRC) without proved FH mutation/LOH.
Results: FHRCC cohort included 8 males and 5 females, with age range of 24-65 years, and tumour size of 0.9-18 cm. FHLRC group included 5 males and 5 females, age range 21-82 years, and tumour size of 2.6-11 cm. FHRCC: mixed pattern was present in 7/13 cases, papillary in 3/13, tubulopapillary-cystic in 2/13 and solid sarcomatoid in 1/13. Eosinophilic cells were present in 8/13, macronucleoli in 13/13 (4 focally), perinucleolar clearing in 10/13 (7 focally). FHLRC: mixed pattern was present in 5/10 cases - tubulopapillary pattern was present in 4/10, tubulo-cystic in 1/10, only papillary in 4/10, and tubulary 1/10. Macronucleoli were present in 10/13 (1 focally), perinucleolar clearing in 8/10 (2 focally).
Conclusion: Renal cell carcinomas from both groups showed significant overlap in histological growing pattern and cytologic features. It is impossible to separate FHRCC from FHLRC based only on morphology. Due to the limitations of immunohistochemistry, analysis of FH gene is only reliable method for separation of FHRCC from their mimickers.

OFP-13-008
Prognostic value of E-cadherin and P-cadherin immunoexpression in pT3 prostate cancer
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Background & Objective: Prostate cancer (PCa) represents the most common malignancy and a major cause of cancer-related death in men. Despite being referred as "high risk cancer", pT3 tumours do not exhibit a uniformly poor prognosis after radical prostatectomy (RP). Loss of E-Cadherin has been associated with poor prognosis, while the role of P-Cadherin in PCa is still widely debated. We aimed to assess the prognostic value and impact on survival of E-Cadherin and P-Cadherin immunoexpression in pT3 PCa.
Method: RP specimens of 102 PCa patients were retrospectively queried (1999-2014). All patients were treated at our institution by the same multidisciplinary team. Clinical and histological material was reviewed. A representative block was selected for tissue micro-array (TMA) construction(3cores/case). E-Cadherin immunoexpression was assessed with digital image analysis system (H-score method), with cases categorized as E-Cadherin-high/low when above/below the 30th percentile(P30). For P-Cadherin, the scoring criteria currently used for HER2 in gastric cancer were applied.
Results: Patients with pT3b (vs. pT3a) and higher Gleason Groups (vs. lower) displayed worse disease-specific survival (DSS) [HR:4.58, 95%CI:1.49-14.05; HR:9.65, 95%CI:1.25-74.89]. There was an association between E-Cadherin and P-Cadherin immunoexpression (p=0.019); considering E-Cadherin-low patients, 97% were P-Cadherin negative. E-Cadherin-low patients displayed worse DSS, although it did not reach statistical significance (HR:2.65, 95%CI:0.81-7.88). However, considering only pT3b patients, those with low E-Cadherin immunoexpression displayed significantly worse overall-survival (OS) and DSS (HR:3.69, 95%CI:1.18-11.50; HR:5.90, 95%CI:1.40-24.81). No significant differences in survival were found for P-Cadherin.
Conclusion: Lower E-Cadherin immunoexpression discriminated a subgroup pT3b patients with poorer survival. The role of P-Cadherin in PCa might be context-dependent and deserves further investigation.

OFP-13-009
FOXC2 regulating epithelial-mesenchymal transition is a marker of aggressive prostate cancer
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Background & Objective: Epithelial-mesenchymal transition (EMT), characterized by reduced E-cadherin and increased N-cadherin expression (E/N-cadherin switch), is important for tumour cell invasion and metastasis, and is a feature of aggressive carcinomas. The objective of our study was to examine the EMT-regulator FOXC2 and the cell adhesion molecules E- and N-cadherin, in different human prostatic tissues with focus on EMT, clinico-pathologic phenotype and patient prognosis.
Method: Sections from 338 radical prostatectomies (Haukeland University Hospital, Norway, 1986-2007), 33 castration resistant prostate cancers, 33 soft tissue metastases, 13 skeletal metastases and 41 prostatic hyperplasias were immunohistochemically stained for FOXC2, E- and N-cadherin.
Results: In univariate survival analyses, using the clinically important subgroup of 198 patients with Gleason score 7, high FOXC2 expression and E/N-cadherin switching were significantly associated with shorter time to clinical recurrence, skeletal metastases and cancer specific death. In multivariate Cox proportional hazard analysis, high FOXC2 (HR 1.9, p=0.018; HR 3.7, p=0.003; HR 4.9, p=0.001) and the E/N-cadherin switch (HR 2.6, p=0.009; HR 4.1, p=0.002; HR 7.6, p<0.0005) were independent predictors of time to these end-points, together with Gleason grade groups (GG3 vs. GG2) and pathologic stage (>=pT3 vs. pT2). In benign prostatic hyperplasia, FOXC2 was significantly weaker than in the other tissue groups, and E/N-cadherin switching was not observed.
Conclusion: FOXC2 expression and a switch from E- to N-cadherin predict aggressive prostate cancer. Factors regulating or signifying EMT can be useful as prognostic biomarkers and are potential targets of cancer therapy.

OFP-13-010
PBRM1 and BAP1 expression in renal cell carcinoma
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Background & Objective: PBRM1 and BAP1 genes are located on chromosome arm 3p, which is deleted in the majority of patients with clear cell subtype of renal cell carcinoma (RCC). Here, the loss of expression of PBRM1 and BAP1 proteins was studied and correlated with the pathological features in RCC subtypes.
Method: Immunohistochemistry was performed on FFPE samples of 73 consecutive RCC nephrectomy or biopsy specimens (59 clear cell, 6 chromophobe, 5 papillary, 2 unclassified and 1 clear cell papillary) to evaluate PBRM1 and BAP1 staining of the nuclei. The reactions were simply read as positive or negative. None of the patients received prior therapy.
Results: The loss of PBRM1 or BAP1 protein was observed in clear cell RCC, while in the non-clear cell types both markers were retained. In clear cell RCC, PBRM1 and BAP1 expression was PBRM1+ BAP1+ in 29.8% of tumours, PBRM1− BAP1+ in 44%, PBRM1+ BAP1− in 15.2% and PBRM1− BAP1− in 11%. We compared PBRM1+ BAP1+ clear cell RCCs with PBRM1− or BAP1− cases, and we found that the latter were associated with high ISUP nuclear grade (p=0.021), but the pT stage (p=0.44), the tumour size (p=0.85) and the presence of necrosis (p=0.98) displayed no significant associations.
Conclusion: Loss of PBRM1 and BAP1 appears to be specific for clear cell RCC, thus their use as clear cell RCC specific markers should be considered. Also, the inactivation of PBRM1 or BAP1 may facilitate tumour dedifferentiation, and it may worsen the patient outcome.

OFP-13-011

Multi-stage pathological and immunohistochemical characterisation of N-butyl-N-(4-hydroxybutyl)-nitrosamine-induced murine bladder cancer

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Background & Objective: N-butyl-N-(4-hydroxybutyl)-nitrosamine (BBN)-induced bladder tumours in mice represent an attractive model of muscle-invasive bladder cancer (MIBC), which mimicks the basal-like transcriptomic subgroup. Lineage tracing studies in mice suggested that MIBC, including basal tumours, arise from carcinoma in situ (CIS) lesions. However, in routine pathology practice, the majority of human CIS express a luminal immunohistochemical (IHC) phenotype CK20+. In this context, we sought to characterize early stage lesions occurring in BBN-exposed mice, using IHC markers of basal and luminal subtypes
Method: To study multiple stages of tumour progression, 35 mice bladders were obtained at different time points following oral BBN exposure of a maximum of 14 weeks. Morphological and IHC analysis of basal (CK5, CK6, CK14), luminal (CK20, GATA3, FOXA1) and proliferation (Ki67) markers were performed.
Results: Morphological analysis identified a spectrum of lesions during BBN exposure, including isolated early lesions -hyperplasia (n=1), dysplasia (n=3) or CIS (n=4)- pTa (n=13), pT1 tumours (n=10) and MIBCs (pT2 and pT3, n= 6). Squamous differentiation was observed in 79% of pTa-pT3 tumours. A basal IHC pattern was identified in 2 of 3 dysplasia lesions and in all CIS lesions, which were associated with high proliferation (Ki67≥20%). pTa to pT3 cases displayed a basal-like phenotype in 86% of cases.
Conclusion: Our study shows that BBN-induced bladder tumours at both CIS and invasive stages are of basal-like IHC phenotype, suggesting that BBN-treated mice may represent a model of basal CIS. Further genomic and transcriptomic analyses of stage-specific lesions following laser-capture microdissection are ongoing.

OFP-13-012

Osteonectin overexpression in the case of prostate cancer with intraluminal inclusions

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Background & Objective: Osteonectin (OSN) is secreted by osteoblasts during bone formation, initiating mineralization and promoting mineral crystal formation at sites of ectopic calcification. Also OSN was found in many types of human malignant tumours. The aim is to study the OSN expression in patients with prostate cancer (PC) and the presence of intraluminal inclusions (prostatolithes and amyloid cells).
Method: OSN expression was investigated in tumours and in the adjacent prostatic tissue of 30 PCs with intraluminal inclusions and 30 PCs without them by immunohistochemistry. In each group 15 samples refer to moderately differentiated G2 and low-differentiated G3 tumours. Samples were fixed, embedded in paraffin, and analized for OSN accumulation using the anti-OSN antibody, followed by DAB detection substrate and counterstained with Mayer's haematoxylin.
Results: OSN expression was increased in PC tissues with pathological inclusions in comparison to those without them ($p<0.001$, Student test). Osteonectin was mostly localized in tumour cells cytoplasm, its expression was not observed in tumour microangiourea cells and in stroma. It was found that the OSN expression by tumour cells reduced during reduction of the malignant tumour differentiation (comparison of subgroups G2 and G3) ($p<0.001$ and $p<0.01$ respectively for groups I and II).
Conclusion: OSN overexpression in tumours and in the adjacent prostatic tissue of PCs with intraluminal inclusions may be regarded as a prospective role for the osteosteogenic phenotype development of tumour cells and for the bone metastasis promotion.

Tuesday, 11 September 2018, 17:15 - 19:15, Room B1
OFP-14 | Joint Session: Endocrine Pathology / Head and Neck Pathology

OFP-14-001

Differentiated thyroid carcinoma of the paediatric age: genetic and clinical scenario

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Background & Objective: Follicular-derived differentiated thyroid carcinoma is the most common endocrine malignancy in children. The different clinical and pathological features between paediatric and adult thyroid carcinomas could be related to a different genetic profile. However, few studies are currently available and most of them involved a limited number of patients and mostly focused on radiation-exposed population. A greater knowledge of the genetics might improve the diagnostic frame and lead to an individualized therapy.
Method: We studied 57 paediatric patients who underwent surgery for diagnosis of differentiated thyroid carcinoma between 2000 and 2017. The presence of mutations in BRAF, NRAS, PTEN, PIK3CA genes, and in TERT promoter, were analyzed through sequencing. RET/PTC rearrangement has been investigated with Fluorescent in situ hybridization. Clinical-molecular features of paediatric patients were compared with those of 165 adult patients.
Results: In paediatric age, male gender and subjects < 15 years have a more extensive disease and more frequent lymph nodes and distant metastasis. Compared to adults, in paediatric patients there is a more frequency of lymph nodes and distant metastasis ($p=0,01$); moreover, paediatric patients are more prone to have a second treatment ($p<0,01$). The frequency of BRAFV600E mutation is lower in paediatric DTCs ($p<0,01$). NRASQ61R, NRASQ61K and TERTC250T are rare in children and adolescents; no mutations were found in PTEN and in PIK3CA.
Conclusion: Paediatric differentiated-thyroid cancer has a greater aggressiveness at diagnosis and a greater risk of recurrence than adult's one. Differently from adult, point mutations have not a genetic key role.

OFP-14-002

Specific molecular mechanisms of tumour progression from well differentiated to poorly differentiated thyroid carcinomas identified by next generation sequencing analysis

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Background & Objective: The molecular background of thyroid cancer histotypes, including poorly differentiated carcinoma, has been investigated in recent years using high throughput technologies. However, molecular studies specifically designed to explore the mechanism of tumour progression from well-to-poorly differentiated forms are still missing
Method: Fifteen cases of poorly differentiated carcinomas with associated well-differentiated papillary or follicular components have been micro-dissected to isolate and characterize at the molecular level the two tumour populations using the Oncomine Focus Assay (IonTorrent platform, ThermoFisher Scientific) covering somatic CNA and fusions in 52 cancer relevant genes
Results: Eleven cases yielded adequate DNA and RNA for next generation sequencing analysis. A high prevalence of alterations in the RAS (5/

11 cases) and PIK3CA/AKT1 (7/11 cases) pathways was observed, in most instances mutually exclusive. In 10/12 mutated cases, RAS and/or PIK3CA/AKT1 mutations were present in both tumour components with similar allelic frequencies, thus underlying their role as driver mutations. However, all but one case showed discordant molecular profiles at least in one of the genes investigated. RET and MET were predominantly altered in the well differentiated components, only (1/1 and 2/3 mutated cases, respectively). By contrast, EGFR and PDGFRa/KIT genes were altered almost exclusively in the poorly differentiated component (2/3 and 3/4 mutated cases, respectively, the latter genes always associated to cases with well-differentiated papillary histotype)
Conclusion: These data show a high molecular heterogeneity in poorly differentiated carcinomas associated with a well differentiated component, and identify novel molecular markers of tumour progression including tyrosine kinase receptors that might represent novel potential therapeutic targets

OFP-14-003
The "don't eat me" signal CD47 – a therapeutic option in human anaplastic thyroid carcinoma?
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Background & Objective: Anaplastic thyroid carcinoma (ATC) is one of the most aggressive human cancers and has a dismal prognosis. CD47 is a "don't eat me" signal which prevents cancer cells from phagocytosis by binding to SIRP-alpha on macrophages. So far, the role of macrophages and the CD47-SIRP-alpha signaling axis in ATC is not well understood.
Method: We analyzed 20 primary human ATCs for macrophage markers and CD47 expression by immunohistochemistry. ATC cell lines were assessed for CD47 expression by flow cytometry. CD47 was blocked in in vitro phagocytosis assays of co-cultured macrophages and ATC cell lines. Anti-CD47 antibody treatment was administered to immunocompromised mice subcutaneously xenotransplanted with ATC cell lines as well as to double-transgenic mice that develop orthotopic ATCs after tamoxifen induction.
Results: Human ATCs had a mean macrophage infiltration of 25%, a weak CD47 expression and a moderate expression of calreticulin, the dominant pro-phagocytic molecule. Surface CD47 and calreticulin were highly expressed in 8/8 ATC cell lines as analyzed by flow cytometry. Blocking CD47 increased phagocytosis of ATC cell lines in vitro compared to isotype control. Anti-CD47 antibody treatment significantly delayed tumour growth and increased the frequency of intratumoural macrophages in ATC xenotransplanted mice. In double-transgenic mice, anti-CD47 treatment resulted in increased intratumoural macrophage frequencies without affecting tumour growth kinetics.
Conclusion: ATCs express CD47 and are heavily infiltrated by macrophages. Anti-CD47 treatment increases phagocytosis of ATCs by macrophages in vitro and in vivo and might be a promising therapeutic option for ATC patients.

OFP-14-004
Neuroligin 2 is a novel immunomarker of neuroendocrine cells and tumours
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Background & Objective: Neuroligin 2 (NLG2) belongs to a family of proteins with predominant brain localization whose activities are related to inhibitory synapses. A strong immunoreactivity for NLG2 was incidentally observed by our group in islet cells of pancreas. This prompted an extensive investigation of NLG2 expression in other neuroendocrine (NE) cells and tumours.
Method: A series of 236 NE-neoplasms was collected from the pathology files of the University of Turin and tested immunohistochemically for NLG2 (polyclonal rabbit antibody, Synaptic Systems, Germany). These included lung carcinoids (100), gastroenteropancreatic NETs (22), parathyroid (20) and pituitary (9) adenomas, medullary thyroid carcinomas (30), pheochromocytomas (15), high grade pulmonary and extrapulmonary NE carcinomas (17), Merkel cell carcinomas (10), mixed adeno-NE carcinoma (8), and NE-breast carcinomas (5). Control non-NE lung, breast, colorectal, pancreatic adenocarcinomas were evaluated.
Results: NLG2 was expressed in 94% of NENs, irrespective of the site of origin, with a diffuse cytoplasmic distribution in variable intensity and percentages of tumour cells (5-90%). Peritumoural normal pancreatic, intestinal and pulmonary neuroendocrine cells had a similar immunoreactivity. Well differentiated tumours generally expressed NLG2 to a higher extent than high grade NE carcinomas. All control non-NE neoplasias were negative, except occasional cells in rare pancreatic and breast adenocarcinomas, representing focal NE differentiation as demonstrated by chromogranin A co-localization in double stainings.
Conclusion: NLG2 may be a valid adjunct to other pan-NE markers to define the NE phenotype irrespective of the primary location, with special reference to well differentiated neoplasias.

OFP-14-005
The role of class III beta-tubulin in invasive potential of thyroid carcinoma and its clinical significance
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Background & Objective: Class III beta-butulin (TUBB3) is known to take part in the invasive growth and metastasis in some tumours. In this study we aimed to evaluate clinicopathologic significance TUBB3 in thyroid carcinoma.
Method: A total of 166 cases of papillary thyroid carcinoma (PTC), including 136 conventional (C) PTC, 13 follicular variant (FV) PTCs and 17 anaplastic thyroid carcinomas (APC), were collected and immunohistochemistry (IHC) for TUBB3 was performed. Expression of TUBB3 protein and mRNA were investigated in normal thyroid epithelial cells, CPTC and APC cell lines.
Results: Expression of TUBB3 were significantly different among the three types of tumours, which revealed higher proportion and intensity of both tumour cells and stromal cells in CPTC and APC than in FV PTC. In CPTC group, the proportion of TUBB3 in tumour cells was associated with older age. And the intensity of TUBB3 in tumour cells was associated with lymph node metastasis. In survival analysis, the proportion of tubulin was associated with inferior recur-free survival (p=0.05). In vitro cell line studies, western blot and RT-PCR analysis in baseline and after invasion assay were generally concordant with the IHC results with APC showing higher expression of TUBB3 in both baseline and invasion assay than in CPTC.
Conclusion: Our results suggest that tubulin might participate in invasive growth and metastasis in PTC, being a potential target for therapy in patients with aggressive disease course.

OFP-14-006
Non-invasive follicular thyroid neoplasm with papillary-like nuclear features: clinicopathological aspects, outcome and genetic profile of 42 cases
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Background & Objective: It is now admitted that non-invasive encapsulated follicular variant of papillary thyroid carcinoma has an indolent

clinical behavior. Recently, the term non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) was introduced to emphasize the low biological potential of these tumours. The objective of this study was to describe clinicopathological, evolutive features and molecular profile of a series of NIFTP

Method: After reviewing all the slides of encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC) from the archives of Pathology Department of Habib Thameur Hospital of Tunis between January 2000 and August 2015, 42 cases fulfilled the criteria of NIFTP. The mutational profile, using pyrosequencing, of codon 600 of the BRAF gene and codons 12, 13, 59, 61, 117 and 146 of the NRAS and KRAS genes were studied.

Results: The mean age was 41 years with a sex ratio M/F of 0,1 (4/38). Fourteen patients (95%) have done total thyroidectomy. The mean size of the tumour was 3,6 cm. No lymph node metastases were observed in all cases. Thirtyfour (94%) NIFTP were classified as stage I or II according to UICC. Molecular analysis revealed RAS gene mutations in 18 cases (45%), BRAF gene mutation in 5 cases (12%). Eighteen cases (43%) were not mutated. The mean follow-up was 30 months. No patient died, recurred or had distant metastasis during follow-up.

Conclusion: Histological, molecular and evolutive characteristics of NIFTP confirms their low malignant potential and provides supporting evidence for the nomenclature shift and the inclusion of NIFTP into the latest WHO endocrine tumour classification scheme.

OFP-14-007

Impact of race/ethnicity on oncogenic driver mutations prevalence and outcomes in thyroid nodules

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Background & Objective: A previous study showed evidence of racial disparities in clinical behavior of thyroid carcinoma subtypes. We aimed to evaluate the racial disparities impact on oncogenic driver mutations in a subset of thyroid neoplastic lesions.

Method: We identified 424 thyroid nodules with corresponding fine needle aspiration and ThyroSeq testing performed at our institute between February 2015 and September 2017. The self-reported race/ethnicity distribution was 29% whites, 31% blacks, 20% Hispanic, 10% Asians, and 12% Unknown.

Results: Of 424 nodules, 125 with definitive histologic diagnosis. The surgical resection prevalence was 30% among racial/ethnic subgroups [p=0.21]. A 64.8% of the resected nodules had a neoplastic lesion (62 had positive molecular-test). Classic Papillary Thyroid Carcinoma (PTC) was 43.33% in whites and 33.33% in Hispanics; Follicular Variant Papillary Thyroid Carcinoma (FVPTC) was 31.58% in blacks; Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP) was 57.14% in Asians [p=0.007]. In PTCs, whites (54% BRAF-V600E, 38% RAS mutations); blacks (100% BRAF-V600E); Hispanics (40% BRAF-V600E, 20% NRAS); and Asians (67% NRAS). In FVPTCs, blacks (83% RAS mutations); whites (33% NRAS); and Hispanics (50 % NRAS). No FVPTC was diagnosed among Asians. 57% of NIFTPs had RAS mutations. No NIFTPs were diagnosed in white and blacks.

Conclusion: We found racial/ethnic disparities in the genomic alterations of the subtypes of neoplastic thyroid lesion including prevalence of BRAF and RAS mutations, and other oncogenic drivers detected by ThyroSeq test. These results stress the importance of maintaining awareness of how racial differences may affect the diagnostic utility of molecular testing platforms and thus influence patient management.

OFP-14-008

Mutational analysis of ossifying fibromas of the jaws and craniofacial skeleton

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Background & Objective: Ossifying fibroma (OF) is a benign neoplasm of the jaws and craniofacial skeleton characterised by progressive growth with bony expansion. Three distinct variants are recognised: cemento-ossifying fibroma (COF), and two juvenile types: psammomatoid (JPOF) and trabecular (JTOF). There are considerable clinicopathological overlaps between these lesions, resulting in significant diagnostic challenges. Further genetic analysis of OF is required to better understand their origins and identify potential diagnostic markers. We aimed to establish protocols for whole exome sequencing (WES) from decalcified, formalin-fixed paraffin-embedded (dFFPE) tissue, and to explore possible genetic origins of OFs.

Method: 3 different methods of DNA extraction were assessed (Qiagen QIAamp, Qiagen GeneRead, Covaris truXTRAC) and WES was conducted on 8 cases of OF. Alignment and variant calling were performed with online analytical software Galaxy tools. Variant annotation and prioritisation used multiple tools, including, Ensembl VEP, ClinVar and SIFT, to identify key variants based on their significance to tissue expression and known pathogenicity.

Results: The Qiagen GeneRead method gave the best yield of DNA. 1,615 variants (minimum read depth = 35) were filtered to 9 variants within 7 genes (BCLAF1, ANKHD1, CDC27, FARP2, FRA10AC1, HEXB and PDE4DIP) based on tissue expression, impact type and predicted pathogenicity. Variants did not distinguish between OF types. No common variants were identified amongst odontogenic or non-odontogenic samples.

Conclusion: DNA extraction from dFFPE tissue can result in a sufficient yield for conducting WES. This study has identified new candidate gene mutations, opening new avenues of investigation for potential biomarkers in this group of rare lesions.

OFP-14-009

Defining HPV-driven neoplastic transformation infection in oropharyngeal carcinoma. A moving target in head and neck oncology

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Background & Objective: Oropharyngeal squamous cell carcinoma (OPSCC) treatment relies on HPV status definition. Viral oncogene mRNA identification is the gold standard for HPV-driven oncogenesis, but for its technical complexity algorithms pairing DNA and p16 expression, as indirect evidence of E6 activation, are currently used. Recently, HPV oncogene mRNA in situ hybridization (ISH) on routine slides has been proposed as a stand-alone test for OPSCC classification. We compared mRNA rt-PCR and ISH with HPV DNA and oncogene target expression in 54 consecutive OPSCC to define their ability to identify oncogenic infections

Method: Frozen samples were used for HPV E6 mRNA qRT-PCR. HR-HPV mRNA ISH, SPF10 LiPA genotyping and mmunostains for p16, pRB, p53 were performed on fixed samples

Results: HR HPV mRNA qRT-PCR was positive in 31 samples (57.4%) and mRNA ISH in 24 (44.4%). Of the 7 mRNA PCR+/ISH- samples, 2 expressed p16 and HPV16 DNA; 5 were negative for p16 but expressed HR-HPV DNA. These 5 samples also expressed pRB. All HR-HPV DNA+ cases, including the 5 that were p16-, expressed viral mRNA by qRT-PCR; all HR-HPV DNA- cases, including 4 that were p16+, were negative for viral mRNA

Conclusion: Discordant cases complicate studies comparing HPV identification strategies. We confirmed the occurrence of p16 expression independent of viral oncogenesis. Our findings of mRNA qRT-PCR+/ISH- cases with no p16 expression/pRB loss challenges the assumption of a necessary correlation between HPV oncogene expression, pRB pathway inactivation, and more generally, HPV-driven neoplastic transformation,

and suggest that analysis of HPV-oncogene target proteins may improve classification of discordant OPSCC.

OFP-14-010

The need for intra-operative assessment of resection margins in oncological surgery, with focus on the head and neck region: a review of the literature

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*Erasmus MC, Otolaryngology, Rotterdam, The Netherlands

Background & Objective: Intra-operative assessment of the resection margins can help the surgeon to achieve complete tumour removal. However, there is no consensus on the indication for performing intra-operative assessment. The aim of this study is to give an overview of literature on the need for intra-operative assessment and to compare two different methods: specimen driven and wound bed driven.
Method: A literature search was performed in the Medline-, Embase- and the Cochrane Collaboration, from 2000 to 2017. The studies were clustered per surgical discipline and anatomical site. Information on type of study, type of surgery, frequency and method of intra-operative assessment, and the author's results/conclusion were recorded.
Results: Sixty-eight studies reporting on intra-operative assessment in oncological surgery were found: 6 skin cancer surgery, 6 gynaecology, 13 breast, 14 urology, 13 gastro-intestinal and 14 head and neck. The frequency and method of intra-operative assessment, and the author's conclusions varied widely between surgical disciplines. Most studies recommended the intra-operative assessment. For the head and neck region, 4 studies compared the two different methods and recommended the specimen driven assessment.
Conclusion: This review demonstrates that there is relatively scarce evidence on the need of intra-operative assessment of resection margins, implying that this technique is not standard practice in oncological surgery. However, for head and neck, all authors recommend specimen driven intra-operative assessment. This is in accordance with the experience at our institute. Finally, current American Joint Committee on Cancer (8th edition) guidelines also recommends specimen driven intra-operative assessment in the head and neck region.

OFP-14-011

Relocation of inadequate resection margins in the wound bed during oncological surgery

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Background & Objective: Intra-operative assessment of the resection margins on the specimen provides immediate feedback to the surgeon on whether an additional excision is needed. However, relocation of an inadequate margin from the specimen to the wound bed has been shown to be difficult. The objective of this study is to assess a new method for relocation of inadequate tumour resection margins in the wound bed after intra-operative assessment of the resection specimen.
Method: During surgery for oral cavity cancer, the surgeon placed numbered tags on both sides of the resection line in a pair-wise manner. The tags were placed along superficial and deep resection lines. After resection, one tag of each pair remained fixed on the specimen and the other tag remained in the wound bed. Upon detection of an inadequate margin in the resection specimen, the numbered tags were used to relocate the inadequate resection margin in the wound bed.
Results: The method was applied during 80 resections for oral cavity cancer, for which intra-operative specimen-driven assessment of resection margins was performed. In 31 resections an inadequate margin was detected. Based on the paired tagging method an accurate additional resection was achieved.
Conclusion: Paired tagging facilitates a reliable relocation of inadequate margins, enabling an accurate additional resection during the initial surgery. It is expected that implementation of paired tagging will lead to a higher number of adequate tumour resections and thereby will improve patient outcome and/or reduce adjuvant therapy and the related morbidity.

OFP-14-012

Objective intra-operative assessment of the resection margins to facilitate head and neck cancer surgery

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Background & Objective: Adequate resection margins are a crucial prognostic factor in oncological surgery. For head and neck, with its complex anatomy, this is a challenge. Frozen sections have known limitations and are not suitable for bone. Our aim was to find an objective method for fast and reliable intra-operative assessment of the resection margins, including bone. For this we explored Raman spectroscopy.
Method: Experiments were performed on freshly resected specimens from 56 patients with oral cavity squamous cell carcinoma (OSCC), including those who underwent mandibulecotomy.
Results: Raman spectroscopy can discriminate OSCC from healthy soft tissue with 99% sensitivity and 92% specificity, and the border of the tumour can be determined. In addition, during mandibulectomy tumour can be detected in bone resection margins with high sensitivity (96%) and specificity (83%).
Conclusion: Our results are promising and show, for the first time, that an objective technique like Raman spectroscopy could be applied intra-operatively in OSCC surgery to evaluate resection margins, including bone. This method could facilitate adequate resection in head and neck oncological surgery.

Poster Sessions

Sunday, 9 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-01 | Breast Pathology

PS-01-001

PDL1-expression in triple negative breast cancer: analysis of two different antibodies and their prognostic values

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Background & Objective: Programmed cell death protein ligand1(PDL1) expression plays an important role in inflammatory response to tumour cells. We compared two different PDL1 antibodies in triple negative breast cancer (TNBC).
Method: Ventana SP263 and BioCare RbMCAL10 antibodies were performed on 51 TNBC cases. Percentages of membranous and

cytoplasmic expression were assessed in neoplastic cells (NC) and tumour-infiltrating lymphocytes (TIL). Groups and cut-off values for PDL1 expression were 0(0%), 1(1-9%), 2(10-49%), and 3(50% and above).

Results: Mean age was 52.7 (32-84). The diagnoses were medullary-like carcinoma (n=23), ductal carcinoma (n=20), metaplastic carcinoma (n=5) and basal-like carcinoma (n=3). In NC, mean PDL1 expression was 11% and 11.3% with SP263 and RbMCAL10, respectively. Mean PDL1 expression was 15.4% and 16.8% in stromal lymphocytes wtih SP263 and RbMCAL10, respectively. There was high correlation between 2 antibodies ($p<0.01$). PDL1 expression in NC was also corralated with PDL1 expression in TIL with both antibodies. TIL density and PDL1 expression in NC were positively associated with both antibodies. There was no statistically significant association between PDL1 expression and other prognostic parameters (age, tumour-subtype, histological grade, lymphovascular/perineural invasion, survival, and metastasis).

Conclusion: We found a strong correlation between two antibodies in TNBCs. In discordant cases, RbMCAL10 detected higher PDL1 expression generally. Between 2 antibodies, PDL1 expression in neoplastic and TIL compatments were corralated, but the relationship was stronger in the neoplastic compatment compared to TIL. The density of tumour infiltrated lymphocytes had a positive relationship with both antibodies in neoplastic compartment.

PS-01-002

Atypical lipomatous tumour of the breast – reporting a not-so-rare entity in an extraordinarily rare location

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Background & Objective: Atypical lipomatous tumour/well-differentiated liposarcoma (ALT/WDL) of the breast is a very rare malignant tumour accounting for less than 1% of all breast malignancies, which was first reported by Neuman in 1862. It features amplification of the 12q13-15 chromosomal segment, which includes the genes MDM2, CDK4, and HMGA2. ALT is a low-grade tumour which rarely metastasizes.

Method: We report the case of a 49-year-old female with no family history of breast cancer presenting to our clinic with a firm and imprecisely delimited tumour mass of approximately 3/1/1 cm, located in the retromammary space of the right breast.

Results: Histopathological examination revealed a neoplastic proliferation composed of lipoblasts and fusiform cells. Lipoblastic areas (representing 20% of the tumour mass) were composed of round lipoblasts with multivacuolated cytoplasm and slightly enlarged, hyperchromatic and eccentric nuclei. The fusiform cells featured vesicular nuclei and eosinophilic cytoplasm and were arranged in a solid-infiltrative pattern. Mitotic count was 8-9 mitoses/10HPF. Immunohistochemistry revealed diffuse reactivity for Bcl-2, S100, MDM2 and Vimentin, as well as negative expression of ER, PR, Mammaglobin, CK 7, h-caldesmon, CD10, CD34 and Desmin, with a Ki-67 index of 60%. Although malignant phyllodes tumour with liposarcomatous differentiation and myofibroblastoma were proposed as main differentials, the ancillary tests were highly suggestive for the diagnosis of atypical lipomatous tumour of the breast.

Conclusion: We present an extremely rare case of atypical lipomatous tumour with unusual presentation, where besides the atypical site of involvement, the lipoblastic areas represented only a small part of the tumour, causing differential diagnosis difficulties.

PS-01-003

Thymidylate synthase, Cyclin D1 and Ki-67 expression in hereditary and sporadic breast cancer

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Background & Objective: Thymidylate synthase (TS) is involved in DNA biosynthesis (Rose et al.,2002; Yu et al.,2005). Cyclin D1 (CycD1) regulates cell cycle and growth of estrogen-responsive tissue (Roy et al.,2006; Ezzat et al.,2012). Few studies have highlighted the immunohistochemical profile (besides molecular type) of hereditary breast cancer (HBC) regarding TS and CycD1. Aim of this study is to compare TS, CycD1 and Ki-67 expression in hereditary and sporadic breast cancer.

Method: A retrospective study included 110 cases of invasive breast cancer. Cases were classified as hereditary (45) by BRCA1/2 mutation testing in peripheral blood. Control group comprised 65 tumours. Expression of TS, CycD1 and Ki-67 was detected by immunohistochemistry and graded by percentage. Data were analyzed using descriptive statistics and Mann-Whitney U-test. $p<0.05$ was considered significant.

Results: In HBC, TS was expressed in 66.7% of cases, contrasting with 29.2% ($p<0.001$) in control group. CycD1 was expressed in 95.6% and 83.1% of HBC and control cases, respectively ($p<0.001$). HBC was characterized by the following mean values: CycD1, 83.5±21.9% [95% confidence interval: 76.9–90.1]; TS, 28.7±32.3% [18.9–38.4]; Ki-67, 37.8 ±27.8% [29.4–46.1]; control group: CycD1, 27.8±27.7% [20.9-34.6], TS, 4.5±10.4% [1.9–7.0]; Ki-67, 12.4±2.9% [11.7–13.1]. Median values in HBC was: CycD1, 91.0% (interquartile range, IQR:19.0); TS, 20.0% (IQR:50.0); Ki-67, 32.0% (IQR:51.0); in controls: CycD1, 20.0% (IQR:37.5); TS, 0.0% (IQR:6.0); Ki-67 12.0% (IQR:0.0).

Conclusion: HBC is characterized by distinctive overexpression of TS, CycD1 and Ki-67 indicating differences in cell proliferation and DNA synthesis. These markers can add informative value in HBC evaluation.

PS-01-004

Malignant adenomyoepithelioma with chondrosarcoma: a case report and review of the literature

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Background & Objective: Malignant adenomyoepithelioma is a rare biphasic tumour with neoplastic epithelial and myoepithelial cells. We aimed to present this rare case with macroscopic and microscopic features.

Method: The case we reported here was a 67 years-old woman who had a mass in her right breast. On the PET-CT scan for staging, there was a pathologically increased 18F-FDG uptake in the subareolar area of the right breast. Patient underwent right modified radical mastectomy. The diagnosis was made by macroscopic, microscopic and immunohistochemical studies.

Results: Macroscopically, there was a white-greyish tumour mass in the subareolar region with irregular borders and focal hemorrhagic areas. Microscopically, neoplastic lesion composed of epithelial and myoepithelial cells, a focal pleomorphic adenoma-like area and a chondroid area with an atypical tripolar mitosis compatible with chondrosarcoma. Myoepithelial cells had focal necrosis and increased mitotic activitiy. İmmunohistochemically, neoplastic myoepithelial cells were diffusely nuclear positive with p63 and focally positive with SMM, SMA, calponin, cytokeratin-19 and cytokeratin 5/6. Neoplastic epithelial cells were diffusely positive with cytokeratin-19 and cytokeratin-7 and focally positive with cytokeratin-5/6. There was a strong nuclear positivity in the area of chondrosarcoma and focal positivity in some myoepithelial cells with S-100 staining. Estrogen reseptor was very rarely nuclear positive in tumoural cells. GATA-3, Chromogranin-A, Synaptophysin and p40 were negative.

Conclusion: After reviewing the English literature, to our knowledge, this is the first case of malignant adenomyoepithelioma with chonrosarcoma. We presented a rare case and review of the literature with malignant adenomyoepithelioma.

PS-01-005

Correlation of changes of estrogen receptor and progesterone receptor expression levels in locoregional metastases of breast cancer comparing with primary tumour

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Background & Objective: Discordance of biomarker expression in primary tumour and metastases is the possible reason of insufficient effectiveness of the antitumour therapy. Research objective: to evaluate correlation of changes of estrogen receptor (ER) and progesterone receptor (PR) expression in locoregional metastases of breast cancer compared with primary tumour.
Method: Postoperative samples of primary tumour and metastatically affected lymph nodes of 104 patients with invasive breast carcinoma of no special type without neoadjuvant therapy were studied immunohistochemically with monoclonal anti-ER and anti-PR antibodies (clones 1D5 and PgR-636). Staining results were evaluated using Allred score. Spearmen's rank correlation coefficient was calculated for differences of ER and PR expression levels between metastatic and primary tumours.
Results: ER expression levels in metastases and primary tumours were different in 67 of 104 cases (64,4%, 95% CI 54,4-73,4%), PR expression levels – in 64 of 104 cases (61,5%, 95% CI 51,5-70,8%). Correlation coefficient of ER and PR expression level differences between metastasis and primary tumour was 0,49 ($p<0,001$) for all cases. Analyzed in groups, formed according to primary tumour ER expression level (first – 0 and 2, second – 3-6, third – 7-8 Allred scoring points) correlation coefficients were 0,24 ($p=0,19$) in first, 0,67 ($p<0,001$) in second and 0,19 ($p=0,32$) in third groups.
Conclusion: Changes of ER and PR expression levels in locoregional metastases compared with primary tumour of breast cancer are correlated. Statistically significant correlation was indicated in the whole sample (weak correlation) and in the group with intermediate ER expression level in primary tumour (intermediate correlation).

PS-01-006

Paget breast cancer immunoprofile as Toker's cells: a case report

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Background & Objective: Paget's disease or Paget breast cancer is a rare and unusual breast cancer. The appearance of the disease may be associated with invasive or noninvasive tumour mass and rarely without an underlying neoplasm. The aim of this paper is to present a case of Paget's carcinoma without an underlying carcinoma (PCWUC), arising from Toker's cells.
Method: The patient was 70-years old woman with ulcerative and crusted changes of the nipple and areola. We examined a large number of sections taken from biopsy and surgical specimen of the nipple, areola and underlying breast tissue. All slices were processed and stained with standard procedures (haematoxylin–eosin) and immunohistochemical technique.
Results: Epidermis and distal lactiferous channels were infiltrated with Paget cells resembling atypical neoplastic altered Toker's cells. Using immunohistochemistry, we found a clear demarcation between normal epithelial cells from malignant cells infiltrate. Cytokeratin 7 was positive only in tumour cells, but high molecular and low molecular weight cytokeratins were only positive in normal epithelial cells. Underlying breast tissue did not contain any tumour cells.
Conclusion: The same immunoprofile of Toker's cells and PCWUC cells suggests a common histogenesis.

PS-01-007

Quality assurance of Ki-67 proliferative index measurement in breast cancer reporting

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Background & Objective: Ki-67 has prognostic and predictive value in invasive breast carcinoma (IBC), but clinical uptake is hampered by suboptimal accuracy, reproducibility and standardisation. Published guidelines have addressed standardisation of pre-analytical and analytical factors, however, the practicalities of ongoing monitoring Ki-67 quality have not been discussed. We aimed to evaluate the quality of the established digital Ki-67 IBC reporting practice at our tertiary institution.
Method: In the four years since initial validation work, we completed a series of internal and external quality assurance (QA) projects. For internal QA we undertook an interoberver agreement study of the four pathologists involved in Ki-67 reporting, an interlaboratory agreement study across separate sites reporting Ki-67 and audited the year-to-year Ki-67 values. External QA was investigated by comparison of our Ki-67 data against published datasets.
Results: We demonstrated excellent concordance ($R=0.91$-0.97) and good agreement ($K=0.76$-0.96) between pathologists and excellent concordance ($R=0.94$) and a very good agreement ($K=0.80$) between laboratory sites. There was no significant difference in Ki-67 data from year-to-year, which demonstrated expected associations with clinico-pathological parameters. Descriptive Ki-67 statistics were comparable to those of Ki-67 datasets reported in other studies and our data separated into similarly proportioned 'high'/'low' groups when dichotomised as per their protocols.
Conclusion: Our studies provide evidence of adequate internal and external QA for our digital Ki-67 IBC reporting service. Given the absence of a formal breast Ki-67 QA program, our approach could be emulated as a framework for Ki-67 QA in IBC.

PS-01-008

Comparative analysis of peritoneal carcinomatosis in patients with a history of breast cancer: breast cancer metastasis versus second primary tubo-ovarian and peritoneal cancer

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Background & Objective: Causes of peritoneal carcinomatosis (PC) in patients with a history of breast carcinoma include both metastatic breast carcinoma (MBC) and primary peritoneal/ovarian carcinoma (PPOC). The origin of PC is important to determine the appropriate treatment strategy. Cytological examination of the peritoneal fluid (PF), which may be the first diagnostic approach to PC, is of distinct value in confirming the presence of malignant cells and determining the origin of PC.
Method: We analyzed the clinicopathological and cytomorphological characteristics of 33 patients with a history of breast carcinoma whose PF cytology contained malignant cells. Cases showing positive immunoreactivity for PAX8 and WT1, and a lack of GATA3 expression were considered as PPOC.
Results: Sixteen developed PC caused by PPOC. PPOC patients were characterized by early-stage primary breast carcinoma, absence of nonperitoneal MBC before the detection of PC, and normal serum levels of CEA and CA15-3. Fourteen PPOC patients had pathogenic germline BRCA mutations. Cytological examination revealed that most of the PPOC cases had a dominant

papillary arrangement of the tumour cells with severe nuclear pleomorphism, occasional bizarre nuclei, and atypical mitotic figures. Patients with PPOC who underwent cytoreductive surgery had a significantly longer survival time compared to those who did not, or MBC patients.
Conclusion: In patients with a history of breast carcinoma presenting with PC, the presence of early-stage primary breast carcinoma, no prior nonperitoneal MBC, and a dominant papillary cellular arrangement pattern in the PF cytology were independent predictors of PPOC. Cytoreductive surgery significantly improved survival for patients with PPOC.

PS-01-009
Breast implant capsule-associated pathology: from "common" to "rare" to "unique"
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Background & Objective: The use of breast implants (BIs) for augmentation has become commonplace. It is believed that BIs could infrequently be associated with haematologic malignancies but they do not increase the risk of conventional mammary carcinoma.
Method: Cases: Common – Silicone mastitis. Rare – BI-associated anaplastic large cell lymphoma (BI-ALCL) with unusual clinical presentation and BI associated mammary fibromatosis. Unique – Metaplastic sarcomatoid squamous cell carcinoma.
Results: 77-year-old woman with silicone mastitis due to free liquid silicone injection into breasts for augmentation which caused breast deformities and pain. 69-year-old woman diagnosed with BI-ALCL who had a history of bilateral mastectomies with textured saline implant reconstruction. Initial skin breast biopsy was diagnostic of ALCL and axillary lymph node was positive for CD30-positive lymphoma cells. 52-year-old woman with BI associated mammary fibromatosis. 41-year-old woman presented with pain and breast swelling after saline breast implant augmentation 7 years ago. Implant capsule was thickened and on excision adjacent friable mass was demonstrated. Pathology revealed metaplastic sarcomatoid squamous cell carcinoma. Subsequent MRI showed chest wall mass requiring radical modified mastectomy and chest wall resection.
Conclusion: Because of rarity and unusual clinical presentation, BI associated pathology may go under recognized. It is important to increase awareness of these unusual entities. The aggressive behavior of the tumours presented in this series underscores the importance of excluding malignancy by pathologic examination in patients with long-standing BIs who present with acute onset of unilateral breast pain, breast enlargement and delayed periprosthetic fluid collection.

PS-01-010
Higher tumour cell proliferation in breast cancer of the young
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Background & Objective: Breast cancer (BC) in adolescents and young adults (AYAs; 15-49 years at diagnosis) is associated with aggressive tumour features. We aimed to investigate tumour cell proliferation markers in AYAs.
Method: The proliferation marker Ki67 was analyzed by immunohistochemistry on TMA slides of breast cancer FFPE tissue from two population-based cohorts: One AYA series (n=378) and one series of patients aged 50-69 years (n=546). mRNA microarray data from the METABRIC and TCGA cohorts (n=2283) was used to investigate gene expression signatures reflecting tumour proliferation.
Results: The AYAs demonstrated higher Ki67 levels compared to BC patients ≥ 50 years (median Ki67 10.1% and 6.8%, respectively; P<0.0005). Higher Ki67 levels were found in BC of AYAs <40 years compared to AYAs 40-49 years (median Ki67: 16.1% and 8.6%, respectively; P=0.009). High levels of Ki67 among AYAs were associated with high histologic grade, ER and PR negativity, larger tumour diameter and shorter survival (all P<0.0005). When adjusting for tumour size, histologic grade and lymph node status, Ki67 maintained independent association with prognosis in ER positive AYA cases (HR 4.8; 95% CI 1.9-12.1, P=0.001). Higher mRNA proliferation scores in the young, and associations between high scores and shorter survival, validated our results (all P<0.0005).
Conclusion: BC of the young demonstrate higher tumour cell proliferation compared to older patients. Higher levels of proliferation indicators associate with aggressive tumour features and reduced survival in AYAs and may potentially contribute to the more aggressive breast cancer seen in the young.

PS-01-012
Relationship of axillary total tumoural load (TTL) by PCR (OSNA) in early breast cancer, pathological variables and clinical outcomes
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Background & Objective: The study of sentinel lymph nodes (SLN) assessed by PCR (OSNA) creates a new variable, Total Tumour Load (TTL; defined as the total number of CK19 mRNA copies in all positive SLN). The latest edition of the Spanish Oncological Gynaecology Society (SEGO) Guideline (2017) proposes a complete axillary lymph node dissection (ALND) when TTL is 15,000 or more in early breast cancer. We are using OSNA to assess SLN and Z0011 criteria to complete ALND. We want to determine the correlation between TTL and pathological variables and clinical outcomes and if TTL is useful to decide complete ALND.
Method: Clinicopathological and follow up data were obtained from all patients with invasive breast cancer and SLN assessed by OSNA between 2011 and mid-year 2014.
Results: A total of 167 patients underwent SNB assessed by OSNA. 54.49% were luminal A, 25.14% luminal B, 11.9% triple negative, 4.9%, Her2 positive and 4.19% luminal B-Her2 positive. TTL was cero in 92 cases and greater in 75 cases; 40 cases higher than 15,000 copies. Only 12 cases met Z0011 criteria. 3 patients have had locoregional relapse and 5 metastatic disease. 7 have died, only two from metastatic breast cancer.
Conclusion: 1. Using Z0011 criteria, we have adequate clinical outcomes with a low rate of ALND 2. If we had based the axillary management on TTL values we would have multiplied the number of ALND by a factor of 2,4 (from 12 to 29). 3. We have observed a tendency to higher TTL in luminal phenotypes and to lower TTL in HER2 positive and triple negative subtypes.

PS-01-016
Clinical study on detection of sentinel lymph node metastasis in breast cancer by one-step RT - PCR
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Background & Objective: To investigate the sensitivity and specificity of SLN detection by reverse transcription-polymerase chain reaction (RT-PCR), which quantifies the expression of mammaglobin and cytokeratin-19 genes to determine SLN status.
Method: According to the AJCC, different numbers of breast cancer T47D cell were implanted into the lymph node metastasis model by cell

culture, and according to the CT value the metastasis of SLN was determined. RT-PCR was performed on odd-numbered blocks of 256 clinical SLN, and the corresponding SLN even blocks were paraffin-treated. The clinical and pathological data of the patients with metastasis and no metastasis were compared.
Results: Lymph node-negative, isolated tumour cells, micrometastasis, macroscopic metastasis, positive reference with the increase of tumour cells, RT-PCR CT value is getting smaller and smaller. This study analyzed 256 sentinel lymph nodes which are from 150 cases breast cancer patients, of which 40 SLN cases could expres human mammagloglobin and CK19, and the positive rate of the samples was 15.60%. The specificity of molecular detection of BLN (90.65%) and negative predictive value (96.04%) clearly demonstrated its reliability in guiding ALND decision-making.
Conclusion: The results of RT-PCR in detecting sentinel lymph node metastases> 0.2 mm are similar to those of permanent histology. RT-PCR has objective and rapid output advantages, which is proved to be true and reliable. Therefore, RT-PCR method can be used intraoperatively to decide whether to carry out axillary lymph node dissection.

PS-01-017
The role of T-lymphocytes in brain metastasis formation of breast cancer
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Background & Objective: To develop brain metastasis, breast cancer (BC) cells need to cross the blood-brain barrier (BBB). Previously, we identified the T cell response as an important pathway in helping primary BC to develop brain metastasis. Here, we aim to identify the T cell subpopulation and their secretion factors that facilitate brain metastasis formation of BC.
Method: We FACS-sorted CD3+, CD3+/CD4+, CD3+/CD8+ and CD14+ fractions of a fresh Ficoll PBMC-isolation from whole-blood of a healthy donor. All sorted cell fractions were studied at their naïve and PMA-activated status, following co-culture with BC cells. We used our in vitro BBB model for functional studies. In addition, we studied the function of interferon gamma (IFNγ) - one of the main factors secreted by T cells. IFNγ was used to activate naïve CD3+ T cells, and to affect BC cells directly.
Results: All naïve subpopulations of T cells did not enhance the ability of BC cells to cross the BBB. PMA activation increased the trespassing of BC cells through the BBB model significantly. Remarkably, BC cells that were co-cultured with CD3+/CD8+ T cell fraction were able to trespass the BBB to a higher extent (p=0.009). BC cells that were directly treated with IFNγ were not able to trespass the BBB. However, INFγ pre-treated CD3+ T cells increased the ability of BC cells to cross the BBB (p=0.006).
Conclusion: Activated T cells, especially CD3+/CD8+ T cell subpopulation, increase the ability of BC cells to cross the BBB. Furthermore, IFNγ is an important molecule in that pathway.

PS-01-018
The prognostic value of the tumour-stroma ratio in invasive breast carcinoma
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Background & Objective: Complex interactions occur between cancer cells and the tumour microenvironment. A high amount of stromal cells reflects a disturbed microenvironment. The prognostic value of the tumour-stroma ratio (TSR) is confirmed by stromal disalignment, stromal lymph node invasion and changed immune status of tumours in breast cancer patients.
Method: Women with invasive breast cancer (T1-4, N1-3, M0) who underwent an axillary lymph node dissection were retrospectively selected. TSR assessment was performed on H&E stained tissue sections of primary tumours and corresponding tumour-positive lymph nodes. Stromal organization was analyzed using image analysis software. Immunohistochemical staining was performed for human leukocyte antigen (HLA) class I, HLA-E, HLA-G, regulatory T cells, natural killer cells and cytotoxic T-lymphocytes to determine the immune status.
Results: Stroma-high correlates with worse RFS (P<0.001). A significant relationship was observed between stroma consisting of organized collagen and pathological response to neoadjuvant chemotherapy (P = 0.002). Patients with primary tumour stroma-low/lymph nodes stroma-low showed strongly improved 10-year RFS rates compared to patients with primary tumour stroma-high/lymph nodes stroma-high (58% versus 8%). Ten years RFP for patients with a stroma-low tumour /high immune status profile was 87% compared to 17% of patients with a stroma-high tumour/ low immune status profile (P <0 .001).
Conclusion: Determination of TSR is cheap, fast and simple to apply. Patients with a stroma-high tumour have worse outcome. Response on therapy is strongly dependent on stromal alignment. The prognostic value of the TSR can be further refined by including lymph node stromal involvement and immune status profile.

PS-01-019
Adenomyoepithelioma with carcinoma of the breast: case report with next generation sequencing
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Background & Objective: Adenomyoepithelioma (AME) is characterized by a proliferation of two cell populations - epithelium-lined spaces in a background of myoepithelial cells. Each of these two components has the potential for malignant transformation, resulting in a rare diagnosis of AME with carcinoma. Few case reports, and even fewer molecular studies, of AME with carcinoma have been published. One author reports a mutation of the TP53 gene in a case of AME with carcinoma.
Method: A case of AME with carcinoma is identified. Tissue has been selected for Next Generation Sequencing, with results pending.
Results: A 70 year old female presented with a three month history of a palpable, 7 cm, rapidly growing breast mass. Core biopsy showed a malignant biphasic lesion, favoured to be AME with carcinoma. Mastectomy pathology confirmed the diagnosis. Sentinel lymph node biopsy was negative and CT showed no evidence of distant metastases.
Conclusion: We report a case of AME with carcinoma. Our patient will require close clinical follow-up because of the known aggressive nature of this rare tumour and potential for metastases. Although the current role for chemotherapy in the management of AME with carcinoma is unclear, if a unique genomic signature can be established, it is potentially targetable with future therapies.

PS-01-020
PDL1 expression in triple negative breast cancer – core needle biopsy versus lumpectomy
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Background & Objective: Recent studies have shown that PDL1 positivity was most frequently observed in the subgroup of triple negative breast cancer. The intratumoural heterogeneity of PDL1-expression in breast cancer is also addressed in previous studies. In current trials the scoring system for evaluating PDL1-status changed from TPS (tumour proportion score) to CPS (combined positive score). The aim of our study was to compare PDL1-positivity in core needle biopsies and lumpectomy or mastectomy specimen. Furthermore the big difference between the applied TPS and CPS should be demonstrated.

Method: Immunohistochemical staining for PDL-1 (Biocare CAL 10) was performed on triple negative breast cancer specimens obtained from 79 patients which had core needle biopsy or lumpectomy/mastectomy performed in the breast health care centre of KH Hietzing/Vienna. We evaluated PDL1 expression in 42 core needle biopsies and 37 lumpectomy/mastectomy specimens. At first the PDL1 expression was determined by the TPS and classified as positive if TPS ≥1%. Secondly the CPS was performed on all TNBC cases and classified as positive if CPS>1. The staining results of the core biopsies were compared with those of the lumpectomy specimen of the same patients.
Results: 20% of the samples showed a TPS ≥1% and 66% a CPS>1. There was 62% concordance between the core needle biopsies and the lumpectomies of the same patients.
Conclusion: Core needle biopsies are a valid method to evaluate PDL1 status. Compared to the TPS the CPS increases the number of patients who will receive an immune therapy.

PS-01-021
High Pregnane X Receptor (PXR) expression is associated with poor prognosis in patients with invasive breast carcinoma
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Background & Objective: Pregnane X Receptor (PXR) has been involved in human malignancy, either by directly affecting carcinogenesis or by inducing drug-drug interactions and chemotherapy resistance. The present study aimed to evaluate the clinical significance of PXR expression in invasive breast carcinoma.
Method: PXR protein expression was assessed immunohistochemically on formalin fixed paraffin-embedded breast cancer tissue sections obtained from 148 patients and was statistically analyzed with clinicopathological parameters and overall and disease-free patients' survival.
Results: PXR positivity was noted in 79 (53.4%) and high PXR expression in 48 (32.4%) out of 148 breast carcinoma cases. High PXR expression was positively associated with histological (p=0.0305) and nuclear (p=0.0112) grade and tumour cells' proliferative rate (p=0.0051). Associations between high PXR expression and estrogen and progesterone receptor negative status were also recorded (p=0.0314 and p=0.0208, respectively). High PXR expression was associated with shorter overall survival times (log-rank test, p=0.0009). In multivariate analysis, high PXR expression was identified as an independent prognostic factor of overall patients' survival (Cox-regression analysis, p=0.0082).
Conclusion: The present data support evidence that PXR is related to a more aggressive invasive breast carcinoma phenotype, being a strong and independent prognosticator of poor prognosis.

PS-01-022
Association of serum 25-hydroxy vitamin D level and invasive breast cancer risk among Sudanese patients: a case-control study
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Background & Objective: Although suggested by several epidemiologic and experimental studies, results regarding the role of 25 hydroxy vitamin D [25 (OH) D] in the development, progression and prognosis of breast cancer have been inconclusive. This study aimed to assess the possible association between 25 (OH) D serum levels and invasive breast cancer risk in Sudanese women.
Method: This case-control study was conducted on 333 Sudanese women (100 with newly diagnosed invasive breast cancer and 233 matched non-cancer females). Serum 25 (OH) D was measured through a competitive Electrochemiluminescence immunoassay.
Results: Age ranged from 28 to 85 years with a mean (±SD) of 48.10(±12.11) years. 76.9% of breast cancer patients and 83.5% of non-cancer women had vitamin D serum levels below 20ng/ml (deficient) (P 0.077). The correlation between vitamin D level and histologic type, clinical stage and molecular subtypes of breast cancer was not significant (P. values 0.755, 0.073 and 0.192, respectively).
Conclusion: This study showed a trend towards marginal statistical significance between serum 25 (OH) D level and invasive breast cancer risk (P=0.077) and clinical stage (P=0.073), but not with histopathological type and molecular subtypes (P. values 0.755, 0.073 and 0.192, respectively). Further studies are necessary to additionally affirm these findings.

PS-01-023
Prognostic value of ALDH1 expression between invasive ductal carcinomas containing micropapillary components and invasive ductal carcinoma, NST groups
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Background & Objective: In our study, immunohistochemical expression profile of ALDH1, a stem cell marker, was evaluated in invasive ductal carcinoma, NST (IDK, NST) and invasive ductal carcinomas containing micropapillary component (MPKIDK). The relationship between ALDH1 and clinical-pathological, prognostic parameters of tumours investigated.
Method: Between 2010 and 2016, 105 cases were included in the study which were evaluated as IDK, NST and MPKIDK in our laboratory. Immunohistochemically, MPKIDKs were selected based on the EMA positivity pattern. Tumours were immunostained with ALDH1 antibody. No staining in tumour cells: negative; less than 10% weak or focal staining: 1+; moderate intensity in 10-50% staining: 2+; more than 50% strong cytoplasmic staining was assessed as 3+. No staining with ALDH1 in stromal cells or staining with less than 10% was negative; more than 10% of the staining was positive.
Results: There was no significant difference between clinical-pathological, prognostic parameters, tumoural ALDH1 expression ratio and staining intensity in IDK, NST and MPKIDK groups. ALDH1 was significantly higher in Ki-67 proliferation index 3+ staining cases than the 1+ cases (p=0,048). Stromal cells showing ALDH1 staining around the peritumoural area were more intense but ALDH1 positive stromal cells showed less density in the surrounding benign ducts.
Conclusion: Elevated Ki-67 proliferation index and ALDH1 expression can be used as supporting markers for detecting potentially aggressive tumours in invasive ductal carcinomas. According to our results we suppose that ALDH1 positive stromal cells with high density in the peritumoural areas may have protective effect and stromal response against development of malignancy.

PS-01-024
Positive axillary lymph node status pre-neoadjuvant chemotherapy (NACT) is associated with a high rate of post-NACT sentinel lymph node biopsy positivity
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Background & Objective: Pre-operative axillary lymph node (LN) assessment informs surgical treatment of the axilla in management of primary invasive breast cancer. In patients undergoing primary surgery, a positive LN predicts significant disease burden warranting progression to direct axillary node clearance (AXCL). In patients with a positive LN who subsequently receive NACT with a good radiological response, post-NACT sentinel lymph node biopsy (SNLB) is performed to assess the need for AXCL. This study investigates the correlation between pre- and post-NACT LN status, related to tumour biomarker profile.
Method: The study comprised 93 patients with a positive pre-NACT LN, assessed using ultrasound guided FNAC, who were diagnosed and treated

at SVUH between 06/15-07/17. Two patients had multifocal disease. Tumour biomarker profile was 46 hormone receptor (HR)+HER2-, 37 HER2+, 12 triple negative (TN)

Results: Following post-NACT imaging, 51/93 patients (55%) had SLNB and 42/93 (45%) proceeded to direct AXCL. 33 patients who underwent direct AXCL had further nodal disease (79%). 30/51 (59%) SLNB were positive; 26 progressed to AXCL with further nodal disease in 9 (35%). Post-NACT LN positivity was associated with HR+HER2- biomarker profile ($p < 0.05$).

Conclusion: Our findings suggest that in patients with positive pre-NACT LN FNAC, there is a high incidence of post-NACT SLNB positivity and requirement for AXCL, regardless of imaging findings. Based on current data, HR+HER2- biomarker profile is significantly associated with a higher rate of SLNB positivity, compared with HER2+ and TN tumours.

PS-01-025

Impact of decalcification on prognostic/predictive indicators in bone metastases from breast cancer. An experimental study

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Background & Objective: Prognostic/predictive indicators (ER, PR, Ki-67, HER2) in bone metastases from breast cancer are of paramount importance for adequate treatment decisions, but immunohistochemistry (IHC) on decalcified specimens is considered unfeasible and/or its results unreliable. Retrospective investigations found significant discrepancies between primary breast carcinoma and metastases, depending on true disease changes and pre-analytical variables as decalcification.

Method: In order to assess the reliability of IHC, a so-called experimental decalcification was performed on primary breast cancer tissue using ethylendiaminetetraacetic acid (EDTA). In 5 cases, tiny portions from primary tumours were decalcified for one hour after fixation; in 5 cases, one-hour decalcification was performed on paraffin blocks of primary tumours. Histological sections were immunostained for ER, PR, and Ki-67 using DAKO OmnisTM automated platform. HER2 status was tested by DAKO HercepTestTM. The results of the original report were used as standards.

Results: ER and PR immunostains of decalcified tumours gave results comparable to the original reports. Ki-67 appeared significantly lowered in nearly all the samples decalcified after fixation and in 1 sample undergone surface decalcification. HER2 passed from 1+ to 0 score in 1/5 samples decalcified after fixation, without variations in the remaining four and in all samples exposed to surface decalcification.

Conclusion: The percentage and intensity of immunostaining for ER, PR and HER2 is not hindered by decalcification of fixed biopsies or paraffin blocks. Ki-67 is severely effaced by decalcification after fixation, but not after paraffin decalcification. EDTA decalcification of paraffin blocks appears a reliable method to perform IHC on bone metastases from breast cancer.

PS-01-027

Oestrogen receptor antibodies and their performance in the UK National External Quality Assessment Scheme for Immunocytochemistry and In Situ Hybridisation (UK NEQAS ICC & ISH)

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Background & Objective: UK NEQAS ICC & ISH conducts assessments of oestrogen receptor (ER) immunohistochemistry (IHC) at quarterly intervals. At each run, the Scheme assesses participant's stained slides for technical quality and gathers detailed information on primary antibodies and other methodological parameters. We examined these data for assessment runs conducted between 2007 and early-2018.

Method: Data were extracted from the Scheme's database and analysed in respect of performance of primary antibody clones and IHC staining platform suppliers.

Results: Between 2007-18, 34 ER assessments were conducted (10,321 submissions). Median number of participating laboratories at each run was 333 (range=264-368). In total, 546 laboratories participated (from 61 countries); 36% were from the UK, contributing 50% of the data-sets. In 97% of submissions, one of four primary antibody clones was used (1D5:7%; 6F11:48%; EP1:8%; SP1:34%). The mean pass-rate was 91%. For each individual clone mean pass-rate (trend, between first and last use) was: 1D5:81% (96-67%); 6F11:88% (97-94%); EP1:98% (67-100%); SP1:97% (96-100%). IHC staining platforms from 3 suppliers were represented (those used by <20% of participants excluded), Agilent-Dako:20%; Leica Biosystems:25%; Ventana:40%. Non-automated staining was used for 2% of submissions. Mean pass-rates (trend) for each was: Agilent-Dako:90% (99-94%); Leica Biosystems:89% (100-100%); Ventana:96% (100-99%); non-automated:82% (100-67%). Additional methodological analyses will be presented and 10-year performance trends will be examined.

Conclusion: Analysis of the data has shown performance differences between ER clones and IHC staining platforms.

PS-01-028

Clinical significance of EphA2, EphA4 and EphA7 expression in triple negative invasive breast carcinoma

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Background & Objective: Ephrin receptors (Ephs) are frequently overexpressed in a wide variety of human malignant tumours, being associated with growth, invasion, angiogenesis and metastasis. The present study aimed to evaluate the clinical significance of EphA2, EphA4 and EphA7 expression in triple negative breast carcinoma (TNBC).

Method: EphA2, EphA4 and EphA7 protein expression was assessed immunohistochemically on formalin fixed paraffin-embedded TNBC tissue sections obtained from 52 patients and was statistically analyzed with clinicopathological parameters and overall and disease-free patients' survival.

Results: EphA2, EphA4 and EphA7 positivity was noted in 52 (100%), 27 (51.9%) and 43 (87.8%) out of 52 TNBC cases, respectively and high EphA2, EphA4 and EphA7 expression in 26 (50.0%), 25 (48.1%) and 32 (61.5%) cases, respectively. EphA2 expression was positively associated with tumour cells' proliferative rate ($p=0.0054$), EphA4 expression with the presence of lymph node metastases ($p=0.0444$) and EphA7 with histological grade ($p=0.0647$). Enhanced EphA2 expression was associated with poor overall and disease-free patients' survival at both univariate ($p=0.0006$ and $p=0.0141$, respectively) and multivariate ($p=0.0041$ and $p=0.0232$, respectively) level.

Conclusion: EphA2, EphA4 and EphA7 may be implicated in the malignant transformation of TNBC and especially EphA2 may be considered as a strong prognosticator of poor prognosis and possible treatment target.

PS-01-029

Tumour-infiltrating CD8+ lymphocytes after primary systemic therapy predict clinical outcome in patients with breast cancer

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Background & Objective: Tumour-infiltrating lymphocytes(TILs) have prognostic values in breast cancers. This study was performed to investigate changes of TIL subsets after primary systemic therapy (PST) and their prognostic significance in breast cancer.

Method: 155 patients who had received anthracycline- or anthracycline and taxane-based PST and had residual disease were included. The change of intratumoural and stromal TIL subsets (CD4+, CD8+, FOXP3+ TILs) in pre- and post-PST breast cancer samples and their association with clinicopathologic features and patient survival were analyzed.

Results: Intratumoural CD4+ and CD8+ TILs increased, but stromal TILs decreased after PST. As for FOXP3+ TIL, both intratumoural and stromal TILs

decreased after PST. The chemo-responsive subgroup showed the same pattern of change in CD8+ TILs as in the whole group, but the chemo-resistant subgroup did not show significant change. Survival analyses for each TIL subset and their ratios revealed that only high CD8+ TIL infiltration after PST was an independent prognostic factor for favorable survival outcome. In subgroup analysis by pre-PST CD8+ TIL status, high CD8+ TIL infiltration after PST was revealed as a favorable prognostic factor in the pre-PST high CD8+ TIL subgroup, but not in the low CD8+ subgroup. Prognostic significance of high CD8+ TIL infiltration after PST was also found in hormone receptor-positive subgroup and in the chemo-resistant subgroup.
Conclusion: This study showed that CD8+ TIL subset moves from stromal to intratumoural compartments during PST, especially in chemo-responsive tumours and that CD8+ TIL status in residual tumours after PST can serve as a useful prognostic marker in patients with breast cancer patients who receive PST.

PS-01-031
Tumour associated macrophages as potential prognostic biomarkers in breast cancer
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Background & Objective: Tumour associated macrophages (TAMs) are activated macrophages with tumour progression in various cancers. They can polarize M1 or M2 types. M1 has a pro-inflammatory function and kill pathogens. Conversely, M2 shows immunosuppressive and promote tumour growth. There are various markers of TAMs. CD11c is regarded as a specific M1 marker and CD163, revealed in M2. CD68 is known as a pan-macrophage marker. We evaluated the relationship between clinicopathological parameters and the immunohistochemical expression of CD163, CD11c, and CD68 in invasive breast cancer (IBC) and the prognostic value of macrophage localization with tumour stroma (TS) and tumour nest (TN).
Method: IHC of CD68, CD11c, and CD163 was performed on TMA of 367 IBC. The number of CD68+, CD11c, or CD163+ macrophages in TN versus TS was counted. The correlations between CD68+, CD11c+, and CD163+ macrophages and the clinicopathological parameters were analyzed. Additionally, we assessed the impact of CD68+, CD11c+, and CD163+ macrophages in TS and TN on DFS and OS.
Results: Infiltration of CD68+, CD11c+, and CD163+ macrophages into TS or TN has a significant clinical relevance with positive correlation with higher histologic grade, increased Ki-67, and ER and PR negativity in TN. CD163+ macrophages in TS and TN have positive correlation of T stage. Furthermore, CD163+ macrophages in TN were an independent prognostic factor with reduced OS and DFS. Conversely CD11c+ macrophages in TS were an independent prognostic factor for improved OS and DFS.
Conclusion: TAMs in the TS is an independent predictor of tumour progression in IBC. It also can be a significant unfavorable prognostic factor and a potentially useful diagnostic and prognostic marker for IBC.

PS-01-032
Efficacy of radiotherapy after breast conserving surgery depending on the presence of tumour infiltrating lymphocytes (TILs)
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Background & Objective: To evaluate the effect of postoperative radiotherapy (RT) after breast conserving surgery depending on stromal-tumour infiltrating lymphocytes (sTILs) in the primary breast tumour.
Method: 1178 patients with breast cancer stage I and II were randomized to postoperative RT or not within the SweBCG-91RT trial. Median follow-up for ipsilateral breast tumour recurrence (IBTR) was 15.2 years. Blocks were collected from 1003 patients. Subtyping was performed with immunohistochemistry. sTILs were scored in 941 patients using haematoxylin-eosin stained full tissue sections.
Results: The sTIL score was <10% in 669/941 (71%) of all the patients. sTILs values were well balanced between the treatment arms. In a multivariable regression analysis with RT and sTILs as explaining variable and IBTR as outcome variable the hazard ratio for RT versus no RT was 0.48 (95%CI 0.34-0.66) in the low sTILs subgroup (<10%) and 0.77 (95%CI 0.54-1.11) in the high sTILs subgroup (>10%). Test for interaction between RT and sTILs did not reveal a significant interaction (p=0.19).
Conclusion: RT reduced the risk for IBTR significantly. Lower values of sTILs indicated numerically lower risk for IBTR. However, sTILs did not significantly interact with the effect of the postoperative radiotherapy.

PS-01-033
Sentinel lymph node biopsy (SLNB) versus axillary lymph node dissection (ALND) following neoadjuvant chemotherapy in women with node-positive breast cancer at diagnosis: retrospective study
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Background & Objective: The meaning of small volume metastases in the sentinel node (SN), performed after neo-adjuvant chemotherapy is still subject of debates. Purpose of the present study is to present data from a cohort of patients, cN+ who become cN0 after NAC.
Method: Sixty-four cases cN+ (cytologically proven nodal-disease) before NAC and cN0 after NAC, received SNB. Relation between SN status and axillary dissection was examined.
Results: SNB resulted negative in 36 cases and no axillary dissection was performed. The remaining 28 cases were classified as macrometastases (8), micrometastases (15) and isolated tumoural cells (ITC)(5). Axillary dissection was performed in 20 cases. The number of cases showing further axillary involvement was: 4\cr8 in cases with SN macrometastases; 4\cr9 in cases with SN micrometastases and 1\cr3 in cases with SN ITC. Furthermore, all nodes showed treatment effects (fibrotic areas and hyaline scars, aggregates of foamy histiocytes). For each case a comparison with histotype, grading and biological parameters (ER, PGR, Ki-67 and HER-2) was done. The lymph node final status was also correlated with the degree of tumour regression at the level of mammary neoplasia.
Conclusion: The meaning of micrometastases and ITCs is different in the neoadjuvant setting than in the adjuvant setting. When ITCs are present in the lymph-node, it cannot be considered pathological complete response (pCR). The present data indicate that small volume metastases after NAC can indicate residual axillary disease.

PS-01-034
Primary breast lymphoma. Presentation of eight cases with literature review
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Background & Objective: Lymphomas rarely affect the breast, the majority being secondary. PBL accounts for 0.04%-0.5% of breast malignancies and less than 0,5% of all malignant lymphomas and about 2% of extranodal lymphomas. Recognition of breast lesions as haematolymphoid is critical to distinguish them from other entities occurring in the breast. We present eight cases PBL and we review the relative literature.
Method: Eight patients, seven women and one man, without a history of previous lymphoma, were diagnosed having PBL, during a seven years period, among 21030 breast malignancies (percentage: 0,04%). Average age was 66 years (range: 48-94). Seven patients presented with a palpable, painless mass while in one the lesion was detected by routine mammography. One patient had bilateral involvement. Breast biopsy or partial mastectomy with lymph node dissection were performed in six and two cases, respectively.
Results: On histology, tumours consisted of neoplastic cells with lymphoid morphology that tended to infiltrate around and within mammary units.

Immunohistochemical analysis confirmed their B-cell lymphoid origin. Four MALT lymphomas, two DLBCL and two follicular lymphomas were diagnosed. The patient with bilateral lesion had additionally lymph node involvement. Subsequent CT scans and bone marrow biopsies showed no evidence of extra-mammary disease. All patients received a combined chemotherapy regimen. After an average 45 months follow-up period there was no recurrences.
Conclusion: PBL is a rare breast malignancy. Accurate and early diagnosis is critical to avoid unnecessary surgery and ensure access to appropriate treatment.

PS-01-035
The value of tumour infiltrating lymphocytes (TILs) for predicting response to neoadjuvant chemotherapy in breast cancer: a study in a hospital complex
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Background & Objective: The link between the immune system and cancer is well known. Lymphocytes are the effector cells that mediate the immune response. The validity of the histological assessment of the tumour infiltrating lymphocytes (TILs) in cancer has been standardized by The International TILs Working group. The aim of the study was to analyze the association between TILs and the grade of response to neoadjuvant chemotherapy (NAC).
Method: The stromal TILs on haematoxylin and eosin (H&E) stained tumour sections were analyzed by light microscopy following the International TILS Working Group tutorial in 122 unselected patients. These patients were diagnosed of breast carcinoma (BC) at the Department of Pathology (Hospital Complex of Navarra) and treated with NAC between 2011 and 2017. The TILs were scored in three categories: 1-10%, 11-20% and more than 20%, and studied the association with other biomarkers and intrinsic BC subtypes.
Results: We observed a statistically significant association between TILs score >20% and the pathologic complete response (pCR) to NAC (Miller-Payne:5) (p=0.026). This association is also significant if we considered the grades 4-5 of Millar-Payne Grading System. We did not find any association between the density of TILs and no expression of ER (P=0.69), ki67 expression (p=0.19) or the HER2/triple-negative subtypes (p=0.92).
Conclusion: •BC with ≥20% of TILs is more likely to reach pCR. •The TILs assessment in needle core biopsy can predict the response to NAC and help for clinical decision. •The TILS assessment following the standardized International TILS Working Group approach is feasible in all the Departments of Pathology.

PS-01-036
Discrepancy in hormones and growth factor receptor expression in primary versus metastatic breast cancer
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Background & Objective: Breast cancer can metastasize anywhere in body. Many researches show that the molecular profile may change when cancer metastasize. But there exist few data about metastases to the skin worldwide. This study aims to evaluate retrospectively discordance of hormonal receptor status among primary and metastatic (recurrence) breast cancer, particularly in skin. Our study is the first in Georgian population.
Method: We analyzed medical records of 109 women with breast cancer relapse who developed recurrence in lung (32), liver (27), skin (29) and bone (21).
Results: We revealed that all 29 cases with positive ER status remained positivity in skin mts. PR-negative status was stable in 7 cases; 0 case was changed from negative to positive. 12 cases changed from PR-positive to PR-negative and 10 case remained stable positive status; Negative HER2 status was staid stable in 17 cases and 6 cases was changed from negative to positive, 0 case lost HER2 receptor and 5 case staid stable positive status. We also revealed that the fastest relapse in skin was developed in 2 years and the latest recurrence in 10 years. We revealed that out of 29 patients 26 had PR/ER (+).
Conclusion: We find out also that there was no significant correlation between grade and recurrence in skin. No changes were identified in grades between primary and secondary tumour. In skin metastases most discordance revealed in PR status, where 41% of patients' skin mts became PR-negative. HER 2 status was changed also from negative to positive (in 20%), no discordance was found in HER2 (+) status

PS-01-037
ALDH1L1 downregulation and hypermethylation in breast cancer
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Background & Objective: Investigation of ALDH1L1 expression and pattern of promoter methylation in breast cancer and analysis of association of these features with clinical characteristics of the tumours.
Method: Thirty primary tumour specimens and thirty matched histologically normal tissues were obtained from patients diagnosed with stage I-III breast cancer prior to radiation or chemotherapy. Expression level of ALDH1L1 was evaluated by quantitative PCR. Treatment of the genomic DNA with sodium bisulfite and targeted high-throughput sequencing (MiSeq, Illumina) were applied to assess methylation level of ca 100 CpG sites in promoter region of the gene.
Results: Expression of ALDH1L1 was considerably suppressed in all tumour specimens: on average, more than 10-fold downregulation was observed. Hypermethylation of the gene promoter region was also revealed in the majority of breast tumours. We have demonstrated statistically significant negative correlation between average methylation level of promoter region and expression level of ALDH1L1 gene. Moreover, high-throughput bisulfite sequencing of the gene promoter allowed us to specify CpG sites, which hypermethylation was associated with gene expression. However, no significant correlation was observed between the gene expression or promoter methylation level and clinical characteristics of the tumours.
Conclusion: Strong downregulation and hypermethylation of ALDH1L1 already at early stages of breast cancer argue that suppression of ALDH1L1 is a prerequisite for malignant transformation and the gene is highly likely to be a tumour suppressor but not a suitable marker for differential diagnostics of breast tumours.

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PS-01-038
Hormone receptor status in invasive breast carcinoma – single institution results of more than 10,000 consecutive cases
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Background & Objective: Immunohistochemical demonstration of hormone receptors (HR) is a crucial factor for management of invasive breast carcinoma (IBC). Regular monitoring of HR assessment results is recommended, however published data on expected patterns of HR status and expression are scarce.
Method: Institutional database was searched for primary IBCs in the period 2006-2017. ER and PR were assessed immunohistochemically. IHC protocols were EQA monitored. Cut-off was 1%. Analysis was performed to obtain data (average and annual variation) on HR, ER and PR status, level of ER and PR expression (% of stained tumour cells), co-expression of ER and PR and PR expression in ER negative IBCs.
Results: 10637 consecutive IBCs were identified. 87% were HR positive, 87% ER and 76% PR. ER and PR expression was strong (>80% positive cells) in 78% and 43%, intermediate (1-80% positive cells) in 8% and 33% and negative in 14% and 24% respectively. 75% were ER+/PR+,

12% ER+/PR-, 0.5% ER-/PR+ and 13% ER-/PR-. Annual variation was minimal in all parameters. PR expression in ER negative tumours was very low (1-9% positive cells) in 71% and rarely intermediate or high.
Conclusion: 87% IBCs were HR positive, 87% ER positive and 76% PR positive. ER expression was predominantly strong or negative and rarely intermediate while PR expression was usually strong or intermediate and less frequently negative. ER-/PR+ IBC were very rare and in these PR expression was usually very low. Annual variation was minimal if methods are subjected to regular EQA monitoring.

PS-01-039

Adenomyoepithelioma and malignancy in association with adenomyoepithelioma, 4 cases from a single center

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Background & Objective: We aimed to present unusual cases; 1 adenomyoepithelioma and 2 malignancy arising from adenomyoepithelioma.
Method: Three cases diagnosed as adenomyoepithelioma (Case 1), low grade mucoepidermoid carcinoma (Case 2) and malignant adenomyoepithelioma (Case 3) were re-evaluated, retrospectively.
Results: Case 1: Tumor showed well-defined borders and composed of both epithelial and myoepithelial cell proliferation in a tubular growth patern. Although this case, had a history of adenomyoepithelioma 9 years ago from another hospital, no necrosis, mitosis, cytonuclear atypia were detected in current lesion. Case 2: Tumor showed lobulated borders. Microscopically, while some of these lobules correlated with adenomyoepithelioma with papillary growth pattern, the rest of the tumor showed solid-cribriform proliferation of different type of epitelial cells. These cells composed of intermediate, epidermoid type cells and sparsely mucinous cells with low grade cytonuclear features. Ki-67: 10-15% Case 3: Tumor displayed extensively cystic-hemorrhagic areas with expansile borders. Microscopically, tumor showed several types of growth patterns and epithelial cell shapes. While some areas composed of solid proliferation of polygonal cells with clear/eosinophilic cytoplasm, other areas composed of cribriform proliferation or irregular nests including plasmocytoid type cells within the myxoid matrix. Osteoid/osteochondroid formations were present. Necrosis and 12 mitosis/10HPF were detected. Some of papillary type of benign adenomyoepithelioma foci were noted at the periphery of the tumor. No accompanying in situ/invasive carcinoma were determined. Ki- 67: 35%. Metastasis to axillary lymph nodes and/or distant organs were not determined in last 2 malignant cases.
Conclusion: Because of the rarity of these lesions, we found them worthful to present.

PS-01-040

Tumour-infiltrating lymphocytes (TILs) as a predictor of response to neadjuvant chemotherapy in breast cancer

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Background & Objective: Breast cancer is a heterogeneous disease with different molecular subtypes. The HER2-positive (HER2+) and the triple-negative (TN) subtypes have shown improved survival when neoadjuvant therapy results in a complete pathologic response (CRp). Since there is a link between the abundance of TILs and the occurrence of CRp, TILs evaluation is becoming an important aspect of routine histopathologic examination. Our aim is to explore the correlation between TILs presence and CRp achievement in our cases.
Method: This study has included patients with invasive ductal carcinoma diagnosed in our centre in 2017 and treated with chemotherapy. Following literature recommendations, TILs were examined in tumour stroma using haematoxylin-eosin (HE)-stained slides and the findings were expressed as the percentage of tumour stromal area occupied by mononuclear inflammatory cells/total tumour stromal area. The correlation between TILs and CRp was analysed with the IMB-SPSS programme.
Results: Fifteen patients (9 HER2+ and 6 TN) have been studied. Sixty per cent of patients (66% HER2+ and 50% TN cases) achieved CRp, while the rest showed a partial response. Of the cases with abundant TILs (≥30, n=6) 83% showed CRp, whereas CRp was observed in 55% of instances with few TILs (<30, n=9). These differences didn't reach statistical significance (p=0.28), probably due to the limited number of cases studied.
Conclusion: Our preliminary results indicate that a high TILs percentage is associated with a positive CRp. TILs evaluation, which can be done on HE-slides without recourse to immunohistochemestry, is thus emerging as a useful predictor of response to neoadjuvant chemotherapy in breast cancer.

PS-01-041

Lymphoepithelioma-like breast carcinoma. Report of a case

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Background & Objective: We present a case of lymphoepithelioma-like carcinoma of the breast (LELC-B) a very rare primary breast carcinoma with 33 cases reported in the English literature.
Method: A 57-year old patient was admitted due to palpable lymphadenopathy of the left axilla. On clinical examination a small palpable lump of the left breast was found followed closely by FNA cytology that was positive for malignancy.
Results: Grossly, the tumour was relatively well circumscribed with hard consistency measuring 22 mm. Microscopically on low power examination it was multilobulated with lobules divided by fibrous septa. Higher power examination revealed small tumour islands and trabeculae consisting of highly atypical cells, with abundant eosinophilic cytoplasm embedded in a lymphocyte rich stroma which surrounded and intermingled with the tumour cells often obscuring their epithelial nature. Metastatic disease was found on 8 lymph nodes. Immunohistochemical study was positive in the tumour cells for the epithelial markers AE-1/AE-3, Cytokeratin 8/18 and Cytokeratin-7 and negative for Cytokeratin-20, CD3, CD20, CD15, CD30 and CD79a confirming the epithelial nature of the neoplasm. E-Cadherin was positive whereas ER, PR, C-ERB-2 and CD117 were negative, with Ki-67 staining 80% of the tumour nuclei. Epstein-Barr virus was not detected by in situ hybridization. Type 16 HPV was detected by PCR and in situ hybridization.
Conclusion: The diagnosis of LELC-B was made. The patient received adjuvant chemotherapy and RT. Forty-eight months later there is no evidence of recurrence or metastasis. LELC-B is a rare primary breast carcinoma with unique morphology, excellent response to treatment and favorable outcome.

PS-01-042

The diagnostic value of liquid-based cytology in thyroid fine needle aspiration: an institutional experience

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Background & Objective: Fine needle aspiration (FNA) is often the first step procedure because it is easy, reliable and economical to evaluate thyroid gland nodules. Liquid based cytology (LBC) is a method developed to evaluate gynaecologic cytologic specimens and it is now applied to cytologic materials obtained from thyroid FNA. İn our study, we aimed to determine the diagnostic value of LBC method in assessment of thyroid nodules.

Method: Between 2014 and 2017, FNA biopsy was performed on the thyroid node of 7387 patients in the presence of ultrasonography. Diagnoses of the specimens were made according to the Bethesda System for Reporting Thyroid Cytopathology (2010). Gathered during a period of 4 years, 581 cases with surgical resection were included. Sensitivity, specificity, accuracy were calculated.
Results: A total of 581 histologically confirmed cases, 16.9% (98/581) were male and 83.1% (483/581) were female. The risk of malignancy of cytology category was calculated 3.6 % of nondiagnostic,1.6 % of benign cytology, 12.2% of atypia of undetermined significance/follicular lesion of undetermined significance, 16.4% of follicular neoplasm/suspicious for a follicular neoplasm, 74.3% of suspicious for malignancy cytology and 100% of malignancy cytology. The specificity of thyroid fine needle aspiration biopsy was 100% and sensitivity was 83.3%. Diagnostic accuracy was 98.4%. False positivity was not observed. False negativity rate of cases was 0.9%.
Conclusion: LBC may be an indispensable cytology method in the evaluation of thyroid nodules because it is particularly suitable for use of ancillary methods such as immunohistochemistry and molecular assays.

PS-01-043
Acinic cell carcinoma of the breast associated with high grade ductal carcinoma: a case report
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Background & Objective: Acinic cell carcinoma (AcCC) of the breast is a rare, special type of breast carcinoma that shows morphologic overlap with those of the salivary glands. AcCC of the breast has morphological features similar to microglandular adenosis, and as Rosen has stated and recent molecular studies support, AcCC is in fact "invasive carcinoma with acinic cell differentiation arising in microglandular adenosis." In the current WHO classification, it is recognised as a rare type of triple-negative breast carcinoma. One third of reported cases have been associated with ductal carcinoma NOS, usually poorly differentiated triple-negative.
Method: We present a 60-year old patient who in a first needle core biopsy was diagnosed with high grade ductal carcinoma NOS, triple-negative, and with features that were interpreted as carcinoma involving microglandular adenosis on the periphery. A second needle core biopsy from microcalcifications adjacent to the main mass showed only AcCC carcinoma, also triple-negative. The patient recieved neoadjuvant chemotherapy and the posterior surgery showed minimum residual high-grade carcinoma, and more extensive residual AcCC. The sentinel node biopsy was negative.
Results: This case presents a wide morphologic spectrum, from microglandular adenosis to high grade poorly differentiated carcinoma. The interest is not only academic.
Conclusion: The recognition of this entity is important to avoid interpreting areas of microglandular-like adenosis as benign in a well-differentiated AcCC, both in a needle biopsy and in surgical margins.

PS-01-045
Primary mucinous cystadenocarcinoma of the breast: report of a rare case
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Background & Objective: Primary mucinous cystadenocarcinoma of the breast is an extremely rare entity and, to the best of our knowledge, only a few isolated cases have been reported in the literature. It is defined as a cystic tumour, composed of tall, columnar cells with abundant intracytoplasmic mucin and basally located bland nuclei.
Method: Our patient, a 59-year-old woman, presented with a mass in the right breast, measuring 0,9 cm in maximum diameter. Lumpectomy and sentinel lymph node biopsy were performed.
Results: Macroscopically, the neoplasm was well-circumscribed, solid and cystic, grey to white and was partially filled with mucoid material. Histological features were consistent with mucinous cystadenocarcinoma of the breast. Immunohistochemically, the tumour was negative for estrogen and progesterone receptors and HER2, whereas the Ki-67 proliferative index was 15%. The 3 sentinel lymph nodes were negative.
Conclusion: Primary mucinous cystadenocarcinoma of the breast is an extremely rare entity. Although in the 2003 WHO classification of breast tumours it was classified as a variant of mucin producing carcinomas, the term was abandoned, due to its rarity, in the latest WHO classification. The tumour usually occurs in older female patients, displays unique pathological features resembling an ovarian mucinous neoplasm and despite its usual triple negative immunoprofile seems to have a favorable prognosis after complete resection. A thorough clinicopathological correlation is necessary in order to differentiate primary mucinous cystadenocarcinoma of the breast from metastatic mucinous neoplasms originating from distant organs, mainly ovaries and pancreas.

PS-01-046
Comparison of immunohistochemical markers before and after neoadjuvant chemotherapy in breast cancer and their use as predictor od response
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Background & Objective: Changes in tumour markers between biopsies performed before and after neoadjuvant chemotherapy (NAC) are controversial. The aim of this study is to compare immunohistochemical (IHC) expression of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (Her-2) in breast cancer before and after treatment and to correlate the expression of tumour markers with response to NAC.
Method: Retrospectively analysis of 132 patients with locally advanced breast carcinoma diagnosed on core needle biopsies and surgical specimens was performed. IHC staining for ER, PR, Her-2 were available before and after NAC.
Results: Pre-chemotherapy IHC revealed 96 (72,73%) ER+, 80 (60,61%) PR+ and 39 (29,55%) Her-2+ cases. Nine (8,04%) ER+, thirteen (11,61%) PR+ and four (3,57%) Her-2+ patients lost positivity after NAC. Initially two (1,79%) ER-, eight (7,14%) PR- and three (2,68%) Her-2- tumours were positive after NAC. Patients with Her-2 positive and PR negative tumours before NAC demonstrate significantly higher pathological complete response.
Conclusion: No significant changes were seen in steroid receptors and Her-2 status before and after NAC but retesting of these markers in residual tumour shoud be considered to improve future tailored adjuvant therapies. The predictive factors of the pathological complete tumour response to therapy are the negative status of PR and Her-2 positive status.

PS-01-047
Prolactin and circulating vitamin D levels as risk factors for benign breast tumour
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Background & Objective: Recent studies showed that increased prolactin (PRL) level and vitamin D (VD) deficiency may play a certain role in breast cancer. To evaluate the role of prolactin and circulating vitamin D level in patients with benign breast tumours (BBT).
Method: 134 patients with fibrocystic mastopathy including 92 women with a diffuse form of mastopathy (DFM) and 42 patients with fibroadenoma (FA) and 134 healthy women were examined. All women underwent a visual

examination, ultrasound diagnostics of mammary glands, digital mammography (under 40 years). Prolactin and VD levels were measured by ELISA. Statistical analysis done with SPSS Statistics v.20.
Results: More than half of women with DFM (59.7%) have a VD deficit compared to healthy women (7.3%). BBT patients characterized by lowering VD level (17.8±0.23 ng/ml and 20.50±0.37 ng/ml in DFM and FA respectively and 27.35±0.16 ng/ml (p-value <0.001). Furthermore, we found that in the VD deficiency mean PRL level was much higher compared to a group with normal VD supply (289.4 mU/l and 232.2 mU/l respectively). Significant negative correlation between PRL and VD was found only in DFM patients (r= -0.2106, p = 0.026).
Conclusion: Patients with DFM are characterized by low VD availability and by the highest values of prolactin which serves as an independent marker for breast cancer. Thus, correction of VD deficiency in patients with DMS can be an effective means of primary prevention of breast cancer.

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PS-01-048
Malignant phylodes tumour with rhabdoid and chondroid differentiation in a patient with Hashimoto thyroiditis
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Background & Objective: Malignant phyllodes tumours are rare entities, accounting for 0.18% of all breast tumours. The microscopic features of these tumours may occasionally include heterologous sarcomatous elements, however rhabdoid differentiation is an exceptional finding.
Method: A 49-year-old woman presented to the Emergency Department with a 6-months history of rapidly growing ulcerated left breast mass. Ultrasonography of the left breast identified a dense large lobulated mass measuring 12x10 cm, accompanied by lymphadenopathy of the left axilla. A diagnosis of high grade sarcoma with myoid immunophenotype was established on core needle biopsy. In addition, PET-CT examination revealed a solitary nodule of the left thyroid lobe (9 mm), leading to the suspicion of primary breast tumour with metastases in lymph nodes and thyroid. The patient underwent mastectomy and hemithyroidectomy.
Results: On gross examination, the thyroid showed a whitish, well delimitated nodule (1 cm), which on microscopic examination prove to be Hashimoto thyroiditis. The mastectomy specimen revealed multiple subcutaneous nodules with ulceration, with nipple and areola involvement. On cut section, the tumour (17x13x11.5 cm) was multinodular delineated by fibrous septs, containing myxoid, cystic and necrotic areas. The microscopic appearance was of a malignant stromal proliferation with chondroid and rhabdoid features, and with occasionally leaf-like projections. Axillary lymph node showed only reactive changes. Based on histological examination and in correlation with immunohistochemistry, the final diagnosis was malignant phyllodes tumour with chondroid and rhabdoid differentiation.
Conclusion: We described a rare case of malignant phyllodes tumour with uncommon histological and clinical presentation.

Sunday, 9 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-02 | Cytopathology

PS-02-001
Can Survivin, IMP3 and GLUT-1 be helpful in the differential diagnosis of peritoneal effusion cytology?
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Background & Objective: The morphological differential diagnosis between malignant epithelial tumours and reactive mesothelial hyperplasia can be extremely challenging. The aim of this study is to determine whether there is a difference in the human insulin-like growth factor II mRNA binding protein 3 (IMP3), glucose transporter 1 (GLUT-1) and survivin staining between invasive malignant epithelial tumour cells and reactive mesothelial hyperplasia.
Method: We evaluated the staining of these markers on tissue microarray blocks prepared from cell blocks of 37 malignant and 17 benign peritoneal effusions.
Results: Nuclear survivin staining was observed in 56,8% (21 cases) of malignant cases and 16,7% (3 cases) of benign cases (P=0.013) where as cytoplasmic survivin staining was positive in 100% (37 cases) of malignant and %94,1 (16 cases) of benign cases (P=1.0). Strong GLUT-1 staining was seen in 31,4% (11 cases) of malignant cases, where as in only 5,6% (1 case) of benign cases (P=0.041). Positive staining for IMP-3 was observed in 27,0% (10 cases) of malignant and 50% (9 cases) of benign cases (P=0.168).
Conclusion: Nuclear survivin positivity and strong GLUT1 staining in malignant cases are potentially useful markers in differential diagnosis of malignant epithelial cells and reactive mesothelial hyperplasia. IMP3 staining has no significant difference between malignant and benign cases.

PS-02-003
How does knowledge of hpv status affect pathologists' final cytologic diagnosis?
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Background & Objective: Human papilloma virus (HPV) testing is commonly used as an adjunct to cytology for cervical cancer screening. Our aim is to find out if knowledge of HPV status has any affect on cytologic diagnosis.
Method: The cytology results of 27014 women with median age of 40 who had cervical screening between 2012 and 2017 were reviewed. Patients were evaluated with co-test (PAP smear+HPV test) after May 2015. Cervical cytology results before co-test period (n: 16254) were compared with the co-test period in which HPV status was known to the pathologist as a second part of this study, random 50 cases of cervical cytology were evaluated twice (blinded and unblinded to HPV status) independently by two (senior and inexperienced). pathologists.
Results: Overall epithelial cell abnormality diagnosis had increased from 1.3% to 4% after the start of co-testing. The difference was most prominent in LSIL (from 0.2 % to 1.7%) (p, <0.05). ASC/SIL ratio decreased from 2 to 0.79 with HPV co-testing. For the 50 cases reviewed by 2 pathologists, ASC/SIL ratio decreased from 0,67 to 0,43 for senior pathologist and 1,88 to 0,73 for inexperienced pathologist after unblinded screening.
Conclusion: The interpretation of cervical cytology is relatively subjective. Our findings show that knowledge of HPV status affects desicion making and increases sensitivity. Also helps espescially less experienced pathologist to classify borderline cases.

PS-02-004
Preoperative diagnosis of poorly differentiated thyroid carcinoma by fine needle aspiration cytology
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Background & Objective: Poorly differentiated thyroid carcinoma (PDTC) is a rare but aggressive thyroid malignancy. Due to its aggressive nature, preoperative recognition is tremendously important for planning patient's management. According to some experts PDTC diagnosis can

be established only on histology. The aim of this study is to present three cases in which PDTC diagnosis was made on FNA (fine needle aspiration) cytology and to highlight those features which should raise suspicion of this rare condition.
Method: All three cases were males older than 55 years. Each presented at consultation for a gradually growing mass on the left/right side of the neck. One patient had a second tumour mass in the manubrium. FNA was recommended and was performed from the tumour and the bone mass.
Results: On cytology all three cases were similar: hypercellularity, no colloid, but extensive necrotic background. Cells were small and monotonous and were disposed either as individual dispersed cells or grouped in insular or trabecular arrangements. The nuclei were round/oval, with smooth contours and small-inconspicuous nucleoli; some cells had plasmacytoid appearance. The cytoplasm was ill-defined, sometimes finely granular. In all three cases a high mitotic rate was noticed. In one case typical papillary carcinoma cytology was associated with previously described aspects. The pathological examination of the surgical specimens confirmed the PDTC based on Turin criteria.
Conclusion: We have demonstrated that in some cases, PDTC diagnosis is possible in cytology as well. Three cytomorphological features were predictive for PDTC, others having limited value: monotonous appearance of the cells, necrotic background and mitosis.

PS-02-005
Comparative characteristics of neutrophil extracellular DNA formation during incubation with breast carcinoma autologous cells of different molecular-genetic subtype
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Background & Objective: Depending on the initiating factor and the tumour cell properties of breast carcinoma, neutrophils are able to perform effector functions through either active phagocytosis or cytotoxic action, including the formation of neutrophil extracellular traps.
Method: 20 females of each group with breast cancer: luminal type A, luminal type B HER2 positive or HER2 negative, HER2 positive nonluminal type, triple negative type. Pure fractions of neutrophils were incubated with tumour cells at 37° C to assess the neutrophils functional activity. Their ability to form extracellular networks served as an indicator of neutrophils functional activity.
Results: The study revealed that during incubation of tumour cells of the luminal type A breast carcinomas, the number of extracellular DNA networks formed by them predominated over those in the carcinoma group of luminal type B HER2-negative, but there was significantly less aggressive forms of nonluminal carcinomas (triple negative type). Thus, all breast cancers tumour cells of any molecular-genetic type were activating cells, but the cells of clinically more aggressive forms showed the maximum values of the studied indicator.
Conclusion: Having low expression on receptor cells to progesterone (luminal type B, HER2 positive), the presence of HER2 overexpression (triple negative type, nonluminal), and the approximation to basal cell differentiation (triple negative type) demonstrates a much more pronounced ability to activation of neutrophils.

PS-02-006
Tall cell variant of papillary thyroid carcinoma: report of a case with tall cell variant clues in thryroid fine needle aspiration cytology
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Background & Objective: The thyroid fine needle aspiration cytology (FNAC) has proven that it was an important tool to characterise thyroid nodules, mostly to discriminate malignant (primitive or secondary) from benign lesions. The tall cell variant (TCV) of papillary thyroid carcinoma (PTC) is an important agressive subtype and usually associated with higher extrathyroid extension and distant metastasis.
Method: A 53-years-old woman presented a rapidly growing left thyroid nodule without thyroid dysfunction symptom but associated with compressive symptoms. Thyroid ultrasound was performed and showed a suspicious complex nodule measuring 8,4 cm in its largest dimension without lymphadenopathy (classified as TI-RADS 4b based on the Thyroid Imaging Reporting and Data System). CT-Scan confirmed these results.
Results: FNAC of this left thyroid nodule was performed and showed isolated or aggregated numerous atypical cells characterized by high nuclear-cytoplasmic ratio, an eosinophilic abundant cytoplasm, proeminent intranuclear pseudo inclusions and nuclear grooves. Neutrophils were the predominant background. Immunochemistry was used on the cell block section: antibodies CK19, HBME1 and PAX 8 were positives. The FNAC was reported as Bethesda VI: malignant, and the histologic diagnostic was PTC tall-cell variant of PTC.
Conclusion: The tall cell variant of PTC is rarely identified on FNAC. Utilisation of ancillary methods such as immunochemistry on cell block could help to identify the tumour as a primitive one and exclude a secondary tumour.

PS-02-007
Retrospective analyses of women with HSIL or more in a countryside city in relation to age, number and interval of cytological exams
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Background & Objective: The Brazilian Cervical Cancer Screening Program recommends screening women between 25 and 69 years of age with cervical smears every 3 years, after two consecutive annual negative smears. Then, in ten years it is expected about 3 to 4 screening exams per women.
Method: This is an observational retrospective analytical study. The analyzed patients were stratified into three age groups. The number of screening exams was analyzed in a period of 10 years previously the histological diagnosis.
Results: After using the exclusion criteria, the sample consisted of 261patients. More than an half of patients were under-screened (less than 3 exams in the previous ten years). 46% of women showed interval between the two last exams before the diagnosis bigger than 3 years. Women between 20 and 24 years represented more than 10% of our population.
Conclusion: In our point of view, the popularization of 3 years interval can be dangerous because women can feel comfortable to not do the exam frequently. Since the number of patients between 20 and 24 years was not irrelevant, it is suggested a close relation between the age of first sexual intercourse and the diagnostic of HSIL or more in young patients. Then, it is questionable if in Brazil the screening should not start previously.

PS-02-008
Can liquid-based cytology help for diagnosing pleural and ascitic effusions?
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Background & Objective: Pleural and ascitic fluid cytology is a simple and accurate diagnostic method to diverse benign and malignant processes. Tissue and organ specificity of metastatic tumour can be supposed by traditional smear cytology with Romanowsky-Giemse staining. But tumour cells being in a fluid can dramatically change its morphology. Thus,

ancillary techniques (such as Immunocytochemistry, molecular testing, PCR) can help a lot. In these cases CellPrep Plus® (Biodyne) looks like the best possible method for samples preparation. CellPrep samples can be preserved for 6 months, what can lower the need of additional aspirations. Well-known methods of liquid-based cytology, such as SurePath® (BD) and ThinPrep® (Hologic), proved itself to be good in cervical cancer screening programs. Nevertheless, they are known as not an adequate method for diagnostic cytopathology, as they change cell morphology and remove background, that is essential for precise diagnose.
Method: In 2017 in our Centre 56 samples of pleural and ascitic fluids were simultaneously studied on traditional smears (with Romanowsky-Giemsa staining) and on CellPrep Plus® liquid-based cytology smears (with Papanicolaou staining). Rare or difficult diagnoses, that were proposed on routine microscopy, were verified with Immunocytochemistry markers, performed on CellPrep material with Automated staining system BenchMark Ultra Ventana – 26 cases
Results: Reports coincided in all 56 cases (100%). Among diagnoses, verified by Immunocytochemistry, were not only ovarian serous and mucinous adenocarcinoma, but also rarer diseases, such as Hepatoid ovarian carcinoma or Pancreatic ductal adenocarcinoma.
Conclusion: CellPrep Plus® data gives additional facilities for investigating pathology diversity of metastatic tumours in pleural and ascitic effusions.

PS-02-009
Role of cytology in the diagnosis of intraocular lesions: a retrospective study of 33 patients

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Background & Objective: Intraocular cytology studies are infrequent due to the risk for serious eye complications and the dissemination of malignant cells, although complications are typically under-reported and the risk of seeding is low when small needles are used. So that, most frequently the diagnosis of intraocular lesions is done by non-invasive studies. Because of therapies are different depending of the disease, a definitive diagnosis must be done. We report our experience in intraocular cytology during the last 10 years.
Method: In a retrospective study over a 10-year period diagnostic cytology was performed on 33 patients with intraocular lesions. The specimens were obtained from fine needle aspiration (FNA) or from vitrectomy-based procedures. Flow cytometry and microbiologic analysis of samples were performed when required.
Results: Out of 33 specimens, cellularity was insufficient in 4 cases (12,1%), 19 (57,6%) were non-neoplastic (ocular amyloidosis, intraocular candidiasis and inflammatory processes), and 10 (30,3%) were neoplastic. Of those neoplastic lesions, 6 (60%) were choroidal melanoma and 4 (40%) were lymphoproliferative disorders. Only one melanoma was confirmed by enucleation, and all lymphoproliferative disorders were confirmed by flow cytometry. No complications were register after the procedure. And no evidence of malignant cells dissemination has been noticed.
Conclusion: In any suspected intraocular malignant lesion, in which enucleation is not the obvious treatment, the standards applied in the treatment should be equivalent to those in other fields of oncology and a diagnosis based on FNA or vitrectomy-based procedures must be done. However, in some cases specimen cellularity may be insufficient for diagnosis and some complications may happen.

PS-02-010
Cytologic diagnosis of noninvasive follicular thyroid neoplasm with papillary-like nuclear features and its impact on the risk of malignancy in the Bethesda system for reporting thyroid cytopathology: an institutional experience

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Background & Objective: Recently, "noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)" has been proposed to replace "noninvasive encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC)" due to its indolent behavior. We analyzed cytologic diagnosis of NIFTP and its impact on the risk of malignancy (ROM) in the Bethesda system for reporting thyroid cytopathology (TBSRTC).
Method: This study included 5549 cases of thyroid fine needle aspiration cytology (FNAC) diagnosed between 2012-2014. Diagnostic categories based on TBSRTC were compared with final surgical diagnosis, and the ROM in each category was calculated.
Results: Of the 5549 thyroid FNAC cases, 1891 cases underwent surgical resection. At the time of final diagnosis, 1700 cases were revealed as PTC, and 25 cases as NIFTP. The cytologic diagnosis of NIFTP were non-diagnostic in 1 case (4%), benign in 5(20%), atypia of undetermined significance (AUS) in 14(56%), follicular neoplasm in 2(8%), and suspicious for malignancy in 3 cases (12%). While none of the NIFTP was diagnosed into malignant category, 8(17.8%) of 45 EFVPTCs with invasion were diagnosed as malignant in FNAC. Collectively, NIFTP/EFVPTCs were less frequently categorized as malignant compared to PTCs. Exclusion of NIFTP from malignant diagnoses resulted in a slight decrease in malignancy rates in some categories without any statistical significance.
Conclusion: The decrease in the ROM was not significant when excluding NIFTP from malignant lesions due to the low frequency of NIFTP. In thyroid FNACs, NIFTP/EFVPTCs were mostly classified into indeterminate categories. Therefore, it might be feasible to separate NIFTP/EFVPTC from PTC on FNAC to guide conservative clinical management with NIFTP/EFVPTC.

PS-02-011
Diagnostic concordance difference between endobronchial ultrasound-guided transbronchial needle aspiration cytology and needle biopsy according to lymph node station

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Background & Objective: Lymph node (LN) metastasis in lung cancer is important factor for patient to determine the prognosis and to decide treatment plan. Endobronchial ultrasound (EBUS) guided transbronchial needle aspiration cytology (EBUS-TBNAC) or needle biopsy (EBUS-TBNB) is one of the useful methods for predicting mediastinal LN metastasis in lung cancer patients. The purpose of this study was to evaluate the concordance between EBUS-TBNAC and EBUS-TBNB according to LN station.
Method: We compared simultaneously obtained biopsy and cytology of 639 patients over 3 years period from January 2011 to Sep 2014. We evaluated 12 sites of mediastinal and intralobar LNs. The mean number of cases per each LN station was 138.4 (3 to 411) and the large number of cases were 556 in LN4R, 479 in LN7 and 192 in LN4L in order.
Results: The EBUS-TBNAC and EBUS-TBNB diagnosis were concordant in 1046 (87.2%) and discordant in 244 (14.7%) cases. Among the location of LN which collected more than 10 cases, the most discordant site was LN4L station (20.8%, 40/192), and the least discordant site was LN12 (5%, 1/20). The incidence of insufficient sample for diagnosis of EBUS-TBNAC was lower than that of EBUS-TBNB (0.7% and 1.7%, respectively) and the most common site of insufficient sample acquisition was LN4L (2.9%, 14/192).
Conclusion: The data showed that there is a clear diagnostic rate differences according to sampling methods of biopsy and cytology, and LN station.

PS-02-012

Endoscopic ultrasound guided fine needle aspiration in pancreatic lesions: a four-year retrospective study with cytohistological correlation and use of DPC4

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Background & Objective: Endoscopic Ultrasound-guided Fine Needle Aspiration Cytology (EUS-FNAC) is the most common procedure to obtain cytological specimen of pancreatic lesions. Rapid-On-Site-Evaluation (ROSE) method has the potential to check the cellular sample and improve the adequacy rates of FNA cytology. DPC4 has been described as a prognostic factor in pancreatic cancer.
Method: A retrospective study was performed on the pancreatic lesions initially diagnosed by EUS-FNAC between 2014 and 2017. EUS-FNAC was performed with ROSE and different needles. In cases of pancreatic carcinomas in 2017, DPC4 was performed in a cell block or, failing that, in the Papanicolau (PAP) smears and in the surgical specimen. The result of staining and the clinical evolution were compared.
Results: In our series, 291 patients underwent EUS-FNA for suspected pancreatic lesion. We standardized the diagnoses according the PSC guidelines (Category I: 14%, II: 43%, III: 2%, IV: 8%, V: 5% y VI: 30%), evaluated the impact of the different needles used and the cell blocks obtained. We also studied 32 cases of pancreatic carcinoma from 2017; 15 men and 17 women, mean age was 68.71 years, category I: 1, II: 3, III: 1, V: 2 and VI: 25; in which DPC4 was performed in 28 PAP, 24 blocks and 9 surgical pieces.
Conclusion: EUS-FNAC gives a valuable contribution in the diagnoses of all kind of pancreatic masses. Using 22G procore and ROSE method we obtained good samples and observed a good correlation between the cytological and histological diagnoses. The positivity of DPC4 indicates a better prognosis in pancreatic carcinoma.

PS-02-013

Intraocular lymphomas. Clinical and cytological perspective

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Background & Objective: Describe the characteristics of intraocular lymphomas (IOL) and analyze the most efficient techniques for evaluation.
Method: Retrospective descriptive study of patients with IOL seen at our institution between 1994-2017. The morphological criteria and the role of immunohistochemistry (IHC) and flow cytometry (FC) were analyzed.
Results: Twenty-five samples from 21 patients were analyzed; 18 cytologies (15 vitreous samples, two aqueous humor and a subretinal aspirate), and seven biopsies (three conjunctiva, one iris, two retina and an enucleation). Eleven patients were diagnosed with primary vitreo-retinal lymphoma (PVRL, 52%), four primary uveal lymphoma (PUL, 19%) and six secondary intraocular lymphoma (SIOL, 28%); 90% of the PVRL and 83% of the SIOL were diffuse large B-cell lymphomas, whereas PUL were extra-nodal marginal lymphomas. A primary T lymphoma and a secondary NK were diagnosed. All the cytological samples but two were diagnostic. The most relevant cytological criteria was cell size; most of the cases had medium and large cells. In more than half of the cases nuclear irregularity and pleomorphism were observed. The finding of lymphoglandular bodies, mitosis and necrosis was infrequent. In 16 of 18 cytological samples IHC was performed and confirmed the diagnosis in 14. FC supported the diagnosis in 6 of 9 cases. All biopsies were consistent with lymphoma diagnosis.
Conclusion: PVRL and SIOL are mostly large B-cell lymphomas. The most efficient technique for diagnosis is cytology combined with immunohistochemistry. Biopsy should be restricted to accessible locations or cases with negative cytology.

PS-02-014

Diagnostic accuracy of endoscopic ultrasound-guided sampling techniques of pancreatic lesions in surgically confirmed cases

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Background & Objective: Endoscopic ultrasound–guided fine needle aspiration cytology and biopsy (EUS-FNAC & EUS-biopsy) are currently the most commonly used sampling techniques of pancreas. This study was aimed to evaluate the diagnostic value of EUS guided sampling techniques in surgically confirmed cases.
Method: A retrospective medical record review of 58 cases of pancreatic lesions with concurrent initial diagnosis by EUS-FNAC & EUS-biopsy and subsequent histologic confirmation by surgical resection between January, 2010 and December, 2013 in Seoul National University Hospital, was done. The diagnoses were compared for statistical analysis for diagnostic accuracy of each procedure. Cases with different diagnosis were considered discordant, and slides were reviewed for analysis.
Results: Compared with final histologic diagnoses of surgically resected specimen, the diagnostic accuracy of EUS-FNAC and EUS-biopsy was 84.5% and 82.8%; sensitivity of EUS-FNAC and EUS-biopsy was 86.3% and 81.5%; specificity of EUS-FNAC and EUS-biopsy was 71.4% and 100%. Combining two techniques diagnostic accuracy progressed to a higher rate to each procedure (91.4% vs. 84.5% and 82.8%, respectively). But the sensitivity and specificity did not show any differences between combination and each procedures. The most common cause of inconsistent diagnosis in EUS-guided sampling techniques is 'insufficient for diagnosis'. The cause of discordance was sampling errors, misinterpretation of suboptimal specimens and misinterpretation of reactive atypia to malignancy.
Conclusion: EUS-FNAC and EUS-biopsy have a comparable diagnostic accuracy, but the combination of these procedures goes favorably.

PS-02-015

The Papanicolau Society of Cytopathology (PSP) pancreato-biliary cytology (pbc) nomenclature: early experience in our centre with endoscopic ultrasound-guided fine-needle aspiration biopsy (eus-fna)

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Background & Objective: The PSP developed guidelines for pancreatobiliary cytology including indications and techniques for EUS-FNA, terminology and nomenclature of pancreatobiliary disease, ancillary testing and post-biopsy treatment and management. The proposed terminology scheme recommends six categories: Nondiagnostic(I), Negative(II), Atypical(III), Neoplastic (Benign: IVa; Other: IVb), Suspicious (V) and Positive(VI).
Method: Pancreatic EUS-FNA performed in 2016 in our institution (81 cases) were revised and reclassified according to the proposed categories. When necessary, radiology of the lesions and the biochemical tests performed were also considered.
Results: There were no changes in the diagnosis in the cases originally considered as "Negative" (14 cases), "Atypical" (5 cases) or "Suspicious" (5 cases). Two of the 3 cases originally "Negative" were reclassified as "Nondiagnostic". Of the 13 cases previously diagnosed as "cyst", 4 were changed to "Nondiagnostic(I)" due to a discordant radiology; 7 to "Negative" category, 1 to "Neoplastic: benign (IVa)" (serous cystadenoma) and 1 to "Neoplastic: other (IVb)" (mucinous cyst). Of the 41 originally "positive" EUS-FNA cases, 3 have been reclassified as a "Neoplastic: other" and corresponding to pancreatic non-high-grade neuroendocrine tumours. The remaining 38 "Positive" cases included 36 adenocarcinomas, 1 lymphoma and 1 metastasis.

Conclusion: Cystic lesions suffered the greatest changes in reclassification due to additional radiological/biochemical information, which increased the diagnostic accuracy and avoided false negatives in potentially malignant lesions. The "Neoplastic: other" category allowed better discrimination in potentially less aggressive neoplasms, specially in neuroendocrine lesions. Moreover, the new terminology is more objective and understandable and promotes adequate patient treatment.

PS-02-016

Diagnosis of soft tissue lesions: role of fine-needle aspiration cytology

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Background & Objective: Fine-needle aspiration cytology (FNAC) is a cost-effective, safe and easy-to-perform technique. However, the role of FNAC in soft tissue lesions (STL) is controversial. Our aim is to assess the diagnostic performance of FNAC in soft tissue lesions.
Method: Retrospective study of all FNAC of STL diagnosed in our institution between 2000-2016 (n=234). Clinicopathological data was collected and cytological results were divided into groups and correlated with histological diagnoses.
Results: Most patient were male (53.4%) and patient age ranged between 15 and 94 years (mean: 61.29). Most lesions were located in the head and neck region. 22.6% of cytologies were non-diagnostic and most lesions were diagnosed by FNAC as carcinomas (33.3%), benign STL (17.9%) or inflammatory lesions (17.9%). Malignant STL comprised only 3.4% of all cases. Biopsy was performed in 36.1% of cases. Non-diagnostic cytologies were mainly inflammatory lesions, and carcinomas were histologically detected in 33.3% of inflammatory FNACs. General and specific concordances were 65.9% and 47.1%. Diagnostic sensitivity, specificity, negative and positive predictive values were 71.4%, 100%, 85.7% and 93.8%, respectively.
Conclusion: FNAC of STL is a valuable tool for diagnosing epithelial cysts, carcinomas, lymphomas and benign STL. However, inflammatory smears can be associated with false-negative cases and in some cases a biopsy is required in order to obtain enough material for immunohistochemical (IHC) study. The availability of a multidisciplinary team, clinical and imaging features, ROSE and IHC and molecular techniques is required for improving the role of FNAC of STL.

PS-02-017

The clinical performance of the ultrasound-guided thyroid fine-needle aspiration cytology and molecular testing at a tertiary care hospital

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Background & Objective: This study aimed to establish a profile of the ultrasound-guided thyroid fine-needle aspiration (FNA) cytology and molecular testing examined at the pathology department of the Goztepe Education and Research Hospital of Turkey.
Method: We reviewed 123 cases diagnosed as atypical by FNA cytology on the basis of the Bethesda system who had undergone molecular testing at this institute between January 2016 to March 2018. FNA samples were tested for BRAF, NRAS, and KRAS point mutations by real-time polymerase chain reaction (RT-PCR). The mutational status was correlated with cytology.
Results: All DNAs from 123 FNA samples could be analysed and point mutations were detected in 49 samples (40%). In 57 AUS/FLUS nodules, 13 samples (23%) had point mutations including BRAF (n=4), KRAS (n=6), NRAS (n=6) and BRAF-KRAS (n=3). In 29 nodules diagnosed as follicular neoplasm or suspicious for a follicular neoplasm, 10 samples (34%) had point mutations including BRAF (n=1), KRAS (n=5), and NRAS (n=4). In 13 nodules diagnosed as suspicious for malignancy, 10 samples (77%) had point mutations including BRAF (n=9), KRAS (n=2), NRAS (n=1) and BRAF-KRAS (n=2). In 24 nodules diagnosed as malignancy, 16 samples (66%) had point mutations including BRAF (n=13), KRAS (n=4), NRAS (n=0) and BRAF-KRAS (n=1).
Conclusion: Molecular analysis of FNA samples might be useful for the diagnosis of indeterminate thyroid nodules. This approach might be expected to reduce repeated FNA, needle biopsy, or diagnostic surgery for indeterminate thyroid nodules. Molecular tests may help clinicians to drive patient care and the surgical decision.

PS-02-018

HPV negative cervical adenocarcinoma – rare case of gastric type diagnosed by cytology

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Background & Objective: To present a case of a patient with gastric type cervical adenocarcinoma, describe the clinical course, diagnostic pathway and the key role of cytology in the diagnostic procedure.
Method: A 56-year-old asymptomatic woman attended the gynaecological clinic for a routine examination. The screening Pap smear was taken and the result was atypical glandular cells possibly of endocervical origin.
Results: The Pap smear revealed sheets and strips with cell crowding and pseudostratification, nuclear enlargement, anisonucleosis, mild chromatin irregularity and prominent nucleoli. The abnormal Pap smear was the first sign of a disease and further diagnostic procedures was suggested. The colposcopy finding was negative (TZ3), the high-risk HPV (Hybrid Capture 2) was negative and the immuno-testing p16/Ki-67 (CINtec Plus) double stain was negative. After two repeated abnormal Papsmears (AGC), fractionated curretage was performed. The histopathological diagnosis was negative. A follow up Pap smear finding was adenocarcinoma in situ with suspicious microinvasion. Abnormal glandular cells showed simillar features as in the initial Pap smear, but more prominent. Some cell group showed feathering and rosette-like arrangement. Three years after the first abnormal Pap smear conisation was performed and the histopathological diagnosis was mucinous endocervical adenocarcinoma of gastric type. The margins were positive and definitive radical operation was performed.
Conclusion: The finding of AGC in Pap smears demands further procedure and should be taken very seriously. We have to be aware of the fact that a small percentage of cervical cancers could be negative in the initial cloposcopy/histology workup, negative for HR HPV as well as p16/Ki-67 immuno-testing.

PS-02-019

Endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) cytology of mesenquimal tumours of the gastrointestinal tract: a 10-year retrospective study of 66 cases

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Background & Objective: Mesenquimal tumours of the gastrointestinal (MTGI) tract due to the deep location are difficult to diagnose by conventional surgery biopsy techniques. EUS-guided FNA has been increasingly used for the preoperative diagnosis of MTGT tract. In reviewing our experience, in this study, our aim is to determinate the accuracy of EUS-guided FNA for the diagnosis of MTGI tract.
Method: Over a 10-year period, a computerized search of the cytopathology laboratory information system was performed and all cases of EUS-

guided FNA in which a clinical diagnosis of MTGI tract was suggestive were identified. All correlating surgical pathology report diagnosis were obtained and retrospectively reviewed

Results: A total of 66 patients were clinically diagnosed as MTGI tract, 26 males, 40 females with a mean age of 65 (range 22 to 84 years). The tumour sized from 0,8 to 10 cm (mean: 4,3 cm). 44 cases had a gastric, 15 oesophagic, 4 duodenal, 2 oesophago-gastric and 1 rectal location. There was cell block (BC) in 71,2 % of the cases. 50% of the cases were hipocellular (36% CB), 34,2% gastrointestinal stromal tumours (GIST) (92%CB) and 15,8% (75% CB) leiomyomas. Immunohistochemistry (IHC) stains were performed (C-KIT, actin, CD34, DOG1 and ki67). Follow-up histology diagnoses were found in 35 (53%): 15 EUS-FNA GIST (all of them histologically confirmed), 8 EUS-FNA leiomyomas (7 confirmed) and 12 EUS-FNA hipocellular (8 GIST, 2 leiomyomas and 2 schwannomas).

Conclusion: EUS guided FNA along with CB and IHC stains are an accurate method of establishing a preoperative pathologic diagnosis of MTGI tract.

PS-02-020

Diagnostic performance of fine needle aspiration for thyroid nodular pathology. Analysis of 921 cases

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Background & Objective: Ultrasound-Guided Fine Needle Aspiration (UG-FNA) for thyroid, has been shown to be sensitive and specific to establish a diagnosis. 921 cases of UG-FNA are presented in order to assess the efficacy and know the performance of this procedure in our hospital.

Method: A descriptive, retrospective, study was carried out, analyzing the thyroid FNA from 2011 to the present year, with a total of 921 cases, reclassifying the cytological diagnoses according to The 2017 Bethesda System for Reporting Thyroid Cytopathology, correlating with clinical data and histological diagnoses in cases with surgical procedure.

Results: In our serie, 921 patients are classified into: Bethesda I: 50.4% (n=464), II: 37.6% (n=346), III: 2.5% (n=23), IV: 5% (n=47), V: 2.3% (n=21) and VI: 2.2% (n=20). The correlation of these results with the surgical sample are: Within Bethesda III, 21.7% malignant histology, 43.5% benign histology and 34.8% without surgical procedure. In Bethesda IV, 19.1% malignant histology, 42.6% benign histology and 38.3% without surgical procedure. Bethesda V, 90.5% malignant histology, with 9.5% without surgical procedure, and Bethesda VI: 75% malignant histology with 25% without surgical specimens.

Conclusion: The sensitivity of UG-FNA for the diagnosis of malignancy is high. There is a good correlation (in categories III and IV) of the risk of malignancy with respect to the 2017 Bethesda System for Reporting Thyroid Cytopathology. This work has led to a prospective work to improve the high percentage of unsatisfactory samples, in collaboration with the radiology department.

PS-02-021

Fine-needle aspiration cytology of the thyroid. A 10-year retrospective study of 3,531 samples from a single institution. Bethesda System and cytology-histology correlation

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Background & Objective: Fine-needle aspiration (FNA) cytology of thyroid nodules is a common practice. Bethesda system for reporting thyroid cytology (BSRTC) is intended to standardize terminology and offers specific cytology categories to facilitate more useful reporting and increased knowledge of the inherit risk of malignancy. This study was conducted to investigate the impact of using BSRTC diagnostic criteria on FNA diagnosis.

Method: All thyroid FNA cases were identified in a retrospective review between January 2008 and December 2017. BSRTC were used: non-diagnostic (BS1), benign (BS2), atypical/follicular lesion of undetermined significance (BS3), follicular neoplasm (BS4), suspicious for malignancy (BS5) and malignancy (BS6). Correlating surgical pathology report diagnosis of BS3, BS4 and BS5-6 were retrospectively reviewed.

Results: 3531 cases of FNA thyroid cytology were diagnosed, 2976 (84%) females and 555 (16%) males, with a mean age of 52 (range 12 to 91 years). There were 1858 (53%) BS1, 1078 (30,5%) BS2, 160 (4,5%) BS3, 279 (8%) BS4 and 156 (4%) BS5 y BS6. There were 431 histological follow ups: 121 (75,6 %) in BS3 with a malignant diagnosis (MD) in 28 (23%), 173 (62%) in BS4 with MD in 21 (12%) and 137 (87%) in BS5 and BS6 with a MD in 83%.

Conclusion: The risk of malignancy in BS3 is 5-15%, in BS 4 15-30% and in BS 5-6 60-99%. Our data reveal a higher percent of MD in BS3 and a slight lower percentage of MD in BS4. BS1 is 53% and liquid base cytology should be implemented to try to reduce it.

PS-02-022

Is the concurrent use of p16 and Ki-67 biomarkers an effective diagnostic tool for low grade squamous intraepithelial lesion of the cervix?

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Background & Objective: The implementation of CINtec PLUS, an immunocytochemical (ICC) assay which features dual staining of p16 and Ki-67, allows the identification of squamous intraepithelial lesions of neoplastic character. The aim of the study was to examine scanned slides of cervical smears stained first by routine (Papanicolaou) method and then in CINtec PLUS, compare the diagnoses and correlate them with histopathological results.

Method: The slides of 176 cases of archival routinely stained cervical smears: 88 LSIL, 58 ASC-US, 10 ASC-H, 10 HSIL and 10 cancers were scanned and destained. After restaining in CINtec Plus, the slides were scanned again, and the digital images were compared, allowing analysis of the very same cells.

Results: In 69% of LSIL, one to several dozens of ICC(+) cells were found, a few positive cells were spotted in only 27% of the ASC-US group, and 80% of ASC-H smears showed positive cells. In 100% of smears harbouring HSIL and cancer there were numerous p16/Ki67(+) cells. The observation period was 3 to 5 years. In one case of ASC-H further histopathological evaluation revealed cancer. In all cytological HSIL and cancer cases there was histopathological confirmation of at least high-grade dysplasia. Repeated Pap test and colposcopy in patients with LSIL and ASC-US showed low grade squamous intraepithelial lesions only in two cases.

Conclusion: Destaining of the routinely processed cytological smears and restaining with CINtec PLUS allows more accurate cytological diagnosis and classification of the smears to a category of high grade squamous intraepithelial lesions.

Sunday, 9 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-03 | Endocrine Pathology

PS-03-001

Histological scores for diagnosis of adrenocortical carcinomas – are they enough?

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Background & Objective: Adrenocortical carcinomas (AAC) diagnosis is a challenge for pathologists, especially in borderline cases. In the last years some

scores have been proposed for the evaluation of AAC; Weiss modified system (WMS) is the most commonly used.
Method: Retrospective evaluation of the ACC (2004-2016): 16 patients, median age of 50.5±10.16years (11F:5M). AAC had a median of 9.35±6.66cm (5.5-28) and 213±765,58g (34-2600). ACC was an incidental finding in 62.5% of patients; hormone production present in 31.3%. Ancillary evaluation: P53, Ki67 and Gordon&Sweet. Application of WMS, Reticulin algorithm (RA) and Helsinki score (HS).
Results: After a median follow-up of 31±48.72 months the overall survival (OS) was of 56.3% and 45% at 3 and 5-years. Disease-free survival (DFS) of 13.5±43.02months: five patients with local recurrence and seven with metastasis. Three lesions were benign with WMS, two with RA and three with HS criteria. Histologic characteristics: 62.5% had vascular invasion, 81.3% had necrosis and 50% had capsular invasion. Majority were staged as T2 (68.8%), and in this subgroup, size>10cm was associated with poorer OS (p=0.036). Ki67 had a median of 9.6±11.76% (2-43.70). Gordon&Sweet showed diffuse loss in fourteen cases and focal in two. P53 had abnormal staining in nine. Higher staging was predictor of poorer OS (p=0.011), as well as more than 5mitosis/50HPF (p=0.012). No factors were identified of better DFS.
Conclusion: Histological scores are precious auxiliaries in the ACC diagnosis, but can miss some borderline cases. The conjugation of size and weight can be helpful in some situations. Staging and mitotic index are powerful predictors of OS.

PS-03-002

Ribonuclease T2 (RNASET2) expression in the spectrum of neuroendocrine neoplasms of the lung. Relationships with hypoxia-related mechanisms and microvascular patterns

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Background & Objective: RNASET2 exerts several different activities in neoplastic cells since the early steps of tumour development such as growth suppression and antiangiogenic activity. No data on its expression in neuroendocrine neoplasms of the lung (Lu-NENs) are available. We investigated RNASET2 expression in well-differentiated (WD) and poorly differentiated (PD) Lu-NENs. In addition, we explored possible relationships between RNASET2 expression and a series of immunohistochemical markers related to hypoxic stress, apoptosis, proliferation and angiogenesis.
Method: Twenty-nine surgically resected Lu-NENs diagnosed between 2007 and 2016 were analyzed and compared to normal lung tissues from six lobectomies. Immunohistochemical stains for RNASET2, HIF-1 alpha, CAIX, M30, synaptophysin, chromogranin A, CD31 and CD34 were evaluated. RNASET2 expression was also measured with quantitative RT Real Time PCR. HIF-1 alpha expression in transfected cells was evaluated 48h after transfection by western blot analysis.
Results: Our results showed a significantly higher expression of RNASET2, HIF-1 alpha, and CAIX in PD Lu-NENs, associated with a higher proliferation and apoptotic rates, as well as a lower microvessel density (MVD) compared to WD Lu-NENs. In vitro, we demonstrated an overexpression of RNASET2 consequent to the activation of HIF-1 alpha.
Conclusion: We suggest that in PD Lu-NENs, RNASET2 expression may be induced by HIF-1 alpha. In this aggressive group of cancers, RNASET2 fails to exert the growth-inhibiting effects described in other types of neoplasms. However, it may contribute to the typical phenotypic alterations seen in poorly differentiated Lu-NENs, such as low MVD, high apoptotic rate and extensive necrosis.

PS-03-003

IgG4-related hypophysitis: report of two cases and revision of the literature

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Background & Objective: IgG-4 related disease (IgG4-RD) encompasses different disorders, sharing biochemical and morphological features. Elevated IgG4 serum levels may be elevated. The pituitary gland is a rare target site and IgG4-related hypophysitis (IgG4-RH) is not yet well characterized among primary hypophysitis. Here we present two cases of IgG4-RH and review the literature, to discuss the histopathological criteria for the diagnosis.
Method: Case 1: a male patient aged 66 presented with hyperprolactinemia and hypogonadism. MRI showed a sellar/extrasellar mass. A non-functioning (NF) pituitary neuroendocrine tumour (Pit-NET) was hypothesized and the patient underwent trans-sphenoidal surgery (TSS). Case 2: a female patient aged 22 presented with headache and galactorrhea. MRI showed an intrasellar mass, suggesting a Pit-NET. From PubMed data base (https://www.ncbi.nlm.nih.gov/pubmed), we selected all case reports of IgG4-RH, using the key words hypophysitis [AND] IgG4. Clinico-pathological features were recorded and compared with those of our cases.
Results: In both cases, pituitary tissue with an abundant lymphoplasmacytic infiltrate, storiform fibrosis and high numbers of IgG4 plasma cells per HPF were observed and IgG4-RH was diagnosed. We retrieved 17 histopathologically documented cases of IgG4-RH from previous literature. Our overall review highlighted that specific criteria for IgG4-RH are missing, despite the differential diagnosis of this condition from other primary or secondary hypophysitis is therapeutically crucial.
Conclusion: IgG4-RH is a rare condition, which benefits from corticosteroidal therapy and should be differentiated from other conditions affecting the pituitary gland. Our results suggest that diagnostic criteria for IgG4-RH should be better defined and may be different from those applied for IgG4-RD in other organs.

PS-03-004

Primary pigmented nodular adrenocortical disease - the role of the pathologist in the diagnosis of hereditary syndromes

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Background & Objective: Primary pigmented nodular adrenocortical disease (PPNAD) is a rare cause of ACTH-independent Cushing's syndrome, which can be either isolated or associated with Carney Complex (CC). The latter is a rare familiar syndrome, usually caused by a germline mutation in the PRKAR1A gene. Herein we report a case of CC diagnosed after histological evidence of micronodular adrenal hyperplasia (MiAH).
Method: A 17-year-old girl was referred to our hospital due to obesity and Cushingoid appearance. She had a family history of sudden death (father). Endocrinological workup confirmed the diagnosis of ACTH-independent Cushing's syndrome. MRI disclosed normal adrenal morphology. Scintigraphy displayed focal left adrenal hyperfixation, being consistent with a functional adenoma. Left adrenalectomy (12g) was performed.
Results: Grossly multiple brown nodules (largest dimension <5mm) were seen throughout the cortex and, occasionally, in the periadrenal tissue. Histologically, the nodules were composed of lipofuscin-containing cells. The diagnosis of MiAH, most probably corresponding to a PPNAD, was made. Molecular study revealed a heterozygous inactivating germline mutation of PRKAR1A, supporting the diagnosis of CC. Follow-up disclosed no other features of CC.

Conclusion: CC is a rare familiar syndrome with an autosomal dominant inheritance characterized, among others, by endocrine hyperactivity, which presents more often with Cushing's syndrome caused by PPNAD. Diagnosis of this rare condition can be challenging as imaging may not always identify the bilateral micronodular changes, which require a definite pathological diagnosis. This case represents an extremely unusual hereditary syndrome and highlights the importance of observation and documentation by pathologists.

PS-03-005

PDCD1 (PD-1) promoter methylation as a new prognostic marker in localised (stage I-II) Merkel cell carcinoma

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Background & Objective: Merkel cell carcinoma (MCC) is an aggressive neoplasm, whose prognostic criteria are a matter of dispute, specifically for localized (stage I-II) tumours. Programmed death-1 (PD-1) proved to be a key player of the tumour microenvironment, with agents blocking the PD-1/PD-L1 axis showing efficacy in these patients. DNA promoter methylation of programmed cell death 1 (PDCD1, PD-1) was evaluated as a prognostic biomarker in MCC.
Method: We collected clinical, pathological and follow-up data of 62 Merkel cell carcinomas of the skin. PDCD1 methylation (mPDCD1) was retrospectively assessed by bisulfite-Sequencing. Prognostic parameters were evaluated with Kaplan-Meier failure estimates, log-rank tests and Cox proportional hazards regression.
Results: There were 36 (58.1%) men and 26 (41.9%) women, aged from 60 to 95 years (74.6±10.7). Stages I and II were prevalent (56.5%), with only 6.4% patients in stage IV. High level of mPDCD1 was found in 37.1% of patients, unrelated to stage ($\chi 2 = 0.290$, p=0.590). High mPDCD1 was associated with a significantly shorter overall survival in stage I and II (HR=3.05, p=0.021), even adjusting for age and tumour size (HR=3.29, p=0.017). In the overall cohort, older age (HR=2.15, p=0.041) and tumour size >2cm (HR=2.12, p=0.040) were the only parameters associated to a shorter overall survival.
Conclusion: Our data support the role of the PD-1/PD-L1 interaction in creating a local tumour-specific immune response, representing a favorable prognostic factor in localized Merkel cell carcinomas and providing a rationale to improve investigation of PD-1/PD-L1 axis, as currently studied in melanoma and head and neck squamous cell carcinomas.

PS-03-007

Clinico-pathological features of adrenal tumours in young adults, a retrospective study

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Background & Objective: Adrenal tumours are rare in patients aged below 40 years. The aim of this study is to describe the clinico-pathological features of adrenal tumours in young adults.
Method: We retrospectively analyzed clinical and pathological data of 296 adrenal tumours treated at our institution from January 2000 to December 2017. Score of Weiss, PASS and Biceglia were established.
Results: 49 out of 296 patients (were under 40 years old (range age, 18 to 39.9 years). 12 patients were male (24%), and 37 were female (76%). Most tumours were pheochromocytomas (n=20) followed by adrenal cortical adenomas (n=13). Adrenocortical carcinoma was less presented (n=2). One composite pheochromocytoma was observed in patient with neurofibromatosis type 1. Three patients had bilateral pheochromocytomas; two of them had a Multiple Endocrine Neoplasia Type 2B. One patient had metastatic pheochromocytoma and succinate dehydrogenase subunit B mutation. The highest PASS and Weiss scores were respectively 14 and 3 (mean of 3 median of 2).
Conclusion: Adrenal tumours in young adults represent in our study 18 % of all adrenal neoplasms. They are most frequent in women. Pheochromocytomas are the most frequent tumour observed in our series and tend to have a low PASS score. Some cases are observed in familial syndromes. Adrenocortical carcinoma is uncommon in young adults and represents less than 4% of cases.

PS-03-008

Ultrastructure cell-cell interconnections in neuroendocrine neoplasms of the pancreas

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Background & Objective: Potential role for desmosomes and gap junctions in cancer progression has been suggested based on a variety of experimental clues. Difference in cell-cell interconnections between benign insulinomas and more aggressive nonfunctioning (NF) neuroendocrine tumours of the pancreas is generating scientific interest
Method: The material from 18 patients with insulinomas and 15 NF neuroendocrine tumours was investigated using electron microscopy
Results: Insulinoma cells were connected to each other and held together by desmosomes, providing a very tight connection. Desmosomal complexes were characterized by increased osmiophilia and increased length. The presence of a large number of mature desmosomes between tumour cells in insulinomas explains their strong adhesion. A significant number of gap junctions were determined in insulinoma. In NF tumours was dominated by simple contacts. Plasmolemma of the contacting cells are clearly visualized. Desmosomes were rare, were poorly developed. Gap junctions were isolated. Ruptures of intercellular contacts with the formation of cytoplasmic bridges led to the formation of syncytia-like structures in both insulinomas and NF tumours. In insulinoma near the rupture of membranes was determined by strong intercellular connections such as desmosomes. In the NF tumours did not note the "consolidation" of the rupture site. Predominance of weak simple contacts, reduction of desmosomes in NF can contribute to easier separation of individual tumour cells and formation of metastases
Conclusion: The acquisition of an invasive phenotype and further the ability to metastases NF tumours of the pancreas in comparison with the insulinoma was confirmed at the ultrastructural level, the peculiarity of intercellular interactions

PS-03-009

Pathological evaluation of prognostic parameters in tall cell thyroid carcinoma: a study

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Background & Objective: Tall cell variant (TCV) of papillary thyroid cancer (PTC) represents an aggressive variant of PTC and should be reported when 10% is present in an otherwise usual PTC. Aim of this study is to evaluate the correlation between different rates of TCV with the most important histological prognostic parameters to stratify patients for a correct management.
Method: We analysed 96 patients with a TCV pattern of PTC and on those were evaluated the rate of the TCV variants 0-20% (group 1), 21-49%(group 2), 50% or higher (group 3). The three groups were matched with the following prognostic parameters: multifocality, invasion of thyroid capsule, peritumour vessels invasion and cervical nodal metastases (subdivided into micro- and macrometastases).
Results: Out of 96 cases 41 were in group 1, 38 in group 2 and 17 in group 3. Regarding the group 1 21 cases were multifocal, 22 infiltrate the

thyroid capsule, 21 showed vessels invasion, 22 had nodal metastases (17 of them resulting macrometastases). In group 2 20 were multifocal, 21 showed capsule and 5 vascular invasion, 27 presented nodal metastases (20 macrometastases). In group 3 10 were multifocal, 15 showed capsule infiltration and 3 vascular invasion, 15 presented nodal metastases (13 macrometastases)

Conclusion: Although the series is still limited the statistical analysis shows significant correlation between groups 1 and 3 for capsular invasion ($p = 0.0163$), for vascular invasion ($p = 0.0216$) and nodal metastases (0.0163) and a correlation between groups 2 and 3 for capsular invasion ($p = 0.0299$) confirming the aggressiveness of TCV in PTC.

PS-03-010

DICER1 alterations are more frequent in oncocytic, follicular and rare aggressive variants than in classical papillary thyroid carcinoma

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Background & Objective: Dysregulation of DICER1 has been described in different human tumours. Due to insufficient data indicating the risk of thyroid cancer in the presence of germline and somatic mutations of DICER 1, we analyzed the presence of DICER 1 alterations in Papillary Thyroid Carcinoma (PTC) cases obtained from The Cancer Genome Atlas Research Network.

Method: Histomorphology characteristics of 501 PTC cases from TCGA were re-evaluated. Genetic information concerning DICER 1 status was extracted from TCGA. DICER1 germline alterations with allelic frequency lower than 0.02 (n=14) were selected for analysis; as well as cases presenting DICER 1 somatic mutations (n=3). Clinical information - when available- was added.

Results: The 14 cases with DICER 1 germline alterations in less than 0.02% were diagnosed as oncocytic variant (n=7), follicular variant (n=4), classical PTC (n=2) and one columnar-cell variant. Somatic DICER1 mutations were detected in 3 PTC cases; oncocytic variant (n=2) and one follicular variant. In total 9 cases of the oncocytic variant PTC and 5 cases of follicular variant of PTC out of 17 cases presented DICER1 mutations. The percentage of DICER 1 mutation is higher in oncocytic variant of PTC (9/156) as well as in follicular variant (5/131), and in rare aggressive variants (1/24) than in classic PTC (2/164).

Conclusion: DICER1 alterations were encountered more frequently in oncocytic, follicular and rare aggressive variants of PTC than in classic PTC using the TCGA data. The association of DICER 1 with the aforementioned variants may open an avenue for research and will be explored in our laboratory.

PS-03-011

Impact of thiadiazines and lipoic acid on protection of pancreatic islets, liver and kidney in diabetic rats

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Background & Objective: Treatment of diabetes mellitus (DM) requires antidiabetic drugs with multiple impacts. Previously, we have identified synthetic 1,3,4-thiadiazine derivatives, L-17 and L-14, which combine antioxidant and antiglycative properties. The aim of the work is to reveal whether L-17 and L-14 can contribute to the pancreatic islet, liver and kidney protection in diabetic rats when compared with a natural antioxidant lipoic acid (LA).

Method: Forty male Wistar rats weighing 220-250 g were used in accordance with the ethical principles of the Directive 2010/63/EU. Alloxan was injected intraperitoneally (300 mg / kg) that provides a model type 1 DM. Aqueous solutions of the drugs were administered intramuscularly (40 mg/kg per day, 12 injections for 30 days) to diabetic and healthy rats. Biochemical, morphometric and immunohistochemical investigations were performed.

Results: We revealed an increase in diameter and cell number in the pancreatic islets after LA and L-17 administration to healthy rats. The injections of L-17, L-14 and LA to diabetic rats were accompanied by a decrease in glucose, glycated hemoglobin and creatinine content, but not the aminotransferase activity (AST, ALT). An increase in the number of β-cells occurred only in diabetic rats treated with LA and L-14.

Conclusion: Therefore, L-17, L-14 and LA reduce hyperglycemia and kidney damage marker without ameliorating liver damage markers in diabetic rats. The impact of L-14 on the β-cell survival is comparable to that of the LA and is more pronounced than that of L-17.

PS-03-012

Prevalence and clinicopathological features of papillary thyroid carcinoma – analysis of the cases of a single institute for a period of 20 years

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Background & Objective: Among the many variants of papillary thyroid carcinoma (PTC), papillary microcarcinoma (PMC) is the one with excellent prognosis and increasing incidence worldwide over the last 20 years. The aim of this study was to analyze the prevalence and clinicopathological features of PMC in our institute for a period of 20 years.

Method: A total of 1374 consecutive patients with PTC, including 618 patients with PMC, who received surgical treatment from 1996 to 2015 were included. The prevalence and clinicopathological features of cases with PMC were compared to the cases with other variants of PTC during the individual 5-yrs (1996-2000, 2001-2005, 2006-2010 and 2011-2015) and 10 -yrs (1996-2005 and 2006-2015) study periods.

Results: PMC was the most frequently diagnosed variant of PTC (45%) in our series of PTC, with increasing prevalence by 18% during the second 10-yrs period. PMC was more common in females (89%) than in males (11%, $p<0.0001$) and 77% of all cases were aged below 55 yrs. The tumour size varied from 0.2 to 1.0 cm, in 43% - up to 0.5 cm. The percentages of histologically diagnosed thyroid capsule invasion, tumour multifocality and lymph node metastasis were low – 2%, 8%, and 11%, respectively. There was relationship between LN metastasis and tumour multifocality ($p<0.001$), and size ($p<0.05$).

Conclusion: Our results show that PMC was the most common variant of PTC, also with increasing prevalence for the study period. In small number of patients are present lymph node metastasis and multifocality and their identification preopreratively is essential for the choice of treatment.

PS-03-013

NIFT-P and cytology – can overtreatment of thyroid tumours be reduced?

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Background & Objective: The recognition of NIFT-P by WHO Classification of Tumours of Endocrine Organs (4th edition) as a low malignant potential tumour is associated with a significant impact in fine needle aspiration (FNA) cytology interpretation and categorization in Bethesda System for Reporting. Recalculation of the risk of malignancy (ROM) is therefore needed for each Bethesda category.

Method: Between 2006-2016, 11639 thyroid nodules were submitted to FNA in Centro Hospitalar de São João. We reviewed the cytological and histological features of the 345 surgical specimens classified as follicular variant of papillary thyroid carcinoma. The cases were reclassified

according to NIFT-P criteria. ROM before and after reclassification were calculated for each Bethesda category.
Results: 109 cases were reclassified as NIFT-P (31.6%). The decrease in ROM before vs after reclassification was statistically significant ($p<0.05$) in the indeterminate categories: in Bethesda category III (atypia/follicular lesion of undetermined significance) the decrease was 4.9% (17.8%-12.9%); in Bethesda category IV (follicular neoplasm/suspicious for follicular neoplasm) the decrease was 10% (37,5%-27,5%); in Bethesda category V (suspicious for malignancy) the decrease was 13.5% (80.2%-66.7%).
Conclusion: Our results concur with those of other published series: a decrease in ROM was verified mainly in the intermediate categories. Therefore, we suggest that whenever a follicular patterned tumour with papillary-like nuclear features is considered in a FNA specimen, the Bethesda category IV should be used instead of a Bethesda category V, thus leading to lobectomy instead of total thyroidectomy. With this approach patients may be spared from overtreatment.

PS-03-014
EGFR mutation in thyroid carcinomas
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Background & Objective: The majority of thyroid cancers are well differentiated carcinomas. However, some of the well differentiated carcinomas as well as other carcinomas of the thyroid show an aggressive course. There is no specific treatment except RAI. Epidermal growth factor receptor (EGFR) mutations are commonly used for targeted therapy in lung adenocarcinoma There are few data on EGFR mutations in thyroid cancer in the literature. The aim of this study was to investigate the presence of EGFR mutations, especially in aggressive thyroid carcinomas.
Method: In a retrospective study, we studied 118 patients with thyroid carcinoma and followed up between 2002 and 2017. EGFR mutation status in exons 18, 19, 20 and 21 was examined from the paraffin blocks of patients by real-time PCR (Cobas® 4800).
Results: Classic or tall cell variant of papillary thyroid carcinoma was diagnosed in 37 out of 118 patients. These patients had lymph node or distant metastasis or recurrent disease. 8 patients were diagnosed with follicular carcinoma, 5 of them were encapsulated with capsular and vascular invasion and 3 patients were widely invasive. Seventeen patients had poorly differentiated carcinoma and 32 were anaplastic thyroid carcinoma. Twenty-four patients had medullary carcinoma with a lymph node metastasis greater than 1 cm in diameter. EGFR exon 18, 19, 20 and 21 mutations were not observed in any of the 118 cases.
Conclusion: Although there are several immunochemistry studies reporting overexpression of EGFR in thyroid carcinomas, molecular evidence is lacking. Targeted therapies to treat thyroid carcinoma remain an area of research.

PS-03-015
Extra-islet insulin-producing cells in experimental diabetes mellitus and at modulation activity of macrophages
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Background & Objective: Damage and dysfunction of β-cells lead to hyperglycemia. That is why β-cells are the main target of regenerative therapy of diabetes. Insulin-producing cells (IPC), located solitary or in clusters, may occur in acinar part or in ducts of the pancreas. Proposed, that formation of such cells occurs due to the damage of pancreas, mediated by macrophage infiltration of organ. Strategy, aims to proliferation and maturation of these specific β-cells subpopulations, may represent a promising direction in the regulation of hyperglycemia. Objective: to characterize quantity, localization, functional activity of extra-islet IPC in diabetic rats and after modulation macrophage activity.
Method: 20 Wistar rats were divided into 4 groups: 1 – control; 2 and 3 – 30 and 60 days of streptozotocin-induced diabetes correspondingly, 4 – 30 days of diabetes + injection of 3-aminophtalhydrazine derivatives, which modulate macrophage activity and reduce inflammation. Insulin-positive cells were detected by immunohistochemistry.
Results: In 30 days of diabetes number of solitary IPC in acinar part increased more than 3 times with normal functional activity level and decreased in 60 days. Number of IPC in ducts at diabetes almost unchanged. Modulation of macrophages activity promotes increase the number of solitary IPC in acinar and ductal parts and ductal insulin-positive clusters as well; growth of functional activity of extra-islet IPC was detected.
Conclusion: Exposed increase of number and functional activity of endocrine extra-islet cell subpopulations proves heterogeneity and plasticity of pancreatic cells, due to which they can serve as an additional source of β-cells, while macrophage-centered therapy offer promising possibilities at correction of hyperglycemia.

PS-03-017
Modeling effect of heavy metals salts and glucocorticoids on the secretion of parathormone in the experiment
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Background & Objective: In some regions of Ukraine there is an increase in the accumulation of heavy metals in soil and drinking water. In this work is studied the functional state of the parathyroid gland and adrenal glands of rats under conditions of influence of salts of heavy metals.
Method: The experiment was conducted on 24 rats aged 5-6 months. Animals received drinking water, saturated with a combination of salts of heavy metals: zinc, copper, iron, manganese, lead and chromium. The rats were withdrawn the experiment by decapitation under etheric anesthesia according to ethical norms. The concentration and indexes of cortisol COR (nmol/L) and parathormone PTH (pg/ml) concentration and indices were determined by auto immunohymoluminescence assays in serum.
Results: In experimental animals, the level of COR was <27.6±4.8nmol/L, which is 2.6 times less in the control animals. These data correlate with the optical density indexes, which are inversely proportional to the concentrations of the hormone and are 5.49±0.53, which are 2.0 times higher than in the control animals. The concentration of PTH in control and experimental animals does not reveal significant numerical changes and is <3.0pg/ml. However, the optical density of PTH according to the manufacturer's annotation is directly proportional to the concentration of the serum hormone and is 56.1±1.52, which is 18.3% less than in the control animals.
Conclusion: Heavy metals salts have a negative modeling effect on the level of glucocorticoids, which in turn stimulates dysfunctional disorders from the side of the parathyroid glands in the form of hypofunction.

PS-03-018
Manifestation of the regenerative potential of beta cells of pancreatic islets during modulation of macrophage activity under conditions of experimental diabetes mellitus
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Background & Objective: Damaged pancreatic tissue possesses the ability to regenerate itself. Modulation of macrophages activity stimulates regeneration of different tissues, which may express in the increase of size, quantity and functional activity of cells and may use to restore the structure and function of pancreatic islets in therapy of diabetes. Objective: to characterize quantity, functional activity and rate of

proliferation of β-cells in the islet of Langerhans at macrophage modulation in experimental diabetes type 2 (CD2).
Method: 15 Wistar rats were divided into 3 groups: 1 – intact, 2 – 60 days of CD2 (streptozotocin-nicotinamide model), 3 – after 30 days of CD2 3-aminophtalhydrazine derivatives, which modulate macrophage activity, were injected for 30 days to reduce inflammation. Insulin-positive and Ki-67-positive cells were detected in pancreas tissue by immunohistochemistry, using fluorescent marker. Optical density of insulin in β-cells was measured.
Results: Damage of insulin-producing islet apparatus in experimental CD2 involves decreasing of quantity and functional activity of β-cells and quantity of islets as well; proliferation level of β-cells higher than at intact rats, which have no Ki-67 positive cells at all. At macrophage modulation functional activity of β-cells and quantity of Ki-67-positive cells significantly increases in comparison with CD2 and intact meanings.
Conclusion: Appearance of proliferating islet β-cells at experimental diabetes may be considered as a compensation of reducing their quantity. Sharply increased quantity of proliferating islet β-cells in addition with the growth of their functional activity during macrophages modulation may be used in the treatment of diabetes.

PS-03-019
The oncofoetal protein IMP3 can predict aggressive behaviour and poor clinical outcome in neuroendocrine tumours
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Background & Objective: Oncofetal protein IMP3 or insulin like growth factor 2 mRNA binding protein 3 (IGF2BP3) is expressed in tissues in the early stages of embryogenesis. In normal tissues of adult organisms, IMP3 is not detected.
Method: We measured the expression of IMP3 in 55 neuroendocrine tumours (NET) of different localization and malignancy: 27 NET pancreas (25 G1-G2, 2 G3), 8 stomachs (3 G1-G2, 5 G3), 8 intestines (6 G1- G2, 2 G3), 5 Merkel G3 carcinomas, 33 lung tumours (6 typical and atypical carcinoids - TC, ATC, 9 small cell and 3 large-cell NEs). The comparison group consisted of 24 adenocarcinomas (AC) (6 pancreas, 6 stomachs, 3 intestines, 9 lungs) and 7 squamous cell lung cancers (SCLC).
Results: IMP3 expression was observed in the cytoplasm of cells 20/26 (76.9%) of NEC G3 (2/2 pancreas, 4/5 of the stomach, 2/2 of the intestine, 4/5 of Merkel's carcinoma, 12/12 of the lung) and was absent in all 40 highly differentiated NET (34 NET pancreas, stomach and intestine G1-G2 and 6 TC and ATC lungs). In the comparison group, intensive expression of IMP3 was observed in 71.2% (19/24) AC (6/6 pancreas, 5/6 of the stomach, 2/3 of the intestine, 6/9 of the lung) and 85.7% (6/7) of the SCLC. IMP3-negative were more often highly differentiated AC lungs (like lapidary type AC lung).
Conclusion: The expression of IMP3 in neuroendocrine tumours of any site is a marker of an aggressive behavior and poor clinical prognosis that differs little from that of adenocarcinomas.

PS-03-020
Multiple scoring systems in oncocytic adrenocortical neoplasms: which fits better with patient's outcome?
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Background & Objective: Oncocytic Adrenocortical Tumours (OATs) diagnostic criteria have been matter of debate. The aim of the study was to compare different scoring systems and correlate them with follow-up.
Method: We reviewed 21 OATs of patients who underwent surgery in our institution from 2007 to 2017. We assessed the Weiss score (WS), Weiss revisited score by Aubert (WR), Linn Weiss Bisceglia score (LWB), Helsinki score (HS), and "reticulin" algorithm (RA). Each score were established with full agreement among five pathologists.
Results: WS classified 57.2% (12/21) as benign and 42.8%(9/21) as malignant; WR 71.4% (15/21) as benign and 28.6 (6/21) as malignant; LWB 52.3%(11/21) as benign, 19.1% (4/21) as "uncertain malignant potential" and 28.6%(6/21) as malignant; HS 80.9% (17/21) as non-metastatic potential vs. 19.1%(4/21) as metastatic potential; RA 42.9% (9/21) as benign with no altered reticulum framework and 28.6%(6/21) with irregularly thickened and frayed fiber vs. 28.6 (6/21) as malignant. In malignant tumours, according to the LWB score, Ki67 presents an average of 12.4%(range:2.7- 18.89). Follow-up information was available for 17/21 patients (mean of 1169 days). None of our court died of disease or showed any signs of local recurrence, two patients (9.5%, 2/17) developed distant metastasis.
Conclusion: LWB downgraded malignant OCTs in contrast to WS and WR; while HS eliminated "uncertain malignant potential" category and seems to better predict patients' outcome.

PS-03-021
EWSR1 rearrangement is a common molecular alteration in thyroid tumours
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Background & Objective: EWSR1 rearrangements were recently demonstrated by our group as a frequent event in papillary thyroid carcinoma (PTC) and in carcinoma of the thyroid with Ewing family tumour elements (CEFTE). We have looked for EWSR1 rearrangements in different types of follicular derived thyroid tumours.
Method: Fluorescence in situ hybridization (FISH) technique was performed on 4-μm paraffin embedded tissue sections from: 1 follicular adenoma (FA), 4 hyalinizing trabecular adenomas (HTA), 12 PTCs, 1 follicular carcinoma (FC), 3 Hürthle (oncocytic) carcinomas (OC) and 5 anaplastic (undifferentiated) carcinomas (AC). FISH was carried out using Vysis EWSR1 Break Apart FISH Probe (Abbott Molecular, Illinois, USA) and Vysis RET Break-Apart FISH Probe (Abbott Molecular). In each case, 50 nuclei were scored for the presence of EWSR1 and RET rearrangements. Cases were considered positive for EWSR1 rearrangement and/or RET rearrangement when 5% or more of the nuclei with the break-apart signal were detected, respectively.
Results: Positivity (in percentage) for EWSR1 rearrangements was detected in 1/1 FA (26%); 4/4 HTAs (6%, 13%, 28% and 34%); 9/10 PTCs (4%, 6%, 13%, 17%, 17%, 24%, 25%, 32%, 33%, 42%); 1/3 OCs (0%, 3%, 16%); and 4/4 ACs (6%, 14%, 19%, 22%). No RET rearrangements were detected.
Conclusion: Although more studies with a greater number of cases are necessary, our results suggest the participation of EWSR1 rearrangements in the tumourigenesis of different thyroid tumour histotypes. The existence of a roughly similar percentage of these rearrangements in well-differentiated and anaplastic thyroid carcinomas does not mean that they play a role in tumour progression.

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PS-03-022
Clinical utility of EZH1 mutations in the diagnosis of follicular-patterned thyroid tumours
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Background & Objective: Follicular-patterned tumours of the thyroid gland are characterized by a predominantly follicular growth pattern. They

frequently harbor RAS mutations, not BRAF mutations. Technological advances in molecular testing have discovered novel RAS-type mutations. However, clinical significance of these mutations remains unknown.
Method: We investigated the prevalence and clinical impact of mutations of BRAF, NRAS, HRAS, KRAS, EZH1, EIF1AX, and TERT genes by Sanger sequencing in a series of 201 follicular-patterned thyroid tumours including follicular adenoma (n=40), Hürthle cell adenoma (n=54), non-invasive follicular thyroid neoplasms with papillary-like nuclear features (NIFTP; n=50), follicular thyroid carcinoma (FTC; n=40), Hürthle cell carcinoma (n=10), and poorly differentiated thyroid carcinoma (PDTC) arising in a well differentiated follicular neoplasm (n=7), and 120 classic papillary thyroid carcinoma (PTC).
Results: Two hot spots of EZH1 mutations were only found in in RAS-negative follicular-patterned tumours. EZH1 mutations were detected in 3% of follicular adenoma, 20% of Hürthle cell adenoma, and 10% of minimally invasive Hürthle cell carcinoma. Thyroid tumours with EZH1 mutations reported in the literature were benign in most cases. Otherwise they were minimally invasive or non-invasive thyroid cancer on histologic examination. EIF1AX mutation was found only in one follicular adenoma. We confirmed the presence of RAS mutations and BRAF K601E mutation in benign, borderline, and malignant follicular-patterned tumours. No BRAF V600E was found in 201 follicular-patterned tumours. This study also confirmed the occurrence of TERT promoter mutations in high-risk thyroid cancers.
Conclusion: These genetic markers can be used for the diagnostic purpose and risk stratification of thyroid nodules.

PS-03-023
Predictive factors for malignancy and recurrence in ovarian goiter: a case series of 56 patients
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Background & Objective: Ovarian goiter (OG) is a mature teratoma composed predominantly of thyroid tissue (>50%) disclosing the same spectrum of histologies of thyroid gland. Malignant ovarian goiter (MOG) represents 0.01% of ovarian tumours and 5 to 10% of OG. Mixed tumours with thyroid and carcinoid components are called strumal carcinoid (SC) and are potentially malignant. Because of its rarity, diagnostic criteria and treatment are not consensual. Objectives: To better classify OG according to criteria for high-risk progression and relapse in order to treat them appropriately. To examine whereas criteria of malignancy for thyroid primitive tumours were also applicable in cases of OG and whether they are predictive of outcome and relapse.
Method: A pathological and clinical review of 56 cases of OG diagnosed at Institut Gustave Roussy over 17 years was done. Tumours were classified according to the 2017 WHO classification system.
Results: 56 cases: 18 benign OG, 22 SC and 16 thyroid carcinomas of various types. Overall survival was 100% at 5 years with a median follow-up of six years (no documented disease-associated- death). Recurrence occurred in 2 of 4 cases with capsular rupture and both cases with peritoneal or ovarian implants. The only distant metastatic case was of neuroendocrine component.
Conclusion: This is the second largest series of OG. Histologic classification of thyroid malignancy did not affect overall survival or tumour progression. Factors predictive of recurrence seem to be ovarian capsular rupture which correlates with a lesion size of >10 cm, presence of peritoneal implants and presence of a neuroendocrine component.

PS-03-024
Papillary thyroid microcarcinoma: the rate of lymph node metastasis
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Background & Objective: Papillary thyroid microcarcinoma (PTMC) is defined as a malignancy sized up to 1 cm that often diagnosed accidentally. The aim of this study was to analyze the frequency of lymph node metastasis (LNM) in patients with this disease in the post-Chernobyl fallout area.
Method: Patients (n=122) with PTMC were admitted to the hospital during January to March 2015 for treatment with total thyroidectomy (all of them) and simultaneous lymph node neck dissections (91.2%).
Results: It was men to women ration as 1:4 (26/21% and 96/79%, correspondingly). The age of patients ranged from 16 to 93 years, the average age was 47.6 years (47.7 – for women and 46.9 – for men). PTMC size ranged from one to 10 mm, microscopic extrathyroid extension to the fat tissue was detected in 74/60.7% cases. Tumours were monofocal (110/90.2%) and bilateral (12/9.8%). Solitary lesions commonly located in the right (65/59%) or left (33/30%) lobes and rarely in the isthmus (12/11%). Nodal disease was detected in 49 (40.2%) patients: 24 patients had N1a, 25 - N1b.
Conclusion: More than 40% of patients with papillary thyroid microcarcinomas had the LNM at presentation. Surgical treatment of PTMC should not differ from the management of more sizable papillary thyroid carcinoma.

Sunday, 9 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-04 | Gynaecological Pathology

PS-04-001
Universal Lynch syndrome screening in endometrial cancer: two years of experience
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Background & Objective: Lynch syndrome (LS) is an autosomal dominant cancer susceptibility syndrome characterized by increased risk for developing several cancers. Endometrial carcinoma (EC) is the sentinel cancer in >50% of women. Recently, universal screening for patients with EC has been advocated but still lacks consensus. We prospectively implemented universal LS screening in our institution.
Method: From 1 January 2016 to 31 December 2017, in all patients with endometrial carcinoma a four-antibody panel immunohistochemistry (IHC) for MLH1, PMS2, MSH2 and MSH6 was performed. The complete absence of nuclear staining in tumour cells for one or more markers was deemed indicative of mismatch repair (MMR) deficiency. All patients with any pattern of MMR loss were offered germline mutation testing.
Results: 35 patients were screened (mean age of 72years). 10 (28,6%) presented abnormal MMR IHC: 5 showed dual loss of MLH1/PMS2, 1 dual loss of MSH2/MSH6, 2 isolated loss of PMS2 and 2 isolated loss of MSH6. 8 accepted germline mutation testing. 2 (5,7%) were confirmed to have LS, 1 with germline MSH2 and 1 with germline MSH6 mutation. Only 1 of these patients would have been identified if LS-associated clinical data and morphologic features had been applied.
Conclusion: Besides the still small number of patients, our results are concordant with previous similar studies and support the universal screening of Lynch syndrome (LS) in patients with endometrial carcinoma given the proportion of patients that would have been missed with strategies that rely only on Revised Bethesda Guidelines.

PS-04-002
Uterine tumour resembling ovarian sex cord tumour with granulose-like differentiation - a case report
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Background & Objective: Uterine tumours resembling ovarian sex cord tumours (UTROSCT) represent an extremely rare type of neoplasms (< 0,5%

of all uterine malignancies). Etiology is uncertain, but there are many theories: derivation from uncommitted mesenchymal stem cells or from ovarian sex cord cells which have been displaced during embryogenesis, overgrowth of sex cord elements within endometrial stromal neoplasm or adenosarcoma. They can be mistaken for leiomyomas, because of the similar symptomatology (menorrhagia, pelvic pain, pressure).
Method: We report a case of a 46-year old woman who presented to our hospital for menorrhagia. The clinical diagnosis was uterine leiomyoma. She then underwent total hysterectomy with bilateral adnexectomy. The specimen was sent to our Pathology Department for histopathological examination.
Results: Macroscopic examination revealed two uterine nodules: a 35 mm whitish, firm subserosal nodule, which was microscopically confirmed as a leiomyoma, and a 70 mm, well-circumscribed, yellowish, soft intramural nodule. Microscopy of the second nodule showed a rather well circumscribed proliferation of small cells, with monomorphic, vesicular nuclei, forming a microfollicular pattern. Differential diagnosis included: leiomyomas (different subtypes), endometrial stromal tumour and endometrioid carcinoma with sex cord-like features, adenosarcoma. In order to establish a positive diagnosis, immunohistochemical stainings were performed: sex cord markers (calretinin, inhibin, melan A - negative; CD 56 - positive); PR, vimentin, WT1 - positive; AE1/AE3, ER, CK 7, PAX 8, CD 10, EMA - negative.
Conclusion: UTROSCT is very rare finding in uterine specimens. Particularities of this case are granulosa-like morphology with microfollicular pattern and coexistance with a leiomyoma.

PS-04-003
An adenocarcinoma of mammary-like glands of the vulva presenting with inguinal adenopathy: a case report of a rare entity
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Background & Objective: Adenocarcinoma of mammary-like glands (MLG) of the vulva is an extremely rare entity derived from anogenital MLG. To the best of our knowledge, less than 30 cases have been reported.
Method: We report a case of a vulvar adenocarcinoma of MLG presenting with left inguinal metastasis.
Results: A 53-year-old female presented with weight loss and left inguinal lymphadenopathy. A complete PET-CT scan revealed no additional lesions. The lymph node was excised and pathological examination was consistent with a metastatic CK7 positive adenocarcinoma. Clinical observation, including mammary and gynaecological examination, was unremarkable. Endoscopy and imaging studies, including mammary and gynaecological MRI, were normal. Six months later, a small nodule in the vulvar labium minor was detected in the gynaecological evaluation and biopsied. Histological examination revealed an infiltrating solid and tubular adenocarcinoma located in the lamina propria with no connection to the epithelium. The cells had large, pleomorphic nuclei with prominent nucleoli. Pancytokeratin AE1/AE3, cam5.2, CK7, GATA3, GCDFP-15 and mammaglobin were positive. Estrogen and progesterone receptors were negative. Retrospectively, additional immunohistochemical stains (GATA3, mammaglobin and GCDFP-15) were performed in the lymph node and were positive. Immunohistochemical staining for ERBB2 was positive (+3) in both the primary and the metastatic lesions. The diagnosis of an adenocarcinoma of MLG of the vulva with a lymph node metastasis was established.
Conclusion: Adenocarcinoma of the MLG of the vulva is a rare entity. Its diagnosis, namely in the metastatic setting, requires a high level of suspicion and clinical and imagiological correlation.

PS-04-005
CADM1, MAL and miR-124 promoter methylation as biomarkers of progression in cervical cancer
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Background & Objective: Molecular tests for hrHPV detection have shown a sensitivity of 90-95% for the detection of high-grade intraepithelial lesions/cervical intraepithelial neoplasia grade 2-3 and CC (HSIL/CIN2+), but have a relatively low specificity, as many hrHPV infections will never progress to CC. This prospective study analyzes whether the CADM1, MAL and miR124 promoter methylation analysis could detect those patients with HSIL/CIN2+, and thus, have a role in the triage of hrHPV-positive women.
Method: Prospective study that included cervical biopsies form 131 women referred to the Colposcopy Clinic from January 2013 to December 2015. Eight patients had a negative biopsy and were negative for hrHPV, 19 had a low-grade squamous intraepithelial lesion/cervical intraepithelial neoplasia grade 1(LSIL/CIN1), 30 had HSIL/CIN2, 60 a HSIL/CIN3, and 14 a cervical cancer (CC). DNA extraction was performed from formalin-fixed paraffin-embedded tissue after bisulfite treatment. A standardized, multiplex quantitative methylation specific PCR was used to identify the methylation status of the promoter regions. The proportions of methylation-positive samples per histological diagnosis were compared using the Mann-Whitney U test.
Results: DNA methylation of at least one loci was detected in 12,5% (1/8) of normal samples, 31.5%(6/19) of LSIL/CIN1, 83.3%(25/30) of HSIL/CIN2, 81.6%(49/60) of HSIL/CIN3 and 100%(14/14) of the CC ($p = <0.001$). miR124 and MAL were the most frequent methylated loci in HSIL/CIN2+ (66.6% and 56.6% for HSIL/CIN2; 68.3% and 60% for HSIL/CIN3; and 92.8% and 78.5% for CC, respectively). Methylation of CADM1 was the most specific for the detection of HSIL/CIN2+ and HSIL/CIN3+ lesions, whereas miR124 was the most sensitive.
Conclusion: CADM1, MAL and miR-124 promoter methylation could be a useful biomarker of progression in women with hrHPV associated cervical lesions.

PS-04-007
Primary retroperitoneal borderline mucinous cyst of Mullerian origin - a case report
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Background & Objective: Retroperitoneal mucinous cysts are extremely rare, mostly occurring in women. Our objective is to present a new case of a retroperitoneal borderline mucinous cyst of Mullerian origin.
Method: A 38-year-old woman, with a history of laparoscopic surgery performed 3 years ago for a benign retroperitoneal cyst in the left hypochondrium, was admitted to our hospital for tumour recurrence. Another laparoscopic intervention was performed with incomplete excision due to adherence to the left colon wall. No lesion was observed in the ovaries, fallopian tubes, pancreas or kidneys.
Results: The specimen was composed of multiple fragments of cyst wall measuring 80/75/7 mm, with a smooth, white-greyish surface, and a 7 mm diameter white nodule. Histopathological findings revealed a densely fibrotic cystic wall, lined by a single layer of columnar cells with areas of nuclear atypia, either nuclear enlargement or vesicular nuclei. The nodule showed glands lined by a mucinous epithelium of endocervical-type, with intraluminal projections, some with a more complex architecture, lined by stratified, enlarged, hyperchromatic nuclei. The nodule stroma had an "ovarian-like" pattern and was composed of spindle cells with little cytoplasm and indistinct borders. Immunohistochemistry confirmed the Mullerian origin.
Conclusion: This is a very uncommon case of a retroperitoneal mucinous cyst of Mullerian origin. The particularities of this case are the borderline aspect, resembling ovarian mucinous tumours and the "ovarian-like" stroma. Close adherence to surrounding structures prevented the complete excision of the cyst, leading to a recurrence. Open surgery was proposed to the patient and will probably follow.

PS-04-008

Mesothelial cyst of round ligament of uterus presenting as inguinal hernia in a young female – a case report

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Background & Objective: Cysts of the round ligament of the uterus are a very rare finding. The literature reveals 10 cases of mesothelial cysts between 1980 and 2013. They are usualy misdiagnosed as inguinal hernias or adnexal masses and occur in women in their late third or fourth decade. Our objective is to present a new case of a round ligament cyst of the uterus.
Method: A 29-year old female patient presented at Elias Hospital with a groin mass. The clinical diagnosis was of incarcerated right inguinal hernia, for which the patient underwent surgery.
Results: We received a specimen consisting of a greyish mass surrounded by fat, measuring 30/15/10 mm, with elastic consistency, a cystic apearance on serial sections, and containing a clear liquid. Histology showed the cyst was lined by a monolayered flatened epithelium, with areas of cuboidal cells. The cyst presented focal areas of moderate lymphoplasmacytic and neutrophilic inflamation, congestion and reactive epithelial cells, and was surrounded by a fibrocollagenous stroma including smooth muscle fibers, fatty tissue, dilated blood vessels and some nerve fascicles and striated muscle fibers at the periphery. We perfomed immunohistochemistry to distinguish between a mesothelial and a serous origin. Calretinin, vimentin, and WT1 were positive and EMA was negative, thus confirming the mesothelial origin of the cells.
Conclusion: Although it is such a rare encounter, a mesothelial cyst of the round ligament should be included in the differential diagnosis of other groin masses in women such as inguinal or femoral hernias, lipomas or hydrocele of Nuck's canal (Nuck's canal cyst).

PS-04-009

Immunohistochemistry for detecting colorectal (CRC) and endometrial cancer (EC) patients at risk for Lynch Syndrome (LS). Utility of a 2-antibody panel

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Background & Objective: Currently, testing for mismatch repair deficiency proteins (MMR-P) in CRC and EC is initiated by performing IHC with a 4-antibody panel (MLH1, PMS2, MSH2 and MSH6). Due to the binding properties of the MMR heterodimer complexes, gene mutation and loss of MLH1 and MSH2 invariably result in the proteolytic degradation of their obligatory partners PMS2 and MSH6, but not conversely.
Method: To analyze the expression of MMR-P by IHC in patients with CRC and EC. We propose that a 2-antibody panel (PMS2 and MSH6) can be sufficient to detect cases of MMR-P expression deficiency.
Results: We collected 2 cohorts of CRC and EC patients from the records of our institution: (1) A retrospective series of 200 unselected patients with CRC and (2) a prospective series of 108 unselected patients with EC. In all cases, a 4-antibody panel was performed.
Conclusion: Of the 308 tumours tested, 65 (21%) showed abnormal staining for at least one MMR-P: 51 cases (78.5%) showed concurrent loss of expression of MLH1 and PMS2, 3 (4.5%) concurrent loss of MSH2 and MSH6, 4 (6%) loss of PMS2 alone, and 7 (11%) loss of MSH6 alone. No cases showed isolated loss of expression of MLH1 or of MSH2. CONCLUSION: Our findings suggest that a 2-antibody panel is as effective as the current 4-antibody panel in detecting MMR-P abnormalities. This approach has cost-effective implications for an IHC panel that is being widely used as the first line of screening for LS.

PS-04-010

c-KIT immunohistochemistry and KIT mutational status in mesonephric carcinomas of the female genital tract

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Background & Objective: Mesonephric carcinoma is a rare gynaecological malignancy. Approximately one-third of patients will suffer from local recurrence or distant metastases. To date, no targeted therapeutic options have been identified. Based on limited case reports, c-KIT immunohistochemical expression has been reported in female adnexal tumours of Wolffian origin (FATWO), and targeted therapy with imatinib has been attempted with mixed success. Currently, it is unclear whether c-KIT immunohistochemical expression is seen in mesonephric carcinomas and how this correlates with KIT mutational status.
Method: Using whole sections, we assessed the immunohistochemical expression of c-KIT in a series of 11 mesonephric carcinomas of the female genital tract (5 cervical, 3 uterine corpus, 1 ovarian, 1 broad ligament, 1 pelvic tumour). The intensity of staining and proportion of cells showing cytoplasmic/membranous staining were recorded. Plasma cells served as an internal control. KIT was sequenced using a next generation sequencing panel which targets 120 hotspots and 17 exons in 33 known actionable cancer genes. This panel includes exons 9, 11 and 13 of KIT, and 6 hotspots (T670, D816, D820, N822, Y823, A829).
Results: c-KIT immunohistochemical expression was observed in the vast majority of mesonephric carcinomas, 9 of 11 cases (82%). Staining was moderate to strong in intensity and ranged from 5% to 80% of cells (average 34%). DNA has been extracted and the KIT molecular results are pending.
Conclusion: c-KIT immunohistochemical expression was observed in a large number of mesonephric carcinomas. KIT mutational results will be known shortly, allowing us to assess whether c-KIT immunoexpression correlates with mutational status.

PS-04-011

Morphological substrate and molecular mechanisms of pregnancy failure in women with undifferentiated connective tissue dysplasia (uCTD) and hereditary thrombophilia (HT)

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Background & Objective: HT and uCTD seem to have general pathogenesis and may lead to infertility. The aim of the study: to determine the morphological substrate and molecular mechanisms of pregnancy outcomes violations in women with uCTD and HT.
Method: 130 patients of reproductive age women with primary infertility (main group) and 11 patients of control group (surrogate mothers). Patients of the main group were divided into subgroups: 1A - with infertility and HT (91), 1B with infertility, HT and uCTD (19), 1B - with infertility and uCTD (20). Endometrial biopsy specimen was taken on the 6-8 day after ovulation with following morphological and immunohistochemical study with primary antibodies to LIF, PAI-1, osteopontin. Blood samples were taken in subgroups 1A and 1B for PAI-1 and homocysteine, methionine test; polymorphisms of: FII, FV (Leiden), FVII, FXII, FXIII, GpIa, GpIb (5), GpIb (T145M), GpIIIa, PAI-1, FBGb, MTHFR, MTRR, MTR, SLC19A1, angiotensinogen M235T and T145M, angiotensin-converting enzyme, homo- or heterozygosity.
Results: The most favorable outcomes were observed in subgroup 1B, least - in 1A. we revealed significant differences in hemostatic system only in the frequency of disaggregated thrombopathy development - 88% in group 1B and 55% in group 1A. There was slowing of endometrium maturation with decreased expression of LIF, PAI-I and osteopontin in main group.
Conclusion: In patients with HT, uCTD, and more with combination of HT and uCTD genetically determined predisposition to impaired

implantation develops, due to remodeling of the endometrium, leading to the development of infertility and violation of pregnancy outcomes.

PS-04-012

Extragenital neoplasias involving the uterine cervix: a case series of diagnostic biopsies

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Background & Objective: Involvement the uterine cervix by extragenital neoplasia is a rare event. Diagnostic challenges ensue from the small size of biopsies and the fact that many primary tumours have been reported to metastasize to the cervix. We aimed to describe a case series of cervix biopsies diagnostic of secondary involvement.
Method: We retrospectively (2012–2017) identified twelve patients with involvement of the uterine cervix by extragenital neoplasias diagnosed in biopsies. Clinical files and histological material were reviewed.
Results: Median patient age was 70 years (range:42-89). Pathological findings were consistent with cervix metastases from tumours originating in gastrointestinal tract (n=7) and breast (n=4). These included 3 poorly cohesive adenocarcinomas and 3 lobular carcinomas, respectively, frequently showing signet ring morphology. Additionally, involvement of the cervix by a diffuse large B-cell lymphoma was also found. Biopsies were usually limited to small tissue fragments, ranging from 3 to 10mm. Immunohistochemistry study was done in the majority of cases (n=10), using a large panel (mean of 6 antibodies). In five patients the primary tumour was previously known (mean of 7 years prior). Cervix involvement was the first histologic diagnosis of an extragenital primary neoplasia in the remaining patients. Almost all patients (n=10) had widespread disease at the time of cervical biopsy.
Conclusion: Carcinomas of the gastrointestinal tract and breast, frequently with signet ring morphology were the more common metastases from an extra-genital site involving the cervix. Combining all clinical and pathological data is essential for a correct final diagnosis.

PS-04-013

Villoglandular adenocarcinoma of the vulva: case report and literature review

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Background & Objective: Primary adenocarcinomas of the vulva are rare entity. Within them, the intestinal subtype (known as villoglandular adenocarcinoma, cloacogenic carcinoma or cloacogenic adenocarcinoma) is an exceptional finding. These tumours share morphological features with colon adenocarcinomas. Villoglandular adenocarcinomas may originate from cloacal remnants but the mechanisms of development of this vulvar mucinous lesion are controversial.
Method: We present a case of villoglandular mucinous adenocarcinoma of the vulva in a 56-year-old patient with no relevant medical history. A partial vulvectomy was performed in which a brownish-colored papillary-excrescent lesion measuring 2.5 x 1.7 cm was observed. In microscopic findings, we identified a branched villous-papillary lesion with 2 mm invasion formed by atypical pseudostratified cylindrical cells with interspersed goblet cells. Immunostains (IHC) and PAS stains were performed.
Results: Globet cells were PAS positive and tumoural cells showed strong and diffuse positivity for CK20 and CDX2 markers and CK7 and estrogen receptors were negative.
Conclusion: The exact mechanism of the development of intestinal tumours in the female genital tract is not known. Several reports support the hypothesis that intestinal neoplasia of the vulva could develop from cloacal remnants. We present a case of an exceptional entity in the vulva with IHC CK7-/CK20+, which could support this hypothesis.

PS-04-014

Endometrial changes related to long term use of the levonorgestrel releasing intrauterine system

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Background & Objective: Those who have been practicing diagnostic pathology for half a century, in keeping with knowledge and morals of the time, have been noticing changes in the structure of organs, due to therapeutics. We decided to study the endometrial changes owing to the insertion of the so called levonorgestrel-releasing intrauterine system.
Method: 25 samples of endometrium, of a period of six months until March 2018, after 5 years of implantation of levonogestrel, when removed to be replaced. Patients´ ages ranged from 28 to 51; two categories, a younger purposed for contraception (5), ages around 40-50 meant chiefly for functional disturbances (20). Biopsies done during hysteroscopy, Specimens stained with H&E and immunohistochemistry: CD138 for plasma cells (2)
Results: Hypotrophy; micropolypoid indentations; pre/pseudodecidualized stroma; large cells, with slightly eosinophilic cytoplasm, intermingled with spindled vacuolated ones; myxoid degeneration; foci of crowded small round cells, including plasma cells; glands lined by cells with infra and supranuclear vacuoles, also fully secretory; atrophic, lined by flattened epithelium, often cystic; rarely, oxyntic metaplasia. Vessels forming aggregates, as of granulation tissue; deposits of fibrin; coarse deposits of calcium salts.
Conclusion: Iatrogenic deviation from normal predecidual/decidual aspects, interpreted as result of continuous stimulation by gestagens, without a proliferative phase, and of inflammation. One should speculate about what comes next, if the patient decides to no longer use the device, envisaging fertility. What the consequences will be of so prolonged use of instilled gestagens. Furthermore, consequences, in the long run, of the persistent stimulation by pituitary hormones, with no due response by the effector organs

PS-04-015

Uterine leiomyoma with diffuse perinodular hydropic degeneration, focal symplastic change and adjacent myometrial hydropic change: unique features of a rare variant of a common tumour

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Background & Objective: Leiomyoma is a common tumour of the uterus with a wide spectrum of histological appearances. Although hydropic degeneration within a leiomyoma is not uncommon, accumulation of oedema fluid around the fascicles of neoplastic smooth muscle bundles is rare and gives rise to an unusual variant known as perinodular hydropic degeneration in leiomyoma (PHDL). Concurrent focal symplastic change within PHDL and hydropic changes in adjacent non-neoplastic myometrium have not previously been described. The recognition of PHDL with symplastic change is crucial as it may mimic other uterine disorders, such as myxoid leiomyosarcoma or intravenous leiomyomatosis.
Method: We report a 46-year-old Chinese woman who presented with abnormal uterine bleeding. Magnetic resonance imaging of the pelvis showed a large mass within the anterior myometrium with cystic changes and a heterogenous appearance, suspicious for a uterine sarcoma. Total hysterectomy and bilateral salpingectomy were performed.
Results: Grossly, a large, relatively circumscribed tumour, which consisted of multiple pale fleshy nodules separated by oedematous connective tissue, was seen in the anterior myometrium. Histologically, the nodules comprised intersecting fascicles of smooth muscle cells separated by oedematous, hypocellular fibroconnective stroma. Foci of symplastic change characterised by nuclear enlargement, hyperchromasia and pleomorphism

without mitotic activity were discerned. Hydropic change was also seen in the adjacent non-neoplastic myometrium. No dissecting tumour satellite nodules were evident. Alcian blue mucin stain was negative.
Conclusion: PHDL with symplastic change and hydropic change in adjacent normal myometrium is an extremely rare variant of uterine leiomyoma that has not been described in the literature. Its recognition is important as it may mimic malignant lesions of the uterus both radiologically and histologically.

PS-04-016
Characteristics of the niche of uterus fibroid stem cells in simple and lypoleiomyomas
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Background & Objective: The modern concept of uterus fibroids (UF) development is based on arising from fibroid tumour stem cells located in special niche in tissue. Aim to characterize a possible niche of tumour stem cells in UF.
Method: biopsy and operative material of 54 patients 27-55 years old with simple type UF and 12 patients with lypoleiomyomas (LLM) were analyzed. Patients were divided in two groups: with large leiomyomas, more than 6 sm in diameter (30 patients) and control with UF and LLM, less than 4 cm in diameter (24). Immunohistochemistry (IHC) with semiquantative analysis determined the expression of nestin, connexin, CD117, PD-ECGF TGFβ, Ki67, Vimentin.
Results: IHC showed increased expression of nestin, connexin, CD117, PD-ECGF TGFβ, , Ki67, Vimentin in separate cells of perivascular growth zones in UF and LLM. Cells with expression of nestin, connexin, CD117, TGFβ, Vimentin may be considered stemless cells. It was found that LLM commonly contained adipocytes adjacent to stemless cells not only in the perivascular region, but also in the foci of adipose tissue inside tumour parenchyma.
Conclusion: Niche of tumour stem cells in simple UF and LLM are localized in the perivascular regions of UF and LLM and are characterized by the presence of stemless cells inside them, that is shown in the enhancement of expression of the stem cell markers - nestin, connexin, CD117, PD-ECGF TGFβ, Vimentin. Adipocytes in LMM in perivascular zone also may be considered as potential markers of tumour stem cells niche.

PS-04-017
Clinicopathologic features of colonic endometriosis simulating colon neoplasia
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Background & Objective: Endometriosis is frequent among premenopausal women. Colonic endometriosis accounts for most extrapelvic cases and may clinically simulate colon neoplasia. We aimed to describe the clinicopathological features of colonic endometriosis clinically simulating colon neoplasia.
Method: We retrospectively (2007-2017) identified three patients with colonic endometriosis diagnosed in resection specimens, with a presurgical presumptive diagnosis of colon neoplasia. Clinical and imagiological records were retrieved from the patients' files and histological features were reviewed.
Results: All three patients were pre-menopausal, nulliparous women, presenting with abdominal pain. Imaging and endoscopic studies showed a stenosing colonic lesion in two patients and in the third patient colonic mass concomitant to a left ovarian tumour. Pre-surgical biopsies only denoted non-specific inflammatory colitis. The patients underwent surgery under presumptive diagnoses of primary colon neoplasias and secondary involvement by ovarian tumour. Intraoperatively, inspection of the abdominal cavity raised suspicion of pelvic peritoneal endometriosis in two cases. Perioperative pathological examination excluded primary colon malignancy in all patients. Macroscopically, the lesions were described as subserosal/submucosal masses or colonic wall thickening, and the mucosa was grossly spared. Microscopic examination was diagnostic of colonic endometriosis, showing endometrial glands and stroma infiltrating the serosa/subserosa, muscularis propria and, in two cases, focally reaching the mucosa. All cases had lymph node involvement. The third patient had a concomitant diagnosis of synchronous endometrioid ovarian and uterine carcinomas, with loss of expression of MSH6.
Conclusion: Diagnosing colonic endometriosis is clinically challenging. Peri-operative examination should be considered when the clinical picture is unclear, as it may prevent overtreatment.

PS-04-018
Expression of VEGF and SOD3 in the placenta of pregnant women with breast cancer
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Background & Objective: To study the expression of VEGF (vascular endothelial growth factor) and SOD3 (superoxide dismutase-3) by immunohistochemical methods in the placenta of pregnant with breast cancer (BC).
Method: Studied 45 placentas: group I - placentas from women who had BC diagnosed during pregnancy but did not receive treatment (n=11), group II - placentas from women who received BC-chemotherapy during pregnancy (n=19), group III (control) - placentas from puerperas with-out pathology (n=15). Performed a morphological study of the placentas and quantitative analy-sis of immunohistochemical reactions of VEGF and SOD3 in syncytiotrophoblast (STB) and endothelium of capillaries (EC) in terminal villi.
Results: The lowest VEGF expression in STB were found in group I (10.9% and 20.5% less than in group II and III, respectively). The minimum value of VEGF in the EC were in group II (30.4% and 23.0% less than the values of groups III and I, respectively). The lowest SOD3 expression was in group II (less by 4.6% and 9.6% in STB and by 26.3% and 12.2% in EC compared to groups I and III). The SOD3 expression in the EC of the placenta of group I exceeds the corresponding values of the control group.
Conclusion: Decreased expression of VEGF and SOD3 in terminal placental villi reflects the processes of placental damage at BC and chemotherapy. Multidirectional changes in the intensity of the SOD3 reaction indicate the development of compensatory reactions aimed at neutralizing the increased intake of oxygen radicals.

PS-04-019
Evaluation of platelet to lymphocyte and neutrophil to lymphocyte ratios as potential biomarkers of endometrial pathology in postmenopausal women
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Background & Objective: Systemic low-grade inflammation has been investigated extensively in the field of cancer the last years. Neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte (PLR) ratios seem to be promising markers and have been previously reported in various tumours. The purpose of the present study is to investigate if these ratios differ in postmenopausal patients with evidence of endometrial pathology. A significant contribution is that it is based on a significantly larger cohort compared to previous evidence in the field.

Method: We retrospectively searched patient records and identified postmenopausal patients with evidence of endometrial pathology (vaginal bleeding or endometrial thickness ≥ 5 mm determined by ultrasound examination). The study based on a cohort of 178 patients that underwent dilatation and curettage between January 2013 and December 2016. The statistical analysis was performed with the IBM SPSS statistical package.
Results: Overall, 106 women with endometrial cancer and 72 controls were included in the present study. The total number of white blood cells was comparable between the two groups (6,815 (4,010-16,270) vs 7035 (3,520-15,530) p=.373). Similarly, neither NLR (1.70 (0.27 – 25.79) vs 1.93 (0.71 – 12.18) p=.102) nor PLR (0.12 (0.02 – 1.51) vs 0.12 (0.05 – 0.69) p=.767) differed between patients with benign endometrial pathology and those with endometrial cancer.
Conclusion: Our study suggests that neither PLR nor NLR may serve as potential markers for the prediction of endometrial cancer. However, future cohorts are needed to elucidate this field

PS-04-020
Uterine adenosarcoma: a case report and literature review
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Background & Objective: Uterine adenosarcoma is a rare mixed tumour composed of malignant stromal and benign epithelial elements. It occurs in any age, but it is mainly found in women after menopause. It commonly arises from the endometrium, but in rare cases it may appear in the endocervix and within the myometrium. The diagnosis is based on symptoms, such as vaginal bleeding, pelvic pain or vaginal discharge, and on histopathologic exam. we report a case of a patient diagnosed with uterine adenosarcoma.
Method: Biopsy was made.
Results: A 62-year old female patient presented vaginal bleeding after menopause. An ultrasonography revealed an endometrial mass. A biopsy of the lesion acquired nine soft, elastic, irregular, brown fragments measuring 2.2 × 1.2 × 0.3 cm. Histopathological exam showed low cylindrical glandular or cubic epithelium with either nuclear atypia or evidence of cytoplasmic eosinophilia, or both. The epithelium surrounded the stroma, which was composed of nests of spindle or rounded cells, forming a periglandular belt occasionally, where nuclear atypia is more evident. Mitotic index: two mitotic figures per ten high power fields.
Conclusion: This case showed many of the distinctive characteristics of the rare uterine adenosarcoma, reinforcing that one should consider the diagnosis of adenosarcoma if spindle cells are found in an endometrium biopsy. Its treatment of choice is total hysterectomy with salpingo-oophorectomy. Adenosarcoma has a relatively low malignant potential, if not associated with sarcomatous overgrowth or myoinvasion. Patients with one or both of these features have a less favorable prognosis.

PS-04-021
Clinicopathologic and molecular characteristics of mesonephric adenocarcinoma arising from the uterine body
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Background & Objective: Mesonephric adenocarcinoma (MNAC) is a rare tumour of the female genital tract mainly occurring in the uterine cervix. To date, only a few cases of MNAC arising from of the uterine body (UB-MNAC) have been reported. The clinicopathologic and molecular characteristics of UB-MNAC remain unknown.
Method: We investigated the clinical, histopathologic, immunohistochemical, and genetic features of UB-MNAC.
Results: In total, 11 cases were included. Six patients developed metastatic disease, most commonly in lungs (5/6). Histopathologically, UB-MNAC was characterized by an admixture of tubular, glandular, papillary, retiform, glomeruloid, sex cord-like, and comedonecrosis-like architectural patterns. Three adverse pathologic characteristics, including advanced International Federation of Gynecology and Obstetrics stage, high mitotic activity, and presence of lymphovascular the invasion, were independent factors predicting the development of metastasis. All cases were positive for GATA-binding protein 3 and paired box 2 expression and showed wild-type p53, patchy p16, and preserved PTEN expression, as indicated by immunohistochemistry. Next-generation sequencing using 12 samples (11 primary tumours and 1 metastatic tumour) revealed 42 single nucleotide variations in 16 genes, mostly in KRAS (10/12) and ARID1A (9/12). Copy number variation was found in 16 genomic regions, and consisted of 57 gains and 10 losses, with 1q gain (11/12) being the most prevalent.
Conclusion: UB-MNAC displays an aggressive biological behavior, with a tendency to metastasize to the lungs. Adverse pathologic characteristics reflect the aggressive nature of UB-MNAC. Distinct molecular features of UB-MNAC include frequent somatic mutations of KRAS and ARID1A and gain of 1q.

PS-04-022
Clinical validation of next generation sequencing for identification of BRCA somatic mutations in high grade serous ovarian carcinoma (HGSoC)
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Background & Objective: To establish the feasibility in the clinical practice of targeted next generation sequencing (T-NGS) for BRCAs mutational analysis in order to identifying both somatic and germinal mutations starting from Formalin Fixed Paraffin Embedded (FFPE) tissue.
Method: T-NGS analysis of all coding and flanking intronic regions of BRAC1/2 genes was performed on 17 samples of HGSoC collected at the Cannizzaro Hospital (Catania, Italy). The GeneReaderTM NGS System (GeneRead®QIAact BRCA 1/2 Panel, Qiagen) was the NGS platform used and results were compared with germline analysis previously obtained from corresponding blood samples.
Results: All FFPE cases were genotyped successfully with both good libraries and sequencing CQ metrics. All germline mutations previously identified were confirmed on tumour tissue analysis (concordance 100%) and three of them showed additional somatic alterations, underlying the loss of function of BRCA genes in these patients. Among the three cases without germline variants, two harbored pathogenic somatic mutations (BRCA1_c.80+1G>T; BRCA2_p.N372H) and one presented a silent passenger variant (COSM148280). Most of the genetic variants identified were previously reported in the main mutational databases, except one likely pathogenic and two variants of unknown significance. The diagnostic workflow for T-NGS did not impact in the turn-around time (5 days).
Conclusion: GeneReader NGS is a valuable and feasible tool in molecular testing for somatic BRCA analysis starting from routine tumour tissue. The present study underlines the possibility to assess both somatic and germline mutations form FFPE routine archival material, thus increasing the number of patients suitable for targeted therapy.

PS-04-024
Ki67 expression as prognostic factor in advanced cervical cancer in patients treated with concurrent chemoradiotherapy
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Background & Objective: Determine the correlation between Ki67 expression by immunohistochemistry and local failure-free survival (LFFS), progression-free survival (PFS) and overall survival (OS) in a group of patients with locally advanced cervical cancer treated with concurrent chemoradiotherapy
Method: The study was performed in a group of 186 patients with advance cervical cancer (Squamous cell carcinoma 155, Adenocarcinoma 31) treated with chemoradiotherapy The specimens from the cervix before radiation therapy were immunohistochemical stained with Ki67/MIB1 antibody. Patients were stratified according to Ki67 expression in three groups (Group 1 :< 40%, Group 2: 40-70%, and Group 3 :> 70%).
Results: We found that with a Ki-67 / MIB-1 cut-off higher than 40% was more acceptable to identify a highly proliferative tumour. Of the 186 biopsies, 12 (6.45%) were ascribed to the Group 1, 75 (40.32%) to Group 2 and 99 (53.23%) to Group 3. Ki-67 index of 40% or greater correlated significantly with a better response to radiation compared with those with lower expression Low levels of Ki67 were associated with a higher rate of pelvis relapse, decreased progression-free survival (PFS) and overall survival (OS). The survival rate at 3 years for group one was 44%, while for group 2 and 3, 79 and 84% respectively.
Conclusion: The low expression of Ki-67/MIB-1 had significant association with poor prognosis in cervical cancer, both in local failure-free survival (LFFS), progression-free survival (PFS) and global Survival (OS) in patients treated with chemoradiotherapy

PS-04-025
ANXA1 protein overexpression contributes to a good response of ovarian carcinoma to chemotherapy
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Background & Objective: Epithelial Ovarian Cancer (EOC) is the highest gynaecological cause of cancer deaths. ANNEXINE A1 (ANXA1) protein has been implicated in aggressiveness of several cancers. Here, we evaluated ANXA1 protein expression in EOC clinical samples.
Method: Using immunohistochemistry (IHC), we retrospectively assessed ANXA1 expression in epithelial cells of 121 pre-chemotherapy EOC samples and 40 normal ovarian samples from patients treated at Salah Azaiez Institute. We compared ANXA1 expression in normal versus cancer samples and searched for correlations with clinicopathological features.
Results: Fifty one percent of tumour samples showed positive epithelial ANXA1 staining versus 26% of normal samples (p=1.16E-02, Fisher's exact test). We showed that epithelial ANXA1 expression was associated with good response to chemotherapy (p=1.68E-02, Fisher's exact test).
Conclusion: Epithelial ANXA1 overexpression in tumours could be an early diagnostic protein and contribute to the good response to chemotherapy in EOC cases, suggesting a potential therapeutic interest of ANXA1 activation for targeting tumour epithelial cells.

PS-04-026
Stromal expression of MARCKS protein and resistance to chemotherapy in ovarian carcinomas
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Background & Objective: Epithelial Ovarian Cancer (EOC) is the most lethal gynaecological cancer. Identification of new therapeutic targets is crucial. MARCKS protein expression found to be implicated in cancer aggressiveness.
Method: We measured MARCKS protein expression in normal ovarian and EOC samples and searched for correlations with clinicopathological features. MARCKS status was evaluated by immunohistochemistry in 118 tumour samples and 40 normal ovarian samples. Expression was assessed on the epithelial and stromal cells. We compared MARCKS expression in normal versus cancer samples and with histopathological features.
Results: In tumour samples, the staining was observed mainly in stromal cells notably fibroblasts and to a lesser degree in tumour epithelial cells (p=2.37E-05). A correlation was found between stromal MARCKS expression and resistance to chemotherapy (p=3.9E-0.02). There was no correlation between stromal IHC MARCKS statutes and the other clinicopathological features
Conclusion: Stromal MARCKS overexpression in tumours might contribute to cancer-associated fibroblasts activation and explain the poor prognosis of EOC. Targeting stromal activation by inhibition of MARCKS might represent an approach targeting the cooperative tumour stroma of EOC.

PS-04-027
Leiomyoma with bizarre nuclei. A study of 108 cases focusing on clinicopathological features, morphology and fumarate hydratase alterations
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Background & Objective: Leiomyoma with bizarre nuclei (LBN) is a rare variant of uterine smooth muscle neoplasm. Recent studies suggest fumarate hydratase (FH)'s involvement in these tumour's pathogenesis. We analysed 108 cases focusing on clinical features, morphology, immunohistochemical and mutation analyses of FH and compare them with another 92 smooth muscle tumours – 50 usual leiomyomas (UL) and 42 leiomyosarcomas (LMS).
Method: Tissue microarrays were prepared and immunohistochemical analysis of FH was performed. Coding regions of FH were Sanger sequenced in 120 cases (53 LBN, 47 UL and 20 LMS).
Results: Follow-up data was available in 92 patients, and 19% patients showed local clinical recurrence after myomectomy. Two other patients presented with LMS – one in a vaginal stump and second in uterus. These tumours arose independently of LBN. FH expression was lost in 61% of LBN, 2% of UL, and 0% of LMS. Most LBN cases without FH expression show histologically prominent eosinophilic nucleoli, rhabdoid-like cells, and staghorn vessels. Pathogenic or probably pathogenic mutations were more frequent in LBN (51%) and LMS (45%), compared to UL (15%).
Conclusion: LBN is a rare neoplasia with a benign behavior. Aberrant FH expression is common in LBN, but rare or absent in UL and LMS. Negative expression of FH may represent an efficient screening method for FH aberration associated disorders.

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PS-04-028
Genital type rhabdomyoma; a rare case
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Background & Objective: Genital type rhabdomyoma of cervix is an extremely rare tumour which presents as a cervical polypoid masses. It is essential to differentiate it from benign and malignant mimickers.
Method: A 47-year-old patient presented with menorrhagia and pelvic pain to gynaecology clinic. During pelvic exam; a cervical polyp was detected. Polypectomy specimen was received in formalin. Specimen diameter measured 4 cm and showed a white lobulated surface. Immunohistochemical stains were conducted in order to identify the tumour.

Results: On microscopic examination the polyp was covered by non-keratinizing squamous epithelium. There was well-vascularized tissue, composed of fusiform or stellate cells, arranged in a myxoid stroma. The stroma showed numerous spindle cells with abundant eosinophilic cytoplasm, vesicular nuclei placed peripherally or centrally and conspicuous nucleoli. The cytoplasm of these cells was cross-striations were readily visualized. Nuclear atypia is absent and mitotic figures were not seen. Immunohistochemical studies showed positive cytoplasmic staining for desmin and myogenin in the cells with rhabdomyoblastic differentiation. Staining for cytokeratin and S100 was negative in these cells. The diagnosis of genital type rhabdomyoma was made.
Conclusion: Genital type rhabdomyoma is a rare benign mesenchymal tumour with distinctive clinical, pathological and behavioral features. The genetic alterations of genital type rhabdomyoma are unknown. The prognosis of rhabdomyoma of uterine cervix is excellent with surgical intervention and complete removal. We reported this case because of the rarity of these tumours in extracardiac localization and to point to differential diagnosis.

PS-04-029

Utility of P16 expression on differential diagnosis of cervical intraepithelial neoplasms; how applicable for the novice in pathology

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Background & Objective: P16 immunhistochemistry is used to fascilitate the diagnosis of cervical intraepithelial neoplasia. Our aim is to investigate p16 expression patterns in differential diagnosis of cervical precursor lesions and to see its applicability for the inexperienced in pathology.
Method: Representative sections from the colposcopic biopsies of 45 patients with diagnosis of chronic cervicitis (n = 12), CIN1 (n = 12) CIN2 (n = 14) and CIN 3 (n= 7) were selected and immunohistochemically stained with p16. P16 staining pattern was classified as negative(0); patchy (1); block positive less than 1/3(2), less than 2/3 (3) and more than 2/3 (4). The results were evaluated independently by medical students without pathology experience and a gynaecologic pathologist.
Results: All chronic cervicitis cases showed less than 1/3 of basal staining, whereas 85.7% of CIN3 cases showed more than 1/3 (p=0.02). Negative or patchy staining pattern was observed more frequently in chronic cervicitis than CIN1 (p = 0.014). Although CIN1 and CIN2 cases were not differentiated by p16 expression, there was significant difference between CIN 1 and CIN2/3 combined (p=0.001) 92% compatibility was determined among the evaluators.
Conclusion: P16 expression is increasing gradually from CIN1 towards CIN3. It is seen that p16 expression is useful in nonneoplastic/neoplastic discrimination and CIN1/CIN2-3 discrimination. This method can be easily applied even by persons who have no experience in pathology and can prevent the difficulties in making histopathological diagnosis.

PS-04-030

Chemotherapy response score after neoadjuvant chemotherapy in ovarian advanced high-grade serous carcinoma correlates with peritoneal cancer index

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Background & Objective: Ovarian high-grade serous carcinoma (HGSC) is frequently associated with peritoneal carcinomatosis. Patients with advanced stage HGSC can be treated with neoadjuvant chemotherapy (NACT) prior to debulking surgery (DS). The chemotherapy response score (CRS), developed and validated by Böhm et al, is a three-tier histopathologic scoring system for measuring response to NACT in interval DS specimens of HGSC. We aim to determinate if CA-125 levels and peritoneal cancer index (PCI) after NACT correlate with CRS in our series.
Method: 22 cases of HGSC treated with NACT and interval DS at our institution from 2014 to 2018 were included. In each case, one omental slide showing the maximum tumour was selected. Two pathologists scored each slide according to CRS. Ca-125 levels and PCI after NACT were collected from medical records. CRS was correlated with PCI and the decrease in Ca-125 levels. Statistics were performed using Mann-Whitney and Wilcoxon tests.
Results: All patients showed a reduction in Ca-125 levels (ranging from 32.04% to 98.37%). IPC after NACT ranged from 1 to 28. CRS was as follows: CRS1: 6 cases, CRS2: 9 cases, and CRS3: 7 cases. PCI showed an overall significant correlation with CRS (p =.004) and differences when comparing CRS1 vs CRS3 (p=.002) and CRS2 vs CRS3 (p=.003). There was no significant difference in CRS1 vs CRS2 (p=.328).
Conclusion: PCI and CRS showed good correlation in our series. Although no significant correlation was found between CRS and CA-125, a larger sample may minimize power issues. Additional cases and outcome data will be evaluated to determine the clinical significance of CRS.

PS-04-031

Primary lymphoma of the female genital tract. Three new cases

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Background & Objective: Primary lymphoma of the female genital tract (PLFGT) is an uncommon entity. The most common location is the ovary and the most common type of is diffuse large B-cell lymphoma (DCBCL). Aim is to analyse all cases of PLFGT in our hospital and to compare the clinical and pathological features to those described in the literature.
Method: Cases were collected retrospectively from the last 18 years; revision of clinical and the anatomopathological features were performed.
Results: Three cases with diagnosis of PLFGT were found, with a mean age of 53 (range 29-81). The most common clinical feature was vaginal bleeding (2/3). The most frequent location was cervix (2/3), with the highest Ann Arbor stage and positivity for tumour markers. 2/3 cases had completed remission. All cases had final diagnosis of DCBCL, and 2/3 cases were germinal centre subgroup. One case of these two ones was positive for C-MYC, BCL-2 and BCL-6 by immunohistochemistry (IH) and only BCL-2 was translocated by FISH. The case activated B-cell-type expressed C-MYC and BCL-6 by IH but FISH was not valorable.
Conclusion: LPTGF is an uncommon entity, which most common location is the ovary. In our revision the most common location was cervix. The mean age, the histology type and the most frequent clinical features are according to literature. Tumour markers are high in the most advanced cases as described in the literature. All cases were treated according to the protocol and had a favourable evolution, which is characteristic of LPTGF, opposite from what occur with secondary lymphoma.

PS-04-032

Renal cell carcinoma with bilateral ovarian metastasis

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Background & Objective: We report a case of Renal Cell Carcinoma (RCC) with bilateral metastases to the ovaries. Ovarian metastasis of RCC is rare with a number of 38 cases in the English literature
Method: A 45-year-old patient with a history of RCC was admitted to the hospital due to symptoms of ascites (abdominal pain, increased abdominal girth and dyspnea). Ultrasound examination revealed a 9.4 cm solid-cystic mass on the left adnexal region. Metastatic disease in the greater omentum, paraortic and retroperitoneal lymph nodes was found on further imaging studies. Tumour markers were normal. A second primary neoplasm was

suspected. Therefore an hysterectomy and bilateral salpingo-oophorectomy, omentectomy and appendicectomy were performed.
Results: On gross examination the tumour of the left ovary measured 9.8 cm and was predominantly cystic. On microscopic examination both ovaries, the greater omentum the right fallopian tube and the peri-appendiceal fat were infiltrated. The tumour consisted of nests and glandular structures with areas of papillary formation. The cells had moderately atypical nuclei without significant pleomorphism and abundant clear cytoplasm. Few mitotic figures were found. Areas of necrosis were also observed. A prominent thin walled vascular network was present. Immunohistochemical study was positive for RCCma, CD-10 and Vimentin and negative for CK-7 and WT-1 confirming histological findings.
Conclusion: The diagnosis of malignant neoplasm with morphological and immunohistochemical features consistent with metastatic RCC was made.

PS-04-033
Atypical polypoid adenomyoma: Clinicopathological characteristics of 7 cases
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Background & Objective: Atypical polypoid adenomyoma (APA) is a rare benign mixed epithelial and mesenchymal tumours of uterus. We investigate the clinicopathological characteristics of 7 cases of atypical polypoid adenomyoma.
Method: This is a retrospective analysis performed in the Department of Pathology of University Of Health Sciences Antalya Training and Research Hospital, Antalya, Turkey over a period of 6 years (March 2012- March 2018) which involved a total of 7 cases with APA.
Results: A total of 7 patients were diagnosed with APA. Revised and reconfirmed 7 cases of the diagnosis. On microscopic examination, architecturally and cytologically atypical endometrial glands separated by intersecting fascicles of smooth muscle cells were seen in all cases. One case included focal atypical endometrial hyperplasia within it. The median age was 49,4 years (range: 37 – 66 years). 4 patients were premenopausal, 3 patients were postmenopausal. The most common symptom was abnormal uterine bleeding (4 patients). Lesions were obtained by using dilatation and curettage in 5 cases and myomectomy in 2 cases. The median level of CA125 was 21,5 U/ml (range: 6,4 – 69,6 U/ml) and it was within a normal range.
Conclusion: The most important entity in the differential diagnosis is atypical hyperplasia or endometrioid adenocarcinoma. APA have high risks of residual lesions and recurrence. Close follow-up with hysteroscopy and biopsy examinations are important for those patients with conservative treatment.

PS-04-034
Primary primitive neuroectodermal tumour of the cervix and ovary: a report of two cases
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Background & Objective: Primary primitive neuroectodermal tumour (PNET) of the cervix and ovary is a very rare entity, with 21 and 100 cases described respectively. PNET has been grouped into two major categories: Peripheral (with EWSR1 rearrangement) and central. We describe the clinicopathological features of two new cases.
Method: First case: 25-year old woman with uterine bleeding and lower abdominal pain for three months. CT revealed a 10 cm mass in the cervix. Hysterectomy, double adnexectomy and bilateral pelvic lymphadenectomy were performed. Second case: 48-year old woman with alterations of menstrual cycle and abdominal distension for two months. CT revealed a 10 cm mass in left ovary. Ovarian surgical protocol was performed.
Results: Microscopically both cases showed a malignant neoplasm composed of round cells of intermediate size, immunoreactive for FLI1, CD99, vimentin and CD117. Cytokeratin, Inhibin, CD10, LCA, HMB-45 were negative. SALL4, SOX2, synaptophysin were negative in the first case and positive in the second. Molecular study by FISH showed breakdown of the EWS gene (22q12) only in the first case. Primary PNET was diagnosed in both cases. Both patients were treated with chemotherapy, the first case is free of disease 4 years after diagnosis, the second case had progression of the disease and died 8 months after diagnosis.
Conclusion: PNET arising from cervix and ovary is very rare and represents a real diagnostic challenge. Immunohistochemistry and molecular study are fundamental for an accurate diagnosis and for discarding other tumours. The distinction of central and peripheral PNET may have prognostic and therapeutic implications.

PS-04-035
Primary clear cell carcinoma of the cervix: report of 10 cases and review of the literature
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Background & Objective: To explore the clinical diagnostic and therapeutic characteristics, prognostic factors of patients with primary clear cell carcinoma of the cervix.
Method: The clinical, pathologic and follow-up data of patients with primary clear cell carcinoma of the cervix treated in our institute from Jan 2003 to Dec 2014 were collected and analyzed retrospectively. The relative literature was reviewed.
Results: The average age was 54.6 with extremes ranging from 36 to 76 years. No patients were exposed to diethylstilbestrol (DES) and none had a screening smear. The primary symptom was mostly irregularly vaginal bleeding. 2 cases were of stage I b, 4 of stage IIa, 3 of stage IIb and 1 of stage IIIa. All cases were negatif for p16 (INK4a) in histology. All of patients underwent neoadjuvant radiotherapy with or without chemotherapy followed by total hysterectomy with bilateral salphingoophorectomy and pelvic lymph node dissection. There was no relapse or metastasis after 4 years of follow-up in 5 cases. One patient was lost to follow-up just after the intervention and four had recurrence or metatases.
Conclusion: Clear cell carcinoma is a rare entity that does not seem to be related to HPV. Its clinical and pathological features and prognosis differ from those of conventional adenocarcinoma.

PS-04-036
PD-L1 expression in cancer tissues vs. soluble sPD-L1 in the plasma of patients with ovarian epithelial carcinoma
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Background & Objective: The immune checkpoint PD-1/PD-L1 pathway has been recently revealed as a major target for therapeutic interventions. Indeed, PD-1/PDL1 blocking agents have been approved for the treatment of melanoma and advanced/metastatic lung, head-neck, and urothelial cancer.
Method: In the current study, we examined in parallel the expression of PD-L1 in neoplastic tissue and the plasma (soluble sPD-L1) of seventeen (17) patients with epithelial ovarian carcinoma.
Results: Soluble sPD-L1 levels were significantly higher in the plasma of patients with ovarian cancer compared to healthy women (median/range 103/29-178 vs. 63/47-98 pg/ml; p=0.01). Immunohistochemical analysis

of cancer tissues from these patients showed a mixed cytoplasmic and membrane expression of PD-L1 in a varying percentage of cancer cells: 6/17 (35.3%) were negative, 4/17 (23.5%) showed reactivity in 20-50% and 7/17 (41.2%) in 60-90% of cancer cells. PD-L1 was also expressed in the tumour-associated lymphocytes and macrophages in 10/17 (58.8%) cases. Stroma PD-L1 expression was not related to cancer cell expression. There was no statistical difference in the concentration of sPD-L1 between the groups of patients with negative, low or high cancer cell PD-L1 expression.

Conclusion: Aside from cancer cells, immune infiltrating cells may be involved in the immune suppression characterizing a subset of ovarian cancer patients. The presence of high PD-L1 amounts in the plasma of patients may also neutralize anti-PD-L1 antibody therapies. The optimal biomarkers for the administration of therapeutic anti-PD-L1/PD1 antibodies remains a subject for investigation.

PS-04-037

Incidental gonadal germ cell tumours at the time of prophylactic gonadectomy in patients with Swyer syndrome - a report of 3 cases

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Background & Objective: Swyer syndrome (46,XY pure gonadal dysgenesis) is an uncommonly encountered condition in which gonadectomy is recommended upon diagnosis due to a significant risk of malignant transformation of the dysgenetic gonads. The aim of this study was to present our experience with incidentally found germ cell tumours in patients with Swyer syndrome.

Method: We report the clinico-pathological characteristics of 3 cases of female phenotypic patients presenting with primary amenorrhea who underwent prophylactic bilateral laparoscopic gonadectomy with salpingectomy following a diagnosis of Swyer syndrome. At the time of diagnosis, they were 17 to 20 years old. The presenting features were hypogonadotropic hypogonadism and 46, XY karyotype. A hypoplastic uterus with normal looking fallopian tubes and bilateral gonads were detected by ultrasonography and confirmed during laparoscopy. The patients with dysgerminoma underwent postoperative chemotherapy. All three patients are alive and well 70, 115 and 144 months following surgery.

Results: The histopathological examination of the streak gonads which were completely sampled and embedded revealed the presence of bilateral predominantly "burnt out" gonadoblastoma in all patients. In addition, in two patients, a coexisting dysgerminoma of 1.5 and 3.8 cm in diameter FIGO stage IC1 in the right gonad was confirmed. The sequencing of the SRY gene of the patient with bilateral gonadoblastoma without dysgerminoma overgrowth revealed a C/G substitution at the first nucleotide of codon 133, leading to Arg/Gly replacement in the SRY protein.

Conclusion: Our data suggest that patients with gonadal dysgenesis and 46, XY karyotype should be referred for bilateral gonadectomy and their operative specimens should undergo meticulous histopathological examination because of the high risk of neoplastic transformation.

PS-04-038

A clinicopathologic study of early stage placental mesenchymal dysplasia

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Background & Objective: To elucidate clinicopathologic features of early stage placental mesenchymal dysplasia (PMD).

Method: Ten cases of PMD with gestational age less than 20 weeks were clinicopathologically analyzed with an immunohistochemical study of p57 (Kip2) (p57).

Results: Maternal ages ranged from 23 to 40 years. Five patients were initially diagnosed as partial partial mole (PM) and one was as complete mole (CM) with twin on ultrasound examination. The gestational periods ranged from 12 to 19 weeks. One case was associated with Beckwith-Wiedemann syndrome. Histologically, early stage PMD was characterized by moderate swelling of stem villi with cistern formation, myxoid change, dilated veins, mild stromal cell proliferations, and the absence of trophoblastic hyperplasia. Dilated subchorionic vascular vessels with or without luminal thrombosis, or chorangiosis, which were observed in the third trimester PMD, were not found. Regarding p57, villous stromal cells were diffusely positive in 3 cases, focally positive in 5, and uniformly negative in 2.

Conclusion: Early stage PMD can be clinically or pathologically misdiagnosed as abortion, PM, or CM with a twin. Histologic features in early stage PMD are less distinctive compared with those of PMD in the third trimester. The diagnostic clues are moderate swelling of stem villi with cistern formation, myxoid change, dilated veins, and mild stromal cell proliferations and the absence of trophoblastic hyperplasia. The p57 immunohistochemical study may be useful for differential diagnoses in equivocal cases. It is important to identify PMD cases in early stage to choose appropriate treatments.

PS-04-039

E-cadherin expression in high grade serous ovarian carcinoma – clinicopathological study

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Background & Objective: E-cadherin is epithelial cell adhesion molecule, which has been downregulated in various malignant epithelial neoplasms. We aimed to evaluate its expression in high grade ovarian serous carcinomas (HGOSC) of advanced stage.

Method: We analysed immunohistochemical expression of E-cadherin and compared it to multiple clinicopathological data and overall survival in 76 cases of HGOSC in advanced stage (FIGO III-IV). Presence of signal, its distribution (membranous and/or cytoplasmic), percentage of positive tumour cells and intensity of staining (mild, moderate and strong) were evaluated.

Results: The mean age of the patients was 58,74 years (24-78), with the majority (56,6%) in stage IIIC, 28,9% in stage IIIB, 10,5% in stage IIIA and 3,9% in stage IV. The mean post-operative survival period was 35,36 months (1-90 months). Immunohistochemical analyses showed membranous and/or cytoplasmic localisation of E-cadherin in all cases. In 68 cases (89,5%) more than 10% of the tumour cells were positive, and in the reminding 8 cases (10,5%) the positivity was present in less than 10% of the tumour cells. We observed heterogeneous intensity of the signal, with dominant strong signal in most of the cases (68.4%), moderate in 25% cases and mild signal intensity in 6,6% of the cases. The statistical analysis showed that both low intensity of signal and expression in less than 10% of the tumour cells were associated with shorter overall survival in patients (Kaplan-Meier, $p<0.001$).

Conclusion: The study shows that the decreased E-cadherin expression in tumour cells of HGOSC is associated to adverse prognosis, making it a potential prognostic marker.

PS-04-040

Pure primary squamous cell carcinoma of the ovary

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Background & Objective: We present a case of pure primary Squamous Cell Carcinoma of the Ovary (SCCO). Pure primary SCCO is a very rare tumour with less than 40 reports in the English literature.

Method: A 54-year-old female patient with history of conization of the cervix 23 years ago because of cervical intraepithelial neoplasia III, was admitted to the gynaecology department due to gradually worsening abdominal pain lasting for four months. Imaging studies revealed a cystic lesion with solid components, originating from the right adnexa with measuring 8,6 x 7,6 cm. Patient had a total hysterectomy, bilateral adnexectomy and omentectomy. Grossly, the tumour was mainly cystic and partly solid. On microscopic examination the ovary was extensively infiltrated by a malignant tumour that was composed of polygonal squamoid cells devoid of keratin pearls or individual cell keratinization. Nuclear pleomorphism and few intercellular bridges were observed. Mitotic figures were numerous. Extensive necrosis was also present. Evidence of any other associated lesions such as dermoid cyst, Brenner tumour, or endometriosis was not found. Immunohistochemical study was positive for CK7, CK5 and P63, negative for CK20, TTF-1, GATA-3 and P16. Ki-67 index stained 40% of tumour nuclei.
Results: The neoplasm was diagnosed as morphologically and immunohistochemically consistent with pure primary SSCO. The patient received adjuvant chemotherapy and died 9 months after surgery.
Conclusion: SCCO is a rare tumour with poor response to chemotherapy. Disease outcome is poor. Tumour stage and grade is correlated best with overall survival.

PS-04-041
Myeloid sarcoma of the vagina: a case report
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Background & Objective: Myeloid sarcoma (MS) is a rare solid extramedullary tumour consisting of immature myeloid cells and commonly associated with acute myelogenous leukemia (AML). Sometimes it appears as a neoplasia without prior evidence of leukemia. In the latter situation, patients usually develop AML within a few days to several months. MS may occur at almost any anatomic site. Involvement of the female genital tract is uncommon. We report a case of MS observed in a vagina.
Method: A 16-year-old female patient was hospitalized with complains of acute vaginal bleeding for some days. On colposcopic examination on the anterior wall of the vagina a cyanotic dense tumour-like lesion was found in the form of a cauliflower with a decay, filling the vagina, measuring 2.5 x 3.5 x 2.7 cm. Tissue samples were investigated histologically and immunohistochemically.
Results: Microscopic evaluation of the vaginal lesion revealed a diffuse dense cellular infiltration of stroma by moderately sized immature cells with scanty cytoplasm. Some of them had blastic morphology and visible nucleoli. Many cells were myeloid or atypical mononuclear with round to oval or irregularly shaped, angulated nuclei, irregular nuclear contours, fine chromatin. There were a lot of small capillaries and larger dilated vessels, areas of necrosis with ulceration. Immunohistochemical staining was positive for CD45, MPO, lysozyme, CD117, CD68. Ki67 reached about 50%. MS was diagnosed and careful examination of the patient identified AML.
Conclusion: The histologic diagnosis of MS is difficult especially in unusual location without AML clinical manifestations. Histological signs of myeloid differentiation in tumour and immunohistochemistry help make the correct diagnosis.

PS-04-043
Mixed carcinoma (adenoid basal carcinoma and microinvasive squamous cell carcinoma) of cervix: a case report
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Background & Objective: Adenoid basal carcinoma (ABC) is often associated with squamous intraepithelial lesion or another carcinoma subtype. The presence of any invasive carcinoma subtype with ABC should be reported as a mixed carcinoma.
Method: A 77-year old multiparous woman was referred to hospital for abnormal bleeding. Total abdominal hysterectomy and bilateral salphingooferectomy was performed. On macroscopic examination, there was no marked mass in the cervix.
Results: On microscopic examination, lobular clusters of basaloid nests and a few glands were separated by unaltered endocervical stroma. Additionally, cervical intraepithelial neoplasia 3 were found along side of the superficial and glandular epitelium. At the same time, dysplastic epithelium of the cervical gland showed microinvasion through the cervical stroma which was not greater than 3 mm.
Conclusion: The differential diagnosis of ABC includes adenoid basal hyperplasia, adenoid cystic carcinoma, basaloid squamous cell carcinoma and neuroendocrine carcinomas. In this case report, we reviewed an uncommon tumour and discussed differential diagnosis.

Sunday, 9 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-05 | Nephropathology

PS-05-001
A retrospective clinical and pathological study of 11 patients with kidney granulomatous vasculitis without glomerular involvement
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Background & Objective: Renal failure resulting from granulomatous vasculitis without glomerulonephritis was rarely reported. The aim of this study was to describe the characteristics of patients with kidney biopsy showing such features.
Method: We retrospectively analyzed the clinical, biological and histological data of patients from 4 French nephrology centers, between 1984 and 2016.
Results: Eleven patients (5 male, mean age 55.4 years, range 30-73) were included. Clinical presentation was a flu-like syndrome with hyperthermia (n=11), myalgia/arthralgia (n=7). All patients displayed acute renal failure (mean serum creatinine: 4.4 mg/dL, range 1.3-9.5, mild proteinuria (0.8 ±0.2 g/d) and inflammatory syndrome (median CRP 104, range 19-209). Microscpic hematuria was inconstant (n=7). All kidney biopsies showed granulomatous inflammation of the walls of interlobular arteries. The final diagnoses were sarcoidosis (n=2), microscopic polyangiitis (n=2), granulomatosis with polyangiitis (GPA) (n=1), polyarteritis nodosa (PAN) (n=1). For 2 patients, drug-induced vasculitis was evoked and could be related to antibiotic and non-steroidal anti-inflammatory drugs. For 3 patients, final diagnosis could not be definitively established, and drug-induced, infectious, PAN or cryoglobulinemia were presumed etiologies. Follow-up was marked by one death (1 PAN patient due to cerebral hemorrhage), 2 chronic renal replacements (1 GPA and 1 sarcoidosis) and kidney function improvement for the remaining patients (median eGFR 64 ml/min/1.71m2, range 11-104). Drug-associated vasculitis suspected patients were younger with better renal outcome (eGFR 74 and 104 ml/min/1.73m2).
Conclusion: A final diagnosis could be challenging to reach for this rare renal vasculitis. Drug-induced vasculitis group seemed to harbour the favourable prognosis.

PS-05-002
Membranoproliferative glomerulonephritis due to visceral leishmaniasis in an immunocompromised patient: a case report and literature review
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Background & Objective: Membranoproliferative glomerulonephritis (MPGN) is a pattern of injury characterized by mesangial and endocapillary proliferation, double contours along the capillary walls, and lobular accentuation of the capillary tufts. Infections are an important cause of MPGN that are usually associated with an immune complex–mediated MPGN.
Method: To report a case of MPGN with Leishmaniasis in a patient HIV infected, we describe the clinicopathological details and review the literature.
Results: A 50 year-old male patient with history of HIV infection was admitted to our hospital due to a nephrotic syndrome. Physical examination showed gross edema of legs and reddish, papular skin lesions on the chest and abdomen The laboratory analyses revealed a low viremia and CD4 count of 519 cells/mm3. Peripheral blood counts showed anemia and thrombopenia. A renal biopsy was performed to determine the cause of proteinuria and on light microscopy we observed a MPGN pattern in the glomeruli with interstitial inflammatory infiltrate mostly of lymphocytes. Into the capillary lumen of the glomeruli there was numerous Leishmania amastigotes. There were 2 glomeruli present for immunofluorescence microscopy and showed bright staining for IgM, IgG, C1q and C3 and lower for C4. After the diagnosis also the bone marrow was involved and the patient started with liposomal amphotericin B as suppressive therapy.
Conclusion: Diagnosis of Visceral Leishmaniasis (VL) in HIV infected patients can be difficult due to atypical presentations like that in our case. The VL relapses and depend on the immunologic status of the patient.

PS-05-003
The histopathological spectrum of monoclonal gammopathies of renal significance: a single centre experience
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Background & Objective: Monoclonal Gammopathy of Renal Significance (MGRS) encompasses renal histopathological entities caused by Monoclonal Immunoglobulins (MIg) in patients who do not meet criteria of symptomatic lymphoma or myeloma (MM). We describe the spectrum of MGRS histopathological diagnoses in our centre.
Method: Native renal biopsies (2006-2017) that met the following criteria were included: evidence of MIg or light chain in glomeruli, tubules, vessels and/or interstitium. C3GN and TMA cases associated with MIg were excluded.
Results: MIg-associated lesions were identified in 163/4,374 native biopsies (3.7%). After exclusion of symptomatic MM and lymphomas, 68 biopsies (1.5%) were consistent with MGRS. Median age at diagnosis was 65 years (range 25-87). Renal histological diagnoses included: amyloidosis (n=28, 41%), Proliferative GN with MIg Deposits (PGNMID) (n=13, 19%), MIg Deposition Disease (MIDD) (n=12, 18%), Light Chain Tubulopathy (n=5, 7%), Type-1 Cryoglobulinaemic GN (n=6, 9%), Intracapillary Monoclonocal IgM without Cryoglobulin (n=2, 3%), Crystal Cryoglobulinaemia (n=1, 1.5%) and Fibrillary Light Chain restricted GN (n=1, 1.5%). Serum Free Light Chain assay was performed in 42 patients and had an abnormal ratio in 24. Haematological diagnosis was possible in bone marrow histology (BMAT) in 53 patients. These included MGUS (n=30, 56.6%), smouldering myeloma (n=17, 32%), lymphoplasmacytic lymphoma/Waldenstrom's macroglobulinaemia (n=2, 3.7%), chronic lymphocytic leukaemia (n=3, 5.6%) and marginal zone lymphoma (n=1, 1.8%). 8/13 PGNMID and 3/12 MIDD cases did not have a detectable clonal B cell or plasma cell clone in BMAT.
Conclusion: MGRS are increasingly recognised since the term was introduced in 2012. Renal histopathology must be interpreted in conjunction with haematological diagnosis to guide treatment.

PS-05-004
Serum uromodulin correlates with kidney function in patients with membranous nephropathy and nephrotic syndrome
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Background & Objective: Recent studies have shown that serum uromodulin may serve as a biomarker of kidney function, allowing the identification of early stages of chronic kidney disease (CKD). A reduced number of functioning tubules in CKD may correspond to reduced urinary and serum concentrations of uromodulin. We analyzed the serum uromodulin concentration in patients with membranous nephropathy (MN) and nephrotic syndrome and correlated its concentration with biomarkers of kidney function and parameters of CKD obtained from renal biopsies.
Method: Serum uromodulin, serum creatinine and estimated glomerular filtration rate (eGFR) were assessed in 67 patients with nephrotic syndrome and biopsy proven MN and compared with 30 healthy individuals with normal serum creatinine. Interstitial fibrosis and tubular atrophy (IFTA) were scored according to the Banff criteria for transplant kidney. Univariate correlations between serum uromodulin and creatinine, eGFR and IFTA were calculated using Pearson's correlation coefficient.
Results: The serum uromodulin concentration in healthy controls was significantly higher from patients with MN and eGFR MDRD >90 ml/min/1.73m2 (CKD stage I) and patients with MN with CKD stage II –V ($p<0.00$). Decreased uromodulin serum concentration significantly correlated with increased serum creatinine, advanced CKD stage, decreased eGFR and increased amount of IFTA in patients with MN and nephrotic syndrome.
Conclusion: Our study indicated that uromodulin may allow identification of early CKD stages in patients with MN and nephrotic syndrome. Uromodulin might therefore provide substantial information on tubular function in patients with MN-related nephrotic syndrome and retained eGFR.

PS-05-005
Macrophage abundance predicts allograft long-term function and correlates with rejection and fibrosis in a cross-sectional study of transplanted kidneys
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Background & Objective: Standardized markers based on quantitative and qualitative evaluation and localization of immune cell density in kidney biopsies may improve diagnostic accuracy. Inflammation is difficult to quantify by eye at low densities. We measured macrophage abundances in renal allograft biopsies by digital image analysis.
Method: Kidney tissue of transplanted kidneys from surveillance (36%) and clinically indicated (64%) biopsies (n=350) was stained for macrophages using a monoclonal CD68 antibody (PGM1), scanned (Leica) and whole slide images were analyzed for immunopositively stained area using a digital pixel-based approach (Definiens Tissue Studio). Results were obtained separately for cortex, medulla and extrarenal tissue.
Results: Humoral and combined rejection were associated with increased macrophage infiltration (no rejection: cortex 2.6%; borderline: cortex 1.9%; cellular: cortex 2.5%; humoral rejection: cortex 4.4%; combined rejection: cortex 6.2%; $p<0.05$). The density of macrophages correlated with the time after transplantation: Highest mean values were measured when post-transplant time exceeded 1 year (cortex: 5.8% compared to <1year >90 days (4.1%), <90 days >8 days (1.3%), <8 days (1.5%); $p<0.05$). Evaluation of IF/TA showed an increase of infiltrating macrophages with fibrosis progression (ci0: 1.5%, ci1-3: 4.6%; $p<0.001$). In 6-week-surveillance-biopsies macrophage density was a significant predictor of an eGFR<30ml/min after four years ($p<0.01$).

Conclusion: The findings show that macrophages have essential roles in active rejection, chronic allograft injury and fibrosis and can be used as a prognostic marker in early renal transplant biopsies.

PS-05-008

Crosstalk between NCAM/FGFR and TGF-beta signalings: an in vitro study in cultured human proximal tubular epithelial cells

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Background & Objective: Epithelial-to-mesenchymal transition (EMT) contributes to repair and parenchymal damage during renal fibrosis. Neural cell adhesion molecule (NCAM) and fibroblast growth factor receptor 1 (FGFR1) are considered to be involved in the EMT process. We explored the role of NCAM/FGFR1 signaling and pro-fibrotic gene expression signatures as initiating/driving forces of EMT program in cultured human proximal tubular epithelial cells (hPTEs).
Method: In vitro EMT model of hPTEs in response to TGF-β1 (10ng/mL) exposure and NCAM/FGFR1 signaling responses were analyzed by light microscopy, immune-labeling, qRT-PCR and scratch assays. Modulation of FGFR1 was induced using PD173074 (100nM).
Results: Morphological EMT changes started 48h after TGF-ß1 treatment and was clearly apparent after 72 hours, associated with loss of CDH1 and transcriptional induction of SNAI1, SNAI2, TWIST1, MMP2, MMP9, CDH2, ITGA5, ITGB1, ACTA2 and S100A4. After 24 hours of TGF-β1 exposure at the early stage of EMT, transcriptional induction of several NCAM isoforms along with FGFR1 was observed, implicating a mechanistic link between NCAM/FGFR1 signaling and induction of EMT. These assumptions were further supported by the inhibition of the EMT program after specific blocking of FGFR1 signaling responses by PD173074.
Conclusion: Modulation of NCAM/FGFR1 signaling blocks the EMT program in cultured hPTEs. NCAM/FGFR1 signaling appears to be involved in initial phases of TGF-ß1 initiated EMT of tubular cells and thus could contribute to maladaptive repair and parenchymal damage during renal fibrosis.

PS-05-009

The comparison of the renal cortex and medulla for antibody mediated rejection

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Background & Objective: Peritubular capillaritis (PTc) and C4d expression are important criteria for antibody mediated rejection (AMR). This study aims to focus on cortical and medullary scores of PTc and C4d, and specificity and sensitivity of medulla for AMR diagnosis in the allograft biopsy.
Method: Cortex and medulla of 51 post-transplant biopsies were re-evaluated separately for PTc, C4d expression and acute tubular injury (ATI) according to the Banff 2014 scheme. These parameters and DSA status were compared separately in the medulla and cortex.
Results: There was a significant positive correlation between cortex and medulla for PTc (p= 0,036) and C4d (p= 0,001) scores. There was a significant association for ATI between the cortex (0.004) and medulla (0,076) for DSA positive cases. PTc was not detected either at the cortex or medulla in 26 (51%) cases (p=0, 00). PTc was observed in the cortex and medulla in 17 cases and 3 cases had PTc only in the cortex and 5 cases only in the medulla. The sensitivity, specificity, positive and negative predictive values of medullar PTc, predicting cortical PTc were 85,7%, 86,7%, 81,8%, and 89,7%, respectively.
Conclusion: Medulla is injured during AMR. Some renal biopsies have very limited renal cortex or just consist of medulla. If correlated with DSA, medulla findings can be a significant guide, when the cortex is restricted for diagnosis.

PS-05-011

C3 glomerulonephritis: a department's series

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Background & Objective: C3 glomerulonephritis (C3GN) is caused by deregulation of the alternative complement pathway, with glomerular lesions and predominance of C3 deposits in immunofluorescence (IF). We aimed to determine the frequency and features of C3GN in our patients.
Method: A retrospective analysis was made of all renal biopsies of our deparment over the last 5 years. We selected those where the clinical data, laboratorial, pathological and genetic results were consistent with C3GN.
Results: From 227 cases, 6 were compatible with C3GN. Mean patient age was 46. Four patients had history of arterial hypertension, 1 of type 2 diabetes and 1 of chronic kidney disease. All presented with arterial hypertension, haematoproteinuria, acute kidney disease and low seric C3. Three had nephrotic proteinuria and four needed renal replacement therapy (RRT). Histologically, several patterns of GN were noted: 2 endocapillary (one with crescents and exsudative features), 2 membranoproliferative (1 with crescents), 1 necrotizing crescentic proliferative, and 1 global diffuse glomerulosclerosis. All had predominant C3 deposits on IF and electrodense deposits on EM. Genetic tests revealed homozyguous deletion of CFHR3/CFHR1 in one case. After immunosuppresion, 2 patients had complete remissions and one partial. The others remained on RTT.
Conclusion: C3GN was diagnosed in 2,6% of all RB studied. No uniform histologic features could be found. Patients should undergo genetic and immunologic studies.

PS-05-012

Immunohistochemical study of IgG4 and PLA2R in membranous nephropathy: can it be helpful to discriminate the primary forms of secondary ones? Preliminary results

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Background & Objective: Membranous nephropathy (MN) is more commonly a primary disease (pMN), but it also occurs as a secondary (sMN) to other conditions. The histopathological findings do not allow a differentiation between primary or secondary forms. Most patients with pMN have autoantibodies of IgG4 type against the M-type phospholipase A2 receptor (PLA2R). The aim was to evaluate an immunohistochemical panel with IgG4 and PLA2R in the differential diagnosis of MN.
Method: We studied the presence and distribution patterns of IgG4 and PLA2R in the glomeruli of 30 MN patients, using IHC. The clinical history of each patient was reviewed: MN were diagnosed as primary or secondary based on clinical data.
Results: 30 MN: 21 (70%) were primary, and 9 were sMN, based on clinical data. Only granular membranous deposits were considered as positive. Eleven cases presented granular membranous IgG4 deposits. In 4 cases deposits were diffuse and 7 were segmental and focal. Patients with diffuse deposits had more proteinuria. The 11 cases IgG4 (+), did not present clinically secondary causes of MN. PLA2R deposits were found in up to 100% of the pMN. All cases of Class V lupus MN (7 cases) showed absence of IgG4 and PLA2R deposits.
Conclusion: Preliminary results in our series, showed IgG4 membranous deposits in 36.7% and PLA2R in 70%. IHC of IgG4 showed a sensitivity of 52% and specificity of 100% to differentiate MN. However, IHC of PLA2R seems to be more sensitive and specific for pMN.

PS-05-013

Analysis of renal graft survival with pre-transplantation histological evaluation: the experience of a center

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Background & Objective: The shortage of organs in renal transplantation forced the acceptance of marginal donors. Histological evaluation prior transplantation remains controversial. Analysis of marginal donors with pre-transplantation biopsy: histological score, receptor age, compatibility, time of cold ischemia and on dialysis.
Method: A retrospective and unicentric study was performed, including 127 patients who received marginal donor kidneys after biopsy (2009-2016). Histological evaluation was done using Remuzzi scale, and donors with score >/=4 were excluded. Level of significance set at 0.05.
Results: 204 donors performed the biopsy, with an exclusion rate of 62.3%. The mean score of the excluded donors was 4.8 ± 1.47. Donors had a mean age of 64.3±11.48years, and 54.33% were males. The mean cold ischemia time was 19.39±4.06hours. A total of 127 receptors were evaluated (79.53% male). The mean follow-up time was 4.2±2.3years. Mean receptors age was 57.68years, mean anti-HLA incompatibility was 4.04, and mean time on dialysis was 48.93months. It was found that 18.1% of patients had late function and 4.7% had nonfunctioning kidney. The histological score had no relation to graft function ($p = 0.15$). There was significance of GFR according to age ($p=0.0011$). The 1-year graft survival was 88.1%. The age of receptors and the time on dialysis had significance on graft survival ($p=0.0498$ and 0.0084).
Conclusion: The histological evaluation of marginal donors may have value in the exclusion of grafts with specific histological changes, but, in our cohort, histological score does not correlate with graft survival.

PS-05-015

Biopsy-proven acute tubulointerstitial nephritis in the elderly - a single centre study

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Background & Objective: Acute tubulointerstitial nephritis (ATIN) begins abruptly, manifesting as acute kidney injury. Literature data suggest that the incidence of ATIN in the elderly has grown over the past decade. In view of the above, we decided to establish the prevalence of biopsy-proven ATIN in the elderly, and to compare laboratory and clinical as well as histological pattern of the renal injury in elderly patients and in adult patients with ATIN
Method: Patients who underwent a renal biopsy from 2006 to 2017 were reviewed, and 49 patients were identified with biopsy confirmed ATIN. We divided the population into two groups according to the age: Group I (n=22) adults (18-64 years) and Group II (n=27) the elderly (≤65 years).
Results: The total number of native biopsies was 1623, the overall prevalence of ATIN was 3.02%. Of the 1623 native renal biopsy specimens, 220 were performed in patients aged ≤65 years. During the 17 years of follow-up, there was a significant increase in the prevalence of ATIN in elderly individuals: from 6.45% in the first 4 years of observation (2006-2009) to 14.05% in the last 4 years (2014-2017). Laboratory findings and clinical manifestation were similar in both studied groups, however the elderly had lower eGFR as compared with younger patients. Histological pattern of renal injury was similar in both studied groups.
Conclusion: The study confirmed significant increase in biopsy-proven ATIN in the elderly in the last years. Clinical manifestation, laboratory and microscopic findings in renal biopsies were similar in younger and older groups in patients with ATIN.

PS-05-016

Anti-glomerular basement membrane glomerulonephritis in renal biopsies

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Background & Objective: Anti-glomerular basement membrane (anti-GBM) disease is a rare autoimmune disorder, one of the most severe form of crescentic glomerulonephritis (GN), leading to a rapid loss of kidney function. The aim of this study was to analyse anti-GBM GN clinical and morphological data in native kidney biopsies of adult patients.
Method: 694 kidney biopsies of the City Clinical Pathology Bureau (from 2011 to 2015) stained by haematoxylin and eosin, PAS, Masson trichrome, Congo red, Jones silver have been evaluated with light microscopy. Immunofluorescent staining for IgG, IgA, IgM, C3c, C1q, fibrinogen, k and λ light chains was performed on paraffin sections. These cases were confirmed by elevated serum anti-GBM antibody titers and linear IgG deposition along GBM in glomeruli.
Results: Among all kidney biopsies 5 cases (0.7%) were diagnosed with anti-GBM GN (2 males, 3 females). These cases accounted 3% of 165 with any extracapillary proliferation as well as 15.6% of 32 with extracapillary GN containing more than 50% of damaged glomeruli. In all the cases, the cellular and fibrocellular crescents were observed including 60% to 100% glomeruli, necrotic changes were revealed in three cases. The kidney biopsy was made one to three weeks after the onset of the disease. However, in these samples we already observed global glomerular sclerosis 10% to 75% and interstitial fibrosis 25% to 80%.
Conclusion: Anti-GBM GB is characterized by severe clinical manifestations and significant proliferative and necrotic changes in glomeruli. By the time of biopsy kidney tissue demonstrated high level of global glomerular sclerosis and high percent of interstitial fibrosis, indicating a rapid progression to irreversible changes.

Monday, 10 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-06 | Cardiovascular Pathology

PS-06-001

Histopathological findings in ascending aorta wall with and without dilatation in patients with bicuspid valve

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Background & Objective: we study the thickness (E) of the ascending aortas (AAs) and the histopathological findings in biopsies from patients with and without dilatation with bicuspid valve.
Method: 184 patients with bicuspid valve. AAs diameter ≤ 40 mm was observed in 119 patients; AAs > 40 mm was seen in 65 patients. Biopsy of aorta was obtained, fixed in 10% formaldehyde, processed and stained with H & E, Masson's trichrome and Alcian blue. Histopathological findings were studied in semi quantitative grade (G): G 0 (without injury); G1 (0-10%); G2 (11-25%); G3 (26-50%); G4 (51-100%). E: 1,5 to 3 mm.
Results: AAs without dilatation: E: 1,51 - 2 mm: 46% of patients with G3 42% and G4 13% ; E: 2,01 – 2,5mm: 8% of patients with G3 22% and G4 33%; E: 2,51 – 3 mm: 16% of patients with G3 32% and G4 42%. AAs with dilatation: E: 1,51 - 2 mm: 20% of patients with G3 15% and G4 77%; E: 2,01 – 2,5mm: 20% of patients with G3 38% and G4 54%; E: 2,51 – 3 mm: 26% of patients with G3 18% and G4 76%. Thus 70% of patients with AAs without dilatation present an E between 1,5 - 3 mm and 96% of them have G3, while in the same range of E 66% of patients with AAs dilated showed 46% with G4 and 16% G3.
Conclusion: AAs of patients with bicuspid valves without aortic dilation at the time of surgery presented less injury in arterial wall as compared with patients with dilated AAs.

PS-06-003

Vulnerability of aortic dissection induced by protease digestion

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Background & Objective: Dissecting aneurysms of ascending aorta can cause sudden death. To know the pathogenesis of dissection is important to predict future risk. Speed of sound (SOS) through tissues corresponds to tissue rigidity. Susceptibility to protease treatment may simulate future risk of rupture. Aortae of Marfan syndrome (MS) with dissection, non-Marfan syndrome (non-MS) with dissection, and normal autopsy cases were compared with SOS alteration. Moreover, the difference was analyzed by expression of binding extracellular matrix proteins.
Method: Aortic sections in 10 um thickness were digested with collagenases to be followed their SOS. To compare SOS images, LM changes were compared with elastica-Masson stain. To follow alteration of binding proteins, anti-fibrillin-1 and anti-lysyl oxidase (LOX) were stained.
Results: All dissected MS and non-MS aortae showed greater SOS values compared with normal controls. After digestion, SOS of MS reduced rapidly. Non-MS showed two distinct patterns. One was rapidly declined and the other was slowly decreased. In normal controls, SOS of non-atheromatous portions decreased with aging. MS group were unstained with fibrillin-1 but showed conspicuous LOX stain. Non-MS group were positive for fibrillin-1 and focally positive for LOX. Normal younger adults were negative for fibrillin-1 and LOX.
Conclusion: MS with fibrillin-1 deficiency is susceptible to protease digestion. Non-MS contain at least two heterogenous groups about sensitivity to proteases. Both groups increased in rigidity by overexpression of LOX. Vulnerability of dissection induced by proteases may predict future rupture.

PS-06-004

Hypertrophic cardiomyopathy & sudden cardiac death: unexpected revelation

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Background & Objective: Sudden Cardiac Death in children and adolescents with Hypertrophic Cardiomyopathy (HCM) ranges 6.6%. The authors present a case where the postmortem multidisciplinary approach was relevant not only from a medical point of view but also for the socio-familial welfare.
Method: A 13-year-old male died suddenly during the sports class, at school.
Results: A thourough postmortem examination revealed cardiomegaly with macro and microscopic characteristics of "Hypertrophic Cardiomyopathy"; advising genetic/familiar study. Meanwhile, additional clinical information was obtained, discovering that the victim had a previous diagnosis of "Familiar (father), Non-Obstructive Hypertrophic Cardiomyopathy". In such a setting, the Clinical Geneticist asked our Institution for blood samples for molecular studies on the 'index case' and consequent evaluation of the familiar risk of other sudden deaths. These new studies not only confirmed the genetic mutation on the father's side, but also revealed unsuspected genetic alterations on the mothers' side. This discovery lead to the reorganization of the family clinical counselling and to the reduction of the father's "guilt" (as he confessed), since he thought to be the only responsible for his son's disease!
Conclusion: This case highlights the medical, scientific, socio-familial and "human/emmotional" importance of an accurate, specialized and multidisciplinary postmortem examination.

PS-06-005

Chronic aorta dissection: still dangerous?

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Background & Objective: Chronic Aorta Dissection is that with more than 90 days after the onset of symptoms. Its course may be varied, either stable or presenting complications. The authors report four cases of unsuspected chronic dissection.
Method: Four hypertensive patients, three males and one female, aged between 38 and 79-year-old were referred to a Cardiothoracic Center due to ongoing chest pain (n=1), episode of acute chest pain (n=2) - one of which was followed by an acute ischaemic stroke - and also to perform an elective surgery (n=1). The younger patient had polycystic kidney disease. None had history or previous evidence of acute aortic dissection. Emergency imagiologic studies detected lesions of possible type A aortic dissection in three of them and the other had a mitral valve replacement and an ascending aorta aneurysm removal. The aorta segments were sent to anatomo-pathological examination.
Results: Macroscopic evaluation of the specimens showed dead-end false lumen, that in three cases contained acute thrombus. Microscopic observation (complemented with histochemistry and immunohistochemistry) revealed that the false lumen was not recent and was covered by an organized layer of fibrous tissue, upon which the thrombus was seen.
Conclusion: This study reinforces how life-threatening a chronic aortic dissection can be, not only for existing unnoticed but also due to its possible complications, namely being a nidus for thrombosis and thus a source of emboli, leading to ischaemic events and even sudden unexpected death.

PS-06-006

Histopathologic descriptors of degenerative ascending aortic aneurysms according to disease type

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Background & Objective: To assess whether histopathologic descriptors can differentiate disease types in a sizeable number of non-inflammatory/degenerative ascending aortic aneurysms.
Method: We blindly re-evaluated 236 consecutive surgically resected specimens of degenerative ascending aortic aneurysms using the new AECVP/SCVP consensus statement diagnostic criteria. We excluded specimens with moderate/severe atherosclerosis and/or aortitis according to AECVP/SCVP criteria. The study population included: Group1 - 33 pts with genetic disease (mean age 37 yrs, mostly Marfan patients); Group2 - 104 bicuspid aortic valve (BAV) pts (mean age 54 yrs); Group3 - 99 nongenetic/nonBAV pts (mean age 56 yrs).
Results: Overall medial degeneration (MD) was present in all patients; elastic fibre (EF) (99%) and mucoid extracellular matrix accumulation (MEMA) (97%) were the most frequent alterations. Of the three Groups, Group1 had significantly more severe overall MD (Group1: 42.42%; Group2; 8.65%; Group3: 15.15%) ($p < 0.0001$), as well as more severe intralamellar-MEMA ($p < 0.0001$) or translamellar-MEMA ($p=0.01$), and more severe EF thinning-out ($p < 0.0001$) or EF fragmentation/loss ($p< 0.0001$). Translamellar collagen increase was almost exclusively seen in Group1 (31.25% vs 1.92% in Group2 and 4.04% in Group3) ($p < 0.0001$). Interestingly the 15.15% of Group3 severe lesions were found in younger patients (median age 50 vs 59 of group).
Conclusion: Histopathology discriminates genetic versus BAV and nongenetic-nonBAV patients in terms of severity of lesions. This shows that it can produce valuable diagnostic information, especially for the younger patients of Group3 with severe lesions, who should be further tested in view of possible genetic disease.

PS-06-007

Coronary small vessel disease and myocardial fibrosis over the spectrum of hypertrophic cardiomyopathy: an histopathological study

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Background & Objective: We assessed histopathology of microvascular disease (MD) in hypertrophic cardiomyopathy (HCM) and its relationship with myocardial fibrosis and myocyte alterations and compared pathology findings in obstructive (O)HCM versus endstage (ES)HCM cases
Method: Surgical septal myectomies of 27 patients with OHCM (mean age: 45.4 ± 13.5 yrs) and anterobasal septum specimens of 30 explanted hearts with ESHCM (mean age: 46.8 ± 12 yrs) were retrospectively analysed. MD presence, intimal/medial type and degree (mild: lumen stenosis <30%; moderate: >30% and <60%; severe >60%) were assessed in small intramural coronaries according to lumen diameter: 100-500 micron versus <100 micron. Myocardial fibrosis extent and replacement/interstitial types, and myocyte alterations were recognized.
Results: In 100-500 micron arteries MD was found in 93.3% of ESHCM specimens and in 100% of myectomies, causing severe lumen stenosis in 30% of explanted hearts and 25% of myectomies, and was mixed intimal/medial disease in 80% of ESHCM and 77.8% of myectomies. In <100 micron arterioles MD was less frequent and similar in ESHCM samples (73.3%) and myectomies (77.8%). Fibrosis was more frequent in explanted hearts (36.8% ± 20.4 vs 12.8% ± 8.46) ($p<0.001$), prevalently replacement type (53.3% vs 14.8%) ($p=0.005$). Diffuse myocyte vacuolization was found in only ESHCM specimens (23,3% vs 0, $p=0.011$)
Conclusion: MD is present over the entire HCM spectrum suggesting that it is a constant finding in HCM. Although myocardial fibrosis is present in both ESHCM and OHCM, replacement fibrosis along with advanced myocyte abnormalities are distinctive patterns in ES patients.

PS-06-008

Correlation of histological patterns in temporary artery biopsies with clinical symptoms and analytical data

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Background & Objective: Giant cell arteritis (GCA) is a systemic vasculitis that affecting large and medium vessels, mainly the temporal artery and other arteries of extracranial localization. We review a series of patients with clinical suspicion of GCA proved by a positive temporal artery biopsy (TAB). Our objective is to review the histologic inflammatory patterns in the TAB and their possible correlation with analytical and clinical data.
Method: Prospective study of patients with positive TAB between January of 2016 until January of 2018. Clinical data, included: age, sex, symtomatology, physical examination of the temporal artery, ESR, CRP, hemoglobin. Positive biopsies were classified into four categories: a) inflammation limited exclusively to the small vessels of the adventitia (SVV); b) vasa vasorum vasculitis (VVV); c) inflammation limited to the adventitia (ILA); and d) transmural inflammation (TMI). The presence of giant cells, trombosis and distrophic calcification was also noted.
Results: There were 12 female (57%) and 9 male (43%) patients with a positive TAB, with an average age of 78.9 years. Most of the TABs (90.5%) presented TMI, and only 2 cases (9.5%) had ILA. There were no cases with SVV or VVV. There were no significant differences between the correlation of the clinical and analytical data and the 2 patterns of inflammation observed. In all cases of ILA, the patients had headache, visual symptoms, jaw claudication, systemic symptoms and polymyalgia rheumatica. There were no cases of visual loss.
Conclusion: In our series we didn't observed differences between the patterns of inflammation and the analytical and clinical data. It is important to know these patterns of inflammation in the TAB to avoid false negatives.

PS-06-009

Mature cardiac myocyte hamartoma. Case report and review of literature

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Background & Objective: Primary cardiac tumours are rare and usually benign. Among these, hamartoma of mature cardiac myocytes (HMCM), are extremely rare, with only 23 cases reported in the literature. First described by Tanimura et al. in 1988, HMCM is characterized by localized, disorganized and hypertrophied mature myocytes. Herein we report a further case of HMCM and review the literature on issue.
Method: A 22-year-old woman, complaining of dyspnea and progressively worsening chest pain, was found to have on echocardiography a homogeneous intracardiac mass measuring 31x14mm on the wall of the right atrium. A right atrial resection was done.
Results: The surgical specimen measured 50 x 47 x 6 mm and weighted 24.4 g. Histologic examination of the lesion revealed striking hypertrophy of the myocytes, variably interspersed among interstitial fibrosis, blood vessels and scant adipose tissue. Additionally, scattered inflammatory cells comprising lymphocytes and histiocytes were seen. The myocytes showed disorganization, occasional vacuolization, and marked degenerative features with nuclear irregularities and hyperchromasia. The diagnosis of HMCM was made. After two years follow-up the patient is asymptomatic without signs of recurrence.
Conclusion: HMCM may be detected at any age or location in the heart, preferentially affect males, patients are usually symptomatic, and rarely may be associated with sudden death. Our case was similar to others described in the literature. Since HMCM share common features with other cardiac tumours, clinical diagnosis is quite difficult; therefore pathologists play an important role in the recognition of this entity. Surgery is an effective treatment (even after incomplete resection) in symptomatic patients.

Monday, 10 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-07 | Dermatopathology

PS-07-001

Cutaneous syncytial myoepithelioma: a case report

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Background & Objective: Myoepithelial tumours arising in the dermis, subcutaneous fat or soft tissue are exceedingly rare. Commonly, cutaneous myoepitheliomas behave in a benign fashion, however, local recurrence and metastasis have been documented. We aim to report a case of a morphologically distinct variant, designated cutaneous syncytial myoepithelioma, illustrating its histological and immunohistochemical characteristics and discussing possible differential diagnosis.
Method: A 31-year-old man presented with a 5 mm papular skin lesion, located in the right harm, treated by local excision. Specimen was routinely processed, sections stained with haematoxylin-eosin and immunostains performed.
Results: Histologically the tumour was located in the dermis, displaying expansile, solid sheet-like growth. Tumour cells were uniformly sized, epithelioid to histiocytoid, with ovoid to spindled shaped nuclei and

eosinophilic syncytial cytoplasm. Nuclei were vesicular, with fine chromatin, small or inconspicuous nucleoli and no significant pleomorphism. Intranuclear pseudoinclusions were frequent. Mitoses were scanty and necrosis was absent. The overlying epidermis displayed orthokeratosis. Immunohistochemical study showed diffuse positivity for EMA, S-100 protein and SMA. Keratin staining was multifocal. The deep margin was involved by the tumour.
Conclusion: Myoepithelioma`s morphology may lead to diagnostic pitfalls, particularly in the case of a dermal lesion with spindle or epithelioid cells, thus emphasizing the importance of applying a suitable immunohistochemical panel when a myoepithelial neoplasm is suspected. Since reliable criteria for malignancy are still not established and behavior is unpredictable, patients diagnosed with these lesions should maintain a long-term follow-up. At the time of writing, 11 months after surgery, the patient was alive and well, with no local recurrence identified.

PS-07-002
Diagnostic efficiency of CD1a immunostaining in the diagnosis of cutaneous leishmaniasis
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Background & Objective: CD1a is useful to detect amastigotes in Old World cutaneous leishmaniasis (CL) since it is acquired by leishmania from the host dendritic cells during the inflammatory response. However, its accuracy is unknown. Our aim is to study the efficiency of immunohistochemistry with CD1a in the diagnosis of CL.
Method: We retrospectively reviewed skin biopsies of proven CL based on direct examination, culture and kinetoplast DNA-polymerase chain reaction (PCR) from paraffin-embedded skin sections. For PCR analysis, specimens with a threshold cycle ≤ 32.8 were considered positive. Immunohistochemistry with CD1a (MTB1 clone) was performed. Cases without tissue for CD1a staining were excluded.
Results: Twenty-eight positive skin biopsies were included: 11 positive on direct examination and 17 positive on PCR. CD1a staining was positive in amastigotes in 27/28 cases (96%). All cases (5/5) of zoonotic CL (Leishmania Major) were CD1a positive and 96% of sporadic CL (L. Infantum) were CD1a positive. In comparison with PCR, the sensitivity, specificity, positive predictive value and negative predictive value of CD1a immunostaining were 96.4%, 50%, 93.1% and 66.7%, respectively.
Conclusion: Prior studies have reported a higher sensitivity for CD1a staining in Old World species of leishmaniasis than in New World cases (44). Our results confirm CD1a (MTB1 clone) has a high sensitivity and can be useful to highlight amastigotes in biopsies of Old World cutaneous leishmaniasis. However, there are significant limitations to this screening approach as CD1a has a low specificity in comparison with PCR from paraffin-embedded blocks.

PS-07-003
Clinical case: alopecia - unusual precursor B lymphoblastic lymphoma clinical manifestation
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Background & Objective: To introduce a case-based scientific research of unusual clinical manifestation of skin precursor B lymphoblastic lymphoma (B-LBL)/leukaemia (B-ALL) in a 40-year-old female patient with alopecia. This type of lymphoma is especially rare in skin as a primary tumour and primarily affects children under six years of age (more than 75 % of cases).
Method: In 2014, a 40-year-old female was appointed to dermatologist after six months of multiple alopecia patches on her scalp in frontal and parietal areas.
Results: Pathology diagnosis from the first skin biopsy was B-LBL/B-ALL. On PET-CT scan metabolicaly active lymphoproliferative disease was found on the top of the head, both sides of the shoulders and soft tissues of thoracic wall, as well as in a right ureter. High dose-CHOP chemotherapy was initiated consisting of cyclophosphamide, doxorubicin, vincristine and prednisone. After six months control PET-CT scan demonstrates partial response to treatment. Reconsultation of dermatologist revealed new multiple skin nodules. Pathology diagnosis remains the same as a first one.
Conclusion: Alopecia is autoimmune disorder characterized by patches of non-scarring alopecia usually affecting scalp and body hair. Approximately 2% of people worldwide have this disorder. Rarely one of alopecia cause could be malignant tumour. Precursor B lymphoblastic lymphoma (B-LBL)/leukaemia (B-ALL) constitutes approximately 10% of cases of lymphoblactic lymphoma and less than 10% of all skin lymphomas. Around 80-85% lymphoma cases are of precursor B-cell phenotype. The B-LBL frequently present in the skin, lymph nodes and bone. In adults, B-ALL overall complete remission rate is 60-85%.

PS-07-004
Driver mutations, PD-L1 expression and clinicopathological correlation in desmoplastic melanomas
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Background & Objective: Desmoplastic melanomas (DM) are a rare subtype of spindle cell malignant melanoma, characterized by a delay in the diagnosis and frequent local recurrences. The aim of the study was to collect the clinicopathological characteristics of a series of 27 DM along with investigating actionable driver mutations and the expression of PD-L1.
Method: From formalin-fixed samples hot spot mutations of genes AKT1, ALK, BRAF, CTNNB1, DDR2, EGFR, ERBB2, ERBB4, FBXW7, FGFR1, FGFR2, FGFR3, KRAS, MAP2K1, MET, NOTCH1, NRAS, PIK3CA, PTEN, SMAD4, STK11 and TP53 were investigated in 11 cases using NGS Oncomine Focus Assay (Thermo Fisher Scientific). In addition, in 10 cases BRAF mutations were studied by RT-PCR. PD-L1 expression was investigated by immunohistochemistry using 22-C3 antibody (DAKO) in 23 cases.
Results: Tumours occurred in 20 men (74%) and 7 women (26%), with a median age of 65 years. The most frequent location was the head and neck region. Twenty tumours were histologically pure and 7 mixed-type (with conventional melanoma component). Lymphatic and haematogenous metastases were more frequently found in mixed-type DM. Overall, 33% of DM harboured BRAFV600 mutations; 45,5% TP53 mutations; 9% MET mutations and 0SMAD4 mutations. Seven out of 23 cases expressed PD-L1 (30%).
Conclusion: In conclusion, the mixed-type DM have a worse outcome. BRAFV600 mutations are more frequently found in this DM type; whereas pure DM are usually BRAF wild-type and have frequent TP53 mutations. We have not found a correlation between the PD-L1 expression with the clinicopathological characteristics of DM.

PS-07-005
Chondroid syringoma: analysis of clinical-pathological features. A series of 12 cases
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Background & Objective: Chondroid syringoma (CS) or mixed tumour (MT) of the skin is a rare, bening neoplasm. The most frequent location

are head and neck. It has an inespecific clinical debut and the diagnosis is histopathological. We present 12 patients with skin lesions with pathological diagnosis of CS and their clinical-pathological features.
Method: A search with a diagnosis of MT is performed through the database of the Pathological Departament of the General University Hospital of Ciudad Real (GUHCR) in 8 years, and medical historial are consulted with the electronic program of the Dermatology Departament of the GUHCR. Clinical data and histopathological features of the skin lesions were collected and reviewed.
Results: 12 cases coded as MT of the skin were retrieved. 3 women and 9 men between 29 and 73 years old. Most lesions were on face and scalp, and most frequent presentation was a skin-colored subcutaneous nodule. None was clinically suspected. Histologically, a cellular proliferation in dermis was observed, it was constituted by epithelial and mesenchymal origin cells with a background fibromyxoid matrix and adipose metaplasia in almost all cases. 11 corresponded to apocrine type and 1 to eccrine type. No recurrences were found.
Conclusion: CS should be considered in the differential diagnosis of subcutaneous nodules in head and neck in middle-aged patients. Total excision is the preferred treatment. CS has good prognosis and low potencial of recurrence. It´s a rare tumour whose diagnosis is histological, and we provide data of clinical-pathological correlation and practical histopathological data for help to the differential diagnosis.

PS-07-006
Variation of dendritic cells distribution patterns in mycosis fungoides vs. inflammatory dermatosis
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Background & Objective: Our study aims to identify and characterize variation of distribution of dendritic cells in inflammatory dermatosis and in mycosis fungoides, useful in differential diagnosis and understanding the pathophisiology of these lesions.
Method: Our study included a cohort of 78 patients: 22 with psoriasis, 26 with spongiotic dermatitis (SD) and 30 with mycosis fungoides (MF). Their diagnostics were based on histopathological and imunohistochemical stains. Specific markers for DCs were performed (CD1a, Langerin and CD11c), in order to evaluate the density, localization and distribution pattern of DCs.
Results: In all cases, a high number of DCs was found in epidermis diffusely distributed. The number of intraepithelial DCs was higher in inflammatory dermatosis. Second more frequent pattern was diffuse distribution in papillary dermis. More than a half of inflammatory dermatoses had both diffused DCs in epidermis and in papillary dermis. In comparison to SD and MF, many cases of psoriasis had nodular distribution of DCs in papillary dermis. Only in MF were found DCs dispersed in reticular dermis.
Conclusion: Distribution patterns of DCs emphasized by immunohistochemistry may help in MF and inflammatory dermatosis differential diagnosis.

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PS-07-007
Malignant blue melanoma: an institution experience in 4 cases
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Background & Objective: Malignant blue melanomas (MBM) are melanomas arising in association with blue nevi (BN) or simulating BN, representing a heterogeneous, controversial set of melanocytic tumours. No consensus exists for diagnostic histological criteria or prognostic indicators. MBM differential diagnosis includes mainly atypical BN, melanocytoma and metastatic melanoma.
Method: 212 BN and related tumours were diagnosed in 9 years in our hospital; they include 7 atypical BN and 4 MBM.
Results: Mean MBM patient age was 44 years (range:17-73); there were 2 males and 2 females. The tumours were commonly located on the trunk region (50%). MBMs were typically situated in mid/deep dermis with frequent subcutaneous involvement, composed of large, variable pleomorphic, spindled and/or epithelioid cells. Mean Breslow thickness was 5,28 mm (range: 2,85-6,8 mm); mean mitotic figure count was 5/mm2 (range: 2-11/mm2); one tumour was ulcerated; two MBMs had lymphovascular invasion and 2 perineural invasion. One tumour was negative for HMB45 staining; all cases had Ki67 proliferation index >10%. One MBM patient died of disease (thigh tumour with V600 B-raf mutation and gain of chromosomes 3q,5,8,15,18,20,22,X revealed by comparative genomic hybridization; inguinal lymph nodes and liver metastases after 2.5yrs; vemurafenib treatment till death, 5yrs after first diagnosis); all the other 3 patients are alive and free of disease (4, 46, 44 months follow up).
Conclusion: In our study, MBM showed a predilection for trunk region, large Breslow index and frequent lymphovascular and perineural invasion; overall prognosis apparently is more favourable than classic melanoma with similar stage.

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PS-07-008
Cutaneous amyloidosis as major manifestation of systemic AL-amyloidosis
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Background & Objective: Cutaneous involvement in acquired systemic immunoglobulin light chain (AL) amyloidosis occurs in 30-40% of patients. We report a case of systemic lambda-type AL-amyloidosis, revealed by exuberant persistent cutaneous lesions.
Method: A 70-year-old Caucasian man was referred to our hospital due to hard tight edema, and plaque-like, purpuric and ecchymotic lesions involving the anogenital and inguinal areas, with asthenia and weight loss in the last month. There was no evidence of macroglossia or peri-orbital purpura. Initial routine laboratory tests were within normal values and skin biopsies were performed.
Results: Histology showed diffuse homogenous, hyaline deposits in the dermis, subcutis and vessel walls, consistent with amyloid (Congo-red/polarised light) of the AL-type (immunohistochemistry). The patient developed aspiration pneumonia, after a colonoscopy, complicated by septic shock and multi-organ failure. Serum protein electrophoresis showed no monoclonal peak, but free-light-chain evaluation revealed: lambda - 297mg/L (normal: 110-240mg/L); kappa - 51mg/L (normal: 200-440mg/L) and kappa/lambda ratio - 0.17 (normal: 1.35-2.65), consistent with light-chain plasma cell dyscrasia. Ecocardiography, stage 3/4 chronic kidney disease and abdominal/pelvic CT-scan findings were consistent with advanced systemic AL-amyloidosis. Despite best supportive care, the patient died five months after diagnosis.
Conclusion: AL-amyloidosis can evolve progressively to advanced stages, without specific clinical features, but macroglossia and peri-orbital purpura (<1/3 of cases), not present in our case, should suggest this diagnosis. Clinicians should be aware that cutaneous involvement, despite occasional, may occur in flexural skin, that should be evaluated in a skin biopsy, to establish the diagnosis of AL-amyloidosis, as in the herein case.

PS-07-009

Compound blue nevus (Kamino Blue Nevus): an unusual benign melanocytic lesion

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Background & Objective: Blue nevi are a subset of melanocytic proliferations containing cells reminiscent of the embryonal neural crest–derived dendritic melanocytic precursors. They are common specimens in a general pathology practice, but some of their rare variants may pose diagnostic difficulty. An example of one of these variants is the Compound Blue Nevus (CBN) or "Kamino Blue Nevus".
Method: We present a case of a 42-years-old female with a pigmented lesión in the right submammary región. An exision was performed, due to an increase in size in the course of the previous year.
Results: The surgical specimen was a 6 mm punch biopsy, with a 4 mm brownish, well delimited papule in its center. Histologically, melanocytic proliferation was observed at the level of the papillary and superficial reticular dermis. The melanocytes had a dendritic morphology, with a vaguely congenital distribution. A minute intracytoplasmic melanin pigment granules were identified. In the epidermis, a junctional melanocytic component, in the form of single cells was found, without evidence of theca formation. Immunohistochemistry highlighted the unique histopathologic feature of CBN, namely, single dendritic melanocytes at the dermoepidermal junction with striking intraepidermal prolongations.
Conclusion: CBN is a distinctive variant of blue nevus that may mimic cutaneous melanoma both clinically and dermoscopically. The junctional component of linear melanocytic proliferation in a blue nevus is a rare finding, but an important diagnostic clue to the recognition of CBN.

PS-07-010

Cellular dermatofibroma – a challenging diagnosis

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Background & Objective: Cellular dermatofibroma (CDF) is a dermatofibroma variant with higher rate of local recurrence and, exceedingly rare, distant metastases.
Method: We reviewed 21 cases of CDF diagnosed between 2012-2017 in our department – 6.7% of a total of 312 dermatofibromas; immunohistochemistry for CD34, SMA, Desmin, S100 protein, CD68, factor XIIIa and Ki67 was performed.
Results: The lesions are mostly located on the limbs (upper 52.38%, lower 33.33%, the remainder on trunk 14.28%) with dimensions between 0.6/0.4/0.4-2.5/2.5/2cm; none on head and neck; 3 cases were associated with previous trauma. Male-to-female ratio was 1:2; median age 42 (between 15-64 years). Histopathologically, the lesions were deeply seated with evident grenz zone, highly cellular, with densely fascicular growth pattern, tend to be very infiltrative, 11 extending into the superficial subcutis, 6 being incompletely excised and 4 ulcerated. Typical mitoses were common, 14 cases showed 1-6 mitoses/10HPF; central necrosis was found in 2 cases. Focal positivity for CD34, SMA and Desmin was noted in a minority of cases. Expression of Factor XIIIa was a constant feature. Ki67 index ranged between 0-5%. S100 and CD68 were negative.
Conclusion: Given the high rate of recurrence and the possibility of metastases, even extremely rare, complete surgical excision is mandatory and correct identification of this variant is important for differential diagnosis and prognosis, especially to avoid misdiagnosis of a possibly aggressive lesion such as dermatofibrosarcoma protuberans and leiomyosarcoma. Factor XIIIa is a valuable immunohistochemical marker for differential diagnosis.

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PS-07-011

Hashimoto-Pritzker histiocytosis: presentation of a case and literature review

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Background & Objective: Hashimoto-Pritzker histiocytosis (HPH) is a entity discribed in 1973 as a subtype of Langerhans histiocytosis. It is an infrequent, usually solitary, congenital, cutaneous lesion but always self-healing with an excellent prognosis. We review and analyze the indexed literature to date.
Method: Using the PSPP statistical program, we compiled all the HPH cases published in the PubMed database, analyzing the variables sex, age, lesion size, location, type of injury, resolution times, follow-up and extracutaneous commitment.
Results: We compiled 84 articles describing a total of 139 cases. We found that HPH cases showed a similar proportion of men and women. In 85% of the cases, the lesions were congenital. The size of the lesions was between 5 and 10 mm in 63% of the cases, presenting more frequently as nodular lesions. In 57% the lesions were multiple, with no predilection in their corporal distribution. Only 7% presented extracutaneous involvement, with the affected organs being bone, liver, kidney and lung. The lesions disappeared more frequently between 2 and 6 months of age.
Conclusion: HPH is a relatively recent and infrequent entity that, due to its self-resolution, is likely to be underdiagnosed, with lesions disappearing within a few months of birth.

PS-07-013

Papular epidermal nevus with "skyline" basal cell layer (PENS), and PEN syndrome in triplets siblings

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Background & Objective: Classical epidermal nevi can have an inespecific or subtle histologic pattern that usually needs clinical correlation. However, papular epidermal nevus with "skyline" basal cell layer has characteristic histological features that allow pathologists to make specific diagnosis. 50% of the patients have PENS syndrome, which includes neurological and ophthalmological anomalies apart from polygonal shaped hyperkeratotic papules since birth.
Method: Triplets siblings came up to dermatology department with multiple papular skin lesions in trunk, neck and extremities since birth. The two brothers developed neuro-ocular anomalies; one had squint and mental retardation, and the other one language development problems. Female patient only has skin lesions up today. Sin biopsies were performed of two patients.
Results: Histological examination showed broad, rectangular rete ridged achantosis with characteristic arranged basal cells with palisated nuclei. Clinical data and additional test (MR) were recopilated and studied, then brothers were diagnosed as PENS syndrome while female has PENS limited to skin.

Conclusion: Both histological and clinical features of PENS are diagnostic, hence clinicians and pathologist should be aware of this syndrome to achieve early diagnostic and neuro-development evaluation or treatment. PENS syndrome is not related to epidermal nevi syndrome and has no FGFR3 nor PIK3CA mutations.

PS-07-014

Protein p16 role in seborrheic keratosis

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Background & Objective: Seborrheic keratosis (SK) is a disease of unknown etiology and pathogenesis. Details of the cell cycle destruction by the SK are not revealed despite a number of studies.
Method: To study the p16 expression in patients with multiple and single SK. An immunohistochemistry test with monoclonal antibodies to p16 was accomplished, 20 SK served as a material for the test, which were obtained from patients with multiple SK – 10 patients, and single SK (not more than 10 elements on the skin) - 10 patients. Clinical examination of patients was being conducted, using data from the anamnesis of concomitant somatic pathology.
Results: Intense cytoplasmic and nuclear staining of tumour cells was revealed by individuals with multiple SK in 70% by immunohistochemical test with monoclonal antibodies to p16, 30% of the staining was moderate, diffuse. A positive reaction with antibody to p16 was diffuse, weak by patients with single SK in 80% of the cases, stain of the single cells of the basal layer nucleus was recorded. In 20% the colour of the cells cytoplasm was intense, but as separate focuses, in these cases was revealed insulin resistance. The presence of insulin resistance was revealed from anamnesis by all patients with multiple.
Conclusion: The connection was found between the intensity of the p16 expression and the prevalence of SK. Given the presence of insulin resistance in the anamnesis of patients with multiple SK, an assumption was made about an indirect effect of the p16 expression on hyperinsulinemia. The presence of focal intense reactions with antibodies to p16 by patients with single SK can serve as a predictor of eruptions dissemination in future.

PS-07-015

Squamous cell carcinoma in situ associated with cutaneous infiltrate of chronic lymphocytic leukemia

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Background & Objective: Chronic lymphocytic leukaemia (CLL) is a neoplasm characterized by clonal expansion of B-lymphocytes with distinct morphology and immunophenotype. Although CLL typically follows an indolent course, it is well established that patients have a greater increased risk of developing a second malignancy mostly skin cancer non-melanomas due to ultraviolet radiation exposure and immunosuppression. CLL is the most common type of leukemia in adults, while dermatological literature reporting CLL is limited.
Method: We present an 89-year-old spanish woman with CLL and basal cell carcinoma. She was referred to a dermatologist who noted an erythematous crusted patch on the right temple. There was no clinical suspicion of clinical involvement by CLL. There was no improvement after treatment with topical ingenol mebutate, so a biopsy was obtained.
Results: A conventional histologic examination revealed atypical keratinocytes and a dense dermal infiltrate of monomorphous, small lymphocytes with round nuclei, a regular chromatin dispersion pattern and scarce cytoplasm. The neoplastic lymphocytes were shown to be CD20+ and CD5+. CD 23 and CD43 were unreactive.
Conclusion: CLL characterized by highly biological heterogeneity and variable clinical course. CLL infiltrating the skin is uncommon and can present in many different ways. A dense sheet of monomorphous lymphoid cells should raise the possibility of leukemic infiltration of the skin and may surround epithelial neoplasms such as basal cell carcinoma and squamous cell carcinoma. Treatment is only indicated in case of active disease and may be involved in the keratinocyte dysplasia. The pathogenic relationship between CLL and skin neoplasia is unclear.

PS-07-016

Wrist paraffinoma after self-injection of vaseline: a case report of very late formation

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Background & Objective: Paraffinoma is the rare condition characterized by a replacement of normal subcutaneous tissues by cystic spaces. The changes develop after injection of oily substances and usually have the facial and penile localization.
Method: We present a case of 39-year-old man with paraffinoma of the right wrist dorsal surface after vaseline self-injection performed 25 years ago. The patient has a history of methadone addiction and chronic virus hepatitis C. Three weeks prior his visit patient had superficial wrist injury. Physical examination revealed local inflammation, dermal necrosis, ulceration and solid subcutaneous mass along the wrist dorsal surface reducing the extension of fingers. Debridement surgery followed by examination of removed tissues by light and electron microscopy was performed.
Results: Histopathological examination revealed panniculitis characterized by variably sized and shaped cysts with a Swiss cheese appearance surrounded by multinucleated giant cells and lymphohistiocytic infiltrates. Ultrastructurally, histiocytic intracellular and extracellular vaseline-containing vacuoles were demonstrated. Surgical excision requiring further reconstruction of the patient's wrist dorsal surface was performed, but he escaped from the hospital next day. The patient was admitted to the hospital with a repeated infection after two months and underwent another debridement surgery. Wet-to-dry dressings were applied to obtain granulations of the defect.
Conclusion: Wrist paraffinomas are ultra-rare conditions requiring damaged tissues excision followed by reconstructive surgeries for enhancing wrist functions. Reconstruction is impracticable due to patient's attitude. Complications associated with oily injections may be extremely delayed in spite of putative immunosuppression.

PS-07-017

Acral nevus (melanocytic acral nevus with intraepidermal ascent of cells) in a child. Report of a case and differential diagnosis

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Background & Objective: Acral melanocytic nevi may represent a diagnostic challenge having sometimes worrisome morphological features that overlap with melanoma. Herein we describe a case of acral nevus in a very young child and the differential diagnostic features with melanoma.
Method: A 3 years old child, with a dark brown lesion on the foot, after clinical examination, was referred to surgery. Macroscopic, the resected

skin specimen showed a brown, light irregularly shaped lesion of 5x4 mm in diameter. Microscopic examination was performed.
Results: Histologically, at low magnification, the melanocytic tumour was composed of junctional melanocytes, with only a few dermal melanocytes. The lesion showed a good symmetry with no mitosis or fibrotic change. Focally, „spotty" pigment in the stratum corneum was also noted. Interestingly, there was presence of scatter melanocytes throughout the epidermis, suggesting a pagetoid spreading (so called "Maniac nevus"). However, these pagetoid melanocytes had banal, bland morphology. There was no irregular lympho-histiocytic infiltrate in the dermis.
Conclusion: Acral melanocytic nevi may present atypical characteristics and constitute a difficult diagnosis. A careful evaluation of histologic and clinical features such age of the patient and size of the lesion, are of paramount importance to avoid overdiagnosis of melanoma.

PS-07-018
BRAF mutation testing as a diagnostic tool of undifferentiated/dedifferentiated melanoma
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Background & Objective: BRAF mutations are associated with malignant melanomas (MM) in about 40-50% of cases with V600E which comprises up to 90%. MM, particullary metastases, tend to present with an aberrant immunohistochemical (IHC) features and lack an evidence of melanocytic differentiation. Histologically, these cases are more likely to be poorly differentiated including i.e. spindled or sarcomatoid types.
Method: From archive data bases 9 cases of MM with a second undifferentiated malignancy/metastatic MM were identified. The broad panel of MM IHC were performed and BRAF mutation status was investigated whenever the formalin fixed paraffin embedded material was available.
Results: A group of 9 cases of metastatic MM, with male to female ratio 3:6 and median age 44 years (range 27 to 57 years). Sites of involvement were soft tissue (5/56%), bone (1), axillary lymph nodes (1), adrenal gland (1) and ovary (1). Mean time from primary MM to metastasis was 55 months (range 20 to 108 months). All cases showed a partial or complete loss of the IHC melanocytic markers; all of them were negative for HMB-45 (0/9) and Melan A (0/9) whereas lack of S100 was observed in 6 cases (3/9). BRAF V600E mutation was detected in 6/9 cases (67 %) respectively.
Conclusion: The presence of BRAF V600E mutation in poorly differentiated or undifferentiated malignancies should be helpful diagnostic tool for patients with MM history. Undifferentiated/dedifferentiated metastatic melanoma is likely under-recognized and frequently mistaken for undifferentiated sarcoma or other neoplasms. BRAF V600E is a helpful surrogate marker in classifying such difficult cases and is important in choosing treatment regiments.

PS-07-019
Correlation between genetic mutations and clinicopathologic features in a series of acral melanomas
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Background & Objective: Oncogenic activating BRAF mutations, seen in 40-60% of melanoma, are also seen in acral lentiginous melanoma (ALM), although at a lower incidence. This is the first study from Singapore to correlate molecular findings in acral melanomas with clinicopathologic features and compare with other Asian data.
Method: 142 cases of melanoma with molecular analysis for mutations in exon 15 of the BRAF gene, and exons 9,11,13, and 17 of the ckit in genomic DNA by polymerase chain reaction amplification and direct Sanger sequencing, were retrieved from the Singapore General Hospital files (2007-18)
Results: Of 142 cases, 55 (38%) were cutaneous, 45 (32%) acral and 42 (30%) mucosal. Of 45 acral tumours, 36/45 (80%) were BRAF negative and 9/45 (20%) positive. Of 28 acral cases with ckit mutational analysis, 21/28 (75%) were ckit negative, 5/28 (18%) positive, and 2/28 (7%) inconclusive. The majority of BRAF positive were Chinese ethnic group (6/9), female (7/9), mean age 56 years, located at non-pressure sites (7/9) and the foot (7/9. Tumours which were positive with either BRAF or ckit mutations showed similar incidence of ulceration (60%), lower than cases of BRAF negative (75%) or ckit negative (71%) tumours. ckit positive tumours had the highest incidence of metastasis (80%), and ckit negative the lowest (43%). No major differential was seen in the incidence of metastasis between BRAF positive or negative cases.
Conclusion: The BRAF positive mutation rate in Singaporean ALM was comparable with data from China, Korea, Taiwan and Japan. Findings suggest dyssynchronous incidence of ulceration and metastasis.

PS-07-020
Screening for mismatch repair mutations in sebaceous neoplasm
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Background & Objective: Sebaceous gland neoplasms (SGN), including sebaceous gland adenomas and carcinomas (SGAs-Cs), are rare skin tumours occurring sporadically or as a phenotypic feature of the Muir-Torre syndrome (MTS). MTS patients tend to have multiple malignancies throughout life (most commonly colorectal carcinomas) and require close surveillance; therefore, differentiation between patients with MTS and sporadic SGN has important implications. Our goal is to evaluate the loss of MMR proteins expression using immunohistochemistry as universal screening in sebaceous neoplasm to distinguish MTS from sporadic SGN.
Method: We retrospectively evaluated MLH1, PMS2, MSH2, MSH6 IHC in all the sebaceous neoplasms diagnosed in our hospital in the period 2012-2017. Eleven were SGAs and five were carcinomas.
Results: Three of the eleven sebaceous adenomas demonstrated loss of expression of a MMR dimer (27%). Two of them showed loss of MSH2-MSH6 (18%) and the other one showed loss of MLH1-PMS2 (9%). Colorectal carcinoma was recently diagnosed in one of the patients, both of neoplasms with MSH2-MSH6 loss of expression. In this case there is a great suspicion of MTS. None of the five SGCs showed loss of expression of MMR proteins.
Conclusion: The percentage of cases with loss of expression is high so universal IHC screening of SGN should be investigated as a first line test to identify MTS and to distinguish from sporadic SGN. It is a cost-effective screening approach, available in most departments.

PS-07-021
A curious cutaneous collision tumour: desmoplastic trichoepithelioma and melanocytic nevus
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Background & Objective: Collision tumours are defined as neoplasms of two distinct lineages occuring at the same anatomic location. Various combinations of cutaneous collision tumours have been described, most common of these being basal cell carcinoma and melanocytic naevus. Our aim is to report this rare collision tumour –occuring on the face, which was composed of a desmoplastic trichoepithelioma and melanocytic nevus.
Method: A 61-year-old, otherwise asymptomatic woman presented with a lesion located on her right cheek; physical examination revealed a firm, well-defined, skin-colored papule, 1 cm in maximum diameter.

Results: An excisional biopsy was performed for this lesion. Histopathologic examination showed a biphasic tumour composed of narrow strands of diminutive basaloid cells without atypia or mitoses, and interspersed with keratinous cysts, disposed within a desmoplastic stroma, occasional calcifications and ossifications noted. The preceding were intimately mixed with intradermal nests of melanocytes. Immunohistochemically Melan-A positivity was seen in these intradermal naevomelanocytic nests, and melanocytes along the basaloid cell strands. The diagnosis given was - collision tumour with desmoplastic trichoepithelioma and melanocytic nevus components
Conclusion: Cutaneous collision tumours composed of desmoplastic trichoepithelioma and melanocytic naevus are rare. Their pathogenesis is uncertain, though it has been suggested that these synchronous components may be purely coincidental or might afford an example of epithelial induction by melanocytic nevi. Wariness of rare collision tumours, such as this, affords diagnostic accuracy, translating into accurate incidence and possibly unravelment of their pathogenesis.

PS-07-023
Expression of epithelial-to-mesenchimal transition markers in the foreskin of males with lichen sclerosus
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Background & Objective: Male genital lichen sclerosus (LS) is a chronic and atrophic mucocutaneous condition with complicated by pathological phimosis, paraphimosis and urethral stricture. Epithelial-to-mesenchimal transition (EMT) could play a role in pathogenesis of this disorder. To study the expression patterns of some markers of the EMT in foreskin from males with LS complicated by scarring phimosis.
Method: The study groups included 10 cases of LS and 10 cases of LS complicated by scarring phimosis. Controls were 10 cases of circumcision in healthy males. IHC was performed with the antibodies to cytokeratin Pan (CK Pan), vimentin and β-catenin.
Results: In healthy foreskin CK Pan and β-catenin expression was noted in keratinocytes of all skin layers. In LS forskin (with and without phimosis) loss of β-catenin expression was seen in basal and parabasal layers. Some CK Pan positive keratinocytes (single and small groups) not connected to epidermis were seen within the upper papillary dermis. Vimentin expression in healthy foreskin was seen in skin dendritic cells. In LS cases foreskin the number of vimentin positive dendritic cells was elevated. In LS cases complicated by the scarring phimosis focal vimentin expression in keratinocytes of basal and parabasal layers was also seen.
Conclusion: Disturbances in the expression patterns of some epithelial and mesenchimal markers in the foreskin with LS are shown. Further studies are needed to determine the role of epithelial-to-mesenchimal transition role in the pathogenesis of male genital LS.

PS-07-024
Trap for pathologists: TRAPP - a case report
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Background & Objective: Cutaneous pseudolymphomas refer to a group of benign reactive T or B cell lymphoproliferative processes that mimic cutaneous lymphomas. T cell rich angiomatoid polypoid pseudolymphoma (TRAPP) of the skin is a unique form of T cell rich cutaneous pseudolymphoma and only 18 cases described until now in English literature. This entity is recently described and pathogenesis is unknown.
Method: The paraffin-embedded block, H&E, and immunohistochemistry stained sections sent us for consultation with diagnosis as "suspicious for cutaneous lymphoma".
Results: A 15-year-old girl suffered from a swallowing on her back and the lesion is totally excisioned. The specimen consisted of 0,5cm diameter lesion on the 1,5x1cm dimensions skin. Microscopically polypoid lesion contained thin Grenz zone, hypervascularity under the atrophic epidermis and in the dermis perivascular nodular CD3 predominant lymphocytic infiltration are noticed. Histopathological and immunohistochemical results were compatible TRAPP of skin.
Conclusion: Misdiagnosis of the cases are usual and awareness of the TRAPP is important. Especially epithelioid hemangioma and low-grade cutaneous lymphoma are most frequent concerns but should not fall into the trap of lymphoma and be aware of TRAPP are the main goal of it.

PS-07-025
Can numeric maturation value be used as prognostic indicator and diagnostic tool in cutaneous melanomas (a morphometric study)?
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Background & Objective: Some melanocytic lesions can be difficult to diagnose because of ambiguous histological and immunohistochemical features. Morphometric features of melanocytes in the upper and lower parts of the skin may help to differentiate challenging lesions from melanomas.
Method: We studied 28 cases of cutaneous melanomas (CM), 34 cases of dysplastic nevus (DN) and 40 cases of ordinary melanocytic nevus (OMN). All cases were immunostained with Sox-10. The nuclear areas of 30 melanocytes were measured on each upper (U) and deep (D) parts of the skin in all cases by using image J analysis program. Then, a maturation index (U/D) was calculated for each case. Also cutaneous melanomas were categorized into two groups showing pseudomaturation or not.
Results: Mean maturation index was 1.02±0.27 in CM, 1.24±0.29 in DN and 1.59±0.32 in OMN, respectively. There were statistically significant differences between CM - DN (p=0,002) and DN - OMN (p=0,001) for maturation index. According to log-rank test, there was no significant difference between survival distributions of two melanoma groups (p=0.438).
Conclusion: Calculation of maturation index can be used as a supporting tool for the diagnosis of challenging cases.

PS-07-028
Autophagy related LC3A-expressing stone-like structures in keratoacanthoma
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Background & Objective: Keratoacanthoma (KA) is a common cutaneous lesion, of unknown etiology. The complexity of the lesion has raised doubts regarding the biologic behavior of the disease. In previous studies we showed that LC3A+ stone like structures (SLS) is a tumour-specific marker for epithelial malignancies. Here we examined the expression of SLS in KA.
Method: We assessed immunohistochemically the expression of LC3A protein in 85 KAs. We also examined the Ki-67 proliferation activity and the nuclear expression of mutant p53 protein.
Results: Forty % the examined cases (34/85) expressed a diffuse cytoplasmic LC3A expression pattern (range from 0-70%, median 0%). The SLS pattern, however, was evident only in 4 of the 85 KAs, (4.7%). The p53 oncoprotein was expressed in 1-90% of cells (median 30%), while the Ki-67 index was expressed in 1-50% of nuclei (median 5%). Neither of these two parameters nor the diffuse cytoplasmic LC3A staining was correlated significantly with the expression of SLSs.

Conclusion: SLSs have been linked with an aggressive tumour behavior. The 4.7% expression of SLSs found in KAs may represent a very small fraction of the disease with aggressive biological behavior. Whether an increased LC3A related autophagic activity is a feature defining malignancy of KAs demands further investigation in cases with clinical progression of the disease.

PS-07-029

YAP nuclear localisation in cutaneous melanoma

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Background & Objective: YAP, an effector molecule of Hippo signaling pathway, is expressed at high levels with strong nuclear localization in a number of cancers, including malignant melanoma. In this study, we confirmed a pro-invasive ability of cutaneous melanoma with YAP nuclear expression and analyzed a prognostic role of YAP in cutaneous melanoma that affects metastasis to lymph node and distant organ.
Method: We performed immunohistochemical staining of YAP on formalin-fixed paraffin-embedded (FFPE) tissue.
Results: YAP nuclear localization was identified in 63 cases out of 140 invasive melanomas (45.0%). YAP nuclear localization was more frequent in acral lentiginous and nodular types (P=0.0072) and cutaneous melanomas with YAP nuclear localization demonstrated increased mitotic activity rather than cutaneous melanomas with YAP cytoplasmic localization did (P=0.0490). Cutaneous melanomas with YAP nuclear localization invaded deeper (P<0.0001), more frequently metastasized to the lymph node (P=0.0004), and more frequently metastasized to the distant organs (P<0.0001) than cutaneous melanomas with YAP cytoplasmic localization. In survival analysis, melanoma patients with YAP nuclear localization had poorer disease-free survival (P<0.0001) and overall survival (P=0.0007) using Kaplan-Meier curve. YAP nuclear localization was an independent parameter affecting lymph node metastasis (H.R: 2.270, 95.0% CI: 0.914-5.637, P=0.077) and distant metastasis (H.R: 3.206, 95.0% CI: 1.032-9.961, P=0.044).
Conclusion: Cutaneous melanomas with YAP nuclear localization had histological features of subtype-specificity, increased mitotic activity, and pro-invasiveness with comparison of cutaneous melanomas with YAP cytoplasmic localization. Moreover, YAP localization is expected to be a useful prognostic marker in patients with invasive cutaneous melanoma.

PS-07-030

The histone modification H3K27me3 is reduced in MCPyV-negative Merkel cell carcinomas

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Background & Objective: Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine skin cancer and 80% cases are associated with Merkel cell polyomavirus (MCPyV). Gene expression and chromatin state are regulated by epigenetic mechanisms including histone modification. Loss of histone modification H3K27me3 has been found in some cancers such as malignant peripheral nerve sheet tumours or paediatric high-grade gliomas. We investigated the association of histone modification H3K27me3 with MCPyV status or prognosis in MCCs.
Method: 42 MCC cases used were 20 MCPyV-positive MCCs, 16 MCPyV-negative cases of combined MCC and squamous cell carcinoma (SqCC) and 6 MCPyV-negative MCCs without combined tumours. FFPE sections of MCCs were immunohistochemically stained with anti-H3K27me3 antibody and evaluated using H-score.
Results: The histone modification H3K27me3 was significantly reduced in MCPyV-negative MCCs than MCPyV-positive ones (p=0.001). In 22 MCPyV-negative MCCs, H3K27me3 was significantly reduced in 16 combined MCC and SqCC cases than 6 pure MCC cases (p=0.027). There was no statistically significant difference between the histone modification H3K27me3 and prognosis.
Conclusion: The differences of the histone modification H3K27me3 among MCPyV-positive MCCS and two MCPyV-negative MCC subtypes suggest that there must be the different mechanisms in carcinogenesis among these three subtypes.

PS-07-032

Relevance of perineural invasion in cutaneous squamous cell carcinoma: prognosis and benefits of radiotherapy

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Background & Objective: Cutaneous squamous cell carcinoma (CSCC) with perineural invasion (PNI) has a poor prognosis. Postoperatory radiotherapy (PORT) has been commonly implemented in these cases. Nevertheless, the benefit of PORT in the management of CSCC with PNI is still not well-established.
Method: In this retrospective multicenter study we evaluated a cohort of 110 CSCC patients with PNI. Based on PNI caliber, all cases were subdivided into two groups (> 0.1mm and < 0.1mm). PORT efficiency and clinical outcome were determined for each group.
Results: Patients with PNI > 0.1mm showed a clear benefit of PORT, as demonstrated by long-term survival on both univariate analysis and Cox regression models. However, patients in this group showed a persistent risk of poor outcome (5-fold), metastasis, and death (4-fold). On the other hand, patients with PNI <0,1 mm did not show any benefits with PORT.
Conclusion: Our results seem to indicate that CSCC patients with PNI greater than 0.1mm show an improved clinical outcome after PORT. PORT, however, does not show such clear benefits in cases with PNI of small-caliber nerves.

PS-07-033

Clinicopathological features of melanomas in our university and comparison of meta-analysis in a specific region

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Background & Objective: Malignant melanomas are the most common cause of deaths from skin tumours and the incidence is increasing in the world. The studies including descriptive meta-analysis of this tumour in Turkey are limited
Method: Clinicopathological data of melanoma patients between 1998 and 2018 in Düzce were re-evaluated and compared with meta-analysis consisting 7718 cases in the last 32 years of melanomas in Turkey.
Results: In our study, 39 cases were invasive melanoma, 10 cases were in-situ melanoma and 11 cases were extracutaneous melanoma. While 33 (55%) cases were male (M), 27 (45%) cases were female (F); male / femail ratio was 1,22. Mean age was 57,6. Turkey's male/female ratio was 1,21 and mean age 55,73. The most frequent localization in our series was head and neck; but, lower extremity in Turkey. The most common cutaneous histopathologic subtype was nodular malignant melanoma, followed by superficial spread malignant melanoma, acral lentiginous melanoma and lentigo malign melanoma, respectively. However, superficial spreading malignant melanoma was the most common type in Turkey. In situ melanoma rate was also higher in Düzce compared with Turkey (0,25 vs 0,05).
Conclusion: The industrialization type and sociocultural characteristics of the region may be related to these differences. On the other hand, early detection of the lesions is important for prognosis.

PS-07-034

Histopathological features and Braf status in invasive malignant melanomas: a single center experience of 2 years

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Background & Objective: Invasive malignant melanoma, is an aggressive type of skin cancer and incidence has increased dramatically over the past few decades.
Method: This is a 2 years retrospective analysis. We present our experience with invasive malignant melanoma diagnosed and treated between october 2016- october 2018 in the Department of Pathology of University of Health Sciences, Antalya Training and Research Hospital, Antalya, Turkey. Incisionel biopsies and external center consultations were not included in the study.
Results: This study involved a total of 37 cases. The median age of affected patients was 62,8 (range: 33- 81 years). The female to male ratio was 1.3/1. Revised and re-confirmed 37 cases of the diagnosis, 28 cases were cutaneous, 8 cases were located in anogenital mucosa and 1 case was located in meninges. The most common subtype was nodular melanoma. The most common site is upper extremite and head and neck. The median tumour size of cutaneous tumours was 16,4 mm (range: 3- 40 mm). The median maximum tumour thickness (Breslow) was 4,2 mm (range: 0,2- 16 mm). The most common anatomic (Clark) level was 4 (range: 1- 5). 10 of 28 cases analyzed of BRAF V600 mutations and 4 of 10 (40%) case were positive. All of anogenital mucosal cases and menengial case were negative for PCR-based analyzed of BRAF V600 mutations.
Conclusion: The levels of both melanoma incidence and mortality vary considerably worldwide. The diagnosis of melanoma is based on histopathological examination and immunohistochemical stains, but BRAF mutation analyses is critical to the treatment decision.

PS-07-035

A completely regressed melanoma firstly diagnosed by its abdominal wall metastasis: a case study

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Background & Objective: Complete regression of melanomas is rare and may be correlated with tumours of indeterminate derivation. We describe a case of a metastatic nodule microscopically diagnosed as metastatic melanoma. The primary site was a totally regressed melanocytic lesion in the upper limb.
Method: A 49-years old patient conferred to our hospital because of the presence of a mass of the abdominal wall, 4cm in greatest diameter that was surgically treated. On gross examination the mass was partially-encapsulated, gray-coloured with a fleshy consistency.
Results: Histologic examination revealed a malignant neoplasm comprising of nests of large epithelioid tumour cells with pleomorphic, hyperchromatic nuclei, nucleoli and eosinophilic cytoplasm that were S-100, Melan-A, HMB-45 and MITF positive and negative for epithelial markers. The diagnosis was compatible either with metastatic malignant melanoma or with a clear cell sarcoma. The patient was intimately searched for a melanoma primary and a low back skin lesion was also sent for pathologic evaluation and was compatible with complete regression of melanoma
Conclusion: By the absence of any other primary, the diagnosis of a completely regressed melanoma was made. Although partial regression occurs in 10-35% of melanomas, only 34 cases of totally regressed melanomas have been referred in the literature. The exact mechanism of regression remains to be elucidated however any patient with a metastatic melanoma needs a thorough cutaneous examination.

PS-07-036

Linear sclerodemic lupus erythematosus - a rare variant of linear morphea and discoid lupus erythematosus

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Background & Objective: Linear morphea "en coup de sabre" is a localized form of morphea that represents paramedian face and/or frontal scalp depression concomitant occurence of discoid lupus erytematosus (DLE) and morphea in the same skin lesion is exceptional and has only been reported in lesion less then five patients. This condition has been named "sclerodermiform linear lupus erythematosus" by some authors.
Method: A 25-year-old women, presented with a sclerotic plaque and alopecia with erythematous halo of the forehead over one year. Physical examination was normal. Antinuclear antibodies and anti-ENA antibodies were normal at laboratory examination.
Results: Microscopic findings of two skin biopsiy speciemens from lesion showed hyperkeratosis, atrophy in the epidermis, vacuolation of epidermal basal cell layer and perivascular, periadnexial inflamatory infiltrates in the papillary and reticular dermis. In adition there was hyalinization of the collagen bundles in the reticular dermis. Increased dermal mucin, thickening basal membrane at the epidermis and hair follicular epithelium were observed with periodic acid-Schiff stain.
Conclusion: Overlap syndrome are defined as a disorder that statisfy diagnostic criteria of two or more different connective tissue disease concurently or consecutively. Rarely the overlap occurs at the same tissue site. Our case demonstrates lupus erythematosus and morphea in the same lesion.

PS-07-038

Dermatomyositis as a paraneoplastic syndrome

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Background & Objective: Dermatomyositis (DM) is an uncommon autoimmune disorder characterized by inflammatory muscular and cutaneous disease, its etiology remains yet unknown. Its paraneoplastic character has been demonstrated in up to 20-30% cases in adults, where this entity could reveal primitive malignancy or metastatic relapse. We report a case of a female firstly diagnosed with DM in which there was eventually found a breast invasive ductal carcinoma grade-II. Dermatomyositis may represent a paraneoplastic syndrome of many neoplasms, as breast carcinoma.
Method: We report a case of a 67-year-old female patient with an extensive violaceous rash and progressive proximal muscle weakness resistant to medical treatment. A 4mm skin punch biopsy was performed.
Results: Histological findings: epidermal atrophy, loss of rete ridges, decreased granule cell layer, scattered apoptotic keratinocytes and pigment incontinence. Interface dermatitis with basal vacuolar degeneration. Sparse superficial perivascular lymphoplasmacytic infiltrate associated with intense edema with increased dermal mucin in the upper dermis highlighted by Alcian Blue. Absence of signs of vasculitis. Diagnosis of dermatomyositis was made and its potential paraneoplastic origin was suggested. After a week, the patient was diagnosed with breast invasive ductal carcinoma (G-II).
Conclusion: Dermatomyositis is an idiopathic inflammatory myopathy which affects skeletal muscle and skin. Malignancy should be taken into consideration when a patient is newly diagnosed with DM. In order to do a correct differential diagnosis, a proper clinical correlation is needed to avoid diagnostic pitfalls as the histological findings may resemble other entities, as usual dermatomyositis or acute lupus. With every new diagnosis of DM, malignancy should always be excluded.

PS-07-039

Pigmented epithelioid melanocytoma: a rare borderline melanocytic lesion

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Background & Objective: Pigmented epithelioid melanocytoma (PEM) is a recently proposed term that was previously known as "animal type melanoma". The purpose of this case report is to present a young female with pigmented lesion diagnosed as PEM.
Method: A 17-year-old woman presented with a 0.7x0.7 cm black nodular lesion on the right knee since her childhood. Medical history of the patient revealed no spesific features. There was no personal or family history of skin cancer. A complete excision was performed.
Results: Histopathologically, the lesion was characterized by heavily pigmented epithelioid cells with prominent nucleoli and interspersed melanophages in the dermis and subcutaneous tissue. Mitosis and necrosis were not observed. The depth of invasion was classified as Clark level IV, with maximum thickness of 2,5 mm. The lesion was diagnosed as PEM on final histopathology report.
Conclusion: PEM is a very rare, borderline melanocytic lesion and has regional lymph node metastasis potential. Clinically, PEM occurs any age, but usually children and young adults. PEM is histologically similar to "epithelioid blue nevus" and differantial diagnosis with other pigmented lesions such as heavily pigmented melanoma, regressing melanoma, blue nevus, recurrent nevus, combined nevus, deep penetrating nevus and spitzoid tumour can be difficult.

PS-07-041

The expressions of IDO1/TDO2 in tumour cells and tumour microenvironment are associated with MCPyV status and prognosis in Merkel cell carcinomas

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Background & Objective: Merkel cell carcinoma (MCC) is known as a rare yet aggressive cutaneous cancer with neuroendocrine features and it is related to Merkel cell polyomavirus (MCPyV) in about 80% of cases. Indoleamine 2, 3-dioxygenase 1 (IDO1) and tryptophan 2, 3-dioxygenase 2 (TDO2), the key and rate-limiting enzymes of the tryptophan to kynurenine metabolic pathway, play a role in several cancer types as part of avoiding immunosurveillance process. We investigated the association of IDO1/TDO2 expression with MCPyV status and prognosis in MCCs.
Method: 24 MCPyV-positive MCCs, 13 MCPyV-negative MCCs combined with squamous cell carcinoma (SqCC), and 7 MCPyV-negative pure MCCs were used. FFPE sections were stained immunohistochemically with IDO1 and TDO2 antibodies and examined using H-score.
Results: IDO1 expression in MCC tumour cells was higher significantly in MCPyV-negative MCCs than in MCPyV-positive ones ($p<0.001$). In 13 MCCs combined with SqCC, tumour cells also highly expressed IDO1 in MCCs rather than in SqCCs ($p<0.001$). There was no different TDO2 expression of tumour cells between MCPyV-positive and -negative MCCs. The tumour microenvironment (TME) in MCPyV-negative MCCs expressed TDO2 more frequently than in MCPyV-positive ones ($p<0.001$). MCCs with lower IDO1 expression in tumour cells and MCCs with lower TDO2 expression in TME had better prognosis than otherwise ($p=0.043$, $p=0.008$, respectively).
Conclusion: The different expressions of IDO1 in MCC tumour cells or TDO2 in TME between MCPyV-positive and -negative MCCs suggest that IDO1 or TDO2 plays a role differently in tumourigenesis mechanism and biology of MCPyV-positive and -negative MCCs.

PS-07-042

Interstitial mycosis fungoides: a rare variant

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Background & Objective: Mycosis Fungoides (MF) is the most common form of primary cutaneous lymphoma that presents a wide clinicopathologic spectrum. Histologically, MF generally displays superficial perivascular or band-like lymphocytic infiltrate with epidermotrophism. Infrequently it can show different patterns such as interstitial, lichenoid, spongiotic, syringotropic or granulomatous etc. Interstitial MF is a quite rare form of MF with an interstitial dermal infiltrate mimicking interstitial granuloma annulare, inflammatory morphea and interstitial granulomatous dermatitis. There are few reports and small series regarding with interstitial MF in the literature.
Method: A 38 years old male patient presented with a three years history of slightly erytematous scaly patchy lesions on his trunk and upper extremities. Preliminary diagnoses were MF and morphea.
Results: The first biopsy didn't show an epidermotrophic infiltration. Therefore, we couldn't exclude the diagnoses of early morphea or interstitial MF and suggested follow up with biopsies repeatedly. After two months follow-up the second biopsy revealed epidermotrophism beside the dermal periadnexial interstitial inflammatory infiltrate with predominance of atypical cerebriform lymphocytes. The neoplastic cells showed immunopositivity for CD3 and CD8. Additionally, there was focally absence of CD7 in the infiltrate.
Conclusion: We reported this case as interstitial MF and discussed with the literature.

PS-07-043

Atypical fibroxanthoma arising on chronic burn scar: a rare case report and the review of the literature

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Background & Objective: Atypical fibroxanthoma (AFX) is a low-grade sarcoma, characterized by a population of spindle, epithelioid and pleomorphic cells, mostly on a background of actinic damage in elderly patients. But uncommonly it can develop on a burn scar with or without actinic damage.
Method: A 31-year-old male patient with a history of a thermal burn 20 years ago, admitted to plastic surgery service with the complaint of intractable ulcer despite conservative treatment for 6 months on his mid-back. A solitary, firm, well-demarcated nodule was noted just lateral to the left mid-back, measuring 2x2 cm in size. The surrounding skin showed mild contracture. Wide excision was performed with a clinical diagnosis of Marjolin's ulcer.
Results: Tumour was composed of pleomorphic spindle cells, admixed with multinucleated osteoclast-like giant cells and mononuclear inflammatory cells. Mitotic activity is brisk, including numerous atypical and bizarre forms. There was no epidermal connection or precursor lesion in the epidermis. The overlying epidermis was atrophic. There was neither necrosis nor vascular, lymphatic or perineural invasion. The immunohistochemical staining revealed strong positivity for CD68 and CD10. Neoplastic cells were negative with cytokeratin, p40, p63, HMB45, smooth muscle actin and CD34. Ki67 proliferation index was low (7-8 %). On the basis of the burn scar history, clinical and pathological findings, a final diagnosis of AFX was given.
Conclusion: Herein, we present a rare case of AFX arising on the non sun-exposed area within a chronic burn scar of a young patient.

PS-07-044

Penile intraepithelial neoplasia: case report and review of literature

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Background & Objective: Penile intraepithelial neoplasia (PeIN) is a rare disease that can be associated with great morbidity and mortality. The risk of progression from PIN to invasive carcinoma is estimated to be between 10% and 30%. Treatment options include topical chemotherapy, immunotherapy, laser treatment, photodynamic therapy and surgical excision. Our aim was to evaluate the outcome of both cryotherapy and imiquimod to treat PeIN

Method: A 24-year-old presented with lesion at the meatus on the glans penis of 4 months duration for which he had not previously sought medical attention. He had at the beginning a surgical excision.

Results: Histologic results showed epidermal acanthosis, prominent atypical parakeratosis. The epithelium is replaced by a monotonus population of small to intermediate sized cells. In the uppers layers of the epidermis presence of numerous koilocytes who have vacuolated scant basophilic cytoplasm and indistinct cell borders with shrunked nuclei. There was no evidence of an invasive component. Immunohistochemical (IHC) studies showed positive staining of these cells for p16. Ki67 proliferation index was 90%. Based on these histologic and IHC findings, the final diagnosis of PeIN was established. The limits of excision cannot be evaluated. The postoperative course is marked by a recurrence of the lesion. The patient then benefited from a treatment by cryotherapy and imiquimod with a good evolution and complete disappearance of the lesion.

Conclusion: Given the favorable response and purported benefits of combination therapy, we propose the use of cryotherapy with topical imiquimod in the treatment of PeIN.

Monday, 10 September 2018, 09:30 - 10:30, Exhibition Hall I/II
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PS-08-001

Mixed histiocytosis (Langerhans cell histiocytosis and Erdheim-Chester disease) with vascular involvement: a rare cause of refractory systemic arterial hypertension

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Background & Objective: The co-occurrence of Langerhans cell histiocytosis (LCH) and Erdheim-Chester disease (ECD) is rare. Aim: to report a systemic mixed LCH/ECD with vascular involvement and systemic arterial hypertension (SAH).

Method: A 63-year-old-woman was referred due to refractory SAH, despite treatment with several antihypertensive drugs, diagnosed three years before. The previous relevant medical history was diabetes insipidus, diagnosed at 34y, and LCH of skin/bone/liver at 50y. She was treated with cytarabine for one year.

Results: The patient had no other relevant risk factors for cardiovascular events (e.g. hyperlipidaemia, diabetes mellitus and smoking). Screening for renovascular disease revealed bilateral stenosis of renal arteries, atrophy of the right kidney, and secondary hyperaldosteronism. Angioplasty/stenting of the left renal artery was performed, allowing blood-pressure control (115/66mmHg). Fourteen days later, she was admitted for acute mesenteric ischemia due to stenosis of the superior mesenteric artery, submitted to angioplasty/stenting. To clarify the pathogenesis of the aforementioned vascular stenoses, we re-evaluated the pathological features of previous bone (a) and liver (b) biopsies that revealed: (a) expression of S100+/CD1a+ in bona-fide Langerhans cells, with eosinophils, and sheets of S100-/CD1a- foamy histiocytes, with Touton giant cells, consistent with a mixed LCH/ECD; (b) LCH associated with secondary sclerosing cholangitis.

Conclusion: ECD can be an under-diagnosed cause of multiple arterial stenoses and SAH, but they occur in ~70% and ~20% of ECD reported cases, respectively. So far, 40 cases of mixed LCH/ECD have been reported, but without mention to refractory SAH, as described in the present case, with impact in patients' management.

PS-08-003

Immunohistochemical and ultrastructural analysis of an ALK-positive anaplastic large cell lymphoma presenting with systemic capillary leak syndrome

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Background & Objective: ALK-positive anaplastic large cell lymphoma (ALCL) was initially described in 1982 by Stein and his collaborators as an aggressive T-cell lymphoma with higher incidence in young males and better prognosis that other T-cell lymphomas. It is usually associated with t(2;5)(p23;q35), which gives rise to the NPM-ALK fusion protein.

Method: We report the case of a 38-year-old male presenting to our clinic with uncontrolled anasarca through systemic capillary leak syndrome. The patient was allergic to plasma solutions. Blood tests revealed leukocytosis with neutrophilia and hypoalbuminemia. A thorough ultrasound examination revealed hepatosplenomegaly and enlarged inguinal and supraclavicular lymph nodes. The patient underwent surgical excision of the inguinal lymphadenopathy. Frozen sections revealed a high-grade neoplastic proliferation, which could not exclude the diagnosis of large cell lymphoma.

Results: Histological examination revealed a neoplastic proliferation of discohesive large anaplastic cells, with eosinophilic cytoplasm, round or horseshoe nuclei and high mitotic rate (16 mitoses/10 HPF). Immunohistochemically, the cells were completely negative for AE1/AE3, PAX5, CD5, CD20 and diffusely positive for EMA, CD30 and ALK, the latter having both nuclear and cytoplasmic immunoreactivity. This pattern of staining for ALK is suggestive for the presence of t(2;5)(p23;q35). Electron microscopy revealed enlarged horseshoe nuclei with dispersed chromatin and convoluted contours, some organelles and cytoplasmic cytotoxic granules. The patient died 2 weeks after diagnosis.

Conclusion: Although ALK-positive ALCL usually has a good prognosis, cases with aggressive evolution have been reported in young patients. Prognosis may be correlated with the presence of intracytoplasmic cytotoxic granules, which could be responsible for systemic capillary leak syndrome

PS-08-004

The impact of micro vessel density on patient survival with diffuse large B-cell lymphoma

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Background & Objective: Diffuse large B cell lymphoma is a clinically morphological and molecular heterogeneous disease. Angiogenesis-related signature and gene expression profile were shown to affect patient survival and unfavorable prognostic. The purpose of this study is to assess the prognostic impact of micro vessel density in one series of patients with diffuse large B cell lymphoma.

Method: Eighty patients with diffuse large B cell lymphoma from the Haematology Department of the Coltea Clinical Hospital were included in the study and underwent combined rituximab–R-CHOP treatment. Microvessels were immunostained with CD 34 and VEGFR and quantified manually.

Results: Correlation between VEGFR intensity and CD 34 intensity in diffuse large B cell lymphoma was statistically significant. The patients who presented intensity positivity for VEGFR have shown strong correlation with a highly positivity CD 34 vascularization. The germinal center B cell -like (CGB) type was associated with a low microvessel density and VEGFR negativity and the non-germinal center B – cell like (non-CGB) type was associated with a high microvessel density and an intense positivity for VEGFR. The patients with a low microvessel density (CD 34 positive) and VEGFR negativity correlates with a poor treatment response and also with relapse. The survival rates decrease proportionally with the microvessel density.
Conclusion: These findings highlight the impact of angiogenesis in the outcome of patients with diffuse large B cell lymphoma and may represent an exciting new interest regarding antiangiogenic drugs in clinical trials.

PS-08-006
CD4 positive indolent T-cell lymphoproliferative disorder of the gastrointestinal tract with high proliferative index: a case report and literatures review
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Background & Objective: Indolent T cell lymphoproliferative disorder of the gastrointestinal tract is a clonal T cell lymphoproliferative disorder that can involve the mucosa in all sites of the gastrointestinal tract. Despite the indolent clinical course, most patients do not respond to conventional chemotherapy.
Method: We report a case of CD4+ indolent T cell lymphoproliferative disorder of the gastrointestinal tract involving ileum and oropharynx, and review literatures of all cases of CD4+ indolent T cell lymphoproliferative disorder of the gastrointestinal tract reported to date.
Results: CD4+ indolent T cell lymphoproliferative disorder of the gastrointestinal tract may have malignant potential.
Conclusion: It is necessary to combine imaging, clinical symptoms and pathological diagnosis. Generally, Ki-67 index of this lesion is very low and often less than 10% but may increase to 20% occasionally.

PS-08-007
Primary T-cell lymphoblastic lymphoma of the ovary: insights into a rare case report and systematic literature review
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Background & Objective: Primary ovarian non-Hodgkin lymphomas are defined by Fox criteria and account for 1.5% of all ovarian neoplasms, with primary T-cell lymphoblastic lymphoma of the ovary an extreme rare entity.
Method: A 29-year-old woman with a medical history of Thymoma treated 7 years ago, develops symptoms of increased abdominopelvic volume and irregular menstrual cycle. An abdominal positron emission tomography (PET-CT) was performed and showed bilateral, solid, expansive ovarian lesions, measuring 10 cm to the right and 10.5 cm to the left, without associated lymphadenopathy. Diagnostic left salpingo-oophorectomy under microscopy, demonstrated uniform lymphoid proliferation of intermediate-sized cells, with scant cytoplasm, dispersed chromatin and poorly evident nucleoli. Immunophenotypically was strongly and diffuse positive for CD3, CD10, CD99 and TdT, focal positive for BCL-2, negative for CD20 and with high Ki-67 index. Bone marrow biopsy did not show involvement due to lymphoma. The patient had complete remission of the disease after treatment with BFM 86 protocol.
Results: In a systematic review, only 2 other cases of primary T-LBL of the ovary were found in the English-language literature. Both represented young women as abdominal and/or pelvic pain, as the case reported. Regarding the laterality of the lesion, one case affected both ovaries and another only the right ovary. They also had the same histopathological and immunophenotypic characteristics, being positive for CD3, CD10, TdT and CD99, as in the presented case. Chemotherapy was used as treatment in both, but only 1 with remission.
Conclusion: The few cases of primary T-LBL of the ovary, sharing clinicopathological and phenotypic characteristics.

PS-08-008
Concomitant Erdheim-Chester disease and acute myeloid leukemia: clinical and molecular characteristics of a rare association
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Background & Objective: Erdheim-Chester disease (ECD) is a rare form of histiocytosis frequently associated with mutations of BRAF or other MAPK pathway genes. Recent works have provided evidence of a haematopoietic stem cell origin of some systemic histiocytoses. These discoveries have raised the question of a possible association or even an etiologic relationship between ECD or LCH and myeloid neoplasms. Herein, we report the case of a 71-year-old man with concomitantly diagnosed ECD and acute myelomonocytic leukemia (AMML).
Method: The patient was admitted for cardiac decompensation and imaging studies showed pleural effusion, bilateral perirenal fat infiltration, and symmetrical involvement of proximal long bones. He also developed increasing leucocytosis. Bone marrow biopsy and aspirate showed images qualifying for a diagnosis of AMML.
Results: Perirenal and pleural biopsies revealed infiltration by CD163+, CD68+/-, S100+/-, CD1a- and Langerin-negative histiocytes, some with foamy cytoplasm, prompting a diagnosis of ECD with multisystemic involvement. NGS studies using a myeloid panel in both pleural and bone marrow biopsies revealed a complex profile encompassing NRAS, SRSF2, TET2 and TP53 mutations in addition to BRAFV600E mutation in both specimens.
Conclusion: While most myeloid neoplasms reported so far in ECD patients consist of myeloproliferative neopalsms or myelodysplastic syndromes, co-occurrence of an acute myeloid leukemia is exceptional. Our case is remarkable by the common complex mutational landscape in both ECD and AML. These observations raise the possibility that, in our case, ECD and the myeloid neoplasm may not only share a common cell of origin but also result from linear evolution along the same molecular oncogenic pathway.

PS-08-010
CD23 expression in follicular lymphoma: the IgD clue
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Background & Objective: CD23 defines a recently recognized subtype of follicular lymphomas (FLs) with diffuse pattern and little tendency to disseminate. However, some cases with follicular pattern are positive for CD23 and the influence of CD23 expression in the clinical outcome is controversial. We aimed to assess the expression of CD23 in neoplastic cells and in mantle cells, defined by IgD positivity, in cases with follicular and diffuse morphology and to investigate its possible association with the disease-free survival (DFS) probability.
Method: We retrospectively evaluated 111 biopsy specimens diagnosed as FLs, for growth pattern and grade. The immunohistochemical pattern of expression of CD23 and IgD was recorded.
Results: 79% of cases showed follicular pattern and 21% presented a diffuse component in variably proportion. CD23 expression in lymphoid

cells was observed in 76 cases (69%) and, in 51 of these cases (68%), positive cells were classified as mantle cells, since they showed IgD coexpression and a predominant mantle-like distribution. These mantle cells were significantly more frequent in cases with follicular pattern (p=0,01, X2). Once excluded the mantle cells component, a better DFS probability was observed in diffuse FLs positive for CD23 in neoplastic cells, but not in cases with follicular pattern (p=0,07, Long-Rank). Further analyses with more cases are needed to improve the statistical significance of this result.
Conclusion: Most CD23 positive cells observed in FLs are actually mantle cells, being more frequent in cases with follicular than diffuse pattern. CD23 positivity in cases with at least partial diffuse component seems to correlate with a longer DFS.

PS-08-011
Clonality assessment of disseminated MALT lymphoma
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Background & Objective: Extranodal mucosa-associated lymphoid tissue (MALT) lymphomas account for 7-8% of all non-Hodgkin lymphomas, being the stomach the most frequent location. It is a disseminated disease in approximately 50%of extragastric MALT lymphomas, and 25% of gastric ones. There is very little literature published about the clonal relationship of MALT lymphomas with disseminated involvement. To study clonality of our disseminated MALT lymphomas.
Method: We reviewed all the cases of MALT lymphoma diagnosed in a single centre between 2009 and 2017. Cases that affected multiple locations were selected, both multifocal and multiorgan, excluding those with exclusive skin involvement. Clonality was detected by PCR for IGH (FR3 and FR2), and for IGK.
Results: Our series comprise 80 patients. Disseminated disease was present in 27 (34%) patients, 13 males and 14 females with a median age of 60 years (range: 38-84). Of those, one (4%) patient had multifocal MALT; 22 (81%) patients had multiorgan MALT; and 4 (15%) patients had both. The most frequently involved primary locations were salivary gland (18.5%) and lymph nodes (15%). All patients received treatment: 23 (85%) patients received chemotherapy, 2 (7%) radiotherapy, 1 (4%) surgery, and 1 (4%) chemotherapy plus surgery. Clonality was analyzed in 52 samples from 24 different patients. We could compare 16 patients. In 6 of them (22%), the neoplastic clones were distinct and unrelated.
Conclusion: This is the largest series that compares clonality in disseminated MALT lymphoma. Our results suggest that in an important percentage of cases, rearrangements are not clonally related.

PS-08-012
Low grade B-cell posttransplant lymphoproliferative disorder (PTLD): about clinicopathological details of 6 cases
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Background & Objective: PTLD included a wide spectrum of lymphoproliferative disorders and the histological cases with low grade B cell morphology are very infrequent. The incidence of PTLD depends on several risk factors: transplant type, age of recipient, EBV status before the transplant, and duration and type of immunosuppressive regimen.
Method: Six cases of low grade B cell lymphoma were studied from the 54 PTLD cases of the Department. Clinical data and stains were reviewed and additional immunohistochemical stains and molecular studies were performed.
Results: We evaluated 6 patients (4 females and 2 males) transplanted of heart (1 case) and liver (5 cases, 3 of them related with Hepatitis C virus, 1 Primary Biliary Cirrhosis and 1 Autoinmmune hepatitis). All cases were Marginal Zone Lymphomas (MZL): 4 of MALT lymphoma (one in a salivary gland MZL and three in the stomach), 1 Nodal MZL and 1 Splenic MZL. Histologically showed monocitoid lymphoid cells with plasmacytic differentiation in one of the cases. One of the gastric MZL was *Helicobacter pylori*-associated. All cases was CD20+, BCL2+, BCL6-, CD10- and one of them showed monotypic plasma cells. B cell clonality was detected in all cases. EBV was negative in all cases. After treatment all patients achieved complete remission.
Conclusion: Low grade B cell PTLD appears infrequently and represents only 6 of 54 cases (11%) of our series. All cases were MZL, characteristically EBV negative, with poor relation to *H. pylori* (only one case positive) and negative to MALT-1 rearrangements. These cases appear to be a consequence of continuous of chronic immunological stimulation related to hepatitis C virus or to autoimmune diseases prior to transplantation.

PS-08-013
Lymphoplasmacytic lymphoma/Waldestrom macroglobulinemia is characterised by a paratrabecular and interstitial bone marrow B cell infiltration pattern
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Background & Objective: Lymphoplasmacytic lymphoma/Waldestrom Macroglobulinemia (LPL/WM) is defined by the combination of a LPL with an IgM monoclonal component. The aim of this study was to describe the characteristics of the bone marrow infiltration found in a series of clinically defined LPL/WM.
Method: We have reviewed a series of 25 bone marrow biopsies from 20 cases with a clinical diagnosis of LPL/WM (18 cases) or MGUS (2 cases). All 20 patients had a IgM component (mean 2.4 gr/dL, range 0.3-6,5 gr/dL). Bone marrow infiltration characteristics by morphology, IHC, FCM and allele-specific real-time PCR for the detection of MYD88L265P mutation were analyzed.
Results: Mean age was 73.4 years (range 49-88). Female/male ratio was 2.3 (14/6). The majority of samples showed a paratrabecular pattern (16, 65%), combined with either patchy (7, 44%) or diffuse (5, 31%) and less commonly nodular (4, 25%) interstitial patterns. The other 7 cases showed a non-paratrabecular pattern with interstitial involvement. Bone marrow quantification of B cells by IHC showed invariably higher values than by FCM (median 20% (2-80%) by IHC vs 7% (0-62%) by FCM, p value of the mean difference <0.05). 15 out of 20 cases (75%) were positive for MYD88L265P mutation. Median Variant Allele Frequency of the mutated cases was 0.1 (range 0.04-0.32).
Conclusion: A combined paratrabecular and interstitial bone marrow infiltration pattern is the most common feature found in LPL/WM. Immunohistochemical quantification of B cell infiltrates is superior to FCM. The identification of MYD88L265P wild type cases requires further investigation.

PS-08-014
Immunohistochemical assessment of the PD-1/PD-L1 axis in follicular lymphoma
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Background & Objective: According to recent promising results of combining immunotherapy nivolumab or pembrolizumab) with rituximab in a phase 2 trials concerning follicular lymphoma (FL) treatment the clinical role of PD1/PDL1 expression is of great interest. Programmed cell death protein 1 (PD1) and its ligands (PDL1) expression corresponds with several interactions between tumour cells, T cells and antigen presenting cells as well.
Method: FL cases from 1999 to 2017 were revaluated according WHO 2016 diagnostic recommendations and from formalin fixed paraffin embedded material tissue microarrays were constructed and immunohistochemical (IHC) assessment of PD1 and PDL1 was performed. The scoring methods included quantification (0-none, 1: 0-5%, 2: 6-25%, 3: 26-50%, 4: >50%] and architectural pattern [1: not scored, 2: intra- and perifollicular, 3: interfollicular and diffuse] of IHC stainings.
Results: Group of 88 FL was enrolled into study with male to female ratio 30:58 and median age 61.5 years (range: 28-93 years, SD=15.68). PD1 was expressed in majority of cases concerning FL microenvironment (93.2% positive vs. 6.3% negative) with predilection to intra- and perifollicular localization (57.2% of cases). Quantification analysis revealed the following distribution: 1 - 9.8%, 2 - 45.1%, 3 - 34.1% and 4 - 11.0%. Morphologically FL cells were PDL1 negative but granular and membranous staining was detected in the FL microenvironment.
Conclusion: Predominant PD1/PDL1 expression is localized in FL microenvironment. The FL neoplastic cells are PDL1 negative which correspond with latest independent studies. Still the efficacy of immunotherapy in FL should be better understood and the PD1/PDL1 expression in the context of the microenvironment landscape need to be thoroughly studied.

PS-08-015

Audit of histopathological diagnosis of graft-versus-host disease in a national bone marrow transplantation centre

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Background & Objective: Approximately 160 haematopoietic cell transplants (HCTs) are performed annually at this national centre. Reported incidence rates of graft-versus-host disease (GVHD) range from 9 to 50% in patients who receive allogeneic HCTs. Our aim was to audit the reporting and diagnosis of GVHD in a subspecialised histopathology department.
Method: Biopsies of queried cases of GVHD were identified using SNOMED coding lists from 2016. Day of arrival, anatomical site, patient history, clinical and histopathological diagnosis, and subspecialty of reporting Histopathologist were recorded.
Results: 92 cases of queried GVHD were identified from 63 patients; 19 patients had multiple biopsies. GVHD was confirmed in 44 cases (47.3%), and excluded in 30 (32.2%). The remaining 18 cases (19.3%) were diagnosed as possible GVHD. The most common background pathology was acute myeloid leukaemia (28.6% patients). Cases were fairly evenly distributed through the week and 6 were reported on a weekend call rota. 59/62 (95.2%) skin cases were seen by a dermatopathologist. Only 8/25 (32%) gastrointestinal (GI) cases were seen by a GI pathologist. The four liver cases were signed out by a liver pathologist- one case was confirmed as GVHD (non-hepatitic).
Conclusion: There was a fairly even daily distribution of queried cases of GVHD. The majority of queried skin cases of GVHD were seen by a dermatopathologist. There are diagnostic guidelines for the histopathological criteria for GVHD however there is a need to standardise subspecialty reporting of GVHD cases. Our recommendation is for appropriate subspecialty review of all queried GVHD cases with preparation for after-hours specimens.

PS-08-016

Accurate GCB/ABC classification of de novo diffuse large B-cell lymphoma with aberrant CD10+ MUM1+ phenotype using RT-MLPA assay

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Background & Objective: The cell-of-origin (COO) determination of diffuse large B cell lymphoma (DLBCL) into germinal center B-cell like (GCB), and non-GCB (activated B-cell like (ABC) and unclassifiable) subgroups based on the immunohistochemical (IHC) Hans algorithm remains an approximate approach.
Method: The aim was to verify at mRNA level the COO classification of a subgroup of GCB DLBCL featuring an aberrant CD10+ MUM1+ (DP) phenotype, using the RT-MLPA assay already successfully tested on archival paraffin-embedded formalin-fixed (FFPE) tissues.
Results: 62 CD10+ GCB DLBCL were retrospectively identified from 255 de novo DLBCL treated in our institution between 2006 and 2016, including 22 DP (8.6%) and 40 CD10+ MUM1- cases. RNA were extracted from FFPE tissues for all 62 cases and RT-MLPA evaluated the expression of 14 markers to differentiate ABC from GCB molecular subtypes. Eighty-eight (29/33) of CD10+ MUM1- DLBCL were classified in the GCB subtype (4/33 unclassified). However, the majority of DP DLBCL was classified in the non-GCB subtype (48% (10/21) in ABC subtype and 19% (4/21) unclassified) and only 33% (7/21) in the ABC subtype. Finally, 8/9 DP DLBCL reclassified in the ABC subtype contained more than 80% of MUM1+ tumour cells by IHC.
Conclusion: 67% of DP DLBCL are misclassified according to the Hans algorithm suggesting a cautious interpretation of COO classification of DP DLBCL in routine diagnosis using this algorithm. A high expression level of MUM1+ (> 80%) could help to identify these ABC DP DLBCL.

PS-08-017

Importance of the molecular diagnosis in the treatment of a patient with Edheim-Chester disease

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Background & Objective: Erdheim-Chester disease (ECD) is a rare non-Langerhans' cell histiocytosis with characteristic radiological and histological features. We present a case of ECD in a 46 year old woman with progressive course and multisistemic affectacion over five years. BRAFV600E mutation were detected. The patient was treated with Vemurafenib.
Method: This report describes the case of a 46 year old woman who presented with hypogonadism, diabetes insipidus and amenorrhoea. The cerebral magnetic resonance imaging showed a thickened pituitary stalk. Two years later she presented with pain in the lower extremities. Radiologycal imaging and computed osseous tomography (CT) showed bilateral, symmetrical osteosclerosis involving metaphyseal and diaphyseal regions of distal femur, proximal tibia and fibula. CT body showed interlobar septal and cisural thickening of the lungs, pericardial and pleural effusion and retroperitoneum, periaortic, omentum, perirrenal and mammary glands' soft tissues thickening. She underwent incisional biopsies of the tibia, mamary gland and omentum.
Results: Histologically, the tissue specimens, showed infiltrates of histiocytes with a pale staining, foamy, granular cytoplasm, scattered Touton giant cells and variable numbers of lymphocytes and plasma cells. The immunohistochemical profile of the lesional cell was CD68, S100, Vimentin, Factor XIIIa and CD163 positive and CD1a negative. Mutation of the Braf gene in exon 15 was detected by PCR of DNA extracted from paraffin embedded

samples and treatment with veramufenib was preformed with clinical and radiological improvement.
Conclusion: We concluded that an appropriate preformed histological and molecular diagnosis and treatment would improve the quality of life of the patients.

PS-08-018
Aggressive NK leukemia and intravascular NK/T-cell lymphoma: are they closely related?
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Background & Objective: Due to its low incidence and highly varied presentation forms, Aggressive NK leukemia (ANKL) and Intravascular NK/T-cell lymphoma (INKTL) are both an authentic diagnostic challenge. We report a rare case of an ANKL with extensive intravascular dissemination, in a VIH 49-year-old man, presenting as multiple nodular skin lesions and progressing fatally.
Method:
Results: A skin lesion biopsy showed a proliferation of T-lymphocytes in dermis and subcutaneous tissue. The phenotype was very silent, showing only positivity for CD2, CD3, TIA-1, Granzyme-B and EBER. Surprisingly, the autopsy revealed an exclusive and massive systemic intravascular proliferation of T-lymphocytes with the same phenotype as the previous biopsy. An exhaustive study of bone marrow demonstrated its subtle infiltration by neoplastic cells. Looking for similar cases, we found more than twenty reported cases, referring to an entity not recognized by WHO, but mentioned in the recent update, INKTL. These cases share lots of similarities with our case. As the bone marrow infiltration is difficult to demonstrate, we cannot reject that these published cases could be an ANKL.
Conclusion: ANKL is an aggressive process, which can appear in multiple different forms, so can INKTL. A skin lesion can always be just the tip of the iceberg of a systemic lymphoma/leukemia, and these entities have to be part of the differential diagnostic. Here we describe a rare presentation of ANKL, never described before, in order to contribute to a better description of this entity and to facilitate an earlier diagnostic in coming similar cases.

PS-08-019
Pathologic features of JAK2-positive myelodysplastic/myeloproliferative neoplasms
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Background & Objective: To identify diagnostic pathologic features of JAK2-positive MDS/MPN using BMB in combination with clinical, molecular, laboratory data.
Method: Diagnosis MDS/MPN was established in 84 pts (2014-2017, NRCH). Mutation status JAK2 V617F was assayed in 69/84 pts, median age – 60,5 (range 24-79), m/f ratio is 2:1; median WBC count – 18x10^9/L (2.4-146.0x10^9/L); median PLT – 107x10^9/L (20-708x10^9/L), Hb - 98g/L (54-148g/l). Bone marrow trephine biopsies were studied in all pts.
Results: JAK2V617F-positive mutation status was detected in 15 pts of group MDS/MPN (15/69, 21.7%), predominantly with marked splenomegaly (87%). CMML was established in 60% of all JAK2+MDS/MPN (9/15), atypical CML - in 13.3% (2/15), MDS/MPN-U in 20.1% (3/15), MDS/MPN-RS-T - in 6.7% (1/15). BMB examination in cases with positive mutational status JAK2 V617F revealed hyperplastic bone marrow in all cases, expanded gtanulopoiesis - 86.7% (13/15); in 73% pts MF≥1(11/15). Significant signs of megakaryocyte atypia were found in 66.7% (10/15) in contrast to cases lacking mutJAK2 which demonstrated predominantly dysplasia of different haemopoietic lineage.
Conclusion: Mutation JAK2 was found in 21.7% of cases with MDS/MPN. The distinctive features were splenomegaly and morphological MPN-like features in bone marrow.

PS-08-021
Clinicopathologic analysis of Peli1 expression in diffuse large B-cell lymphoma
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Background & Objective: Pelil is a RING-type E3 ligase modulating multiple signaling pathways in immune cells including Toll-like receptor and NF-kB. Although Peli1 overexpression induced B lymphomagenesis of mainly germinal center B cell-like (GCB) phenotype via oncogenic Bcl-6 activation in transgenic mice, Peli1 deficiency also promoted B cell activation and autoimmunity via enhanced NF-kB signaling, suggesting multi-directional role of Peli1 in B cell proliferation. Herein, we investigated the clinicopathologic correlation of Peli1 and multiple signaling molecules in diffuse large B cell lymphoma (DLBCL).
Method: Immunohistochemistry for Peli1, IRAK1, c-Myc and phosphor-STAT3 (p-STAT3) was performed in tissue microarray in 105 cases of DLBCL (27 GCB and 70 non-GCB; R-CHOP treatment, 88%) with quantitative H-score (Σ proportion (%) x intensity (0, 1, 2, 3); range, 0~300) using image analyzer for Peli1 and IRAK1.
Results: Peli1 expression was positively correlated with multiple signaling molecules including IRAK1 (r=0.216; p=0.030), c-Myc (r=0.206; p=0.037) and p-STAT3 (r=0.255; p=0.010) as well as Bcl-6 (r=0.262; p=0.008). Peli1 expression tended to be higher in GCB than non-GCB subtype (p=0.051). In survival analysis, unlike previous reports, Peli1 was not related with prognosis. Remarkably, in Bcl-6-positive subset (n=46), Peli1low group (<median) predicted shorter progression-free survival (p=0.041, log-rank), in contrast to no different tendency in Bcl-6-negative subset (n=57; p=0.918).
Conclusion: Peli1 may exert complex roles in DLBCL pathogenesis via modulating multiple pathways, beyond the well-known Peli1/Bcl-6-driven lymphomagenesis, which remains to be clarified further.

PS-08-022
Marginal zone lymphoma with calcification, ossification and amyloid deposition
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Background & Objective: Marginal zone lymphomas (MZLs) are rarely associated with amyloid deposits, calcification and ossification. The aim of this case report is to raise awareness regarding this unusual histological finding
Method: An 81-year-old man has undergone a right colectomy due to a previously diagnosed adenocarcinoma of the hepatic flexure. Intraoperatively, a mesenteric nodule, measuring 1,9cm has been discovered
Results: Microscopically, the tumour of the hepatic flexure represented a mucinous adenocarcinoma. The mesenteric nodule showed a dense infiltration of neoplastic lymphoid cells, arranged in a solid pattern of growth around a pink amorphous deposition. Areas of calcification and ossification were also present. The aforementioned cells had intermediate size with pale cytoplasm and irregularly shaped nucleus with inconspicuous nucleoli. On immunohistochemical stains, the neoplastic cells showed the following immunophenotype: CD20+, CD45RA+, BCL2+, CD38–/+, CD3-, CD43-, CD5-, CD23-, CyclinD1-, BCL6-, CD10-, MUM1-, DBA44-, TdT-, κ- and λ-. The immunohistochemical stain for CD23 revealed the presence of remnants of follicular dendritic cell meshwork. The histochemical stain for Congo red revealed that the pink amorphous deposition represented amyloid

Conclusion: MZLs are rarely associated with amyloid deposits, calcification and ossification. Although amyloid deposits in cases of MZLs tend to be peritumoural and organ confined and do not implicate worse prognosis, rarely multiorgan involvement can be observed. In those cases the complications can be critical and cause considerable morbidity. Pathologists should be aware of the association between MZLs and amyloid deposition, in order to inform the clinicians for the appropriate follow up

PS-08-023

The spectrum of haematolymphoid collision tumours: the importance of looking beyond the apparent. Study of 24 cases

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Background & Objective: Collision tumours are rare entities defined by the presence of two histologically distinct tumour types identified within the same anatomic site. Haematolymphoid neoplasms (HN), which coincide with non-haematological neoplasms, can easily be overlooked. We present the characteristics of the collision HN.
Method: Retrospective study (1990-2018): patients diagnosed with a HN during the diagnosis and treatment of a non-haematological neoplasm or vice versa, occurring synchronously as collision tumours. Clinicopathological, IHC and molecular data of each case were reviewed.
Results: A total of 24 cases were identified: 15 male and 9 female (age: 52-90 years). Ten patients had no previous history of a HN. The most common non-haematological neoplasms associated with a HN were from: gastrointestinal (29,2%), skin (25%), genitourinary (25%), lung (12,5%), and breast (4,2%). Only one case had the HN in a lymph node and had metastasis of the non-haematological malignancy in the lymph node as well. The non-haematological neoplasm were: carcinomas (79,1%), benign tumours (12,5%), and sarcomas (8,4%). The HN identified were chronic lymphocytic leukemia/small lymphocytic lymphoma (83,3%), diffuse large B-cell lymphoma (8,3%), marginal zone lymphoma (4,2%), and cutaneous T-cell lymphoma (4,2%). Follow-up: 12 died with disease, 11 alive with disease, and 1 died without disease.
Conclusion: Collision HN with solid neoplasms are rare. If the coexisting HN is low grade, it can be overlooked as it mimics a dense immune response to the non-haematological neoplasm and can be misdiagnosed. In doubtful cases, IHC and molecular techniques can help to delineate the diagnosis.

PS-08-024

The morphometric characteristic of bone marrow megakaryocyte clusters in Ph-negative JAK2 mutated chronic myeloproliferative neoplasms

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Background & Objective: The aim of study was to evaluate mean size of megakaryocyte clusters in bone marrow biopsies of patients with Ph-negative chronic myeloproliferative neoplasms (CMPNs), which may be useful in the differential diagnosis within this group of diseases.
Method: We examined 55 bone marrow biopsies of patients with JAK2-positive CMPNs: 15 patients – essential thrombocythemia (ET), 14 patients – polycythaemia vera (PV), 15 patients – primary myelofibrosis in prefibrotic stage (pre-PMF) and 11 patients with primary myelofibrosis in fibrotic stage (PMF). The slides were digitalized by a Pannoramic 250 Flash III scanner. The coordinates of all megakaryocytes in bone marrow samples were determined and processed with R programming language. For mean megakaryocyte clusters size evaluation was used Parzen-Rosenblatt method. We used one-way ANOVA to determine if the differences between groups were statistically significant.
Results: The mean cluster radius ($\overline{R}$) in ET (standard deviation – SD) = 122 μm (44 μm). $\overline{R}$ in pre-PMF = 191μm (52 μm). $\overline{R}$ in PMF = 209 μm (117 μm). $\overline{R}$ in PV = 187 μm (55 μm). Differences were found statistically significant (p=0.009). Mean megakaryocyte clusters size in bone marrow biopsies of patients with PMF was the biggest, in patients with ET $\overline{R}$ was smaller than in other CMPNs.
Conclusion: The mean megakaryocyte clusters sizes are associated with type and stage of CMPN and influence bone marrow morphology.

Monday, 10 September 2018, 09:30 - 10:30, Exhibition Hall I/II
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PS-09-001

P16 immunoexpression in oral cavity and oropharyngeal squamous cell carcinoma

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Background & Objective: Human papillomavirus (HPV) plays an etiologic role in the cases of oropharyngeal squamous cell carcinoma (OPSCC). P16 is an immunohistochemical marker used for HPV status which has been validated only for OPSCC. In our study, we analyzed histopathologic features and frequency of p16 positivity in oral cavity and oropharyngeal squamous cell carcinomas (OC/OPSCC).
Method: A retrospective review was performed on pathology reports of OC/OPSCC that underwent p16 immunohistochemistry test (IHC) in our institution between 2012 and 2017. A total of 37 patients were analyzed. Histologically, they were separated into non-keratinizing, hybrid keratinizing and keratinizing types. To define positive IHC staining for P16 expression, diffuse >70% nuclear and cytoplasmic staining of tumour cells was taken into account. Statistical analysis was performed on the data.
Results: The mean age was 57 (range, 23-82). Male to female ratio was 3:1. While 17 of them were in oral cavity, 20 were in oropharynx. In 4 patients with OCSCC (23%) and 6 patients with OPSCC (30%), p16 expression was positive. The frequency of seeing of histologic types in oral cavity and oropharynx was 5.8%, 5.8%, 88.2% and 45%, 35%, 20%, respectively. The data comparison between non-keratinizing type and p16 expression were found to be statistically significant ($p<0.05$) while the rest of the data is found to be insignificant.
Conclusion: In conclusion, p16 expression was correlated with non-keratinizing OC/OPSCC. However, we couldn't find an evidence to support that p16 positive OC/OPSCC have favorable clinical outcomes. This result may be explained by the fact that our case count is fewer.

PS-09-002

Immunohistochemical profiling of mucins in sinonasal adenocarcinomas

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Background & Objective: Adenocarcinomas represent 20-25% of sinonasal malignancies. They include salivary and non-salivary types, which can be further divided into intestinal (ITAC) and non-intestinal type (non-ITAC) subtypes. Prognosis is poor and new therapeutical strategies are necessary. Abnormal expression of mucins has been related with prognosis in solid tumours and represents a possible therapeutic target. We investigated the expression of mucins (MUC 1,2,4,5,6) and their prognostic value in a series of sinonasal adenocarcinomas.
Method: Tumours from 66 patients were studied. Clinical, pathologic and follow up data were collected, (range 5-194 months; mean 56). Tumours were classified as ITAC (n=51), non-ITAC (n=2), and salivary glandtype (n=13). Immunohistochemical results were evaluated with a

semiquantitative method, considering both the staining intensity (0-3) and the percentage of positive cells (0-3). For statistical analysis, cases with score >4 were considered positive. All statistical tests were performed using SPSS software. Kaplan-Meier method was used for overall survival. P-values <0.05 were considered significant.

Results: Overall 71.2%of the adenocarcinomas were positive for MUC4, 59.1%for MUC1, 31.8% for MUC2, 24.2% for MUC5 and none for MUC6. Mucins were more expressed in ITAC than in non-ITAC (78,4% versus 46,7% for MUC4, 70% vs. 20% for MUC 1, 41% vs. 0% for MUC2 and 29.4% vs. 6,7% for MUC5). MUC2, MUC4, and MUC5 were significantly more expressed in mucinous ITAC than in the other variants, (P<0.001 and <0.022 respectively). Overexpression of MUC1 was associated with shorter survival (p=0.04), and a similar trend was observed with MUC2 (p=0.07).

Conclusion: Mucins are variably expressed in adenocarcinomas with correlation with prognosis for MUC1 and MUC2.

PS-09-003

Pseudoangiosarcomatous carcinoma of the oral cavity: Report of two cases

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Background & Objective: Acantholytic squamous cell carcinoma (ASCC) is rare in the oral cavity. Pseudoangiosaromatous carcinoma (PAC) is an extremely acantholytic form of ASCC. We report here two rare cases of PAC arising in the oral cavity.

Method: We selected two cases of PAC from our pathology file during 2002-2017 and examined clinico-pathologically.

Results: Case 1 is 79-year-old female, with rapid swelling of right buccal mass. The tumour resection was performed. Local recurrence was found 2 months after operation. Despite of radiotherapy, multiple lung metastases occurred and she died of disease. Histologically, the tumour showed the vascular-like pattern growth of the atypical spindle cells, and hobnail cells were also seen. The red blood cells were seen in the pseudo-lumens. Case 2 is 63-year-old male, with the pain of the right mandible. The bulky tumour was seen in the right oral floor to the mandible, and it occupied the movable area of the tongue. CT indicated left neck lymph nodes, pulmo-hilar lymph nodes and osteolytic metastasis to the Th8. Radiotherapy against the bones was done, but he died of disease after 3 months. Histologically, the biopsy specimen showed the growth of atypical hobnail cells with vascular space-like lumens, like angiosarcoma. Immunohistochemically, both cases were positive for CAM5.2, CK5/6, p40, and vimentin, whereas they were negative for CD31, CD34, factor 8-related antigen and E-cadherin.

Conclusion: ASCC is a rare variant of SCC, and moreover, PAC is an extreme histological subtype of ASCC, which is exceedingly rare. The morphogenesis of PAC is related to loss of E-cadherin, whereas epithelial-mesenchymal transition may also occur.

PS-09-005

Differentiated oral intraepithelial neoplasia (DOIN), an under-recognised entity in the oral cavity

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Background & Objective: Differentiated oral intraepithelial dysplasia (DOIN) was described by Japanese pathologists in 2007 but is not recognized by the WHO. As in the vulva and penis, differentiated dysplasia in the oral cavity is a diagnostic challenge. We determined reliable histological criteria for the diagnosis of DOIN and assessed the usefulness of cytokeratin 13 and 17. The frequency of DOIN in oral squamous cell carcinoma (OSCC) was also estimated.

Method: All OSCC cases from 2014 to 2017 were reviewed for the presence of dysplasia. For differentiated dysplasia histological features were studied in detail, and diagnostic criteria were established. Inter-observer agreement was measured. Immunohistochemistry with CK13 and CK17-MIB1 was performed.

Results: We noted DOIN in 69% (143/207) of OSCC cases. The histological changes of DOIN were conspicuous in only 27% of cases, while in 73% the changes were subtle. Immunohistochemistry with CK13 and CK17 correlated with the histology: loss of CK13 and expression of CK17 in dysplasia.

Conclusion: Differentiated dysplasia (DOIN) is more frequently associated with oral carcinoma than usual dysplasia. In most cases the histological changes are subtle. In this study we have attempted to define the histological criteria. Cytokeratins 13 and 17 can be useful for supporting the diagnosis. Uniform terminology for precursor lesions leads to progress in knowledge and treatment. The WHO recently introduced 'potentially malignant disorders' in the oral cavity, and we hope in future will also recognize differentiated oral dysplasia.

PS-09-006

NUT midline carcinoma: a series of 21 cases of an under-recognised entity from a single tertiary care oncology centre

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Background & Objective: NUT midline carcinoma (NMC) is highly aggressive, under-recognised entity characterized by NUT-BRD4/3 fusion. We hereby, report the clinicopathological features of 21 cases of NMC from a single tertiary-care oncology centre

Method: NUT immunohistochemistry (IHC) using C52B1 antibody clone was performed in 95 cases of poorly/undifferentiated tumours, wherein NMC was suspected morphologically. Clinico-radiological details and histopathological features were recorded.

Results: Twenty-one cases (21/95) were diagnosed to be NMC, as they reveal positivity for NUT-IHC; with age range of 9-61 years (median=25.5years) and M:F ratio of 1:1. Tumour was primarily located in sinonasal region (n=11), lung hilum/mediastinum (n=8) and larynx (n=2). Imaging revealed locally infiltrating lobulated masses with extension into adjacent structures. 11 cases had metastasis at presentation. Histopathological evaluation revealed undifferentiated tumour exhibiting minimal pleomorphism. In addition to characteristic focal abrupt keratinisation (n=14); cytoplasmic clearing (n=10), spindling (n=3) and neutrophilic infiltration (n=2) was also noted. More than half cases (13/21) were initially misdiagnosed. BRD4-NUT gene-rearrangement by FISH was also demonstrated in one case. Multimodality treatment options including chemotherapy (n=5), combined chemo-radiotherapy (n=7), palliative radiotherapy (n=3) & surgery (n=3) were used. Seven patients died of disease with median overall survival of 5.5 months.

Conclusion: This is the first ever documented report on clinicopathological features of NMC from this region. Abrupt keratinisation and lack of pleomorphism in an undifferentiated midline tumour are the clue to diagnosis. Increasing awareness amongst pathologist and use of NUT IHC helps to ascertain the diagnosis of NMC.

PS-09-007

Elevated expression of IMP1-1 in thyroid cancer

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Background & Objective: The IGF-II mRNA-binding protein (IMP) regulates mRNA binding of certain genes. Aim of this study was to

determine if IMP1-1 is involved in the tumourigenesis of thyroid cancer and if there is a difference in IMP1-1 expression within the 4 tumour types: papillary, follicular, medullary and anaplastic carcinomas. For this purpose, the expression of IMP1-1 in thyroid cancer tissues was compared to benign thyroid lesions.
Method: The immunohistochemical evaluation included 95 patients: 26 papillary, 22 follicular, 14 medullary, 4 anaplastic carcinomas and 29 benign lesions (struma, adenomas, Hashimoto thyroiditis). Age of the patients at diagnosis, histopathological diagnosis, tumour size and stage were recorded. All tissues were immunohistochemically stained for IMP1-1.
Results: Our results demonstrated that in the case of all types of thyroid carcinomas compared to benign lesions, IMP1-1 (p=0.007) was significantly increased in the cytoplasm of the respective malignant cells. Additionally, IMP1-1 was higher expressed in papillary (p=0.000) and medullary carcinomas (p=0.021) compared to benign lesions. For follicular and anaplastic lesions, no sig. was observed.
Conclusion: Our preliminary data reveal an important role for IMP1-1 in the carcinogenesis of papillary and medullary thyroid cancer. Thus, IMP1-1 might be a potential novel target for new anti-cancer drugs in thyroid cancer therapy.

PS-09-008
Epithelial-myoepithelial carcinoma of head and neck: a single institution series of classical and 'not-so-classical' subtypes
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Background & Objective: Epithelial-myoepithelial carcinoma (EMC) is a malignant salivary gland neoplasm with dual epithelial and myoepithelial differentiation. Recent evidence has suggested link between EMC and Pleomorphic adenomas (PA), and Adenoid cystic carcinomas (ACC). The present study is a detailed clinic-pathological evaluation of "EMC" cases with special emphasis on variant and hybrid forms.
Method: Archives of a tertiary care oncology center were searched for cases reported as EMC. All the cases were reviewed for relevant clinical (Electronic medical records and patient's charts) and histological parameters.
Results: A total of 25 cases with 28 tumours were retrieved (2005-February 2018). M:F ratio was 1.4:1, with an age range of 35-82 years (mean,55.3; median, 54). Parotid gland was involved in 50.4% cases. palate in 17.9%, and submandibular gland in 11.2% cases. Classic histology was seen in 12 cases, intermediate in 3 cases, and high-grade transformation in one case. Morphological evidence of PA was seen in 5 cases and 4 cases had hybrid EMC-ACC morphology. The myoepithelial cells were clear in 12 cases, spindled in 6 cases and 3 cases had both types. One case each of oncocytic and papillary epithelial morphology was seen. Follow up ranged from 2-312 months with recurrence in 4 cases; the longest interval to recurrence being 25 years.
Conclusion: A substantial number of "EMC" cases have morphological overlap with PA or ACC, thus questioning their true nature. A multicenter collaborative study with detailed molecular analysis of biphasic salivary gland tumours is essential to distinguish true EMCs vs variant/hybrid forms.

PS-09-010
Acantholytic squamous cell carcinoma (SCC) and salivary duct carcinoma ex-pleomorphic adenoma: relationship to aberrant expression of E-cadherin
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Background & Objective: It is extremely rare that squamous cell carcinoma (SCC) arises in the salivary glands. Acantholytic SCC (ASCC) is a rare variant of SCC, which frequently arises in the skin. We report here two extremely rare cases of ASCC, which was the carcinomatous component of carcinoma ex pleomorphic adenoma (CXPA).
Method: We selected "ASCC ex pleomorphic adenoma (PA)" from our pathology file during 2002-2017 and examined them immunohistochemically.
Results: Case 1 is 72-year-old female (the left submandibular gland). She received the resection and radiotherapy, but alive with disease. Case 2 is 67-year-old male (the right submandibular gland). After the resection was done, he is alive without disease. Histologically, two cases involved hyalinized nodules, which were the old PA, and the Roman-arch or cribriform growth areas of the atypical ductal cells at the periphery of the PAs, which were salivary duct carcinoma (SDC): Theses ductal cells were positive for AR and GCDFP-15 and EGFR. The invasive portions consisted of ASCC, which were positive for CK5/6 and p63, but gland-like structures were negative for mucin stains.: Case 1 showed the rhabdoid-like feature, whereas case 2 showed pseudoangiosarcomatous growth pattern. The cytoplasmic immunolocalization of E-cadherin was observed in ASCC (case1), whereas the decreased expression of E-cadherin was seen in ASCC (case 2). In both cases, SDC components were positive for EGFR.
Conclusion: The early phase in CXPA may start as SDC (basal-like phenotype), and the histological change into SCC may occur beyond the fibrous capsule. Acantholysis of SCC is associated with the aberrant expression of E-cadherin due to CDH1 gene mutation.

PS-09-011
Epithelial-myoepithelial carcinoma arising in the nasal cavity: a case report and review of literature
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Background & Objective: Epithelial-myoepithelial carcinoma (EMC) is a rare low-grade malignant neoplasm of salivary glands that usually occurs in the parotid gland. Its development in the nasal cavity is extremely rare. In this location, clinical presentation is not specific and diagnosis is mainly based on pathologic findings. The aim of this sudy is to describe a rare case of EMC arising in the nasal cavity in a 54-year-old male with review of the literature.
Method: The case was retrospectively analyzed and studied with light microscopy and immunohistochemical staining.
Results: The patient was a 54-year-old male with three month's history of progressive nasal obstruction. CT scan examination revealed a nasal tumour that invades the ethmoid bone. Histopathologically, tumour showed typical myoepithelial and ductal cells biphasic differentiation with areas of tumour necrosis and increased mitotic count. The tumour's dual composition of myoepithelial and epithelial ductal cells has been identified immunohistochemically.
Conclusion: EMC is an uncommon low-grade malignancy with good overall survival despite the potential of distant metastasis and local recurrence. Its distinct histopathological features should be recognized by surgical pathologists in order to establish an accurate diagnosis.

PS-09-013
The risk of carcinoma ex pleomorphic adenoma increases with adenoma size
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Background & Objective: The frequency of carcinoma ex pleomorphic adenoma (CXAP) is largely varying in the literature. This variation might be due to different factors such as ethnic background, environmental conditions, but also can be due to the tumour size at diagnosis. We believe

that the latter could be important, since the carcinogenesis in salivary glands is believed to be a multistep process. If this hypothesis was true the probability to find malignant transformation would be higher in larger adenomas. Therefore, we performed a retrospective study comparing the frequency of malignant transformation in adenomas of different sizes
Method: We analized 312 pleomorphic adenomas excised in our service in the last 25 years relating malignization to the larger diameter d of the neoplasia.
Results: Carcinomas were not observed in 58 adenomas with a larger diameter d < 20mm. The frequency of malignization in adenomas within 20mm ≤ d <40 mm was 5,3% (CI95%: 1,92% to 8,68%). For adenomas with 40mm ≤ d this value increased to 16,5 % (CI95%: 8,61% to 24,39%)
Conclusion: These findings favor the concept of multistep carcinogenesis in salivary glands and call attention to the relatively high risk of malignization in tumours larger than 40mm of diameter in our Brazilian population.

PS-09-015
eIF3p110 expression is elevated in thyroid cancer
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Background & Objective: The impact of eIFs in thyroid cancer remains elusive to date, especially regarding the differences between the four major types papillary, follicular, anaplastic and medullary carcinomas. Previous studies indicate an impact of eIFs on tumour growth in aggressive thyroid carcinomas and conventional papillary carcinomas. Aim of this study was to determine which eIF subunits are critically involved in the tumourigenesis of thyroid cancer. For this purpose, eIF expression in thyroid cancer tissue was compared to benign thyroid lesions.
Method: The immunohistochemical evaluation included 95 patients: 26 papillary, 22 follicular, 14 medullary, 4 anaplastic tumours and 29 benign lesions (struma, adenomas, Hashimoto thyroiditis). Age of the patients at diagnosis, histopathological diagnosis, tumour size and stage were recorded. For eIF expression, tissues were stained for eIF1, eIF2α, eIF3p110, eIF3H, eIF4E and eIF5.
Results: Our results demonstrated that eIF3p110 (p=0.047) was significantly higher expressed in the cytoplasm of all types of thyroid carcinoma cells compared to benign lesions. Additionally, eIF3p110 (p=0.030) and eIF4E (p=0.030) were increased in benign lesions compared to follicular carcinomas.
Conclusion: Our preliminary data reveal an important role for eIF3pp110 in the carcinogenesis of thyroid cancer. Thus, eIF3p110 might be a potential novel target for new anti-cancer drugs in thyroid cancer therapy.

PS-09-016
Her-2 status in recurrent pleomorphic adenoma of salivary glands
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Background & Objective: Pleomophic Adenoma (PA) is the most common salivary gland tumour, accounting for the majority of salivary gland neoplasms. The tumour is clinically and histologically described as single nodules. The incidence of recurrence of PA (RPA) after initial surgical treatment is significant, largely depending on the surgical technique employed. RPA is described as a multinodular lesion, with the size of the nodules varying widely, which may reach the skin, muscles and adipose tissue. Furthermore, RPA has a tendency towards developing multiple recurrences, as well as having an increased risk of malignant transformation to Carcinoma ex Adenoma Pleomorphic (CXPA.)Recently, attention has been focused on molecular targeted cancer therapy in various tumours, including salivary gland tumours. This study was conducted to analyze the role of the HER-2 in PA, RPA and CXPA.
Method: A total of twenty PA, eighteen RPA and seven cases of CXPA cases were labeled immunohistochemically for HER-2. HER-2 was evaluated semiquantitatively and graded from 0 to 3+. HER-2 amplification was assessed by chromogenic in situ hybridization (CISH).
Results: Tumours were negative for HER-2 in all cases of PA, RPA and six cases of CXPA. A case of CXPA showed moderate and complete membranous staining and two cases were negative. HER-2 amplification was not observed in any case.
Conclusion: In conclusion, the lack of HER-2 expression in PA and RPA suggests that these proteins are not involved in development and recurrence. Protein expression in CXPA shows that the HER-2 may play role in the progression of CXPA.

PS-09-017
CDC27, CTBP2, HYDIN, and KMT5A genes involved in carotid paraganglioma pathogenesis
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Background & Objective: Carotid paragangliomas are rare tumours of head and neck arising from the tissue of the carotid glomus. These tumours are usually asymptomatic that results in their late diagnostics. In some cases, they are characterized by expansive growth and metastasis. The location of carotid paragangliomas in close proximity of nerves and blood vessels presents problem for surgical treatment. The study of molecular genetic features of carotid paragangliomas will allow to better understand the mechanisms involved in the tumour formation and progression, and to reveal the biomarkers and the novel therapeutic options.
Method: Whole exome sequencing of 52 carotid paragangliomas using NextSeq 500 System (Illumina) was carried out at the EIMB RAS "Genome" Center. Mutation load was estimated as a number of potentially somatic deleterious mutations per megabase of coding regions. In the study, the archival collection of carotid paragangliomas (without paired blood samples) was used, so potential germline mutations were excluded from the analysis by removing all mutations found in 1000 Genomes Project and ExAC databases.
Results: Ten genes (ZNF717, CDC27, FRG2C, FAM104B, CTBP2, HLA-DRB1, HYDIN, KMT5A, MUC3A, and PRSS3) characterized by the highest level of mutation load were found. In CDC27, CTBP2, HYDIN, and KMT5A only the potentially pathogenic mutations were identified using different predicted tools, such as SIFT, PolyPhen-2, MutationTaster, and LRT.
Conclusion: Thus, CDC27, CTBP2, HYDIN, and KMT5A genes were first found to be involved in the pathogenesis of carotid paragangliomas.

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PS-09-018
The expression and prognostic relevance of programmed cell death protein 1 in tongue squamous cell carcinoma
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Background & Objective: Oral and pharyngeal cancer together are the sixth most common cancer worldwide. Prognosis has remained poor as five-year overall survival rates are around 50% for most countries. Due to invasive treatments, there is need for prognostic factors suitable for clinical use. Programmed cell death protein 1 (PD-1) function as an immune checkpoint receptor and is part of patient´s own immune responses for cancer. PD-1 is expressed in tumour infiltrating lymphocytes (TILs) with

many different malignancies and it is widely proposed to be a potential prognostic biomarker. The aim of the current study was to evaluate PD-1 expression and its predictive role in tongue cancer.
Method: The data of tongue squamous cell carcinoma (TSCC) patients (N = 81) treated in Tampere University Hospital between 1999-2013 was used, while control data consisted of benign reason treated patients (N = 48). The formalin-fixed paraffin-embedded samples were stained immunohistochemically and scanned via digital microscope. PD-1 staining was examined semi-quantitatively with NDP view 2 Viewing software.
Results: PD-1 was detected in the cytoplasm of TILs. TSCC patients with strong invasive front (IF) PD-1 staining showed significantly better 5 years overall survivals than other groups (p = 0.014 Fisher´s exact test). High IF PD-1 expression correlated with better survival (p = 0.02 Log-rank test).
Conclusion: Invasive front PD-1 expression could be a potential prognostic marker in TSCC, although invasive front knowledge isn´t always available in diagnostic biopsies. Further research with increased sample size is needed to evaluate whether intratumoural PD-1 could be used to determine patients prognosis.

PS-09-019
Beauty is only mucosa deep - an analysis of oral lumps and bumps caused by cosmetic fillers
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Background & Objective: Injection of dermal fillers into orofacial tissues is becoming increasingly popular for cosmetic purposes, in particular for lip augmentation procedures. Both natural and synthetic filler materials are available, complications of which can produce a spectrum of clinical and histological appearances. We aimed to review the clinicopathological characteristics of dermal filler cases from 2006-2016 reported at the School of Clinical Dentistry, Sheffield.
Method: An archival search of the Pathology database was performed to retrieve cases reported as being consistent with cosmetic fillers. Cases were assessed for clinical presentation, site, provisional diagnosis, histological appearance of the foreign material and for the presence of a host response.
Results: 10 cases of orofacial cosmetic fillers were retrieved. 100% of these cases were from female patients and the mean age of presentation was 47.6 years (range 24-68 years). The lips were the most frequently involved site (80%, n=8). The majority of provisional diagnoses were related to salivary gland disease including neoplasms (30%, n=3), cysts (20%, n=2) and inflammatory disease (10%, n=1). Only two patients reported a history of undergoing dermal filler procedures, which led to inclusion of cosmetic fillers in the differential diagnosis in these cases (20%, n=2). A variety of filler materials were seen, including collagen, hydroxyapatite and silicone, however hyaluronic acid-based materials were the most common (50%, n=5).
Conclusion: Complications of cosmetic dermal fillers are becoming more common and should be considered within a differential diagnosis for unusual orofacial swellings.

PS-09-020
Expression of EpCAM in adenoid cystic carcinoma
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Background & Objective: Adenoid cystic carcinoma (ACC) is an uncommon malignancy of secretory glands with frequent local recurrence and poor long-term prognosis. The mutational landscape of ACC is currently being revealed, but further studies are needed to identify therapeutic targets of ACC. In this study, we investigated the expression of epithelial cell adhesion molecule (EpCAM) in ACCs.
Method: We retrospectively collected 72 cases of surgically resected ACCs. Using tissue microarray, we conducted immunohistochemical staining using the anti-EpCAM antibody. EpCAM expression was analyzed by intensity score analysis and the total immunostaining score.
Results: The positivity was 97.2% (70/72 cases), regardless of the intensity score. A higher histologic grade (P = 0.002) and specific tumour location (non-salivary gland origin, P = 0.042) showed a correlation with higher EpCAM expression. Diffuse, strong EpCAM positivity was associated with distant metastasis (P = 0.037).
Conclusion: We suggest EpCAM as a candidate molecule for a diagnostic and therapeutic biomarker in ACC. Also, ACCs arising from the salivary gland and the non-salivary gland sites, respectively, might display different pathophysiologies in which EpCAM could play a role.

PS-09-021
Role of VEGF, CD1a- and CD83 - positive cells in development of papillary thyroid cancer
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Background & Objective: VEGF is one of the main potential regulators of angiogenesis and cell migration like potential mitogenic factor that affects endothelial cells addition causes an increase in vascular permeability is involved in fenestrated blood vessels in tumour vasculogenesis, and has the ability to inhibit dendritic cells.
Method: We investigated the relationship between the expression of VEGF and CD1a- CD83-positive dendritic cells in the biopsy specimens of 81 patients with papillary thyroid carcinomas (PTC) immunohistochemically with antibodies against VEGF, CD1a, CD83.
Results: In 85.7% of tumours expressing VEGF was observed decreased infiltration of CD1a+ immature dendritic cells in the tumour stroma, while at 72.2% of VEGF-negative tumours was observed a large number of CD1a+ dendritic cells (5.92 ± 10.43 vs. 13.05 ± 17.17cells / mm2, $\chi 2$ = 6.86; p = 0.009, Mann-Whitney U test). Similarly, at 100% of VEGF-positive tumours was observed decreased infiltration of CD83+ mature dendritic cells in the tumour stroma, while 61.1% of VEGF-negative tumours have an increased number of CD83+ dendritic cells (4.12 ± 6.12 vs.1.48 ± 2.11 cells / mm2$\chi 2$ = 7.64 ; p = 0.006). We discover that the expression of VEGF is inversely related to the density of CD1a+ and CD83+ dendritic cells in the tumour stroma in PTC.
Conclusion: In conclusion we may state that VEGF expression in tumour cells of thyroid cancer can induce neovascularization, suppress dendritic cells and can also affect the behavior of dendritic cells in neoangiogenesis.

PS-09-023
Anaplastic myoepithelial carcinoma – report of two cases
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Background & Objective: High grade malignant tumours with a poorly-/un- differentiated morphology pose significant diagnostic challenges. Increasingly, the use of adjunct immunohistochemical and molecular tests to characterize and delineate the histopathologic phenotype of these tumours has become necessary, particularly in head and neck tumours. Recently, several entities with a poorly-/un- differentiated light microscopic morphology have been defined based on specific immunohistochemical and genetic characteristics.

Method: We herein describe two cases of anaplastic myoepithelial carcinoma, one occurring in the submandibular gland and the other occurring in the left nasal cavity.
Results: Both cases showed a poorly differentiated, high-grade morphology and expression of myoepithelial markers by immunohistochemistry. Molecular testing for HPV was negative in both cases. The submandibular tumour showed an aggressive clinical course, with diffuse pulmonary metastases at presentation, whilst the nasal cavity tumour showed localized disease.
Conclusion: We propose that anaplastic myoepithelial carcinomas constitute a distinct category of non-HPV associated poorly-differentiated malignant tumours in the head and neck region.

PS-09-024
Laryngeal papillomatosis: relationship between human papilloma virus type and prognosis
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*Faculty of Medicine of Tunis, Tunisia

Background & Objective: Human papilloma virus (HPV) is causally associated with laryngeal papillomosis especially low risk types 6 and 11. The clinical course is unpredictable. The present study was undertaken to evaluate the occurrence of HPV types in a group of patients with laryngeal papillomatosis and correlation between clinical behavior and HPV type.
Method: Our retrospective study included 14 patients with laryngeal papillomatosis. We detected and identified HPV type by in situ hybridization using 6 probes: 6, 11, 16, 18, 31 and 33.
Results: Among our population study 64% were infants (3-64 years). the sex ratio was 0.4. Recurrence rate was 86%. Obstructive form was noted in one patient. Invasive carcinoma was reported in one patient. In situ hybridation revealed infection mith 11, 6 et 18 HPV types in respectively 100%, 78% et 21% of cases. In all aggressive forms of laryngeal papillomatosis, HPV-11 was detected and HPV-11 in 57% of cases.
Conclusion: It seems that HPV-11 is correlated with agressive forms of laryngeal papillomatosis and neoplastic progression. Thus, an HPV typing is required for predicting prognosis.

PS-09-025
Morphological changes in the jaws osteomielite: 101 cases
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Background & Objective: Jaw osteomyelitis is one of the most frequent inflammatory disease in the maxillofacial area. The study based on retrospective analysis of morphological changes in bone and soft tissues in osteomyelitis of the mandible to predict the prognosis of disease.
Method: More than 400 slides from 101 patients were examined. It was bone fragments in the form of a sequestrum; the granulation tissue from the place of spontaneous rejection or previously deleted pieces of the jaw bone, and granulation tissue protruding from the external and internal orifices of the fistula; excision fistulous passages.
Results: The most common localization was osteomyelitis of the jaws (45%,) at any age (from 2 to 82 years). According to the WHO classification of age groups the predominance of patients 6 (35-44) and 8 (55-64) age groups (28.9% and 22.2%, respectively) was revealed, followed in descending order of cases followed 5 (25-34) -11,1%, 3 (4-14) and 7 (45-54) 8,9%, 4 (15-24) - 6,7%, finally, 2 (1-4) and 10 (75 and older) in the 2.2%. Osteomyelitis in patients was more common in men (78%) than in women (22%). By computer morphometry, a quantitative assessment of the severity of the inflammatory infiltrate, fibrosis, changes in the specific density of bone tissue was carried out.
Conclusion: Due to the duality of processes not only in pathology, but also in normal bone tissue – osteosynthesis and osteolysis, the results of study could indirectly determine the prognosis of the disease on the restored morphological picture of chronic osteomyelitis during remission and exacerbation.

PS-09-027
Histopathologic evaluation of dental follicles associated with impacted third molars
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Background & Objective: Although the surgical removal of impacted third mollars has been widely carried out by dental surgeons, most decisions are based only on clinical and radiographic findings, while histopathologic aspects have been largely overlooked. Hence, this study was aimed at histologically evaluating dental follicles of impacted third molars with no radiographic evidence of pathology.
Method: We conducted both a quantitative and qualitative analysis (using routine H&E staining) of pericoronal follicles removed from impacted third molars and investigated the association with clinical data. The sample included 36 extracted dental follicles of impacted third molars, obtained from 28 patients, which presented with no radiographic evidence of pathologies.
Results: None of the follicles analyzed showed any pathologic entity. The epithelial lining was observed in 61.1% of samples, being identified as reduced enamel epithelium. We found a significant association between the the presence of inflammatory infiltrate and the group aged over 21 years (64.3%; $p<0.05$). Other histopathologic findings showed no relation to the age group ($p>0.05$).
Conclusion: Considering the absence of pathologic lesions, we suggest that further concerns should be addressed to the decision-making process required for the extraction of impacted third molars, particularly in disease-free and young-aged individuals.

PS-09-028
Beyond the diagnosis of sinonasal papillomas: a retrospective analysis of 38 cases, with radiological-pathological correlation and literature review
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Background & Objective: Sinonasal papillomas (SP) are benign epithelial neoplasms arising from the respiratory mucosa lining the nasal cavity and paranasal sinuses. Despite their benign appellation, SP may be locally aggressive, undergo malignant transformation (4%) and, especially when incompletely resected, recur (15-20%). It is widely accepted that SP high recurrence rate is a reflection of incomplete removal, which, in turn, might be the result of insufficient information available to the surgeon. In the absence of universally accepted guidelines for SP reporting, radiologists and pathologists focus on diagnosis, often omitting tumour grading and staging. We aim to call attention to the potentially aggressive behaviour of SP and to propose an integrated radiological-pathological reporting system that may provide the surgeon with more exhaustive data, leading to improved patient management.
Method: We performed a radiological-pathological retrospective analysis of 38 cases collected in our institution (1998-2018). Additionally, a literature review was carried out.
Results: The mean age was 62,9 years (range 45-82), with a male-to-female ratio of 1.8:1. Our series included three (7.9%) exophytic, seventeen (44.7%) inverted and three (7.9%) oncocytic papillomas, while fifteen cases (39.4%) were categorized as “mixed” for their hybrid

morphology. Nine cases (23.7%) showed HPV-induced morphological changes. Twenty-six cases (68.4%) were classified as grade I/II (benign), eight (21.0%) as grade III (dysplastic) and four (10.0%) as grade IV (carcinomatous). We observed substantial correlation between pathological grade and radiological stage.
Conclusion: SP may behave in an aggressive fashion. Our pathological-radiological reporting system is meant to help improve surgical outcome of SP by providing surgeons with additional information.

Monday, 10 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-10 | IT in Pathology

PS-10-001
Automated versus visual estimation of tumour cell counts in colon cancer specimens
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Background & Objective: Molecular studies became a routine part of pathology. Most rely on the analysis of tumoural DNA extracted from formalin-fixed paraffin-embedded (FFPE) tissue containing enough tumour cells (TC). This amount is usually obtained through visual estimation of the proportion of TC per total tissue cells (TCTT). Our study aims to evaluate the utility of automated measurement of TCTT from H&E stained tissue sections of colorectal carcinoma.
Method: We selected one representative H&E slide from 29 cases of colorectal carcinoma that underwent molecular studies in the last year. The TCTT for each slide was reestimated by automated calculation (TM) using the Philips TissueMark Version 3.2.X in the whole slide, as well as by "eye-balling", performed by three different pathologists (A, B and C). No pathologist knew the estimated TM or each others estimations. In the end, A, B and C were compared with each other. In the end, whole slide "eyeballing" and whole-slide TM estimations were compared.
Results: Standard Deviation (STD) was TM=10.29, A=8.80, B=8.20, C=12.06. STD for the pathologists as a whole (A+B+C) was 12.24. Mean absolute deviation (MAD) was TM=10.75, A=8.15, B=9.27, C=8.90 and A+B+C=12.60. Levene's test of variance between TM and A+B+C was 0.5273, and with each pathologist was A=0.2984, B=0.3164 and C=0.6971.
Conclusion: Our results demonstrate that TM is not significantly different from pathologists taken as a group, nor from any pathologist individually. Our results demonstrate that further work is still needed in order to make automated estimation better in the estimation of TCTT in the near future.

PS-10-003
Bridge the distance between pathologist, a pilot project between Egypt & UK
E. Ayad*
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Background & Objective: Telepathology, the practice of pathology at a long distance, has advanced continuously since 1960. The trial for applying telepathology systems in the Middle East began in 1994 in UAE & SA using the static telepathology technology but both trials were limited. The actual practical start began in Egypt in 2002. The Egyptian trial applied the static & dynamictechniques in a pilot project between the Italian Hospital in Cairo (NPO) and the Civico Hospital in Palermo. This project began in 2003 and continued till 2008. We concluded from our experience that telepathology proved to be a very useful and applicable tool for additional consultingon difficult pathological cases especially for emerging countries with limited resources.
Method: In view of this success we have already established our Digital PathologyUnit (DPU) in the pathology department, Cairo University in 2010 using the Whole Slides Image [WSI]. In 2014, we began a pilot project between the pathology department, faculty of Medicine, Cairo University, Egypt & Histopathology Department, St. James University, Leeds, UK to consult problematic cases of CNS tumours through exchanging the virtual slides of the cases.
Results: From 2014 till now we consulted more than 50 cases.
Conclusion: This scientific channel was very useful for exchanging knowledge & offered our patient a highly specialized medical service.

PS-10-004
Bridge the distance between pathologist, the Egyptian National Project of Digital Pathology
E. Ayad*
*Cairo University, Giza, Egypt

Background & Objective: Telepathology, the practice of pathology at a long distance, has advanced continuously since 1960. The trial for applying telepathology systems in the Middle East began in 1994 in UAE & SA using the static telepathology technology but both trials were limited.
Method: The actual practical start began in Egypt in 2002. The Egyptian trial applied the static & dynamictechniques in a pilot project between the Italian Hospital in Cairo (NPO) and the Civico Hospital in Palermo.
Results: This project began in 2003 and continued till 2008
Conclusion: We concluded from our experience that telepathology proved to be a very useful and applicable tool for additional consultingon difficult pathological cases especially for emerging countries with limited resources. In view of this success we have already established our Digital PathologyUnit (DPU) in the pathology department, Cairo University in 2010. The application of WSI technique in teaching [for under- & postgraduate candidates] was greatly successful and encouraged us to create a huge digital pathology library which will expand our Digital Pathology & E-learning programs to cover our staff and students both in Egyptand in the longer term in the wider Eastern Mediterranean. Furthermore, we successfully used the WSI technique in telepathology for consulting a lot of cases through a cooperation program between Histopathology Department, Cairo University & Histopathology Department, St. James University, Leeds, UK. Nowadays we are establishing a network between different cancer centers distributed throughout Egypt with a central digital pathology lab [The Egyptian National Project of Digital Pathology].

PS-10-005
Digital pathology 2.0: a deep learning image analysis tool to identify lung cancer in human tissue samples
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Background & Objective: The microscopic evaluation of cancer is dependent on the experience of the pathologist. Thus, evaluation time and reliability of the diagnosis can vary considerably. To facilitate the diagnostic process, we developed a deep-learning-based image analysis tool that helps to identify lung cancer in tissue specimens.
Method: The study was based on tissue samples of 712 operated lung cancer patients that were compiled into a tissue microarray (TMA). Haematoxylin-eosin stained TMA slides were scanned at 0.5mm/pixel and 707 tissue cores were manually annotated for cancer areas, necrosis, tumour stroma and benign lung tissue by trained pathologists. The cores were divided into training set (354 cores), validation set (175 cores) and test prediction set (178 cores). Finally, 30 cores from the test set were annotated independently by four different pathologists to determine the agreement between the pathologists and the trained model.

Results: The visual comparisons using probability heat maps revealed striking agreements between manual annotations and the predicted cancer areas by the model. The positive predictive value (PPV) on the pixel level was 0.80 with sensitivity of 0.85 and specificity of 0.95 on the whole test set (178 cores). That was in the range of the agreement when four pathologists annotated the same cancer areas in 30 test cores (sensitivity: 0.80-0.91, specificity: 0.94-0.97, and PPV: 0.80-0.91).
Conclusion: In conclusion, we present a deep learning tool that annotate lung cancer in human tissue specimens with a similar accuracy as pathologists. This tool holds the potential to support pathologists in their routine diagnostic process.

PS-10-007
Interoperable access to meta and analytical data of virtual slides
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Background & Objective: In recent years virtual microscopy was introduced into biobank information systems. One of the remaining problems is the lack of established standards for data structures for the exchange of analytical results (e.g. from image processing). Due to these circumstances, the ability to exchange and reuse data between researchers from different working groups / environments is limited. Therefore, we propose a free and extensible interface for exchanging data of virtual slides based on the FAIR data principles.
Method: The aim of this work was the definition of interoperable data structures that contain relevant information of virtual slides (e.g. all contours of cell nuclei). An implementation independent API was defined to handle all user interaction with the underlying data storage. For the realization of the interface the FAIR data principles were considered. To accommodate the diversity of data, the storage of analytical results must be easily extensible through appropriate architecture and modularization. This was realized via a generic plugin interface.
Results: To solve the problem of missing standards of analytical data for virtual slides, we have proposed a free, generic and extensible interface. A key benefit of our solution is the ability for researchers to access data in a simple, platform independent manner based on open standards. Free and easy access to such data can facilitate the application in new fields of clinical research.
Conclusion: The proposed interface helps researchers from different working groups and institutions to exchange and reuse analytical data of virtual slides by using open and established standards.

PS-10-008
Creation and exploration of 3D models based on whole slide images
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Background & Objective: Histological slides provide very limited 3dimensional information. However, there are histological structures with larger extent that can never be fully displayed within one slide. Shape and relative position of those structures can't be evaluated with traditional microscopy or macroscopy. The approach presented here aims at a full automated reconstruction of large-scale 3dimensional information from series of slides to display and explore results in an intuitive way.
Method: Multiple series, containing 40 to 230 slides each, of consecutive histological sections for colorectal tissue distributed on multiple glass slides have been digitized to acquire WSI. Subsequently, all sections have been segmented and aligned with a rigid intensity-based registration using mutual information to create a pre-aligned image stack. Further alignment of neighboring sections has been achieved using an iterative intensity-based recursive pyramid registration with B-spline transformations. For a subsequent refinement, corresponding landmarks were extracted automatically and aligned using thin plate spline transformations.
Results: For all series 3D models were created. The resulting 3D visualization enables pathologists to review relative positions of crypts, adenomas and muscularis mucosa at a glance and allows identification of different types of adenomas. All data are made available using a dedicated graphical user interfaces to interactively explore and measure at different magnifications of the histological image stack.
Conclusion: Applying image analysis and registration to WSI show an irrefutable benefit of digital pathology. The presented method provides a high efficiency to retrieve spatial information from serial sections of histological slides. The method described can be applied to different origin of specimen and stains.

PS-10-009
The proliferation index estimation with MetPiKi software in meningioma tissue samples
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*[2]Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland

Background & Objective: Meningiomas are the group of mostly benign neoplasms derivating from meningothelial cells. Cellular proliferation index correlates with the prognosis. It is calculated as relation of the percentage of Ki67-immunopositive nuclei to the whole number of neoplastic cells' nuclei. Neoplasms with the index greater than 4% are associated with increased risk of recurrence, while even greater values (>20%) correlate with a higher death rate.
Method: The MetPiKi (Method for Proliferation Index in Ki67) is an computerized algorithm capable of automatic quantification of cellular proliferating index in digitalized tissue samples. To achieve satisfactory results, our method employs a variety of thresholds and morphological operations as well as conversion to colour spaces other than RGB. In order to evaluate proposed method, open source semi-automatic software for digital pathology image analysis – called QuPath (proposed by Bankhead, P. et al.) - was used as the reference (ground truth).
Results: The method performance comparison is based on quantity of detected immunopositive and immunonegative nuclei and calculated proliferation index. In 24 fragments of 3 whole slide images of typical tissue with moderate quality and a low amount of artefacts, we achieved quite concordant values. It appears that particularly satisfactory results were achieved for detection of immunopositive nuclei by MetPiKi, while immunonegative objects need improvement.
Conclusion: MetPiKi can become a helpful and time preserving instrument, which should provide objectivity and reproducibility of digital pathology analysis.

PS-10-010
Classification of degree of differentiation of colorectal neoplasm by changes in the betti number
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Background & Objective: Recently, a new method based on the homology theory for analyzing histological digital images has been developed. The Betti number is in general an important index for homology theory, and in this case can be used to assess the degree of connectivity in tissue.
Method: To calculate the Betti numbers, we need to binarize the images so that they can be considered as mathematical objects. We change the binarizing threshold and investigate the relation between the change profile of the Betti numbers and the different types of cancerous tissue. The state of this change can be considered an expression of the strength of the connectivity, and it differs by type of cancerous tissue.

Results: The calculated results can be approximated by quadratic functions. The distribution of the coefficient on the squared term and the x-coordinates of the vertices are shown. We can see a characteristic distribution for each type of cancerous tissue.
Conclusion: As the binarizing threshold decreases, the images gradually fade to white, and the structure of the tissue is lost. Under the proposed procedure, in areas where the connections in the tissue are tight and clear, the one-dimensional Betti number changes slowly. Conversely, where the connections are vague, such as in a background area filled with impurities, it changes very quickly. The state of this change can be considered an expression of the strength of the connectivity, and it differs by type of cancerous tissue.

PS-10-011
A machine learning pipeline for automatic segmentation and grading on digital pathology images that is robust to annotation noise and uses dynamic sampling
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Background & Objective: Grading whole slide images (WSIs) is an important task in the digital pathology for treatment planning, but it suffers from subjectivity and limited reproducibility. It is also time consuming and therefore expensive, hence the need for a robust and automatic solution. State-of-the-art approaches commonly use deep-learning networks that are trained using static training set which consist of image patches pre-extracted from the WSIs. This approach, because of using a fixed dataset, may waste resources on training the model on easy to learn areas instead of focusing more on the harder areas, resulting to a slow training process with lesser model's precision. It is also common that the neural networks are trained using manually annotated WSIs at the pixel level. These annotations are de facto constrained by pathologists' time resource preventing them to draw highly detailed regions such that connective tissue or lumen areas that may be annotated as malignant because of their location within the cancerous areas. This introduces noise in the data and confuses the model during training.
Method: We propose a dynamic approach where difficult to learn areas are dynamically computed using the model's prediction errors. Patches are sampled from regions where the model is the most wrong and/or ignorant. We also propose a training loss that is robust to annotation noise.
Results: Our proposed approach reaches top tier score on Camelyon17 dataset.
Conclusion: We have proposed a novel pipeline that is robust to annotation noise which uses a dynamic sampling strategy for automatic grading that competes with state-of-the-art approaches.

PS-10-012
Feasibility test of the semiquantitative TMA scoring tool Scorenado on a multi-panel immunohistochemistry study regarding endometrial cancer
T. T. Rau*, M. Eichmann, S. Reinhard, S. Imboden, A. Papadia, M. D. Müller, I. Zlobec
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Background & Objective: Standard tissue microarray (TMA) analysis on the microscope is inconvenient due to row-column-orientation and data-management. Digital image analysis is sophisticated but time-consuming. Here we propose an approach that combines the advantages of digitized images, but under control of the pathologist.
Method: Scorenado is a tool developed at our institute for easier scoring and data management of TMA cores. TMAs are de-arrayed to single core images using QuPath scripts. Images are randomized for unbiased scoring. The pathologist tagged percentage immunohistochemical positivity and three-tiered intensity with the embedded scoring systems. Csv-files export results, grid information, the round of scoring and the date. Scorenado was applied to a next-generation tissue microarray (ngTMA©) of endometrial cancer of 225 patients with triplicate cores and stained with 13 immunohistochemical markers.
Results: The multi-panel immunohistochemistry results in 8775 single images to be scored by the pathologist. Using Scorenado, the invested time per original slide of 100 cores was 15-20 minutes. As obstacles, some pictures were out of focus or the TMA grid not well positioned. The data assembling could further be automated and easily assembled to the clinical data set.
Conclusion: Scorenado is a compromise for pathologists sticking to conventional eye-balling TMA analysis, but who want to be equipped with digitized images and easier data handling. The browser-based approach and roundwise data organization helps to assess inter- and intra-observer variability.

PS-10-013
Automatic classification of non-small cell lung cancer histologic subtypes by deep learning
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Background & Objective: Non-small cell lung cancer (NSCLC) encompasses a heterogeneous group of histological subtypes. Whereas well differentiated NSCLC are typically distinguishable by distinctive histologic features such the formation of glandular structures for ADC and the presence of keratin and/or intercellular desmosomes for LSCC, additional immunohistochemistry is often required for poorly differentiated tumours. The objective of this study was to develop an automated framework to classify NSCLC histologic subtypes by deep learning.
Method: A convolutional neural network (CNN) was developed to differentiate ADC from LSCC, on a cohort consisting of 208 NSCLC patients. Patients cohorts were split into a training set (n=140 patients) and test set (n=68). Histologic slides were prepared from formalin-fixed paraffin embedded tumour blocks, stained by Haematoxylin and Eosin. Slides were scanned and 50 frames (128x128 pixels) were prepared for each tumour with a spatial resolution of 2.3μm/pixel.
Results: The performances of the CNN were evaluated on the test set and were compared with the results of three experienced pathologists. In total 66/68 patients were correctly classified using our CNN. Moreover, additional histologic subgroups could be identified based on morphologic similarity without relying on pathologists' labels.
Conclusion: In conclusion, automated frameworks for histologic subtyping of cancer tissues using deep learning algorithms, could serve as potential analytic companion tools for pathologists in order to support routine diagnostic tasks while bringing quantitative data.

PS-10-014
Comparison of transcriptomic data of localised prostate cancer samples from intermediate to high-risk patients
E. Pudova*, E. Lukyanova, K. Nyushko, S. Kharitonov, A. Belova, A. Snezhkina, Z. Guvatova, G. Efremov, E. Slavnona, B. Alekseev, M. Kiseleva, A. Kaprin, G. Krasnov, A. Kudryavtseva
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Background & Objective: Prostate cancer is the second most common cancer in men. Molecular markers, which help distinguish aggressive and indolent tumours, can be helpful for therapy optimization. Genes characterized by altered expression in the high-risk group can serve as potential molecular markers of unfavorable prognosis.
Method: We performed in silico differential expression analysis of The Cancer Genome Atlas (TCGA) RNA-seq data. Localized prostate cancer samples (n = 96, only Caucasians) were divided into the intermediate-risk

(n = 76) and high-risk (n = 20) groups according to the D'Amico classification. Genes identified as potential prognostic biomarkers by previous studies were considered.
Results: Ten differentially expressed genes were identified. Four genes (CYP17A1, FAM72D, UBE2C, and ESM1) showed decreased expression, and six genes (TCN1, SERPINA3, HP, MMP7, S100A9, and FCN1) exhibited increased expression in the high-risk group. These genes are involved in the formation and maintenance of the extracellular matrix (MMP7, S100A9, FCN1, SERPINA3, and ESM1), metabolism (CYP17A1), cell cycle (UBE2C), neuronal formation (FAM72D), congenital immune response (FCN1), proteolysis (HP, FCN1, MMP7, S100A9, UBE2C, and SERPINA3), and inflammation (SERPINA3, S100A9, and HP). Disruption of all these processes is reported in various types of cancer.
Conclusion: After validation in a larger cohort, these genes could potentially be used in a diagnostic panel for the prognosis of localized prostate cancer to optimize treatments for individual patients.

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Monday, 10 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-11 | Other Topics I

PS-11-001
Tumour to tumour phenomenon: report of 3 cases and review of the literature
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Background & Objective: Tumour to tumour is a rare phenomenon with fewer than 100 cases being described to date, but hypothetical any benign or malignant neoplasm can be a recipient for another tumour.
Method: In the literature, meningioma is the most common recipient neoplasm while the lung and breast carcinomas are frequently the donor tumours. We present here 3 cases:
Results: Case1: A 59-year old woman knowm with pulmonary and hepatic metastases presented wit the suspicion of a genital neoplasm. In this case, hysterectomy was performed and the histologic examination showed a conventional leiomyoma harbouring a focus of neuroendocrine carcinoma. Case2: A 59-year ol female came to the hospital with a presumptive clinical diagnosis of nodular goiter and a total thyroidectomy was performed. Microscopic examination revealed in the right lobe an intestinal adenocarcinoma metastasized in a papillary thyroid carcinoma and in the left lob an intestinal adenocarcinoma metastasized in a follicular adenoma. Case3: A 76-year old woman presented to the hospital with hematuria. CT showed a left renal mass. Nephrectomy was performed and following evaluation, the mass was proved to be a clear cell carcinoma including a focus of urothelial carcinoma.
Conclusion: Although the preoperative procedures can help providing useful informations, only the pathological examination can establish a certain diagnostic.

PS-11-002
Percutaneous musculoskeletal core needle biopsy performed by pathologist. Myopathy study
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Background & Objective: Muscle biopsy has a leading role in the diagnosis of neuro – muscular diseases. Obtaining the skeletal muscle sample is usually done by open / bloody surgical procedure, by various medical – surgical specialties. Muscle core needle biopsy is a viable alternative to this surgical procedure. Properly trained pathologist can perform muscle core needle biopsy and ensure the quality of the sample.
Method: Since 1997 to 2017, data of muscular biopsies carried out in the Hospital Universitario Central de Asturias were collected. Samples were classified depending on: origin department, specimen quality (insufficient or not) and final diagnosis.
Results: In the mentioned period, 721 muscle biopsies were performed. 51% men and 49% women. Mean age of 47 years, with a standard deviation of 22 years. 68% were core needle biopsies performed by pathologists. The remaining 32% corresponded to open surgical biopsies performed by non-pathologists. 7% of the samples received were insufficient for diagnosis, with a similar distribution among the different interventional physicians.
Conclusion: The diagnostic performance is similar, when comparing surgical muscle biopsies and muscle core needle biopsies. This study shows that the interventional pathologist is able to optimize the sample collection, implementing a less invasive methodology, safeguarding the quality of the specimen and limiting the economic cost of the procedure.

PS-11-003
Usefulness of ambulatory muscle needle biopsy in rheumatology practice
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Background & Objective: Muscle needle biopsy (MNB) is a faster and less invasive alternative to open biopsy for the diagnosis of some myopathies. However, its use is still limited. Objective: To describe the diagnostic profitability of ambulatory MNB.
Method: Descriptive study including all patients who, from 2005 to 2017, had undergone a MNB in the rheumatologist office of our Hospital for suspected myopathy. Demographics, clinical data and pathologic diagnoses have been recorded.
Results: In these period MNB have been performed on 49 patients (29 women), with mean age of 52 ± 10 years (range 25-70), all with increased muscle enzymes. In 9 cases this was the only finding. Eight patients presented myalgia or weakness as the only symptomatology; twelve patients had an underlying rheumatic or autoimmune disease; in 6 cases the suspicion was dermatomyositis, in 5 cases vasculitis, and in 4 lipid-lowering myopathy. Four patients suffered fibromyalgia and one diabetes. Among the pathological biopsies (39%), histological diagnosis were polymyositis in 12 cases, dermatomyositis in 3 cases, vacuolar myopathy by antimalarials in 3 cases, and necrotizing myopathy in 1 case. In 1/49 cases (2%) MNB must be repeated due to insufficient sample. In 2/49 cases (4%) the histological diagnosis achieved was not concordant with the definitive diagnosis. Only 2/49 (4%) patients presented moderate pain, and one patient presented a haematoma.
Conclusion: Muscle needle biopsy is a quick, simple, non-invasive and safe technique that can be very useful in rheumatology practice, since it has a high diagnostic yield.

PS-11-004
Consultation second opinion and risk assessment of donor in the Italian transplanation network
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Background & Objective: The shortage of organs suggests using donors with malignancies suitable for organ donation. The national guidelines

have classified the different malignancies and stratified level of risk of tumour transmission. In Italy a second opinion works on call for any kind of questions about the risk of neoplastic transmission.
Method: Here we show data collected in two year 2016-2017 including: time of the request, donor data, medical history, risk assigned and transplantation. A "standard" donor is a donor without risk factors, a "non-standard donor", is a donor with neoplasia. The risk is divided into "negligible risk"-very low risk- and "acceptable risk"- increased risk. Unacceptable when the risk is too high for organ utilization.
Results: We evaluated 582 donors: 334 males (57%) and 248 females (43%). Age ranged from 1 to 90, with a median age of 66. Consultation was requested considering medical history in 307 (53%), at pre-transplant assessment in 208 (36%) and during organ retrieval in 142 (24%). Questions evaluated: urological (185: 32%), gastro-enteric (78: 16%), gynaecological (79: 14%), central nervous system (72: 12%), skin (42; 7%), endocrine (41: 7%), lung (27; 5%), haematopoietic (15; 3%), head and neck (10; 2%) and miscellaneous (11; 2%) pathology. The risk was defined standard in 195 (34%) and non standard in 387 (66%): 199 (51%) negligible, 167 (43%) unacceptable and 21 (6%) non specified risk. Transplant was carried out in 391 (67%) of cases.
Conclusion: Although additional efforts in donors setting are required, second opinion increases the number of organs suitable for donation.

PS-11-005
Foetus Acardius
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Background & Objective: Foetus acardius is a rare malformation verified in monozygotic multifetal gestation due to twin-to-twin transfusion syndrome, with an incidence of 1 in 35,000 births. This complication is classified in amorphus, acornus, acephalus and anceps, according to the structure anomalies present. We describe the case of a 20-year-old woman with twin pregnancy, in which one of the fetuses didn't show heart movements.
Method: The ultrasound examination of the first trimester revealed one viable fetus and a second gestational sac with an embryo without heart movements that became an heterogenous mass with a central bony structure, during the pregnancy. A healthy male newborn was delivered at 41 weeks, and also a placenta and a 10cm mass.
Results: Macroscopic examination showed a placenta with two umbilical cords, one long with three vessels and another short, measuring 5cm, bivascular, connected to the mass. Both umbilical cords were united by two major superficial vessels in the fetal portion of the placenta. The fetal mass had 240g and 10x8x6,5cm, presented a lobed surface covered with skin and a cylindrical structure, without differentiated axial organization. Microscopic examination revealed an amorphous fetus with identification of vertebral bodies, cartilage, muscle, fat and neural tissue. No respiratory or gastrointestinal tissues were present.
Conclusion: This case is classified as an acardius amorphus fetus due to the presence of several tissues without recognizable structures. It is included in the acardius myelanencephalus subgroup because of the identification of neural tissue. However, differential diagnosis with placental teratoma is fundamental.

PS-11-006
An atomic level of cancer biology – personal perspectives based on preliminary results of pioneering interdisciplinary clinical-scale cancer tissue investigation with the use of Continuous Flow Isotope Ratio Mass Spectrometer (CF-IRMS)
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Background & Objective: Isotope Ratio Mass Spectrometry (IRMS) applying in cancer research has gave the unique possibility to recognize a previously unknown atomic level of its biology with prospective clinical impact. Recently, IRMS has been shown to be applicable to the direct evaluation of growing in vivo cancer tissues and statistical significance of such measurements has been proved, introducing the project herein to search for novel directions of isotopic research and for new isotopic type of biomarkers which, in addition to well-established prognostic parameters, may appear helpful to limit unjustified failures still observed in oncologic practice.
Method: Multidisciplinary, clinical-scale analysis of nitrogen and carbon isotopic composition in highly selected cancer tissues with the use of a Sercon 20–22 Continuous Flow Isotope Ratio Mass Spectrometer (CF-IRMS) coupled with a Sercon SL Elemental Analyzer for simultaneous carbon-nitrogen-sulfur (NCS) analysis.
Results: There were found variations in the isotopic signatures of the examined tumours suggest metabolic distinctness and modified isotope fractionation patterns specific to their biology. The relation of nitrogen and carbon isotope ratio in tumour tissue to established prognostic parameters, including histological types according to currently used classifications was confirmed.
Conclusion: IRMS method identifies fundamental overall regularities specific for cancer tissue and offers a new perspective of cancer biology investigation in relation to the standards and needs of contemporary oncology as well as further coming personalized therapeutic strategies. Although multidisciplinary studies are based on the ultramodern approaches, their roots still stay in touch with established pathology knowledge and prognostic parameters revealed in histological examination.

PS-11-007
Control of cold ischemia times for fixation standardisation of surgical pieces in tissue processing in our pathology laboratory
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Background & Objective: Reduce and control cold ischemia times to optimize the performance of histochemical, immunohistochemical and molecular processes
Method: Use of molecular fixative based on alcohols and intermediate liquids (PPS) with different times for tissue processing using very low power microwave processor, 60W (Sakura® Tissue-Tek Xpress x120) Implementation of other fixers other than formaldehyde and without Xylene, adjusting the fixation times according to morphological characteristics, size and type of tissue, searching to optimize the antigenic recovery times.
Results: Elimination of formaldehyde use in the tissue processing phase. Protocolization of the fixation times: 10 minutes for cylinders, 15 minutes for endoscopies, 30 minutes for a large piece, 60 minutes for very large pieces with fat tissue, and when they are even more fat tissues for 75 minutes plus. Improvement of the results of immunohistochemical techniques an molecular pathology reducing false negatives. Reduction of the consumption of formaldehyde and alcohols, as well as reduction of the elimination of potentially dangerous toxic waste.
Conclusion: Modification of the work circuit, adjusting and shortening the fixing and processing times, reducing the diagnostic delay in one day Improvement of the ergonomic conditions of the staff. Decreased handling of toxic products (formaldehyde and Xylene) Improvement of sample quality, combining automation and standardization of protocols

PS-11-008

Association of SLC6A4, HTR2A and DRD2/ANKK1 genes polymorphism with stress resistance and work capacity of athletes

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Background & Objective: Physical and psychological demands, expectations and pressure to perform to a high standard are the main stressors which can increase stress and anxiety in professional athletes. It's well known that polymorphisms of the of the serotonin transporter protein SLC6A4 and serotonin receptors HTR2A and DRD2/ANKK1 genes are associated with psychological disorders. L The aim of the study was to evaluate the association of SLC6A4 (rs140701), HTR2A (rs7997012) and DRD2/ANKK1 (rs1800497) genes polymorphism with psychological and emotional status in athletes.
Method: Simple visual reaction time test and Finger-tapping test were used to determine psychological and emotional status in 141 Russian athletes (involved in speed-strength sports (n=30), endurance events (n=41) and mixed sports (n=70)). SNP typing was performed by TaqMan technology using qPCR.
Results: We found that the mental capacity was significantly higher in carriers of the SLC6A4 rs140701 A allele in comparison with GG homozygotes (functional level of the nervous system: 4.49±0.45 vs 4.39±0.89 points; p=0.0001). Furthermore, stability of attention and operative memory were better in HTR2A rs7997012 C allele carriers compared with TT homozygotes (stability of attention and operative memory: 2.29±1.78 vs 1.44±1.61 points; p=0.04). In addition, DRD2/ANKK1 rs1800497 A allele was significantly associated with higher mental endurance both in men (p=0.0001) and women (p = 0.012).
Conclusion: We showed several associations which can partly explain individual differences in response to mental and physical stress in athletes.

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PS-11-009

Primary testicular lymphoma: pathological and immunohistochemical study of two cases

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Background & Objective: Primary testicular lymphoma (PTL) is an uncommon and aggressive form of extranodal non-Hodgkin lymphoma (NHL) accounting for approximately5% of testicular malignancies and 1% to 2% of NHL.
Method: We report two cases of PTL in males aged80 and 70 years, presented with painless inguinal and scrotal masses. Clinical examination revealed a testicular induration. Ultra sonography showed a diffuse testicular infiltration. An orchidectomy was performed.
Results: On gross examination, mean size, of the specimen, was 8cm. Cut section showed a diffuse white tan tumour with focal areas of hemorrhage, without any normal testicular tissue and often extra testicular involvment. The histological examination showed a large round monotonous population of cells showing isokaryosis and scanty cytoplasm. Malignant cells are pleomorphic and non cohesive with large irregular nuclei and prominent nucleoli. The stroma in between showed scanty fibrovascular tissue. Areas of confluent necrosis and vascular invasion were also seen. At the periphery, the tumour show a distinctive intertubular growth pattern with playing of seminiferous tubules by irregular aggregates, clusters and cords of tumour cells. Immunohistochemistry showed that the tumour cells were positive for CD 20, Bcl2 and negative for cytokeratin, CD 3 and CD10. Ki67proliferation index was 90%. Based on these histologic and IHC findings, the final diagnosis of high-grade NHL of B-cell phenotype was considered.
Conclusion: Testicular lymphoma is a rare and deadly form of extra-nodal lymphoma. Histologically, diffuse large B-cell lymphoma (DLBCL) is by far the most common type of NHL. It is associated with a high incidence of recurrence and carries a poor prognosis.

PS-11-010

Increase of automation laboratory preanalytic and analytical phase of a pathology service

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Background & Objective: Improve the quality, safety and traceability of the surgical pieces, avoiding the loss of samples in the processing and securing adequate orientation.
Method: Implementation of carving tables, adapted to new European formaldehyde regulations, equipped with digital photography, voice recognition and traceability systems. Application of new sizing systems, using Paraform safety capsules SAKURA®. It allows the ability to select the appropriate capsule according to the type of tissue, size and orientation of the sample. Strict control and protocolization of fixation times in formaldehyde and molecular solution if is needed. Tissue processing was performed using SAKURA® XPress 120 processor microwave system (avoiding the need of formaldehyde or xylene), SAKURA® AutoTEC at120 automatic block former and tissue sections with SAKURA® AutoSection automatic microtome.
Results: We obtained consistent improvements reducing manipulation and therefore less human error. Work circuits were reorganized, which improved the implementation of continuous workflows, allowing real time adjustments in relation to the workload throughout the day. New norms and guidelines were implemented to prevent labor risks and exposure to toxins or formaldehyde.
Conclusion: We increased patient safety with decreased errors, material loss (when using safety capsules), maintaining the orientation during paraffin block building. Improve control of ischemia times, quality guarantee in the pre-analytic phase and DNA preservation. Decrease in the workload of staff and the automation of the cutting through the AUTOSECTION allows us an optimal orientation of the sample with less loss of material.

Monday, 10 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-12 | Pulmonary Pathology

PS-12-001

NUT carcinoma: a report of two cases and review of the literature

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Background & Objective: NUT carcinoma (NC) is an aggressive, poorly differentiated carcinoma defined by NUT (nuclear protein in testis – NUTM1) gene rearrangement. We aim to clarify its pathologic features to best recognize this entity.
Method: Report of two cases of NC and review of published cases.
Results: The first case regards a 22-year-old-man with multiple left pleural nodules. The second refers to a 56-year-old-man with a mediastinal mass. Microscopically, both cases showed a poorly differentiated neoplasm with a few abrupt foci of epidermoid differentiation. Immunohistochemical study was performed with reactivity for

CAM5.2, AE1/AE3 and p63. In both cases, the tumour cells were immunoreactive for NUT antibody and the diagnosis of NC was rendered. We retrieved 138 cases from the English language literature. NC is most commonly found in the second and third decades of life (46%), although it can affect people of any age without sex predominance. Head and neck were the most frequent locations (36%), followed by lung (34%) and mediastinum (24%). It was initially described as a midline neoplasm, but non-midline locations are frequent as well. 35% patients have metastatic disease at presentation and the median survival is 6.7months. Four large retrospective analyses of poorly differentiated carcinomas identified NC cases there contained only after performing immunohistochemistry with NUT antibody and/or genetic study.
Conclusion: NC should be considered in poorly differentiated/undifferentiated carcinomas with immunoreaction for p63, despite the age of the patient or tumour location; NUT antibody should be included in diagnostic immunohistochemical panels.

PS-12-002
Transbronchial lung cryobiopsy from 2 segments in interstitial lung disease: impact on the diagnostic yield
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Background & Objective: Evaluate if there is an advantage in performing transbronchial cryobiopsies in two separate topographies in the context of interstitial lung disease.
Method: Review of 28 patients, each undergoing transbronchial cryobiopsies in two separate topographies. The two samples of each patient were evaluated by Pathologist A, and a histological analysis was made for each. At a later time, Pathologist B performed the same task. The situations in which the diagnosis depended on the performance of two biopsies were analyzed.
Results: In 18/56 situations (32.14%), the presence of two samples allowed for a final positive diagnosis since one of the two samples was undiagnostic (12 situations of hypersensitivity pneumonitis; 5 of usual interstitial pneumonia; and 1 of descamative interstitial pneumonia). Nonspecific interstitial pneumonia had concordant diagnosis in all the samples. In the remaining situations the diagnosis was the same in both samples or inconclusive in both samples as well.
Conclusion: Performing transbronchial cryobiopsies in two separate topographies in the context of interstitial lung disease provides improved diagnostic yield in hypersensitivity pneumonitis and usual interstitial pneumonia. Different degrees of topographical involvement of these disorders may account for the finding.

PS-12-003
Comparative histopathological-mutational analysis and evaluation of tissue biomarkers in synchronous and metastatic lung adenocarcinomas
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Background & Objective: Adenocarcinoma is the most common lung cancer up to 8% present as multifocal. The distinction of synchronous tumours from intrapulmonary metastasis represents an important problem significantly influencing tumour staging and therapeutic strategies. This definition has been continuously refined. Recently IASLC proposal criteria for resected specimens highlighted the need of a multidisciplinary approach that mainly considers histological features and molecular alterations. The role of other aspects (e.g. imaging or biomarkers) is still debated. We compared histopathological features, molecular signature and tissue biomarkers (ALK, ROS1, PD-L1) in multiple lung adenocarcinomas detected simultaneously in the same patient.
Method: 9 patients surgical resected in 2016 for 2 lesions were grouped as "synchronous" (6) and "metastatic" (3) following the current criteria. The 18 nodules were analyzed for histological features: prevalent pattern, extension of necrosis, inflammation and fibrosis (%) and presence of intra-alveolar, vascular and perineural invasion. Ki67 immunostaining was expressed as %. ALK and ROS1 were scored as 0-3; PD-L1 was evaluated following TPS (Tumour Proportion Score). Mutational analysis of 10 genes was performed by Sequenom "Myriapod Lung Status" kit.
Results: The prevalent pattern was similar in both lesions without difference between the groups. Only KRAS mutations were detected and KRAS mutational status was always different in the two lesions, except for one metastatic case. Interestingly, PD-L1 was highly expressed in all metastatic cases and only in one synchronous lesion with a 100% solid pattern and a high Ki67 value.
Conclusion: These preliminary findings suggest a diagnostic/predictive value of PD-L1 in concomitant lung adenocarcinomas (metastatic and synchronous) but a large case series is mandatory.

PS-12-004
Programmed death ligand-1 (PD-L1) expression in non-small cell lung cancer (NSCLC), results of a single institution
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Background & Objective: In recent years promising results have been reported in immune checkpoint inhibitor therapy in advanced stage non-small cell lung cancer (NSCLC). Programmed death ligand-1 (PD-L1) expression of the tumours has a predictive value of better response. We aimed to investigate the PD-L1 expression rates of the NSCLC cases in our institute.
Method: Immunohistochemical (IHC) reaction for PD-L1 was carried out on 334 NSCLC patients' formalin fixed paraffin embedded material. We used DAKO PD-L1 IHC 22C3 pharmDx antibody on Autostainer Link 48. The basis for grouping were the PD-L1 expression by percentage and the histologic subtype of the tumours. The first group represents the negative cases showed less than 1% positivity, in the second group 1-49%, in the third more or equal to 50% of the tumour cells showed positive reaction. KRAS mutation analysis was performed in 248 cases.
Results: 219 (65,6%) expressed PD-L1 protein of which 121 (36,2%) showed 1-49 % and 98 (29,4%) more or equal to 50% positivity. 301 (90,1%) were adenocarcinomas among which a nearly equal distribution was observed with 34,4%, 36,2% and 29,4% by groups. 28 (8,4%) were squamous cell carcinomas of which one third proved to be negative and 60,7% fell into the second group. In the KRAS mutated group 74,3% of the cases showed PD-L1 expression while in the wild-type group 58,7% proved to be positive.
Conclusion: Two thirds of NSCLC cases showed PD-L1 expression with a nearly equal ratio of the two groups. A relatively high number of KRAS mutated tumours expressed PD-L1 protein and a lower rate of the wild-type cases proved to be positive.

PS-12-005
Mutations at the chromatin remodeling complex subunit and immune phenotypes in lung adenocarcinoma
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Background & Objective: The SWI/SNF complex is key for chromatin remodelling and some of its subunits have been found mutated in cancer. These mutations might be relevant in the tumour mutational burden, generation of neoantigens and MTOR, IFNg pathway regulation.

Method: Using next generation sequencing (NGS) on 93 non-small-cell lung carcinomas (NSCLC), somatic mutations were found in about 10% of them, which prompted us to perform immunohistochemical studies on 50 additional NSCLCs and to analyze the potential correlation between defects in the SWI/SNF complex and their immune phenotype. 250 genes including relevant chromatin regulators were sequenced in the first 93 NSCLCs. 38 samples corresponded to surgical specimens with enough archival tissue to perform immunohistochemical studies. A second cohort of 50 NSCLCs was recently evaluated for SWI/SNF immunohistochemistry and immune phenotype, assessed scoring tumour infiltrating lymphocytes (TILs), according to Immuno-Oncology Biomarkers Working-Group. Intraepithelial and stromal compartments were assessed independently. A semi-quantitative scale was used to grade TILs in each compartment. Samples were grouped for analysis in non-inflamed/inflamed.
Results: 18 samples (first-cohort) resulted SWI/SNF mutant (second-cohort ongoing). Good correlation was found between weak/negative nuclear SWI/SNF immunostaining and mutations (5/8), while strong immunostaining was present in the wild-type samples (30/30). Inflammed tumours were more common among mutant cases (4/6) than wild-type ones (4/17).
Conclusion: SWI/SNF mutations are found in NSCLCs. Among mutant cases, a trend was observed towards more abundant TILs. It could be speculated that these mutations, by altering the process of chromatin remodelling and DNA damage repair, could trigger immune response.

PS-12-006
Bulk tumour cell migration is more common than classical epithelial-mesenchymal transition in lung carcinomas

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Background & Objective: Epithelial-to-mesenchymal transition (EMT) is often described as a requirement for tumour cell migration. However, histopathological findings provide evidence that carcinomas also migrate in cell bulks. The aim of our study was to characterise bulk cell migration in non-small cell lung cancer (NSCLC).
Method: Thirty cases of NSCLC with blood vessel invasion were selected to immunohistochemically identify relevant proteins for bulk cell migration. These proteins were validated in 528 NSCLC cases via tissue microarray (TMA) technology. An additional TMA-analysis was performed for 165 corresponding metastases. Furthermore, the frequency of bulk cell migration was evaluated in 232 adenocarcinomas (AC) and squamous cell carcinomas (SCC).
Results: Bulk cell migration showed many differences in marker expression and regulation compared to classical EMT: The expression of Twist was not associated with TGFbeta1 and Wnt. Slug, betaCatenin, Snail, and Smads were negative in most tumours. E-Cadherin was mostly coexpressed with N-Cadherin. Cytokeratins were coexpressed with vimentin in a few, and with fascin in the majority of cases. Expression of ERK1/2 was downregulated, whereas PLCgamma was upregulated at the invasion front and in metastasis. Brk and Mad were expressed both in the primary tumour and metastasis. In contrast, positivity of Tks5 and Rab40B was confined to the invasion front and metastasis.
Conclusion: Twist, vimentin, fascin, Mad, Brk, Tks5, Rab40B, ERK1/2 and PLCgamma are involved in a mode of carcinoma migration that requires only a partial EMT. This mechanism can be described as bulk-, hybrid-, or complex migration and predominates in pulmonary AC and SCC.

PS-12-008
Pathophysiological features of lung and skin in human SSc and collagen V/C57LB6 mouse model

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Background & Objective: Experimental models are important to understanding of the pathogenesis and new therapies of Systemic sclerosis (SSc). Our proposal was characterise functional, serological and histopathological features of skin and lung in SSc patients and type V collagen (ColV)/C57BL6 mouse model.
Method: The histopathological patterns in skin and lung biopsies of 23 SSc patients and five controls were assessed and compared with female C57BL/6 mice immunized with ColV in Freund´s adjuvant. Mice were euthanized after 120 days and skin and lungs were examined by histology, immunofluorescence, immunohistochemistry, histomorphometry, qRT-PCR, ELISA and pulmonary mechanics.
Results: Immunized mice presented positive antinuclear antibodies and anti-collagen type III and IV autoantibodies in serum. ColV/C57BL6 skin showed increase number of inflammatory cells and collagen type III and V ($p<0.01$) deposition coincident with COL3A1, COL5A1 and COL5A2 gene increased expression. SSc human skin biopsies showed fibrosis with abnormal dermal histoarchitecture and increased ColV in derma and vessels ($p<0.01$). At 120 days, mechanics evaluation of ColV/C57BL6 lungs showed high resistance ($p<0.01$) and elastance ($p<0.01$) coincident with interstitial fibrosis and sclerosis of intrapulmonary arteries. Lungs ColV/C57BL6 also presented increased total collagen by 4-hydroxyproline ($p<0.01$), CD4+ T lymphocytes ($p<0.01$), transforming growth factor beta ($p<0.01$) and connective tissue growth factor ($p<0.01$). Lung and sky biopsies of ColV/C57BL6 demonstrated comparable vascular, inflammatory and fibrotic manifestations of human disease.
Conclusion: We conclude that all typical manifestations of human SSc-related pulmonary and skin remodeling are mimicked in ColV immunized C57BL6 mice, suggesting an appropriate preclinical model to study pathogenetic mechanisms and new target therapies for this disease. FAPESP - FFM

PS-12-009
Comparison between the 7th and 8th edition of the TNM staging system in primary resected pulmonary squamous cell carcinomas

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Background & Objective: The AJCC/UICC TNM classification is a regularly updated standardized system for the description of anatomical extent and stage grouping of solid malignant tumours.
Method: We compared the new 2017 8th edition of the TNM classification with the former 2009 7th edition, in a clinicopathologically well-annotated Western single-center cohort of 354 consecutive pulmonary squamous cell carcinomas (pSQCC), resected 2000-2013, without previous neoadjuvant therapy. Patients with a clinical history of SQCC of other organs were excluded to reliably exclude lung metastases. Patients in whom TNM was unclear due to multiple tumour nodules were excluded. We reevaluated all pathological records and slides and retrospectively validated pleural invasion.
Results: The stage distribution according to TNM 7th edition was as follows: IA (2009): 59 (16.6%), IB: 74 (20.9%), IIA: 72 (20.3%), IIB: 53 (15.0%), IIIA: 79 (22.3%), IIIB: 7 (2.0%), IV: 10 (2.8%). Staging the cases according to TNM 8th edition, 7/354 (2.0%) cases were downstaged, 153 (43.2%) were upstaged; most pronounced between stages IIA(7th) and IIB(8th), and IIB(7th) and IIIA(8th). Both staging systems showed significant prognostic impact for overall survival, disease free and disease specific survival and time to recurrence, but TNM 7th was slightly superior regarding prognostication with lower values for goodness-of-fit criteria (Akaike Information Criterion and Schwarz Bayesian Criterion).

Conclusion: In conclusion, we show a significant stage migration between tumours staged using TNM 7th versus 8th edition, without benefit regarding prognostication in our cohort of pSQCC.

PS-12-010

Fractal dimension of Chromatin is an independent prognostic factor for survival in patients with small cell neuroendocrine carcinoma of the lung

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Background & Objective: The fractal dimension of chromatin characterizes the global organization of the cell nucleus. Previous studies have shown that this variable is an independent prognostic factor for survival or treatment success in leukemias or solid malignant neoplasias. The aim of our investigation was to show whether the fractal dimension of nuclear chromatin in routine cytologic slides of small cell neuroendocrine carcinomas of the lung would also be an independent prognostic factor for overall survival.
Method: Digitalized images of routinely stained cytologic slides from 48 patients were acquired. After segmentation of the nuclei the fractal dimension of chromatin was estimated by an in-house developed software. The prognostic relevance of the fractal dimension was evaluated by Cox regression analyses in comparison with well established prognostic factors.
Results: In the final multivariate Cox regression the fractal dimension of chromatin revealed to be an independent prognostic factor for overall survival together with tumour stage and the clinical Karnofsky performance status.
Conclusion: Our investigation suggests that the global nuclear organization estimated by the fractal dimension of chromatin in routine cytologic preparations is an independent prognostic factor for overall survival in patients with pulmonary small cell neuroendocrine carcinoma

PS-12-011

Simultaneous IHC and FISH biopsy testing offers a more complex understanding of the ALK status complexity in NSCLC: experiences from a series of 1,549 NSCLC biopsies

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Background & Objective: The detection of ALK gene status in adenocarcinoma (ADC) type of NSCLC became an integral part of the biopsy examination. The clinical studies demonstrating benefit of ALK inhibitors were based on ALK status detection by FISH. However, the testing guidelines allow to apply IHC examination of ALK protein expression as a simple method with less running costs which might be validated for therapy.
Method: 1549 biopsies of EGFR non-mutated lung adenocarcinomas were tested immunohistochemically (IHC) using anti-ALK (D5F3) antibody (on Benchmark GX platform, both Ventana) and 1539 of them also by FISH using a) ZytoLight® SPEC ALK Break Apart Probe (Zytovision) and/or Vysis ALK Break Apart FISH Probe Kit to detect rearrangement of 2p23 and in positive cases also by b) ZytoLight® SPEC ALK/EML4 TriCheck™ Probe (Zytovision) to detect ALK/EML4 inversion.
Results: In 2,9% of cases tested by IHC and 6,5% tested by FISH the results were not available either for insufficient tumour cell number or for insufficient FISH signals. 6,6% of the succesfully tested cases showed ALK gene rearrangement by FISH test and 6,3% of cases with available IHC results showed ALK positivity. 26 (1,7%) of all cases with available both FISH and IHC results showed discordancy of both examinations.
Conclusion: Parallel IHC and FISH tests of the ALK status in biopsies of ADC patients represents a challenging and time-consuming method, however even a low percentage of discrepantly positive cases advocate the benefit of such combined approach for the involved patients.

PS-12-012

Yield of bronchoscopic cryobiopsy for the diagnosis of diffuse parenchymal lung disease: our experience in 119 cases

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Background & Objective: Although in some cases clinical and radiographic features may be sufficient to establish a diagnosis of diffuse parenchymal lung disease, surgical lung biopsy is frequently required. A new technique for bronchoscopic lung biopsy has been developed using flexible cryo-probes. In this study we describe our clinical experience using bronchoscopic cryobiopsy for diagnosis of diffuse lung disease.
Method: A transversal study of subjects who has undergone bronchoscopic cryobiopsy for evaluation of diffuse parenchymal lung disease at Navarra Hospitalary Complex during the last 6 years has performed. The cryobiopsy was performed using a flexible bronchoscope to acquire biopsies of lung parenchyma. H&E stained biopsies were reviewed by a lung pathologist. All the cases were discussed in a multidisciplinary committee.
Results: 119 subjects were followed. The mean number of samples per subject was 2.73, obtained 325 valid samples of a total of 372, with a mean area of each sample of 23.41 mm². In 78 of 119 subjects the cryobiopsy were diagnostic, 18 of 119 with a high likelihood diagnosis and 23 of 119 subjects were not diagnosis. The overall diagnostic yield of bronchoscopic cryobiopsy was 81.67% (96/119). Eight of 119 cases included pleura. The most frequent diagnosis was usual interstitial pneumonia (UIP) (n=35). Six of the 23 subjects ultimately required surgical lung biopsy. The significant complications were 8 hemorrhages and 19 pneumothorax.
Conclusion: In patients with suspected diffuse parenchymal lung disease, bronchoscopic cryobiopsy is a promising and minimally invasive approach to obtain lung tissue with high diagnostic yield.

PS-12-014

Microfluidics-based immunofluorescence for fast staining of ALK in lung adenocarcinoma

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Background & Objective: Rearrangement of the anaplastic lymphoma kinase (ALK) is a key oncogenic driver event in lung adenocarcinoma. Therefore, reliable assessment of ALK status is of high clinical relevance. The microfluidic tissue processor (MTP) device is based on a chip-confined low-volume technology allowing for rapid immunohistochemistry/immunofluorescence (IHC/IF) staining of formalin-fixed paraffin-embedded (FFPE) or frozen tissue samples. Here, we aimed to develop a novel ALK IF protocol using the MTP device for FFPE tissue sections.
Method: FFPE tumour whole sections from 14 resected lung adenocarcinoma patients documented to be ALK+ by automated chromogenic IHC and/or FISH (fluorescent in situ hybridization) were re-stained by MTP device using the primary mouse anti-human ALK antibody clone 5A4. MTP-derived IF immunoreactivity was measured by computerized analysis of digitalized images.

Results: The 5A4 antibody yielded saturated immunoreactivity at an incubation time of 4 min on a titration curve ranging from 2 to 32 min. Total staining time on the MTP device was 18 minutes including secondary IgG AlexaFluor-647. MTP-based ALK IF confirmed all 14 cases; with epithelial signal above stromal staining. MTP-IF (mean intensity level 458 to 1301) and chromogenic IHC (H-score 120 to 300) showed an equal range of variation of 2.8 and 2.5 fold, respectively, and a trend for direct correlation (p-value 0.051).
Conclusion: The MTP-based IF is fast and reliable: protocol for immunofluorescent detection of ALK protein with the MTP device confirmed the chromogenic IHC results. We foresee that this approach may allow the current ALK testing to evolve from semi-quantitative to fully quantitative using fluorescent labels.

PS-12-015

Diagnostic consistency among pathologists and malignancy by anatomical site in a cohort of 2,946 lung core biopsy specimens

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Background & Objective: Observational data is not routinely used to assess lung biopsy quality via control charts, as used in statistical process control (SPC)/Next Generation Quality(NGQ).
Method: All in house lung core biopsies at one institution were extracted for the period July 2012-June 2017, and categorized using a hierarchical free text string matching algorithm (HFTSMA) to obtain the anatomical site (AS) (RUL|RML|RLL|LUL|LLL|Lingula|Right Not Otherwise Specified (NOS)|Left NOS), and diagnostic grouping (negative(NEG)|suspicious(SUS)|malignant(MAL)). Pathologist diagnostic rates (PDRs) were calculated and normed by (1) maximal cases read, (2) the standard errors (SEs) to the group median diagnostic rate (GMDR). Normed PDRs were compared on control charts with control lines +/-2 and +/-3 SEs from the GMDR.
Results: The cohort contained 3,051 core biopsy specimens. The accuracy of the HFTSMA was estimated at 97% for all cases and >99% for categorized cases for both AS and diagnosis based on a several audits of >400 cases. Fifteen pathologists interpreted 44to533 cases and together assessed 2,946. The GMDR (normed PDR range) was for NEG_39%(36to44%), SUS_2%(1to6%), and MAL_55%(49to59%). The number of pathologist outliers (P<0.05andP<0.001) were for NEG: 2and0 (of 15), SUS_4and4 and MAL_1and0. Number of biopsies (%malignant of site) varied by AS: RUL_706(58%), RML_219(35%), RLL_489(50%), LUL_562(61%), LLL_326(53%), Lingula_66(38%), RightNOS_233(58%), LeftNOS_209(56%). Cancers were more common in the upper lobe than lower lobe (63%vs37%) and right side than left side (57%vs43%).
Conclusion: In the cohort cancer favoured specific anatomical sites. The pathologist is a predictor of the diagnostic category, suggesting optimization using SPC/NGQ could increase consistency.

PS-12-016

Participating in quality assurance schemes has a major impact in PD-L1 scoring trend in Belgium

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Background & Objective: We organized a Belgian ring trial for PD-L1 IHC staining in non-small cell lung cancer (NSCLC). The trial consisted of 2 rounds, organized in 02/2017 and 02/2018 respectively. In the first round, 24 different sites participated. In the second round, 22 laboratories participated, 16 of which participated also in the first round.
Method: Unstained slides of NSCLC cases were prepared. The first and last slides were stained with PD-L1, using PD-L1 22C3 pharmDX kit of Agilent on an Autostainer Link 48 platform. Each participating laboratory received 2 unstained slides and was asked to return 1 PD-L1 stained slide per case, to report the protocol that was used and their PD-L1 score. The stained slides were evaluated by a team of 3 pathologists trained for PD-L1 scoring in NSCLC by Agilent. Comparison of the evaluation by the pathologists of the different laboratories and the evaluation by the team of referent pathologists was communicated to the laboratories.
Results: The majority of the laboratories used an in-house assay. In the first round 22C3 PD-L1 antibody clone was mainly used. In the second round, a shift to SP263 was observed. Of the participating laboratories, approximately 50% have a Ventana Benchmark apparatus at their disposal. In the first round, a systematic underestimation of the amount of tumour cells with membranous PD-L1 expression was observed. In the second round, the average disconcordance between the pathologists for PD-L1 interpretation dropped from approximately 21% to 8%.
Conclusion: Participating in Quality Assurance Schemes is of utmost importance.

PS-12-017

Coexistence of two missense mutations in the KRAS gene in adenocarcinoma of the lung; a case report

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Background & Objective: KRAS mutations (more frequently G12C & G12V) are present in 15-25% of patients with lung adenocarcinoma. Although the role of KRAS mutations as a prognostic/predictive factor is uncertain in lung cancer, there is suggestion that KRAS mutations negatively impact response to EGFR tyrosine kinase inhibitors. We present a case of lung adenocarcinoma with two coexisting missense mutations in the same exon of KRAS and explore its implications. In colorectal cancer, identifying multiple KRAS mutations is associated with advanced disease.
Method: Mutation screening was performed by next generation sequencing using the Ion Torrent Cancer Hotspot panel.
Results: Two missense mutations; c.34G>T;p.(Gly12Cys) and c.38G>A;p.(Gly13Asp) in exon 2 of the KRAS gene were detected. The two independent variants were confirmed on Integrative Genomics Viewer, suggesting molecularly independent clones. Clinically this was a 63-year old Asian male with other comorbidities (end stage renal failure and renal transplant), presenting with a 6cm spiculated lung mass, bilateral mediastinal lymphadenopathy and lytic bone lesions. EBUS-TBNA of mediastinal lymph nodes showed metastatic lung adenocarcinoma. The patient received palliative radiotherapy and died within two months of diagnosis.
Conclusion: The coexistence of two mutations in the same exon of KRAS gene has not been previously reported in lung cancer. We believe the detection of two mutations in our case indicates presence of two independent clones/subclones. We are further investigating the phenotypic association of this finding. Nevertheless, this patient experienced a very aggressive clinical course which could be related to the underlying molecular events.

PS-12-018

Next generation sequencing in non-small-cell lung cancer patients from northwestern Spain

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Background & Objective: New generation sequencing (NGS) can be an important tool for identification of multiple alterations in a single quick, relatively low-cost test. We compare our experience with NGS in non-small cell lung cancer (NSCLC) with traditional techniques.
Method: DNA from 44 paraffin samples of 39 NSCLC patients were analyzed by NGS: 26 adenocarcinomas, 8 squamous, 2 large-cell neuroendocrine and 3 cases of non-specific (NOS) carcinomas, all previously studied for EGFR (Cobas, Roche), ALK, ROS1 and RET (Vysis, Abbot Molecular). Customized panel was designed to detect structural variants (AKT1, ALK, BRAF, CKIT, CTNNB1, DDR2, EGFR, FGFR1, HER2, HRAS, KRAS, LKB1, NTKR1, NTKR2, NTKR3, MAP2K1, MAP2K2, MET, MYC, MTOR, NRAS, PI3KCA, PDGFR, PTEN, ROS1, RET, SOX2, TP53), and rearrangements (ALK, NTRK1, NTRK2, NTRK3, RET, ROS1), using SureDesign (Agilent). The library was created using SureSelectXT HS Target Enrichment System protocol (Agilent). Illumina technology (MiSeq) was used for sequencing. SureCall and Cartagenia software (Agilent) were used for result analysis.
Results: NGS confirmed 6 translocations and 2 EGFR mutations, already evidenced with traditional techniques, additionally detecting 18 structural mutations. We detected: adenocarcinomas, 2 translocations (RET and ALK) and 14 structural mutations (3 EGFR, 7 KRAS, 2 LKB1, 1 BRAF and 1 MET); squamous carcinomas, 1 ROS1 translocation and 3 structural variants (2 KRAS and 1 LKB1); neuroendocrine carcinomas, 2 translocations and 1 structural mutation in ALK; 3 NOS cases, 1 ROS translocation and 2 KRAS mutations
Conclusion: The NGS is postulated as a feasible alternative for molecular diagnosis in clinical practice due to its sensitivity and specificity.

PS-12-019

Mesothelioma grading system and pleural, extra-pleural and histologic subtypes differences in a Latin-American cohort of patients (preliminary data)

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Background & Objective: A recently described nuclear grading system for mesothelioma has been associated to prognosis. In this series, we have replicated this grading system to a Brazilian cohort of mesothelioma patients, including pleural and extra-pleural samples in order to assess morphologic differences between tissue and histologic subtypes.
Method: Thirty patients previously diagnosed with mesothelioma had their H&E and Immunohistochemistry slides reviewed from the Clinics Hospital (FMUSP) by three lung pathologists, including biopsies and resection specimens from pleural and extra-pleural (omental) sites. Nuclear grading was evaluated as previously published (Kadota et al, 2012). Histologic subtypes were defined as: Epithelioid (Solid, Papillary), Sarcomatoid, Desmoplastic. Tissue homogeneity was evaluated as a minor secondary histologic type.
Results: Of the 30 cases, 17 were from resection specimens, 13 from biopsies, distributed as Solid epithelioid (20), papillary (6), sarcomatoid (2), desmoplastic (2). Nuclear atypia and NC ratio were distinctive factors for the subtypes (p=0.04, p=0.037), as tissue homogeneity for sarcomatoid and desmoplastic (p=0.002). Intranuclear inclusion and proeminent nucleoli were not. Intratumoural infiltrate was predominantly mild. Extra-pleural disease had higher nuclear grading (p=0.0374).
Conclusion: From these preliminary morphological data, we have observed that intranuclear inclusion and proeminent nucleoli, despite location, should warrant Mesothelioma as a differential diagnosis. In a small biopsy, the diagnosis of sarcomatoid and desmoplastic types should be avoided by the possibility of non-homogeneity of sample. For further studies, the extra-pleural and pleural differences will be further investigated, as the intratumoural inflammatory infiltrate, as a possible marker for target therapy.

PS-12-021

PD-L1 (22C3) expression in different samples of non-small cell lung cancer (NSCLC) in correlation with response to Pembrolizumab treatment – a single institution experience

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Background & Objective: Programmed death ligand 1 (PD-L1) expression is used as a predictive marker of response to Pembrolizumab treatment (RPT) for patients with advanced NSCLC. We studied PD-L1 expression in different samples of NSCLC and correlated the Tumour Proportion Score (TPS) with RPT.
Method: We examined FFPE samples of 81 patients with NSCLC: 54 small biopsy, 3 cytology (cytospin) and 24 surgical resection and stained with PD-L1 (clone 22C3) on Dako platform. PD-L1 expression was evaluated on tumour cells (TC). Samples containing 100 or more TC were considered representative. Patients with positive results (>1% TC) were qualified to Pembrolizumab treatment. The qualification criteria were: ECOG 0-1, previous chemotherapy treatment, presence of measurable lesions according to RECIST1.1 criteria and absence of clinically active brain metastasis.
Results: Expression of PD-L1 defined by cutoff values of TPS ≥50% and TPS 1 - 49% were observed in 26 (32,1%) and 22 (27,2%) patients, respectively. 32 patients (20 with TPS≥50% and 12 with TPS 1 - 49%) obtained pembrolizumab. Among patients with TPS≥50%, 2 had partial regression (PR), 8 achieved stable disease (SD), 1 was disqualified because of toxicity, 6 had progression (PD) (2 died) and 3 were lost to follow up. Among patients with TPS 1 – 49%, 4 had PR and SD, 2 - PD and 2 were unavailable for follow up.
Conclusion: All types of samples of NSCLC were adequate for evaluation of PD-L1. Follow up period of 6-8 months does not allow for conclusive correlation between measured expression and RPT. Continued observation is necessary.

PS-12-022

Causality establishment in surgical lung and forensics pathology through characterisation of inorganic tissue – a case report with the Maltese cross example

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Background & Objective: The identification of illicit substances through optical microscopy plays an important role in forensics practices. In this report, we illustrate a case of diffuse-alveolar damage in which the correct identification of pseudomaltese crosses allowed the correct identification of illicit drug use.
Method: A 31 years old male with known drug-abused history (cocaine, crack) was admitted to the emergency room due to abrupt onset respiratory failure associated to chest pain. Imaging studies revealed extensive and diffuse bilateral lung opacities with pleural extension. Immediately after stabilization and transferred to the Intensive Care Unity, an open-field lung biopsy was performed.
Results: Lung biopsy revealed diffuse alveolar damage in acute-proliferative phase, with extensive bronchiectasis in multiple stages of evolution, including fibrosis, associated to granulation tissue. Intima-media vascular thickening was observed, denoting pulmonary hypertension. Perivascular birefringent particles were observed in polarized light, with characteristic pseudomaltese cross morphology, characterizing intravenous emboli of starch, a vehicle in intravenous illicit drugs.
Conclusion: In forensics practice, the establishment of causality plays an essential role. In this report, we illustrate the utility of polarized light microscopy and the importance of determining the characteristics of inorganic material allied to histopathological features to establish causality. Further, we reinforce the importance of distinguishing morphological

aspects of inorganic particles, as the differences between maltese and pseudomaltese cross in order to correctly characterize the organic-inorganic interaction and correctly characterize causality.

PS-12-023

ASCL1 and NEUROD1 expression defines two distinct subtypes of neuroendocrine-differentiated non-small cell lung cancers with different response to chemotherapy

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Background & Objective: The clinical relevance of neuroendocrine differentiation in non-small cell lung cancer (NSCLC) is still a matter of debate and the underlying mechanisms are poorly defined. Recently, two distinct transcriptional profiles have been identified in the small cell lung cancer model, driven by the alternative activation of ASCL1 and NEUROD1 transcription factors. The aim of the study is to investigate the expression and the prognostic role of transcription factors involved in neuroendocrine differentiation in NSCLC patients treated with chemotherapy.
Method: Neuroendocrine differentiation-associated transcription factors ASCL1 and NEUROD1 were analyzed in a cohort of 129 NSCLC patients treated with adjuvant chemotherapy using quantitative real-time PCR and compared to CHGA and the ASCL1-target DLL3. Expression levels were correlated with time to progression at univariate survival analysis.
Results: CHGA was upregulated in 33% of NSCLC patients. NEUROD1 and ASCL1 were both positively correlated with CHGA ($p=0.002$ and $p<0.0001$, respectively) but not each other. DLL3 was upregulated in 30% of cases and strongly associated with ASCL1 expression ($p<0.0001$). High expression levels of both CHGA and NEUROD1 were associated with shorter time to progression ($p=0.04$ and $p=0.002$, respectively), whereas ASCL1 and DLL3 failed to show any statistical significance. Interestingly, the prognostic impact of NEUROD1 was confirmed also in the subset of cases showing CHGA up-regulation ($p=0.01$).
Conclusion: . NEUROD1 represents a candidate prognostic biomarker in NSCLC patients treated with adjuvant chemotherapy. Moreover, ASCL1/DLL3 transcriptional profile is up-regulated in a relevant proportion of NSCLC patients, thus opening to the potential therapeutic use of novel antibodies targeting DLL3 in this subgroup.

PS-12-025

Human leukocyte antigen class I and programmed death-ligand 1 co-expression is an independent poor prognostic factor in adenocarcinoma of the lung

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Background & Objective: Both human leukocyte antigen (HLA) class I and programmed death-ligand 1 (PD-L1) molecules are known to play important roles in cancer immunity. In this study, we evaluate HLA class I expression in resected adenocarcinoma of the lung, and investigate its prognostic impact in correlation with PD-L1 expression.
Method: HLA class I and PD-L1 expression was evaluated by immunohistochemistry in a total of 403 resected lung adenocarcinomas using tissue microarray. Correlations between the expression of HLA class I/PD-L1 and clinicopathologic features and prognostic significance were analyzed.
Results: HLA class I expression was reduced in 91.6%, and more frequently reduced in patients with younger age, absence of nodal metastasis, and low pathologic stage ($p=0.006$, $p=0.028$ and $p=0.007$, respectively). Positive PD-L1 expression in tumour cells was 16.1% (1% cut-off), and associated with poor differentiation, presence of vascular invasion and nodal metastasis ($p<0.001$, $p=0.002$ and $p=0.032$, respectively). On survival analysis, HLA class I or PD-L1 expression alone did not showed any statistical significance. On the integrated analysis, HLA class I (+)/PD-L1 (+) subgroup showed a significant shorter overall survival than others ($p=0.001$). Multivariable analysis revealed that co-expression of HLA class I and PD-L1 was an independent poor prognostic factor of lung adenocarcinoma. ($p=<0.001$, Hazard ratio=5.657 with 95% confidence interval 2.179-14.688)
Conclusion: Lung adenocarcinoma with co-expression of HLA class I and PD-L1 was associated with poor prognosis. This subgroup may evade immune attack by expressing PD-L1 protein despite of HLA expression.

PS-12-026

Consistent and highly reproducible results with PD-L1 22C3 IHC pharmDx in external validation studies on human cancer tissues

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Background & Objective: PD-L1 expression is measured by immunohistochemistry (IHC) and is currently the most advanced potential selective biomarker for response to KEYTRUDA® (Pembrolizumab, MK-3475) anti-PD-1 therapy, allowing identification of Pembrolizumab-responsive patients by a companion diagnostic or complimentary test (PD-L1 IHC 22C3 pharmDx). Objective: Assessment of reproducibility in pathologist scoring of PD-L1 IHC 22C3 pharmDx using specific scoring algorithms
Method: Randomized, multi-site, blinded reproducibility studies were conducted in external clinical laboratories (US and EU) to evaluate Inter-and Intra-observer precision using Tumour Proportion Score (TPS) for NSCLC, and Combined Positive Score (CPS) for gastric carcinoma and urothelial carcinoma indications.
Results: Statistical analysis was performed using Wilson Score Method with Median as Reference and Bootstrap on IHC status. Nine pathologists achieved overall agreement for both Inter-and Intra-observer reproducibility using Tumour Proportion Score (TPS, 1% cut-off) in NSCLC (87.1% Inter-observer agreement/94.3% Intra-observer agreement) or Combined Positive Score (CPS 1 cut-off) in gastric (96.6% Inter-observer agreement/97.2% Intra-observer agreement) and CPS 10 cut-off in urothelial carcinoma (93.9% Inter-observer agreement/95.9% Intra-observer agreement).
Conclusion: External laboratory testing demonstrated that PD-L1 IHC 22C3 pharmDx is a highly reproducible and reliable immunohistochemical method for scoring PD-L1 expression in NSCLC, gastric and urothelial tumour specimens using respective scoring algorithms (TPS and CPS).

PS-12-027

Pathological diagnosis and biomarkers testing in non-small cell lung cancer - a retrospective analysis

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Background & Objective: Lung cancer is one of the major causes of mortality in Portugal. The use of new target therapies has improved survival of patients, with molecular biology having a determining role in selection and individualization of treatments.
Method: Retrospective analysis of diagnosed malignant lung tumours from January 2014 to December 2017.
Results: A total of 283 pulmonary biopsies with malignancies were diagnosed. Mean age at diagnosis was 68 years (range: 36-94 years), 31%

females and 69% males. Histopathological classification was as follow: 76.7% non-small cell lung carcinoma (NSCLC) [of these, 69.6% were adenocarcinoma, 18.4% squamous cell carcinoma (SCC)]; 8.1% neuroendocrine tumours; 2.5% primitive mature B-cell neoplasms and 12.7% metastases to the lung. The vast majority of patients with NSCLC were diagnosed in stage IV (72%). Regarding NSCLC, PD-L1 was performed from January 2017 in 49 cases: 20 showed high-expression (≥50% of neoplastic cells) [14 were adenocarcinoma, 1 SCC], 16 low-expression (≥1<50% of neoplastic cells) [12 were adenocarcinoma, 4 SCC] and 13 were negative. Molecular testing was possible in 136 cases (75 by PCR for EGFR mutations with subsequent FISH for ALK rearrangement; 61 by NGS for EGFR, KRAS, NRAS and ALK): EGFR mutations were detected in 31 cases (22.8%; all adenocarcinomas), ALK in 4 cases of 109 surveyed and RAS in 14 cases of 57 surveyed. In 157 patients follow-up was available, 49 were still alive 29 months after diagnosis.
Conclusion: Our results are similar to those stated in the literature, except in PD-L1 expression, where we found, contrary to reported, higher expression in adenocarcinomas.

PS-12-028
The prognostic value of tumour budding in lung squamous cell carcinoma
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Background & Objective: For lung squamous cell carcinoma (SCC), there is no histological parameter that have been universally accepted as a prognostic factor. But in recent years, tumour budding has been recognized as a prognostic factor in some studies. In this study, the prognostic value of tumour budding in lung SCC were investigated.
Method: We reviewed 36 lung SCC who underwent surgical resection at Baskent University, Department of Thoracic Surgery between 2011 and 2016. Haematoxylin and eosin stained tumour slides were reviewed by 2 pulmonary pathologists. Tumour budding was accepted as the presence of isolated small tumour nests composed of less than five tumour cells in the stroma of the invasive tumour edge and they were counted in 1 high-power field (HPF) at x200 magnification in hot spot areas. The correlation between the clinal parameters and tumour budding was investigated.
Results: Tumour budding was observed in all patients. It was less than 5/1 HPF in 13 patients (36.1%) and equal or higher than 5/1 HPF in 23 patients (63.9%). A statistically significant association was observed between tumour budding and pT stage (p=0.005), TNM stage (p=0.003), the presence of lymph node metastasis (p=0.032) and the presence of metastases (p=0.05). Overall survival was 49±14.6 months in the patients showing <5/1 HPF tumour budding, while it was 30.1±17.7 in the patients who had ≥5/1 HPF (p=0.006).
Conclusion: In conclusion, tumour budding is correlated with poor prognosis in lung SCC and could constitute a part of SCC grading scheme.

PS-12-029
Histological transformation as resistance mechanism of the treatment with EGFR inhibitors in lung adenocarcinoma. Two cases report
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Background & Objective: Patients diagnosed of adenocarcinoma lung cancer treated with therapies directed against the epidermal growth factor receptor (EGFR) use to develope secondary resistance mutations after 12 months of treatment, as the T790M, but some of them present another type of resistance: the histological transformation.
Method: We report two cases of a 50 and 55-year-old women who were diagnosed of a metastatic relapse of lung adenocarcinoma with EGFR mutation. When disease progression was observed, a re-biopsy was made observing a transformation of the histological subtype as a mechanism of acquired resistance.
Results: The needle biopsy of both lung masses showed neoplastic infiltration of adenocarcinoma. In immunohistochemistry, tumour cell showed positivity for CK7, TTF-1 and Napsina-A and negativity for CD56, CK20 and ALK (D5F3). Both cases showed mutation of EGFR (Ex19Del). The re-biopsy after treatment (one case was of an adrenal node, and the other one in a liver node) showed undifferentiated carcinoma formed by small cells in both cases. In immunhistochemistry tumour cells were positive for TTF-1, sinaptofisine and CD56 and were negative for CK7 and cromogranina. Previous mutation EGFR (Ex19Del) persisted in both of them.
Conclusion: To best managing and planing the tratment options on recurrences, it should be mandatory to make a second biopsy in order to detect, not only the most frecuent resistance mechanism (T790M EGFR mutation), but also the histological small-cell transformation.

PS-12-030
Investigation of lung squamous cell carcinoma in multiple squamous cell carcinoma cases
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Background & Objective: The lung is a common site of primary tumours as well as metastatic lesions. Unlike adenocarcinoma, it can be difficult to distinguish between primary or metastatic squamous cell carcinoma in the lung. This differential diagnosis is important for clinical staging and treatments. This study aimed to develop an immunohistochemical panels for primary lung squamous cell carcinoma and metastasis of other organs.
Method: Specimens were obtained from two groups of patients, 9 patients who had a history of SCC of other organs (Group1) and 8 patients who had a multiple lung SCC (Group 2). All specimens were immunosteined with cytokeratin (CK)-CAM5.2, CK5/6, CK7, CK14, CK19, TTF-1, Napsin, p16, p40, p53, RB-1, CD117 and synaptophysin antibodies in each SCC lesions. To determine the primary or metastasis, we also analyzed the sequence of mitochondria DNA D-loop resions in non-neoplastic tissue and tumours from each organ. Furthermore, immunohistochemistry (IHC) of CK-CAM5.2, CK7, CK14 and CK19 were performed on the primary SCC cases of the lung, head & neck and uterine cervix.
Results: IHC panels of CK7 and CK14 showed high coincidence rates in the metastatic cases than in multiple primary cases. Most of primary lung SCC expressed CK-CAM5.2(98%) and CK19(100%), almost all uterine cervix SCC expressed CK19(91%), and all head & neck SCC cases expressed CK14(100%).
Conclusion: The profiling of these antibodies could be useful for distinguishing between primary and metastases SCC of the lung.

PS-12-031
Three cases in a family of hereditary interstitial lung disease with COPA gene mutation
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Background & Objective: Copa syndrome has recently been identified a autosomal dominant syndrome consisting of autoimmune lung, joint and kidney diseases in paediatric patients and it is caused by mutations in the coatomer associated protein subunit alpha (COPα) gene (COPA). In Copa syndrome, the COPA variants in patients impair intracellular protein trafficking and lead to endoplasmic reticulum (ER) stress. Immune dysregulation caused by the stress is considered to bring about diffuse alveolar hemorrhage or intersititial lung disease, arthritis, and glomerulonephritis. We observed the histology of and performed immunohistochemistry for ER stress in the lungs of the cases of interstitial lung disease with COPA mutation.

Method: Patients were a 29-year-old woman, a 4-month-old man who was her son, and a 22-year-old man who was her brother. Three members of the family had open lung biopsy with suspicion of hereditary interstitial lung disease at the age of 2 years, 4 months, and 2 years, respectively. We performed H&E and immunohisitochemical staining for the lung specimens of all cases and analyzed COPA for one of the cases.
Results: COPA showed a novel heterozygous single nucleotide polymorphism (amino acid change p.Val242Gly). Histologically all the cases showed diffuse interstitial fibrosis and lymphoid infiltration with lymph follicules in the alveolar wall. Proliferation of intraalveolar macrophages with cholesterin clefts was seen. Immunohistochemically overexpression of the molecular chaperone binding immunoglobulin protein (BiP) was detected in the lung epithelium and macrophages.
Conclusion: Three cases similar interstitial pneumonia on histology and similar immunohistochemical results. Further functional assessment is necessary to make the final diagnosis of Copa syndrome.

PS-12-032
Primary pulmonary salivary gland-type tumours: a single-institute experience with a focus on the histologic types and clinical outcome
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Background & Objective: Primary pulmonary salivary gland-type tumours (SGT) are uncommon malignancy which derives from minor salivary glands of tracheobronchial tree.
Method: We searched medical records for pulmonary SGT in five years period. Recorded pathological and epidemiological characteristics, based on the population number covered by our institution (approximately population number covered by our institution 1 200 000).
Results: Five cases of primary pulmonary SGT were recorded, approximately 1 new case per year (crude incidence rate 0,8/1.000 000 person/per year). The patients average age was 50,4 (range,30-69), male-to-female ratio 1,5:1. The histologic types of carcinoma were mucoepidermoid carcinoma (MEC, n=3, 60%), adenoid cystic carcinoma (n=1, 20%), and hyalianizing clear cell carcinoma of minor salivary gland (n=1, 20%). Tumours showed low (n=3, 60%), and high (n=2, 40%) histologic grade. Molecular analysis showed presence of MAML2 gene rearrangement in low-grade MEC, and rearrangement of EWSR1 gene in low-grade hyalinizing clear cell carcinoma. From three operable tumours, two were T1 stage without lymphnode metastasis and one T3 stage with multiple lymphnode metastases. Two tumours were unresectable in time of diagnosis and treated with chemo and radiotherapy. All patients are still alive, median follow-up time is 22.6 months (range,10–52).
Conclusion: SGT tumours are extremely rare pulmonary neoplasm with tendency of occurrence in the younger age. Histologic grade and possibility of complete resection are most important prognostic factors. Identification of specific genetic mutations such as rearrangement of MAML2 and EWSR1 genes can be useful for differentiating SGT from other epithelial lung malignancies, especially in small biopsies, and have decisive role in determining definitive treatment.

PS-12-033
Association between pd-l1 expression and driver mutations in non-small-cell lung cancer patients in a specific region
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Background & Objective: Immunotherapeutic approaches to target PD-L1/PD-1 have recently shown great promise in treating patients with non-small cell lung cancer (NSCLC). Very little is known, however, about the coexistence of this biomarker with oncogenic driver mutations used in targeted therapies. We investigated the association between somatic driver mutations and PD-L1 expression.
Method: We retrospectively checked the expression of PD-L1 in paraffin embedded samples from 84 NSCLC patients with molecular alterations in driver oncogenes (EGFR, KRAS, BRAF, ALK, ROS1). The series included: 72 adenocarcinomas, 5 squamous cell carcinomas, 3 adenosquamous carcinomas, 1 neuroendocrine carcinoma and 3 non-small cell lung cancer not otherwise specificied (NOS). Of these, 55 had EGFR mutations, 7 KRAS mutations, 2 BRAF mutations, 18 ALK rearrangements and 2 ROS1 rearrangements. An immunohistochemical study for PD-L1 expression was carried out using clone 28-8 (PD-L1 IHC 28-8 pharmDx, Agilent). Mutational screening for EGFR, KRAS and BRAF mutations (Cobas, Roche), as well as, fluorescence in situ hybridization analyses for ALK rearrangements (Vysis ALK Break Apart FISH Probe Kit, Abbot Molecular) and ROS1 rearrangements (6q22 ROS1 Break Apart FISH Probe RUO Kit, Abbot Molecular) were also carried out.
Results: We found the following PD-L1 expression levels: ≥ 50% in 18% (n=15) of cases; between 1%-49% in another 18% (n=15) of cases; and <1% in 64% (n=54) of cases.
Conclusion: Our results indicate that no significant correlation seems to exist between PD-L1 expression level and these driver mutations used in precision medicine for NSCLC.

PS-12-034
Micro-RNA 215 and 375 regulate thymidylate synthase protein expression in MPM patients
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Background & Objective: Malignant Pleural Mesothelioma (MPM) is a highly chemoresistant and aggressive neoplasm. The standard front-line treatment is Pemetrexed (PEM)-based chemotherapy, whose major target is Thymidylate Synthase (TS), a regulatory enzyme involved in the DNA repair and synthesis. In colon, lung and pancreatic cancer models miR-215 and miR-375 have been shown to target TS, while MPM is actually unexplored.
Method: We screened 71 MPM samples (4 biphasic, 7 sarcomatous and 60 epithelioid types) to detect the miR-215 and miR-375 expression in parallel with TS mRNA and protein levels and in correlation with patient clinical-pathological data.
Results: Both miR-215 and miR-375 were significantly higher in epithelioid hostotype (p=0.003 and p=0.005, respectively). Furthermore, significant direct correlation between TS protein and TS mRNA levels (p=0.03) and inverse correlation between TS protein levels and both miR-215 and miR-375 expression (p=0.009 and p<0.0001, respectively) were found. By contrast, no correlation between both miRNAs and TS mRNA levels was found, thus suggesting a possible post-transcriptional interaction.
Conclusion: Our data show that miR-215 and miR-375 participate in regulating TS expression in MPM. Further studies are required to functionally investigate the mechanisms of TS regulation and PEM sensitivity by miR-215 and miR-375.

Tuesday, 11 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-13 | Autopsy Pathology

PS-13-001
Medical autopsies in problem-based learning medical curriculum at a university
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Background & Objective: Problem-based learning (PBL) has been implemented in medical curriculum around the world. The classical courses as anatomy or pathology are not organized, but students learn the medicine around the problem cases and at the same time anatomy through pathology to diagnostics and treatment is taught. The amount of lectures is limited. At the University of Tampere, PBL method was implemented in a vertically integrated spiral curriculum in the 1990s. No separate pathology course is held, but pathology is integrated to various PBL courses.
Method: To summarize autopsy lessons given in PBL curriculum.
Results: At University of Tampere, there are 6 autopsies in total for each student during the studies from 1st-5th year. Five are integrated into preclinical courses and one is during surgery-internal clinical medicine course. Five of them are compulsory and one is voluntary but attended by the majority of students. Pathology autopsies are performed in small groups (maximum of 8 students) and students can participate in performing the autopsy. Forensic autopsies are taught separately.
Conclusion: PBL medical curriculum at the University of Tampere includes 6 autopsies and they make an important part of the cumulative learning process of pathology. The autopsies are very welcomed by medical students.

PS-13-002
Autopsies in Europe. Results of a survey among the members of the European Society of Pathology (ESP)
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Background & Objective: The autopsy has been an important part of medicine. Decreasing rates are especially critical for surveillance and quality assurance of modern medical practice. To address the situation, we have conducted a survey among the member countries of the ESP.
Method: A survey was sent to member societies of ESP and to members of the Working group Autopsy pathology, with the call for distribution.
Results: Only 8 out of 19 respondents were able to specify the actual numbers of forensic and medical autopsies in their country. In 8 countries no consent from the diseased or next of kin was necessary, while 4 practiced oral and 7 written consent. There was no clear correlation between autopsy rates and type of consent. In some countries with written consent for medical autopsies, a higher autopsy rate was being secured through increase of coronial and/or forensic autopsies. The autopsy rates varied from 3 % to 40%, In most countries, autopsies were performed in public institutions and financed through taxes. UK has introduced autopsy as a sub-specialty of pathology and only 40 autopsies are thus required for the specialization as surgical pathologist. In other countries, the numbers vary from 25 to 480. Forensic pathology is a separate specialty in 15 countries, 5 of which have no mandatory practice in surgical pathology. Only 5 reported on too few autopsies for specialization in pathology. The problem has been solved by allowing jointly co-signatures, visit to other hospitals, and inclusion of forensic autopsies.
Conclusion: The autopsy rates are difficult to evaluate as long as public statistics are missing.

PS-13-003
The importance and role of scientific medical autopsy in opinion of medical staff. Introductory results from the querend
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Background & Objective: The role of scientific medical autopsy is an important issue in medical healthcare. The attitude and opinions on that subject have a great impact on the following use of the obtained information. The wide project involves several medical groups including nurses, midwives, pathologists and physicians (non-pathologists). This study presents part of the results.
Method: The querend consisting of 29 questions divided into three sections: the general information about the respondent, knowledge about the autopsy as a medical procedure, and opinions and attitude towards post mortem examination (PM) was performed in three tranches (two for nurses - N1 and N2, one for midwives - M1). The results were analysed statistically.
Results: Obtained results reveal that major response from nurses (75% in N1 and 65% in N2) and midwives (M1 - 56%) was received from bigger cities (population over 100.000 inhabitants). The distribution among reference levels of hospitals was comparable. Despite the fact that respectively 66% of nurses (N1), 70% (N2) and 85% of midwives had never attended the autopsy, accordingly 67% (N1) and 65 % (N2) and 56% (M1) would attend the procedure. In all groups the respondents agreed (above 90%) that information from the autopsy report are relevant for future treatment and management of the patients.
Conclusion: According to obtained answers the information from PM examination is vital for both patient management, future medical care and plays important role in healthcare quality control assessment.

PS-13-004
Giant cell myocarditis: a case report
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Background & Objective: Giant cell myocarditis (GCM) is an uncommon type of myocarditis that can present with heart failure or ventricular arrhythmia. Its pathogenesis remains unclear, but is attributed to T cell-mediated autoimmunity. We report a case of a 75-year-old female with the following medical history: Dyslipidemia, diabetes mellitus type 1, autoimmune hypothyroidism, pernicious anemia and complete heart block, treated with a pacemaker. She presented to the ER with dyspnea and dysuria. Chronic heart failure was diagnosed and she had a cardiogenic shock and died nine days later.
Method: We performed a complete autopsy. A sample of myocardium was sent for microbiological study. For the microscopic study of the heart, we included sections of the myocardium. CD163, CD3, CD20 and CD68 immunostains were made in order to identify inflammatory cells.
Results: The heart weighed 538g and the macroscopic examination revealed no abnormalities besides the weight and a mild calcified right coronary artery. The aorta had atherosclerosis. Microscopy revealed a severe and diffuse inflammatory infiltrate with T lymphocytes, eosinophils, macrophages and abundant multinucleated giant cells, associated with myocyte necrosis. There was no evidence of infection.
Conclusion: GCM is rare, but it must be differentiated from other disorders with granulomas with giant cells and viral myocarditis. GCM has also been associated with other autoimmune diseases, as in our case.

PS-13-005
Basophil invasion: histological study on normal pituitary glands
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Background & Objective: Migration of corticotroph cells from the intermediate lobe into the posterior lobe of the pituitary gland is called basophil invasion. It seems to be a physiological phenomenon related to the aging process, but its functional significance is still unknown. The aim of our study was to describe the extend of basophil invasion in normal pituitary glands.

Method: Seventy-five pituitary glands obtained from autopsy were examined and all cases with extensive autolysis were excluded. Only 46 cases were suitable for the evaluation of basophil invasion. The mean age was 55 years (between 19 and 91 years). The basophil invasion was classified into three groups based on the extend and number of the areas with corticotroph cells: group 1 (minimal), group 2 (mild) and group 3 (pronounced).
Results: Thirty-four pituitary glands were obtained from males (73%) and 12 from females (26%). Twenty-one cases (46%) were included in group 1, 22 cases (47%) in group 2 and 3 cases (7%) in group 3. No significant statistical differences were found between invasion and sex (p=0.8704) and between invasion and age (p=0.4473).
Conclusion: Despite the lack of statistical relevance in our study the knowledge of this rare phenomenon is mandatory especially in cases with extremely small corticotroph microadenomas which are difficult to identify on MRI imaging and in which the neurosurgeon relies heavily on frozen sections. The identification of the corticotroph tumour on frozen sections is difficult especially in cases with extensive basophil invasion and can lead to failure of surgical treatment.

Tuesday, 11 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-14 | Digestive Diseases Pathology - Liver/Pancreas

PS-14-001
Liver biopsy evaluation of autoimmune liver disease: autoimmune hepatitis and overlap syndrome
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Background & Objective: Autoimmune hepatitis (AIH) is an inflammatory liver disease caused by T cell-mediated immune response targeting hepatocytes. The triggers of AIH are still unknown, but specific genetic and environmental factors are strongly related. AIH may be associated with an autoimmune cholangitis, giving rise to the overlap syndrome (OS). Currently there are not specific diagnostic criteria for OS, which should be classified according to the primary clinical and histological aspects. Liver biopsy is necessary to define the diagnosis of AIH/OS, to evaluate the grading, i.e. the necroinflammatory activity, the staging, i.e. the extent of liver fibrosis, and the response to therapy.
Method: We assessed grading of the hepatitis, liver cell necrosis, plasma cell clusters, cholangitis activity (CA) and pattern of fibrosis in 35 cases of autoimmune liver disease.
Results: 9 cases of AIH and 26 cases of OS were diagnosed. We revealed intense hepatitis activity in 6/9 of AIH and 15/26 of OS cases, CA2-CA3 in 22/26 cases of OS, necrosis in 21/35 cases, 9 with spotty and interface necrosis and 12 with bridging necrosis. Plasma cell clusters were present in all cases analysed. Fibrosis was present in 21/35 cases, bridging fibrosis in 16/35 cases.
Conclusion: In our cases OS is not a rare disease. Since OS is not a specific entity but a spectrum from AIH to AIC, specifying the main disease is an important task of the pathologist in order to avoid undiagnosed OS, that may lead to steroid non-responding patients. Plasma cell clusters represent a relevant tool for the diagnosis of AIH/OS.

PS-14-002
Langerhans cell histiocytosis of the extra-hepatic bile duct – a case report of an uncommon presentation of a rare disease
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Background & Objective: Langerhans cell histiocytosis (LCH) is a rare condition of unknown etiology characterized by clonal proliferation of Langerhans cells. The clinical presentation is heterogeneous and might involve single or multiple organs. Therefore, LCH can range from a benign to a multisystemic life-threatening disease.
Method: We report the case of a 74-year-old man submitted to laparoscopic cholecystectomy. The intra-operatory cholangiography performed during the procedure suggested the presence of a neoplastic lesion involving the bile ducts. The ensuing imaging studies revealed a thickened common bile duct wall and its cytological analysis showed possible malignant features. The Ca19.9 serum levels were largely increased. There was no evidence of dilated intra-hepatic bile ducts suggesting sclerosing cholangitis. The patient was submitted to a cephalic gastroduodenopancreatectomy.
Results: The surgical specimen macroscopic examination showed thickened bile ducts in a 2,3cm extension, in a territory nearly 1,5cm from the Ampulla of Vater. There was no evidence of neoplasia. The histological analysis demonstrated a fibrotic thickened bile duct wall and intense lymphoplasmacytic inflammatory infiltrate, with focal areas of mucosal erosion and ulceration. Focally, there were sub-epithelial aggregates of small/intermediate size cells, with irregular nucleic contours and clefts, vesiculous chromatin and small nucleoli, in a background of eosinophils. The bile duct epithelium had mild and focal cytological atypia, without dysplasia. The mononuclear cells were positive for CD45, CD1a, S100 protein, CD4, CD68 and Langerin. A diagnosis of LCH involving the bile ducts was made.
Conclusion: To our knowledge this is the first reported case describing a LCH exclusively restricted to the extra-hepatic bile ducts.

PS-14-003
Ampullary carcinomas; not rare and worth to know
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Background & Objective: Ampullary adenocarcinomas (ACs) are rarely seen and prognosis is better than pancreatic ductal adenocarcinomas (PDAC). Polypoid and/or flat preneoplastic components are common. ACs were divided into four subgroups according to their location (intra-ampullary/ ampullary ductal/ ampullary duodenum/ampullary-NOS), all with different prognosis. The purpose of this study is to examine the features and prognosis of ACs.
Method: 136 pancreatic resections between 2013-18 were reanalyzed. 53 cases were classified as ‘’ampullary adenocarcinoma” according to gross and microscopic findings. They were reviewed for the site spesific classification. Invasive and if present, preinvasive components were also evaluated. Histological subtypes were redefined as pancretobiliary dominant (PBD), intestinal dominant (ID) and other types. Clinical outcomes were obtained from the medical records and pathology reports. Kaplan-Meier method was used to analyze the survival.
Results: Male/Female ratio was 30/23. Mean age was 60 (36-79). 55% of the tumours had preinvasive component. Mean diameter of the invasive component was 1,6 cm. PBD type was seen in 75%. Survival of PBD type was better than ID type (p=0,014). Location of the tumours were intra-ampullary in 38%, ampullary ductal in 32% , ampullary-NOS in 21% , and peri-ampullary in 8%. Site spesificity did not effect the survival (p=0,078).
Conclusion: ACs need to be defined better by the pathologists, especially by their location and histological subtypes, considering their impact over the prognosis and decision of the chemotherapeutics.

PS-14-004
A rare case of gallbladder pancreatic heterotopia associated with high-grade biliary dysplasia and calculous cholecystitis
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Background & Objective: Ectopic pancreas is defined by the presence of pancreatic tissue without any anatomical connection to the pancreas, within other organs. It is more commonly encountered in the stomach and in the small intestine. Heterotopic pancreas in the gallbladder is a rare occurence, with only a few over 30 cases described until the present day.
Method: A 31-year-old female with no clinical history presented with epigastric and right upper quadrant pain. Seric hepatic enzymes had normal values, and there was no inflammatory syndrome present. Abdominal ultrasound revealed an intracholecystic calculus of 20 mm diameter. The pacient underwent laparoscopic cholecystectomy followed by clinical remission.
Results: Pathological examination showed cholecystectomy specimen measuring 11 cm in length, 2.5 cm in diameter, and 0.2 – 0.3 cm in wall thickness. Intracavitary, there was a calculus measuring 2.5 cm in diameter. Microscopically, chronic active cholecistitis, and a small focus of pancreatic ectopic tissue located in the subserosa of the gallbladder neck, were found. Pancreatic heterotopia consisted of acini, ducts, and islets of Langerhans cells and was therefore classified as type I by the Heinrich classification. Gallbladder epithelium also presented foci of high-grade biliary type dysplasia which came as a surprise, given the age of the patient. Additional levels and blocks were obtained, but no invasive carcinoma was found.
Conclusion: Pancreatic heterotopic tissue in gallbladder is a rare incidental finding, often undiagnosed prior to pathological examination of the surgical specimen. Association with high-grade biliary dysplasia is even rarer, especially in young patients.

PS-14-005
Margin resection status and survival of patients with pancreatic ductal adenocarcinoma submitted to pancreaticoduodenectomy in a high volume centre

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Background & Objective: Pancreatic ductal adenocarcinoma (PDAC) represents 90% of pancreatic tumours and is fatal in almost all patients. Surgical resection is currently the only potentially curative treatment option. The aim of our study was to evaluate the impact of R0 resection on survival in our patients.
Method: Retrospective study was performed in 99 patients who underwent pancreaticoduodenectomy (PD) for PDAC from 2010 to 2015. Clinical files and the slides were reviewed. R1 was defined as the presence of tumour tissue within 1 mm from the margin. Statistical analysis with SPSS version 22.0 and Kaplan-Meier survival curves were performed.
Results: 58 patients showed R0 margin and 41 patients R1. 54% of the R1 showed microscopic vascular invasion and only 22% in the R0 group. R1 margins showed worst survival rates ($p<0.01$). The median survival was 24.4 months for R0 patients and 13.3 months for R1 patients ($p<0.00047$). The margin that showed more survival impact was the vascular. Only 5 patients underwent neoadjuvant chemotherapy and all showed R0 margins.
Conclusion: R0 resection has a positive impact on survival. Further studies should be done on the impact of neoadjuvant therapy in the margin status of PD.

PS-14-006
Glomangioma of the liver - a possibility to consider? Report of a rare case

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Background & Objective: Glomus organs are arteriovenous anastomoses which control the thermoregulation of the extremities. Benign tumours of these glomus organs, glomangiomas, are therefore usually presented as subcutaneous masses of the distal extremities, especially in the subungual area. Case reports of primary glomangiomas in the respiratory and gastrointestinal tracts as well as in the genital organs have been published. Glomus tumour of the liver is extremely rare. Herein, we report a case of a glomus tumour of the liver in a 53-year-old woman.
Method: A 53-year-old female without relevant personal history, was investigated for abdominal pain and performed a computed tomography that revealed a solid, hypervascular liver nodule.
Results: Surgical specimen showed a 5x4.5x2cm subcapsular, spongy, reddish, poorly defined mass. On histological examination it was well delimitated without infiltrative limits. The lesion is composed of small and large vascular spaces small and an intervening densely cellular population of small round bland cells. Immunohistochemistry revealed positivity for CD34, CD31 and actin. The mitotic activity was minimal and a there was a very low Ki-67 proliferative rate. The background liver was unremarkable.
Conclusion: To the best of our knowledge, only a few cases of glomangiomas had previously been reported primarily occurring in the liver. Many differential diagnoses were considered and haemangioma, Kaposi sarcoma and hemangioendothelioma were excluded. Coexpression of actin and CD34 in glomus tumours, although unusual, has been reported in the literature. Even with a reassuring clinical presentation, the low grade histology appearance, low proliferative rate, no infiltrative borders and clear margins, a clinical follow-up was recommended.

PS-14-007
A new scoring system in NAFLD; can it be more practical for evaluating fibrosis and diminish inter-observer variability?

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Background & Objective: Nonalcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease, and its prevalence is increasing worldwide. As the presence of significant fibrosis is associated with poor prognosis and increased mortality; assessment of accurate degree of fibrosis is very important. Currently, two alternative system of scoring with four tiers of fibrosis, NAS and SAF, are commonly used. However, cases with histomorphological features beyond bridging fibrosis but not yet have achieved complete cirrhosis are not categorized in these classification schemes.
Method: In this study, a 6-tiered fibrosis scoring system was used, with cases having advanced fibrosis classified into scores F3 through F6 according to the presence of septations and nodularity, as advised by Bedossa P, et al. 134 cases were re-examined by one surgical pathologist and one experienced hepatopathologist using both the four-tiered and six-tiered fibrosis scoring systems.
Results: For both the 4-tiered and the 6-tiered systems, interobserver reliability was found to be high (Kappa values 84% and 83% respectively, $P<0.001$). Most of the discordant cases were found to be in F2 group. Presence of peri-portal and peri-central sinusoidal fibrosis, with or without non-zonal parenchymal sinusoidal fibrosis is the hallmark of this stage.
Conclusion: The main cause of the discrepancy could be either due to the difficulty in determining periportal fibrosis and/or recognizing the non-zonal distribution of sinusoidal fibrosis.

PS-14-008
Vascularisation of hepatocellular carcinoma nodes depends on the size and degree of histological differentiation

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Background & Objective: Comparative morphological and computer tomography (CT) analysis of the hepatocellular carcinoma (HCC) vascularization depending on the size and degree of histological differentiation.
Method: 40 patients aged 15-83years were examined, 49 nodes of HCC were identified. The multislice-CT with bolus contrast enhancement was

performed before the surgery. On the tomograms were determined: sizes, densitometric parameters, values of the arterial and venous CT-density increments using the coefficient of inflows concentration difference and CT-vascularization indices (CTVI) of the tumour nodes. During morphological study were determined the nodes size, as well as HCC tissue differentiation degree– high-(H), moderate-(M) and poor-differentiated(P) and the microvessel density (MVD) by using CD34.
Results: Groups of nodes were formed according to the size and degree of differentiation. Group I - nodes less than 5cm in diameter(≤5cm): H=8, M=5, P=1. II group - nodes more than 5cm(>5cm): H=13, M=20, P=4. In group I, the maximum values of CTVI were established in the H-HCC tissue (61.1HU), that exceeding by 1.4% and 27.3% the values of M- and P-HCC, respectively. In group II, the CTVI values of H-HCC (66.7HU) were also the highest and exceeded the corresponding values of M- and P-HCC by 5.0% and 24.9%.
Conclusion: CT carrying out with bolus contrast enhancement allows studying the features of HCC nodes blood supply. The maximum values of the CTVI are established in the H-HCC nodes with a diameter >5cm, the smallest ones in the P-HCC nodes with a diameter ≤5cm.

PS-14-009
Prevalence of microsatellite instability in intraductal papillary mucinous neoplasms of the pancreas
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Background & Objective: Microsatellite instability (MSI) due to mismatch repair deficiency (dMMR) occurs at a low frequency in pancreatic ductal adenocarcinomas (PDACs). This phenotype has been associated with responses of metastatic tumours, including PDACs, to immune checkpoint inhibitor therapy. Here we investigated a large series of PDACs for associations between dMMR/MSI and several biologic and clinical parameters.
Method: A total of 445 PDACs were screened for dMMR/MSI, including a multi-centric, consecutively collected, retrospective series (n=428) and a monocentric, consecutively collected, retrospective series of intraductal papillary mucinous neoplasms (IPMNs, n=17).
Results: The frequency of dMMR/MSI in PDACs was 7/428 (1.6%). We found dMMR in a larger proportion of IPMN-associated tumours (4/58, 6.9%) than non-IPMN PDAC (5/385, 1.3%) (P=.02). PDACs with dMMR/MSI showed Lynch-related features, including heterogeneous MMR defects and absence of MLH1 promoter methylation. PDACs with dMMR contained potentially immunogenic mutations due to MSI in coding repeat sequences. PDACs with dMMR or MSI had a higher density of CD8+ T cells at the invasive front than PDACs without dMMR or MSI (P=.08; Fisher exact test). A higher proportion of PDACs with dMMR or MSI expressed the CD274 molecule (PD-L1, 8/9) than PDACs without dMMR or MSI (4/10) (P=.05).
Conclusion: The dMMR/MSI phenotype is rare in PDAC. Around half of all dMMR/MSI cases in PDAC occur in IPMNs. Studies are needed to determine whether these features of PDACs with dMMR or MSI might serve as prognostic factors.

PS-14-010
Blocked cholesterol synthesis induces hepatocellular carcinoma in transgenic mice
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Background & Objective: In Western countries, up to 20% of hepatocellular carcinoma (HCC) evolves from non-alcoholic fatty liver disease due to chronic inflammation that could be driven by metabolic dysfunction. We have developed a liver knockout (LKO) mouse model of lanosterol 14α-demethylase (CYP51) of cholesterol synthesis and observed consequences stretching from severe liver injury to tumour development in later stages.
Method: Male and female Cyp51 LKO mice of progressing age (19 weeks, 12, 18 and 24 months) were sacrificed and liver histology was assessed. Hepatic gene expression was studied by expression profiling and qPCR. We also measured biochemical parameters in plasma.
Results: Histologically, Cyp51 ablation in hepatocytes was characterized by inflammation, ductular proliferation and fibrosis. The hepatocellular damage was confirmed by changes in plasma markers. First HCC cases were observed in livers of one-year-old LKO mice (1/8) that also showed advanced ductular proliferation which was already present in the 19-week old mice. At 2 years, the prevalence of tumours increased and was 3-times higher in females (6/9 vs 2/9). Metastatic HCC was also observed. The transcriptome data in LKOs clearly indicated up-regulated pathways in cancer and extracellular matrix interaction, while multiple metabolic pathways were severely dampened. Diminished was also the activity of transcription factors involved in the cell cycle control, circadian gene regulation and liver regeneration.
Conclusion: We have shown that disturbed cholesterol synthesis induces liver injury and can subsequently lead to HCC. Some of enriched genes and transcription factors in females suggest their higher susceptibility to carcinogenesis.

PS-14-012
Glutamine synthetase, Glypican-3 and Arginase-1 expression in metastatic tumours of the liver
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Background & Objective: Diagnosis of metastatic liver carcinomas (MLCs) vs. hepatocellular carcinomas (HCCs) may be problematic especially in the non-cirrhotic liver. Glutamine Synthetase (GS), Glypican3 (GPC3) and Arginase-1 (ARG1) immunohistochemistry can demonstrate the hepatocellular origin of a given tumour, but they may also be expressed non-hepatocellular tumours. This study aims to investigate the characteristics of GS, GPC3 and ARG1 expression and the value of their combination in MLCs and in HCCs.
Method: Formalin fixed paraffin embedded tissue samples from 86 patients (16 HCCs, 70 MLTs) were stained immunohistochemically for GS, GPC3 and ARG1. Weak staining in >50% or strong staining in <50%or >50% of the tumour was considered positive. Patient files were also analyzed for the confirmation of the primary origin of the tumours. Statistical analyses were made using SPSS version 19.0.
Results: Staining pattern of GS and GPC3 was cytoplasmic. ARG1 staining was cytoplasmic in MLCs, cytoplasmic and nuclear in HCCs. Among HCCs, 100%, 38% and 94% showed positive staining with GS, GPC3 and ARG1, respectively. Overall, MLCs showed positive staining with GS, GPC3 and ARG1 in 73%, 4% and 4% of the cases, respectively. The combination of GS+/GPC3+/ARG1+ was detectable in 38% of HCCs, but in 0% of MCTs. GS-/GPC3-/ARG1- combination was observed in 24% of MLCs. The specificity of GS, GPC3 and ARG1 for HCC was 27%, 96%, 96% and sensitivity was 100%, 38% and 94%, respectively.
Conclusion: Expression of GS in MLTs is high, therefore GS/GPC3/ARG1 should be used as a panel besides other markers when differential diagnosis of MLC vs HCC is challenging.

PS-14-013
Diagnostic utility of Inhibin immunohistochemistry in a multimodality approach to pancreatic cysts
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Background & Objective: Serous cystadenomas (SCA) are benign pancreatic cystic neoplasms (PCN) that despite multiple radiologic, morphologic, and molecular approaches, continue to exhibit diagnostic challenge, and can present difficulties in clincopathologic decision making. Despite the promise of molecular diagnostics, these tests have limited availability in day to day surgical pathology practice. Recent evidence suggests that inhibin is a potentially helpful immunohistochemical adjunct in the diagnosis of lesions cytologically and endoscopically suspicious for SCA.
Method: We retrospectively reviewed 22 fine needle aspirate/biopsies from 14 patients (mean age 58.7, 47-79 years) with pancreatic multicystic lesions radiologically suspicious for SCA (6 body, 2 head, 4 tail, 1 neck, 1 uncinate; cyst size: mean 4.0 cm, 2.0-7.6 cm) as well as ten resection specimens with a histological confirmation of SCA. Immunohistochemistry for inhibin was performed on all cell blocks and representative sections of the resection specimens.
Results: Of the 14 patients with SCA suspicious lesions, 64% (14/22) of fine needle aspirate/biopsy specimens contained epithelial cells positive for inhibin. When selecting for those specimens that exhibited microscopically distinct strips of cuboidal epithelium, the inhibin positivity rate increased to 82% (9/11). Of those individuals who tested negative, repeat biopsy showed that 100% (2/2) stained positively. We additionally confirmed inhibin as a 90% sensitive marker in the 10 patients with resection confirmed SCA.
Conclusion: This study postulates an advantageous decision-making algorithm for how to best confirm SCA and may help to decrease unnecessary follow-up endoscopy or surgical resection, leading to decreased cost and morbidity in those confirmed to have this otherwise benign condition.

PS-14-014
CD73 in hepatobiliopancreatic system: a potential target for immunotherapy and additional tool for the pathological diagnosis
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Background & Objective: expression of CD73 protein in cancer generates immune tolerance and promotes invasiveness via adenosine production. Anti-CD73 targeted treatment could be a promising tool in cancer immunotherapy, but the characterization of CD73 expression in human tissues and tumours has been scarcely studied. Our aim was to investigate CD73 distribution in the hepatobiliopancreatic system (HBP) and related malignancies.
Method: CD73 immunohistochemical expression was analyzed in 132 cases of non-neoplastic and tumoural conditions of the liver, pancreas and biliary tract.
Results: CD73 was expressed in all normal HBP tissues with subcellular-specific patterns of staining: canalicular in hepatocytes, and apical in cholangiocytes and pancreatic ducts. By contrast it was not present in endocrine islets. While CD73 was always present in hepatocellular carcinoma (HCC) (n=17/17) and in pancreatic ductal adenocarcinoma (PDAC (n=32/32), and frequently observed in intra- and extrahepatic cholangiocellular carcinoma (n=28/32), it was detected only in a small subset of pancreatic neuroendocrine neoplasms (n= 6/15) and acinar cell carcinoma (n=2/19). In addition to the specific luminal pattern of staining observed in normal tissues, an aberrant membranous and/or cytoplasmic expression was often observed in HCC and PDAC. These two entities showed the highest extent and intensity of staining as compared to other investigated neoplasms ($p<0.01$). Interestingly, in PDAC, aberrant CD73 expression was inversely correlated with differentiation ($p<0.001$) and was helpful to identify isolated invasive tumour cells.
Conclusion: CD73 expression in HCC and PDAC supports the rationale for investigating anti-CD73 therapies in these conditions. Specific patterns of expression could also be of help in the routine pathological diagnostic workup.

PS-14-015
Malignant transformation of a hepatocellular adenoma in a male individual reveals insights into its molecular trajectories
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Background & Objective: The molecular classification of hepatocellular adenomas (HCAs) may allows us to distinguish between HCAs that are at higher risk to transform into hepatocellular carcinomas (HCC), like beta catenin Exon 3 mutated HCAs (b-HCA). However, given the evidence of various case studies, this is more complex for male individuals, where a resection is generally advised - irrespective of size or molecular classification. With this study, we report molecular insights into the transformation process, on a basis of a particular small HCA (<4cm) on the background of liver cirrhosis in a male individual that transformed into HCC (< 1cm).
Method: Exome sequencing of HCA/Normal/HCC (see above) was performed. With help of the TCGA database, somatic mutations present in transformed HCC were matched towards HCA cases and clinical and molecular data were correlated in a HCC cohort.
Results: We describe a small number of acquired somatic mutations in the transformed HCC, and we correlate the prevalence of these mutations in a cohort of HCA and HCC cases from the TCGA data base.
Conclusion: Together, we name a small number of somatic mutations in this particular case of transformed HCA into HCC, that are also frequently mutated in HCC cases, but not in HCA cases. As an example, mutations of ZFHX4, that have been described very previously to be correlated with survival in HCC. These findings underline the need to explore the molecular basis of HCA transformation into HCC in men.

PS-14-016
Endobiliary colorectal cancer metastases: clinicopathologic analysis in 19 cases
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Background & Objective: Endobiliary metastasis from colorectal carcinoma (CRC) growing within or invading bile ducts is not very common. This pattern differs from CRC with lyphovascular metastases with a more cholestatic presentation. We aimed to search the clinicopathological features of CRC cases metastatic to the liver with biliary ductus invasion (BDI).
Method: Resection specimens of 133 cases of CRC with liver metastasis operated between 2000-2011 were retrospectively evaluated. The demographic data of the patients, number and size of the metastatic foci, type of the resection, presence of BDI, lyphovascular invasion (LVI) and surgical margin involvement by tumour, the pathological features of the primary tumour were evaluated. Nonparametric tests were used for statistical analysis.
Results: BDI was detected in 14% of the cases (n=19) and significantly in male patients ($p=0.043$). There was only one case of pure endobiliary metastasis. Alltough cases with BDI were frequently under 50 years of age (16% vs. 14%) and had more multifocal metastases (19% vs. 12%) this was not statistically significant. Among cases with BDI 74% had segmental resection, the resection margin was free of tumour in 63%. The primary tumour was moderately differantiated adenocarcinoma in 64% and cases with lymph node involvement had a tendency to have more BDI.
Conclusion: In this series, CRC with BDI showed a tendency to occur more frequently in younger (>50) male patients with multipl metastatic foci and LVI in the liver, and with primary tumour metastatic to the lymph nodes. Although liver metastasis of CRC via bile ducts is rarer than vascular route, endobiliary metastasis is an entity that should be kept in mind in the differential diagnosis with biliary intraductal neoplasms.

PS-14-017

Morphologic patterns of IgG4-relateted lesions of different localisation

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Background & Objective: IgG4-related disease (IgG4-RD) is a recently described entity with tumour-like lesions of different localization, abundant IgG4+ plasma cell (PC) within the inflammatory infiltrate, elevated serum IgG4 and good response to corticoid therapy. International Consensus determines the cutoff levels for IgG+ PC number in different organs and tissues. To compare our data on IgG4+ PC number with the International Consensus cutoffs.
Method: 55 cases of IgG4-RD were studied; the followed organs were affected: panceas (32 cases), liver and extrahepatic bile ducts (5 cases), eye (5 cases), salivary glands (5 cases), thyroid (4 cases), orbital soft tissue (2 cases), lymph nodes (3 cases), skin (3 cases), larynx, urethra and retroperitoneum (1 case of each), combined lesions (3 cases).
Results: Mean number of IgG4+ PC reached the Consensus cutoffs in 40 cases (72.7%). Good correlation with Consensus data was seen for pancreas (100% of cases), bile ducts (100%) and lymph nodes (100%). Poor correlation was seen for salivary glands (in 16.7% of cases only IgG4+ PC number reached the cutoff), lacrimal gland (0%) and skin (0%). IgG4+/IgG+ PC relation reached the Consensus cutoff in 48.2 to 100% of cases depending of organ and tissue. Strong background stain with IgG antibody complicates counting of IgG+ PC. We measure IgG4+/CD138+ relation and observed that it comparable with IgG4+/IgG+ relation (42.2 to 98.5%).
Conclusion: The Consensus IgG4+ PC cutoffs for salivary glands and skin are too high and need to be revised. IgG4+/CD138+ PC relation with 40% cutoff could be used without loss of sensitivity for diagnosis of IgG4-RD.

PS-14-018

Long-term follow-up in children with progressive familial intrahepatic cholestasis type 2 after partial external biliary diversion with focus on histopathological changes

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Background & Objective: Progressive familial intrahepatic cholestasis comprises a group of rare cholestaticd isorders of childhood that can lead to liver cirrhosis. Nowadays, the partial biliary diversionp rocedureis therapy of choice in non-cirrhoticc hildren with PFICl or PFIC2 after an uneffective ursodeoxycholic acid therapy. However, partial external biliary diversion (PEBD) is associated with the disadvantage regarding that adolescent patients did not accept a permanent stoma. In some of them (despite good results of this procedure), the ileal exclusion had to be performed many years after PEBD. The aim of this study was to analyze the longterm outcomes of PEBD focusing on histopathological changes.
Method: We examined retrospectively 14 from 5 PFIC2 patients (3 males, 2 females). All the patients underwent a partial external biliary diversion. Before the final decision of closing the stoma, the liver function and a histological activity of the microscopic changesin the liver biopsy specimensw ere assessed.
Results: The characteristic lobular rosette formations of hepatocytes with centrally located bile plugs were found in all patients. C holestasis was observed in each patient, but only in two patients characteristic elongated deposits were seen along the canalicular plate. The majority of hepatocyte showed degenerative changes from mild to severe degree.
Conclusion: The formation of lobular rosettes with centrally located bile plugs and degenerative changes of hepatocytes seem to be the most characteristic microscopic featuresin early liver biopsies in PFIC2 patients. PEBD improved clinical condition of the patients and prevent liver injury.

PS-14-019

Morphological and immunohistochemical classification of a large series of hepatocellular adenomas with follow up correlation

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Background & Objective: Hepatic adenoma (HCA) is a rare benign monoclonal neoplasm, with risk of undergo malignant transformation. Recently, HCA has been categorized into four subtypes with different behaviour: inflammatory (I-HCA), hepatocyte nuclear factor-1 alpha inactivated HCA (H-HCA), β-catenin-activated HCA (b-HCA) and the remaining group "unclassified" (u-HCA). Recently published data about the subtypes of HCA, have not yet had a relevant impact in clinical practice and more data are needed. We have analyzed a Spanish series of HCA with long term follow up using the new WHO classification.
Method: We reviewed morphological characteristics and performed an immunohistochemistry (LFABP, Betacatenin, GS and SAA) to classify a group of 28 HCA. Morphological subtypes were correlated with recurrence and malignant transformation during a follow up of at least 10 years.
Results: According to IHQ and morphological features, 21,42% (6/28 HCA) were H-HCA; 28,59% fulfilled criteria of b-HCA (8/28), and I-HCA were 32,14% (9/28), only 5 cases remained u-HCA (17,8%) (5/28). Surprisingly recurrences were frequent in H-HCA (50%) although all recurrences were as benign lesions (HCA); recurrences in the other 3 subtypes were all as hepatocellular carcinoma. We found 33% of recurrences in both I-HCA and b-HCA but patients with b-HCA had lower survival. Recurrences were 20% in u-HCA.
Conclusion: It is possible to classify hepatic adenomas in the 4 proposed subtypes with clinical and prognosis significance. The new classification system can help to get a better understanding of the natural history of these tumours and a better management.

PS-14-020

Mucinous cystic neoplasm of the pancreas with classic histologic findings of type 1 autoimmune pancreatitis in a patient without IgG4-related systemic disease – a case report

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Background & Objective: Mucinous cystic neoplasm (MCN) is an epithelial neoplasm characterized by mucinous epithelial lining and subepithelial ovarian-like stroma. It occurs predominantly in middle-aged females and is a precursor to invasive carcinoma. Type 1 autoimmune pancreatitis (AIP1), on the other hand, belongs in the spectrum of IgG4-related systemic disease and can present as a pancreatic mass. There is no known association between these two entities in the current literature. Here, we present a case of pancreatic MCN with classic histologic features of AIP1.
Method: We report a case of a 41-year-old female with an incidental pancreatic mass found on MRI. At the time, serum IgG4 levels were not elevated and a differential diagnosis of MCN, intraductal papillary mucinous neoplasm, and pseudocyst was raised. The patient subsequently underwent distal pancreatectomy.
Results: Gross examination of the pancreatectomy revealed a 4.3 cm mass with a centrally located 3.4 cm cystic lesion, confirmed to be a MCN on microscopic examination. The pericystic tissue showed storiform fibrosis, multifocal obliterative phlebitis and a prominent IgG4-positive plasma cell–rich inflammatory infiltrate (up to 75 per high power field) with an IgG4+/IgG+ ratio of 80%. These classic findings of AIP1 were present in the pericystic tissue but not away from the cyst.
Conclusion: To our knowledge, this is the second reported case of pancreatic MCN associated with AIP1-like changes in a patient without

established IgG4-related systemic disease. Awareness of AIP1-like changes around cystic neoplasms of the pancreas may be helpful in preventing misdiagnosis, particularly in needle biopsy or aspiration of pancreatic cystic lesions.

PS-14-021

Liver diffuse pathology: importance of elastometric studies

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Background & Objective: The chronic liver diseases results to the progression of fibrosis stages. It is necessary to improve the diagnostic algorithm for the early fibrosis detection that are asymptomatic for decades. Study objective is to identify the most sensitive liver fibrosis echographic markers.
Method: A standard ultrasound of the abdominal organs and Acoustic Radiation Force Impulse (ARFI) elastometry of the liver were performed on 88 patients with the ultrasound equipment Acuson S2000 (Siemens, Germany). The stages of fibrosis were evaluated on the METAVIR scale.
Results: The most sensitive echographic changes in patients with liver fibrosis: size increase of the liver left lobe, spleen size increase, change in the liver echostructure, ratio of the caudate lobe thickness to the left lobe thickness more than on 1:3. In patients with F1 and F2 stages 1 to 4 ultrasound symptoms were detected, in patients with F3-F4 stages – 3 to 11 symptoms. In 11 % of F3-F4 stages patients only 1-2 symptoms were revealed. In 6 % patients with F1-F4 liver fibrosis no echographic changes were detected.
Conclusion: The presence of 1-2 echographic symptoms of diffuse liver disease should alert the possible fibrosis changes development. The absence of echographic symptoms doesn't exclude fibrosis and cirrhosis. The elastometric studies can detect fibrosis changes when they are not visualized in the standard B-mode ultrasonography.

PS-14-022

Fibrolamellar hepatocellular carcinoma - a tumour which is not really good!

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Background & Objective: Fibrolamellar Hepatocellular Carcinoma (FL-HCC) is a rare variant of hepatocellular carcinoma occurring in younger age group mostly without any underlying risk factors such as cirrhosis and hepatitis. It is believed to have better prognosis than conventional HCC. We reviewed histopathology and clinical course of 14 patients with FL-HCC.
Method: Files of 14 patients were retrieved from the hospital database from 2005 to 2017. Histopathology was reviewed along with immunohistochemistry. Clinical information regarding treatment and follow-up was noted.
Results: The age range was 12-46 years. M:F ratio was 6:8. All patients were HBsAg negative. Serum AFP level were normal in all. Histologically, large oncocytic cells with mild atypia were seen separated by broad fibrocollagenous septa. On immunohistochemistry, all were positive for Hepar1. Only 4 patients underwent resection; all 4 relapsed with metastasis. Five patients died of disease, three were alive with disease. Follow-up information was not available for 3 patients.
Conclusion: Fibrolamellar HCC is a rare variant of HCC with distinct morphological features. All tumours in our series showed characteristitic histological features and posed no diagnostic difficulty. Absence of HBsAg and normal serum AFP levels were present in all. Fibrolamellar HCC is believed to have a good prognosis mainly due to more chances of complete resection and better function of residual liver. However, our study of 14 patients demonstrated aggressive nature of FL-HCC in the form of low rate of operability (4/ 14), metastasis and mortality (5/14) and refractoriness to chemotherapy. None of the patients remained free of disease.

PS-14-023

Lymphoepithelioma-like hepatocellular carcinoma. A case report

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Background & Objective: Lymphoepithelioma-like carcinoma of the hepatobiliary region is very rare and resembles its nasopharyngeal counterpart. Limited literature is available concerning this tumour type and most of the reported cases arising in the liver are Epstein-Barr virus associated cholangiocarcinomas. We herewith present an eightyone-year-old female patient with a history of cirrhosis and fatty liver, admitted to our hospital complaining of upper abdominal pain. A CT scan revealed a 2,5cm diameter tumour of the liver and a segmental liver resection was performed.
Method: Macroscopically, the subcapsular located tumour was well-circumscribed, pale white with solid, soft texture. Histologically, the aforementioned tumour had a component of undifferentiated carcinoma accompanied by a heavy lymphoplasmacytic infiltration. Immunohistochemically, the neoplastic cells were HSP70(+), Glutamine Synthetase (+), HepPar1(-/+), CEA (+), CK8/18(+ focally, dot-like), HLA-DR (+), and CK7(-), CK20(-), CDX2(-). The lymphocytic infiltrate was composed mainly of cytotoxic CD8+ T cells (CD8>CD4). Rare lymphocytes were EBER+ by situ hybridization.
Results: Taking into consideration the histologic and immonuhistochemical features of the neoplasm, the diagnosis of Lymphoepithelioma-like Hepatocellular Carcinoma (LEL-HCC) was established.
Conclusion: Reviewing the literature, LEL-HCC is an extremely rare variant of HCC, with a distinct immune microenvironment and a favorable prognosis.

PS-14-024

Area of residual tumour is associated with clinical outcome in patients with pancreatic cancer after preoperative therapy

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Background & Objective: Preoperative therapy is increasingly adopted in the treatment of pancreatic cancer aimed for a complete resection. However, the impact of pathological factors, including pathological response, as a prognostic factor is not established. Area of residual tumour (ART) has been reported as a potential prognostic marker in other cancers at our institution. We investigated the prognostic pathological factors including ART for pancreatic cancer with preoperative therapy.
Method: Surgically resected specimen from the 47 patients received preoperative therapy from 2006 - 2016 were examined. ART was determined by using morphometric software on maxuimum slice with residual tumour. Pathological response was defined partial as destruction of >50% of tumour cells.
Results: Of 47 pancreatic cancer, resectable, borderline resectable, locally advanced, metastasis were 12 (26%), 18 (38%), 13 (28%), 4 (9%), respectively. 22 (47%) patients received chemoradiation and 25 (53%) patients received chemotherapy before surgical resection. The median value of ART was 166 mm2 (0 – 462). Cases with ART < 150 mm2

showed the significantly less frequencies of lymphatic invasion, perineural invasion, portal vein invasion than cases with ART > 150mm2. The Univariable analysis revealed that ART < 150 mm2, macroscopical tumour size < 20 mm, major artery invasion, and R0 margin status were significantly associated with long overall survival. And ART < 150 mm2, major artery invasion, and plexus of nerves invasion were associated with long relapse free survival. Partial response of preoperative therapy was not associated with clinical outcome.
Conclusion: ART-based assessment may provide useful information of preoperative therapy.

PS-14-025
Profiling the tumour immune microenvironment in pancreatic neuroendocrine neoplasms with multispectral imaging indicates distinct subpopulation characteristics concordant with WHO 2017 classification
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Background & Objective: We successfully determined the difference of immune microenvironments between pNENs and pancreatic ductal adenocarcinomas (PDACs), and the histology-dependent variability among pNENs using multispectral fluorescent imaging system.
Method: Tumour tissue samples including 52 pNENs and 18 PDACs were investigated. The tumour-infiltrating lymphocytes (TILs), their PD-1 and PD-L1 expression in the pNENs were comprehensively and quantitatively analysed and were subsequently compared with those in PDACs.
Results: A principal component analysis revealed that the tissue immune profile is related to tumour histology, with distinct groups being observed for NETs, NECs, and PDACs. While NECs and some PDACs had hot immune microenvironments with abundant TILs, NETs had a cold immune microenvironment with few TILs. Moreover, in NETs, the numbers of intraepithelial PD-1^{high} T cells and PD-$L1^{high}$ Type-II macrophages were elevated according to the grade. Univariate analysis revealed that lymph node metastasis, grade, stage, PD-1^{high} T cells, and PD-$L1^{high}$ Type-II macrophages were predictors for recurrence-free survival (RFS), while grade and PD-1^{high} T cells were prognostic factors for overall survival (OS). We also showed that PD-1^{high} T cells and PD-$L1^{high}$ Type-II macrophages were associated with worse outcome in pNENs.
Conclusion: Our results support the WHO 2017 tumour classification criteria, which distinguish between G3 NETs and NECs.

PS-14-026
Hepatocellular carcinoma in cirrhotic and non-cirrhotic liver
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Background & Objective: Hepatocellular carcinoma (HCC) occurs most commonly in cirrhotic liver (LC) but small percentage occurs in non-cirrhotic liver (NCL). The aim of this study is to make clinicopathologic characterization of HCC, to analyze tumour and non-tumour liver tissue, and the immunoexpression of β-catenin and p53.
Method: We analyzed 60 patients with HCC for cirrhosis, B and C hepatitis (HBV, HCV), serum level of alpha-fetoprotein (AFP), chronic alcoholism, tumour dimension, multiple tumour nodes, lymph node status, histological pattern, tumour grade and survival. Biopsy tumour tissue was investigated for immunoexpression of β-catenin and p53 and non-tumour liver tissue in NCL HCC was analyzed for pathological changes.
Results: There were 8 out of 60 cases of HCC in NCL. Males were more affected and solitary tumours were more frequent in both groups of cirrhotic and NCL HCC. Patients with NCL HCC were older, had smaller tumours, lower AFP and less nodal involvement, not significantly. All HCC in NCL were well differentiated and trabecular type. The risk factors HBV and HCV infection and chronic alcoholism were with similar frequency in both groups. Patients with NCL HCC had non-significant longer survival time. All patients with NCL HCC had liver damage: non-alcoholic fatty liver disease (3 cases), chronic hepatitis (4 cases) and fibrosis (one case). β-catenin reduction and p53 expression in tumour tissue of NCL HCC were lower than in cirrhotic HCC.
Conclusion: Clinocopathological factors of HCC in cirrhotic and NCL, although non-significantly, differ. Investigations are still needed to clarify molecular and other factors which influence survival.

PS-14-027
Cystic fibrosis in paediatric liver transplatation: patterns of fibrosis and vascular lesions
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Background & Objective: Cystic Fibrosis (CF) is a relevant therapeutic indication of liver transplantation. To evaluated different types of vascular lesions and patterns of fibrosis and liver regenerations
Method: 10 Patients were transplanted between 1990 to 2016 from a multicenter of 1253 paediatric liver patients (0,7%). The median age for the transplant was 12 years After weighing, recording the external surface appearance and measuring the liver, at least four different sections were taken from the porta hepatis. Three different sections were submitted from the right and left lobes as well as caudate. Nine livers were evaluated with H&E; Periodic acid-Schiff, Trichrome (Masson), Reticulin stain and Elastic Fibers: Verhoeff-Van Gieson (VVG) stain.
Results: Explant liver of all patients did not show patterns of complete cirrhotic-type regenerative nodules but we found mild to moderate septal fibrosis (F2-F3) alongside with areas of incomplete septal cirrhosis (ICS) We have seen vascular changes like obliterative venopathy, portal vein shunt vessels associated with dense portal fibrosis and lack ort portal tract inflammation. In the liver parenchyma of livers explants we found areas of Nodular regenerative hyperplasia (NRH) close to megasinusoides. Another finding was few isolated arteries unaccompanied by a portal vein or a bile duct. Some large hepatic veins had segmental sclerotic changes. All patients had splenomegaly, thrombocytopenia and portal hypertension 7 also had oesophageal varices.
Conclusion: The livers explantated showed regenerative macronodules associated with severe fibrosis and different types of vascular lesions such as obliterative venopathy portal.

PS-14-028
EBV-associated hepatic smooth muscle tumour (inflammatory miofibrobastic tumour (IMT) pattern) of uncertain biologic behavior after kidney transplant. case report and literature review
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Background & Objective: Epstein-Barr virus (EBV)-associated smooth muscle tumours following solid organ transplantation are a recently described entity extremely rare, with less than 30 cases reported in the literature up to this moment, more knowledge is needed. We describe the clinical, morphological inmunohistochemical and EBV hibridization status of a new liver case with sarcomatous features
Method: A 44 years old woman from Philippines, with a kidney transplant 10 years ago, presented to emergency room with fever and malaise. Ultrasound study showed a 4,3 cm well demarcated mass located in right liver lobule with a suspected diagnosis of liver abcess. Surgery was performed with morphological and inmunohistochemical study.

Results: The tumour showed short interlacing fascicles of moderately differentiated spindled cells with a dense collagenous stroma at the periphery of the tumour and high cellular density at the tumour centre with high mitotic rate (9 /10 hpf). Prominent inflammatory intratumoural infiltrate mainly of T lymphocytes was seen, as it has been previously described in IMT. Tumour cells were stained with smooth muscle markers and EBV infection, was confirmed by in situ hybridization.
Conclusion: Liver IMT-ALK negative is a poorly understood entity with uncertain biological behaviour. This case shows a morphological pattern similar to IMT but in situ hibridization to EBV relates this tumour with smooth muscle tumours-EBV positive. To test EBV in all mesenchymal tumours arising in immunocompromised patients is a diagnosiss clue to find these special tumours with different prognosis and treatment. Sarcomatous features warn about risk of recurrency or metastasis. Literature review shows different specific systemic treatment options including famciclovir and to low immunosuppresive agents to prevent recurrency.

PS-14-029

Liver pseudoprogression in advanced lung squamous cell carcinoma treated with nivolumab: histology and immunohistochemical profile

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Background & Objective: In the era of immune-related therapies, new patterns of response to anti-neoplastic drugs are observed in clinical practice including tumoural pseudoprogression, defined as an apparently increased tumour burden of a given lesion according to Response Evaluation Criteria in Solid Tumours (RECIST) criteria on imaging that is caused by inflammation.
Method: We present a case of a 65-year-old male patient with advanced poorly differentiated squamous cell lung carcinoma who experienced liver progression after first-line chemotherapy and started programmed cell death 1 (PD-1) inhibitor nivolumab as second-line therapy. After five cycles of nivolumab he showed an apparently radiological progression of one of the hepatic lesions and a liver biopsy was performed to rule out pseudoprogression. The aim of our study was to provide an accurate histological description of the hepatic lesion, to quantify the inflammatory component and to define its immunophenotype.
Results: The liver biopsy showed an extensive central area of tumoural necrosis with non-viable tumour cells surrounded by a rim of lymphohistyocytic-rich inflammatory infiltrate with a vague granulomatous pattern. Immunohistochemical analysis confirmed the presence of numerous histiocytes with intense PDL-1 positivity and a predominant T-cell lymphocytic population with a CD4:CD8 ratio of 1:1, numerous CD-103 positive T-cells (100/HPF) and scattered CD56-positive lymphocytes (10/HPF).
Conclusion: In our case, the apparently increased tumour size observed by imaging was actually due to an important lymphohistiocytic infiltrate, with numerous CD103-positive T-cells, associated to tumoural necrosis. Pathological evaluation of growing lesions can aid to rule out pseudoprogression and make clinically relevant decisions.

PS-14-030

Follicular cholangitis in common bile duct mimicking cholangiocarcinoma

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Background & Objective: Follicular cholangitis is a rare variant of chronic cholangitis presenting with biliary stricture and characterized by the presence of florid follicular hyperplasia. Differential diagnosis includes IgG4-related sclerosing cholangitis, primary sclerosing cholangitis (PSC) and cholangiocarcinoma. Correlation of clinical, serological and imaging information is essential to reach the final diagnosis. We report a case of a 75-year-old man with common bile duct (CBD) stricture and clinical suspicion for cholangiocarcinoma
Method: CT-scan revealed CBD stricture and EUS-guided FNA showed few mildly atypical epithelial cells and abundant lymphocytes. Grossly the CBD wall was thickened without evidence of intraluminal mass. The regional lymph nodes were enlarged.
Results: Histologic examination revealed numerous florid lymphoid follicles with prominent germinal centers and intact mantle zones extending from submucosa to periductal soft tissues, with presence of abundant plasma cells. No storiform fibrosis or obliterative phlebitis was noted. Ductal epithelium was spared and showed mild dysplasia focally, with no evidence of high grade dysplasia. Florid germinal center hyperplasia was also noted in all regional lymph nodes. Immunohistochemically, germinal centers in the CBD and lymph nodes were bcl2- and plasma cells were polyclonal with few IgG4+ plasma cells (<15/HPF). The histological and immunohistochemical findings are more consistent with follicular cholangitis
Conclusion: We present a case of follicular cholangitis, a rare new entity which is probably under recognized and should be considered as a differential diagnosis when biliary stricture is present. The absence of periductal storiform fibrosis and elevated numbers of IgG4+ plasma cells rule out IgG4-related sclerosing cholangitis and PSC.

PS-14-031

Evaluation of cdx-2, ttf-1 and pax8 in liver metastases from neuroendocrine tumours - a series of 15 cases

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Background & Objective: Gastrointestinal, pancreatic and pulmonary neuroendocrine tumours (NETs) show similar histologic features. Several immunohistochemical markers have been used to identify the site of origin in metastatic NETs which is important for therapeutic management. We evaluated an immunohistochemistry panel in hepatic metastases from NETs.
Method: We studied 15 cases of hepatic metastases from NETs in a 13-year period. Ten were male and five were female, the average age was 56 years. We evaluated the immunohistochemical expression of CDX-2, TTF-1 and PAX8 and we related the results to the site of origin of the primary NET.
Results: The primary origin was confirmed in 13 cases (5 small bowel, 2 colonic, 2 pulmonary and 4 pancreatic). Six were positive for CDX2: small intestine (5/5) and colon (1/2). Two were positive for TTF1: pulmonary (2/2). Four were positive for PAX8: pancreas (3/4) and one case with unidentified origin. One case was negative for all markers but positive for prostatic acid phosphatase (PAP) which suggested possible rectal origin.
Conclusion: An immunohistochemical panel including CDX-2, TTF-1 and PAX8 is useful in recognizing the primary tumour. The expression of PAX8 (+) with CDX2 (-) can reliably distinguish pancreatic from intestinal and pulmonary NETs. It is important to identify the primary site, especially pancreatic since these patients can benefit from temozolimide-based therapies. In case of negativity for the three markers, PAP can be used to determine a possible rectal origin.

PS-14-032

Multicentric hepatocellular carcinoma in a 31-year-old male with alpha-1 antitrypsin deficiency

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Background & Objective: Alpha-1 antitrypsin deficiency (AATD) is an autosomal recessive disorder with codominant expression that increases

the risk for liver and chronic obstruction pulmonary disease (COPD). There are three phenotypes ZZ, SZ or SS. Most infants are clinically healthy. In ZZ phenotype cirrhosis is present in 2% of the ages 20 to 50. The overall incidence rate of hepatocellular carcinoma (HCC) is significantly lower when compared with other causes of cirrhosis (8,5% vs 31%). We describe a case who required liver transplantation.

Method: A 31 year-old male with a neonatal diagnosis of AATD phenotype ZZ without pulmonary disease and cirrhosis at the age of 17. He has no history of tabaco neither alcohol. Alfa-fetoprotein level is 25 and in radiological imagines the liver also demonstrates several lesions and at least one of 5 cm suggestive of HCC that is confirmed histologically. He has a liver transplantation.

Results: The liver weights 1020 g. The parenchyma is nodular and within the right lobe, there are 4 firm, well and poorly delineated, whitist-tan masses measuring between 2 and 5 cm and one cm one in the left lobe. Microscopic evaluation of the liver disclose cirrhosis, hepatocytes contained diastase-resistence periodic acid schiff (d-Pas) positive intracytoplasmatic granules confirmed immunohistochemistry (alpha-1 antitrypsin) and 5 HCC. These have a trabecular, solid and pseudoglandular pattern. Reticulin stain, CD34 and glypican-3 are done in all tumours and multicentric HCC are diagnosed.

Conclusion: We describe a rare case of a multicentric HCC in a young male with AATD with cirrhosis.

PS-14-033

An exceedingly rare hepatic mesenchymal tumour

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Background & Objective: Lymphangiomas are benign neoplasms regarded as congenital malformations of the lymphatic system. Most lymphangiomas are located in the neck and axilla. Abdominal lymphangiomas account for less than 5%. In most cases, the hepatic lesion is usually part of multi-organ involvement including spleen, kidney and other organs. Hepatic lymphangioma is usually observed in children. To our knowledge, only 17 previous cases of solitary hepatic lymphangioma in adults have been described in the medical literature.

Method: A 74-year-old woman was admitted because of a mass in the right lobe of her liver which was discovered on routine physical examination. Magnetic resonance showed a multi-cystic mass with a central solid component. Preoperative examinations were not sufficient to differentiate the benign or malignant nature of the mass.

Results: Partial hepatectomy was performed and revealed a 8 cm mass. Histologically, a solitary hepatic lymphangioma completely removed was diagnosed.

Conclusion: Hepatic lymphangioma may appear as a simple or multi-cystic mass. Because most lymphangiomas are multi-cystic lesions, they may be confused with other lesions including cystadenoma and cystadenocarcinoma. Isolated hepatic lymphangioma in an adult is extremely rare and lack of specific clinical symptoms, therefore, it is easy to be misdiagnosed. Cystic lymphangioma should be considered as a differential diagnosis when patients present with a multiloculated cystic tumour in the liver. Surgical resection is considered standard treatment. The prognosis following complete resection is excellent and patients have no need for further treatment after resection. Lymphangioma rarely recurs or progresses. The patient has been follow-up for 20 months without evidence of recurrence.

PS-14-034

Difficulties that the pathologist must face to diagnose core liver biopsies of disseminated tumours of unknown origin: review of a case

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Background & Objective: Four percent of diagnosed cases are Tumours of Unknown Origin according to the Spanish Society of Medical Oncology. They have no predisposition for sex, the average age is 60 years and their prognosis is poor (survival: 8-10 months in 85% of cases). The case we present here was a true diagnostic challenge due to its nonspecific clinical presentation, morphology and immunohistochemistry (IHC).

Method: A 76-year-old woman with multiple hepatic, peritoneal and pulmonary masses, the largest of 16 cm. Main antecedents: poorly controlled hypertension, morbid obesity, bronchial hyperreactivity. No pelvic/gastrointestinal organ-dependent masses were observed by NMR. Altered tumour markers: NSE 62.1 ng/mL and β2-microglobulin 3.6 mcg/mL. A liver biopsy was performed for better accessibility.

Results: We received two cores of 0.4 and 0.5 cm in length, both composed entirely of round-epithelioid tumour cells, with oval nuclei, eosinophilic cytoplasm, little atypia and absence of mitosis. IHC: CK-CAM5.2, S100, CD45, Synaptophysin and Myogenin: negative. Vimentin: positive (intense/diffuse). CD99: positive (patched/dim). The initial diagnosis was "Round Cell Sarcoma". Subsequently, with new clinical-radiological contributions, the IHC was amplified, resulting in C-KIT (CD117) and DOG1: positive (intense/diffuse). The diagnosis was changed to "Epithelioid Variant Gastrointestinal Stromal Tumour" (GIST).

Conclusion: The integration of clinical, morphological, IHC and genetic-molecular findings are essential to reach the diagnosis. Primitive Neuroectodermal Tumour with atypical presentation (PNET) was taken into account as a differential diagnosis because it can express CD99, vimentin and even C-KIT, however, DOG1 is a specific marker that helps differentiate them from GIST.

PS-14-035

Malignant solitary fibrous tumour of the liver: a case report

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Background & Objective: Solitary fibrous tumours are benign mesenchymal neoplasms that usually affect the thoracic cavity. Although extrathoracic sites have been previously reported, occurrence in the liver is extremely rare. Also, the malignant behavior of these tumours is uncommon.

Method: A 73-year-old woman presented to the Emergency Department with a 6-months history of hypoglycemia, syncope and upper abdominal pain. On palpation, a mass was identified in the right hypochondrium. Laboratory investigations were unremarkable. Computed tomography scan of the abdomen revealed a giant circumscribed mass in the right liver, measuring 20x16x26 cm. An extended right hepatectomy was performed and intraoperative the liver mass was relatively well delineated, without invasion of the vascular or biliary structures.

Results: On gross examination, the tumour was large (19x16x25.4 cm), lobulated, firm, well-delineated, containing necrotic areas. Microscopic examination revealed a proliferation of fusiform cells arranged in short fascicles with hypo- and hypercellular areas and a variable collagenous background. In areas of high cellularity nuclear crowding, cytological atypia and increased mitotic rate (7-8 mitosis/10 HPF) were observed. Immunohistochemically the tumoural cells were positive for CD34, CD99, and Bcl-2 and negative for cytokeratin, c-kit, S-100, desmin, and actin. Based on the histological examination and in correlation with immunohistochemistry, the final diagnosis was a malignant solitary fibrous tumour of the liver.

Conclusion: We described an uncommon case of solitary fibrous tumour in the liver with malignant features. The definitive diagnosis of this case was confirmed by immunohistochemistry. Due

to the rarity of this tumour, surgery remains the mainstay of treatment.

Tuesday, 11 September 2018, 09:30 - 10:30, Exhibition Hall I/II
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PS-15-001

One-step acid amplification (OSNA) for sentinel lymph node (SLN) assessment in endometrial cancer. A single institution experience

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Background & Objective: OSNA method is widely used in breast carcinoma to asses the metastatic spread to lymph nodes. It has been recently evaluated for endometrial cáncer. We evaluate our center experience in the framework of a multicentric study to validate this method.
Method: A total of 52 SLNs from 26 patients with endometrial carcinoma were enrolled in a 2 years period. SLN were processed as previously consensuated in a protocol and examined by haematoxylin and eosin and cytokeratin 19 (CK19) and the remaining tissue was analysed by OSNA CK19 mRNA. The following parameters (histological type, histological grade, lymphovascular and miometrial invasion) among others were registered. Accuracy of the OSNA assay was evaluated based on histopathological diagnosis.
Results: In our series 85% tumours were endometrioid type, 57,6% cases showed more than half of myometrial invasion; 23% cases showed lymphovascular invasion; 61,5% were grade 2. Using the breast cancer cutoff value for detecting lymph node metastasis by OSNA (>250 copies of mRNA of CK19 for micrometastasis and >5000 copies for macrometastasis) five positive result were given: one macrometastasis (histopathologically confirmed) and four micrometastasis (two of them showed isolated tumoural cells in the histopathological analysis and the other two did not). The sensitivity of OSNA assay was 100%, the specificity was 87.6% and the diagnostic accuracy was 95,9%.
Conclusion: The intraoperative identification and rapid assessment of sentinel lymph nodes by OSNA shows high sensitivity and specificity, reducing surgical staging morbidity and improving the therapeutic strategy in these tumours

PS-15-002

The value of CRIPTO, HOXA9, MGMT, RASSF1A and SCGB3A1 promoter methylation levels for testicular germ-cell tumour subtyping

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Background & Objective: Testicular Germ-Cell Tumours (TGCTs) constitute a heterogeneous group of tumours and differential diagnosis is challenging. Epigenetics may help explain this heterogeneity. We aim to determine the differential patterns of promoter methylation of five genes among TGCT subtypes and assess their potential as subtype-specific biomarkers.
Method: DNA was extracted from a formalin-fixed paraffin-embedded cohort of 161 TGCTs and 16 controls (testicular parenchyma from orchiectomies performed for inflammatory/benign lesions). Bisulfite modification and quantitative methylation-specific PCR (qMSP) was performed for evaluating the promoter methylation levels of CRIPTO, HOXA9, MGMT, RASSF1A and SCGB3A1. Associations with clinicopathological variables were assessed and ROC curves weighed the discriminative power of the gene panel.
Results: CRIPTO, HOXA9, MGMT and SCGB3A1 methylation levels were significantly higher in germ-cell neoplasia in situ (GCNIS)-related TGCTs compared to controls (p=0.0058, p=0.0092, p=0.0268, p=0.0156). Promoter methylation of CRIPTO/HOXA9/SCGB3A1 panel and of RASSF1A best discriminated among controls and Non-Seminomatous Tumours (NSTs, AUC=0.9147) or Seminomas (SEs, AUC=0.8832), respectively. Promoter methylation levels of all genes were significantly higher in NSTs compared to pure SEs($p<0.0001$), with HOXA9/RASSF1A displaying the best discriminative performance (AUC=0.9039). Significant differences in CRIPTO, MGMT and RASSF1A methylation levels were depicted between pure forms and matched mixed components, with the latter showing higher levels. CRIPTO, HOXA9, MGMT and SCGB3A1 methylation levels differed significantly between pre- and postpubertal TGCTs. Higher HOXA9, RASSF1A and SCGB3A1 promoter methylation levels also associated with advanced stage and poorer prognostic grouping.
Conclusion: Combinations of CRIPTO, HOXA9, MGMT, RASSF1A and SCGB3A1 promoter methylation levels discriminate among TGCT subtypes and may constitute useful biomarkers for diagnosis and disease monitoring.

PS-15-003

Gene expression profile in Crohn's disease: preliminary data

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Background & Objective: Crohn's disease (CD) is an immune-mediated chronic of the gastrointestinal tract. The etiology of inflammatory bowel diseases remains undetermined, but the overexpressed immune response in the gut contributes to complications such as strictures, fistulas and perforations. The aim of this study was to identify the differences in gene expression profiles analyzing a panel of candidate genes in the mucosa from patients with active CD (CD-A), patients in remission (CD-R) and normal controls.
Method: Methods Nine adult individuals were enrolled in the study: three with active lesions (CD-A), three in remission (CD-R) and three normal controls. All the individuals underwent mucosal biopsy during colonoscopy. Gene expression profile of 84 genes previously associated with CD was evaluated by PCR array using the Human Crohn's Disease RT2 Profiler PCR Array (PAHS 169Z, Qiagen).
Results: Among the 84 genes investigated, 48 genes differentially expressed in terms of Fold Regulation ($2<FR<-2$) in CD-R (46 up-regulated and two down-regulated) and 64 in CD-A (61 up-regulated and three down-regulated) compared to controls. Genes with statistical significance ($p<0.05$) in CD-A patients compared to controls, were CCL11, CCL25, DEFA5, GCG, IL17A, LCN2, REG1A, STAT3, MUC1, CCR1. In CD-R patients significant genes were CASP1, IL23A, STAT1, STAT3, TNF, CCR1, CCL5, and HSP90B1. CCR1 gene was more expressed in CD-A (FR = 10,39) than in CD-R (FR = 3,36).
Conclusion: Conclusions: Our data suggest that CCR1 gene may be a putative marker of molecular activity of Crohn's disease. Following these preliminary data, a confirmation in larger cohort studies could represent a useful method in order to identify new therapeutic targets.

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PS-15-004

Role of microRNA-1, -205, -210 and -499 in foetal loss syndrome

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Background & Objective: The exchange of information between the functional systems of the mother and the fetus is important for normal pregnancy, development and growth of the fetus. This connection is ensured by microRNAs circulating between the tissues of the mother and the fetus. Thus, the dysregulation of microRNA expression may be associated with fetal loss syndrome. The purpose of this study to compare the relative

expression level of microRNA 210, miRNA 205, microRNA 1, and microRNA 499 in patients with normal pregnancy and fetal loss syndrome.
Method: 34 women aged from 18 to 45 years were examined: 16 pregnant women with fetal loss syndrome, 13 women with normal pregnancy and 10 non-pregnant women. The material for analysis was obtained from 150 μl of plasma and measured by qPCR using TaqMan technology. The relative miR expression level (RQ) was evaluated by Student t-test ($p < 0.05$).
Results: Association with the risk of fetal loss syndrome was reliably detected by almost 2-fold increasing level of miR-1 (RQ 1.87, $p = 0.026$), miR-210 (RQ 1.53, $p=0.036$) and miR-499 (RQ 1.49, $p=0.017$) compared to women with normal pregnancies and non-pregnant women.
Conclusion: We suggest that miR-1, miR-210 and miR-499 can be used in prenatal screening as a risk marker for fetal loss syndrome development.

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PS-15-005

Recommendations to improve the harmonisation of colorectal cancer cell percentage estimation in molecular oncology: a modified Delphi study

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Background & Objective: Results from external quality assessment revealed considerable variation in the way neoplastic cell percentages (NCP) are estimated in samples for biomarker testing. Since testing methodologies require a minimal percentage of neoplastic cells, overestimations might lead to false negative test results. Therefore, we aimed to develop a guideline to improve the NCP determination.
Method: A modified Delphi study was used to reach consensus by 10 gastro-intestinal pathologists from 10 countries with on average twelve years of experience in determining the NCP for colorectal adenocarcinoma. This study included two online surveys and a decision-making meeting. Consensus was a priori defined as an agreement of >80%.
Results: All pathologists completed both surveys. Consensus was reached for 8 out of 19 questions and 2 out of 13 in the first and second survey, respectively. Remaining issues were discussed during the meeting. In total, 24 recommendations were formulated and tested in practice. Major recommendations are: only pathologists can do the morphological evaluation, but molecular biologist/technicians can estimate the NCP, if trained appropriately. The estimation should be determined in the area with the highest density of viable neoplastic cells and lowest density of lymphocytes. Other recommendations concerned: the determination protocol itself, needs for micro- and macro-dissection, reporting and interpreting, referral practices and generalizability towards other cancer types.
Conclusion: The recommendations emerging from this Delphi study may lead to more accurate estimations of the NCP ensuring a correct interpretation of molecular test results. Further studies on variation between pathologists are needed to evaluate the impact of these recommendations.

PS-15-006

Spectrum and frequency of mutations detected by NGS panel in primary melanomas

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Background & Objective: A number of genes have already been described to be implicated in melanoma predisposition (e.g. CDKN2A, CDK4, POT1, BRCA1/2) and pathogenesis (BRAF, NRAS, PIK3CA, PTEN, etc.). Herein we present an NGS analysis of selected genes involved in melanoma development in 80 primary melanomas.
Method: Genomic DNA from 80 FFPE primary cutaneous melanomas (33 nodular and 47 superficial spreading) underwent sequence capture NGS (MiSeq, Illumina) with a custom panel (219 kbp; Roche NimbleGen SeqCap EZ protocol). The data was analyzed by NextGENe (Softgenetics). Only the non-synonymous variants with a minimal average coverage 150x and a frequency ≥10% were evaluated. Selected variants were confirmed by Sanger sequencing. Databases and in silico predictors were used for the pathogenicity determination.
Results: A total of 46/54 evaluated genes carried mutations. Each melanoma demonstrated 0-13 mutations (median 4) in 0-9 genes (median 3), both were equally distributed regardless of stage or location. The BRAF (44/80;55%) and NRAS (24/80;30%) mutations were mutually exclusive. The BRAF mutations correlated with shorter local recurrence-free survival ($p=0.036$). Another relatively frequent class 4/5 mutations were detected in ATM (6/80;7.5%); PPP6C, ZEB2 (5/80;6.3%); and ARID2, BRCA2, TP53 or KDR (4/80;5%). Several novel pathogenic mutations were identified (HNF1B, KDR or ZEB2).
Conclusion: Our results are comparable with other studies, with the addition of several novel variants identified. The characterization of variants and extension of analyzed cohort is ongoing.

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PS-15-007

Adopting HGVS recommendations for reporting of biomarker results: where are we now?

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Background & Objective: The Human Genome Variation Society (HGVS) recommendations for reporting biomarker variants are crucial in molecular pathology for standardization of databases and written reports. External quality assessment (EQA) schemes of the European Society of pathology evaluate correct HGVS practice in diagnostic reports for colorectal and lung cancer. Previous results demonstrated the need for improvement, which is evaluated in this study on a longitudinal level.
Method: Nomenclature was assessed yearly for one and two reports for colorectal and lung cancer, respectively. Different deletions and point mutations were analyzed for the EGFR, KRAS and NRAS genes. A distinction was made between small errors, larger errors with possible interpretation impact, and omitting the variant's nucleotide or protein level.
Results: Reports from 252 unique laboratories were analyzed between 2015 and 2017. The percentage of participants with a nomenclature error decreased from 91.3% (n=115) towards 70.2% (n=104) for lung cancer, and from 74.4% (n=125) to 60.0% (n=105) for colon cancer. Making a combination of different errors for a variant decreased from 54.8% to 26.9% and 19.2% to 13.33% for lung and colon. Participants to all three lung schemes less often obtained a nomenclature error in 2017 (60.6%) compared to one (100.0%) or two (100.0%) participations. The percentage of laboratories with an error in the colon schemes was 55.0%, 71.4%, 62.5% for three, two and one participation(s), respectively.
Conclusion: These results highlight improved HGVS reporting by laboratories for subsequent EQA participations. Currently the 2018 Lung and Colon EQA schemes are ongoing, and data will be included in the analysis.

PS-15-009

Breast cancer subtyping using a novel multiplex RNA expression assay

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Background & Objective: Accurate tumour diagnosis is vital for adequate patient management. The current breast cancer diagnostic workflow is subject to pre-analytic variables, interpretation and defined thresholds. HER2 copy number assessment on 960 breast cancer samples (cBIOPortal, TCGA) is estimated to detect 1.3% amplification in the absence of expression (false positives) and 4.2% diploid with overexpression of the gene (false negatives). Despite updated guidelines, equivocal and inter-laboratory disconcordance persist. Here, we assess the performance of a novel gene expression assay for the diagnosis of breast cancer.
Method: A multiplex branched DNA assay was used to quantify gene expression profiles from 132 formalin-fixed paraffin embedded (FFPE) breast cancer tissue. Tumour area was selected by laser microdissection of haematoxylin and eosin stained membranes, macro-dissection or by taking a 0.6mm core from the FFPE block. Tumour heterogeneity was identified by morphology and immunohistochemical staining.
Results: Measured gene expression profiles characterised Human epidermal growth factor receptor 2 (HER2) status (AUC = 0.950; $p<0.001$), Oestrogen Receptor (ER) status (AUC = 0.934; $p<0.001$) and Progesterone Receptor status (AUC = 765; $p=0.002$) with high accuracy. Moreover, this assay was able to identify heterogeneous receptor expression within tissue biopsies and characterise HER2 in borderline or polysomic cases by fluorescent in situ hybridisation (FISH).
Conclusion: The gene expression assay is a novel, quick and multiplex method that can accurately diagnose breast cancer subtypes, omitting subjectivity of interpretation and minimising technical variation. This method has a wide range of possible applications in the diagnosis of tumours and is adapted to the current diagnostic workflow.

PS-15-011

MicroRNA in situ hybridisation and combinations with immunohistochemistry and mRNA in situ hybridisation in cancer samples

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Background & Objective: MicroRNAs are short, single-stranded sequences of non-coding RNA that have a regulatory contribution to protein expression and comprise an interesting new group of biomarkers. The most frequently described function of microRNAs is the repression of protein synthesis by targeting mRNAs, to which they bind in the 3'UTR. Some miRNAs are cell-specific and the expression is associated with differentiation. The molecular dynamics of a microRNA, its target mRNA and the effect of protein expression makes combined visualization appealing.
Method: The microRNAs were detected in tissue sections by in situ hybridization (ISH) using LNA™ probes. We developed a novel ISH assay for microRNA detection. The assay is based on double-digoxigenin-labeled LNA™ probes and detection can be either fluorescence or chromogenic staining. We combined the microRNA ISH assay with mRNA in situ hybridization using the highly specific RNAscope® probes and immunohistochemistry.
Results: The novel ISH assay for microRNA detection showed improved sensitivity and signal-to-noise and can be used for any LNA™ probe on both FFPE and frozen sections. We have combined the fluorescence assay with immunofluorescence, for double or triple staining, and show a variety of combinations, including examples of combined staining of microRNA-17, IL-1beta mRNA or TNF-alpha mRNA, and cytokeratin proteins in automated triple staining procedures of colon cancer samples.
Conclusion: The combined staining of microRNA and mRNA and protein on the same tissue section is of general interest for exploring how microRNAs (or antisense oligonucleotides) regulate expression of target mRNAs and proteins in individual cells.

PS-15-012

Targeted molecular profiling of poromas and porocarcinomas reveals their genetic heterogeneity and suggest possible role of HRAS and TP53 in their development

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Background & Objective: Cutaneous adnexal tumours comprise different benign and malignant entities whose genetical characteristics are unexplored. Mutations in HRAS were previously reported in subsets of poromas and porocarcinomas, but a more comprehensive genetic view on these adnexal neoplasms is lacking.
Method: The mutational profile of 50 cancer-related genes was evaluated in 12 cases (six poromas and six porocarcinomas) using ultra-deep next generation sequencing. p53 and p16 expression were evaluated using immunohistochemistry.
Results: Non-synonymous mutations were found in two-thirds of both poromas and porocarcinomas. In poromas no more than one mutated gene was found, while porocarcinomas were more heterogeneous with up to six mutated genes per case. Hotspot mutations for subsets of both these tumours were detected in HRAS (p.G13 and p.Q61). Recurrent TP53 mutations were found in all porocarcinomas that harbored mutated genes. In addition, non-recurrent mutations were found in tumour suppressors (RB1, APC, CDKN2A, and PTEN), and genes encoding PI3K-AKT and MAPK pathways (ABL1, PDGFRA, PIK3CA, HRAS, and RET). UV-associated mutations were found in TP53, APC, CDKN2A, PTEN, and RET. Decreased p53 expression was noted in a porocarcinoma with a deleterious mutation of TP53 (p.R306*) and another one without detected mutations. p53 expression was diffuse in other porocarcinomas and more intense than in poromas. A focal loss of p16 was noted in a porocarcinoma with CDKN2A mutation.
Conclusion: Our study confirms and extends the spectrum of mutations in poromas and porocarcinomas. Porocarcinomas exhibited greater genetic variability and frequent TP53 mutations compared to poromas. Mutations in TP53 didn't correlate with p53 loss in porocarcinomas.

PS-15-013

Expression of microRNAs in Wilms tumour with anaplasia

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Background & Objective: Nephroblastoma is the most common abdominal tumour in paediatric age. Anaplastic Wilms Tumour (WT) represents 5% of the renal tumours. This variant has a poor prognostic because resistance to treatment and diagnosis in stage II to IV. Molecular pathways in this variant are poorly studied. The role of microRNAs in the development of the WT is probed; however, the pattern of expression of microRNAs between classic WT and anaplastic WT has not been characterized. The objective was to determine the expression profile between both histological subtypes.
Method: Expression of 756 microRNAs was evaluated in 6 anaplastic WT, 6 classic WT and 8 control group. A total of 55 (7%) microRNAs expressed difference between both tumour types; TaqMan arrays were analyzed and heat maps were generated using the relative quantification values ($2^{-\Delta Ct}$). Data were evaluated comparing tumours with anaplasia against tumours without anaplasia and control cases, and tumours without

anaplasia against control cases. Data analysis was performed with T-student and ANOVA

Results: A group of microRNAs was chosen based on their differential expression, a) WT with anaplasia against WT without anaplasia: miR-29a, miR-200a, miR-139-5p; b) WT with anaplasia against control: miR-141, miR-200a, -200b; c) WT without anaplasia against control: miR-199a, miR-483-3p.

Conclusion: This microRNAs participate in Wnt/B-catenin signaling pathway; regulate migration and are involved in epithelial to mesenchymal transition. The differences in their expression may reflect alteration in different molecular pathways and may delineate a little-explored post-transcriptional regulatory mechanism in this pathology.

PS-15-014

A rapid library preparation method with custom assay designs for detection of variants at 0.1% allelic frequency in liquid biopsy samples

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Background & Objective: Cancer is one of the leading causes of death worldwide and was responsible for 8.8 million deaths in 2015. This number is expected to continue to increase and options for early detection are critical. Non-invasive liquid biopsies from blood samples can be used to examine cell free DNA and RNA derived from tumour cells. This method offers many advantages including screening for diagnosis, monitoring treatment progress and recurrence in the future.

Method: Herein, we describe a new research method for library preparation using the Ion AmpliSeq™ HD Library Kit with custom assay designs from Ion AmpliSeq™ HD Panels for detection of low level variants from liquid biopsy samples. This method includes incorporation of molecular tags that enable 0.1% Limit of Detection (LOD) in circulating free DNA (cfDNA) and dual barcodes for sample identification. This method is also applicable to formalin-fixed paraffin embedded (FFPE) samples. The libraries can be prepared in as little as 3 hours and are compatible for analysis with the Ion GeneStudio S5 system.

Results: Custom assay panels were designed for DNA targets, synthesized, and used to generate libraries with control cfDNA-like samples and FFPE samples containing known variants at 0.1% and 1% LOD respectively. Variants could be detected by sequencing with sensitivity of ≥80% and specificity of ≥98% for cfDNA samples, and sensitivity ≥90% and specificity ≥80% for FFPE DNA samples.

Conclusion: We developed a research method to generate libraries from custom assay designs for liquid biopsy blood samples. For Research Use Only. Not for use in diagnostic procedures.

PS-15-015

BRAF mutation testing in melanoma: a study including Austria, Germany and UK, highlighting concordance for current technologies, and potential requirement of more sensitive technologies in future applications

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Background & Objective: Accurate BRAF mutation testing in melanoma predicts, potential, patient response to therapies targeting BRAF p.V600E, K & R mutations, such as dabrafenib/trametinib. This study was a collaborative approach by laboratories in 3 European countries, to provide insights into their melanoma BRAF mutation testing workflow.

Method: Eight laboratories from Germany, Austria and UK participated in individual discussions to highlight pre-analytic, analytic and post-analytic procedures in their melanoma BRAF testing pathway. Participants were provided with 9 FFPE cell line samples, with various BRAF mutations at frequencies between 1%-50%. Laboratories tested the samples using their routine clinical method.

Results: A range of technologies were used to evaluate the BRAF samples: 1) Real-Time PCR (Roche Cobas z480, Biocartis Idylla), 2) PCR-based Strip Assay (ViennaLab), 3) Pyrosequencing (Qiagen) and 4) Sequencing (NGS (Illumina) & Sanger (LDT)). Sample concordance ranged from 56%-100%. For BRAF samples (p.V600E, K & R) with ≥10% allelic frequency, there was very good concordance (38/39 samples, 97.4%). Highlighted issues included i) failure to detect: p.V600K (<5% mutation; 8/22 samples, 36%); p.V600E (<5%; 3/18, 17%); p.V600E (20%; 1/10, 10%) ii) Mis-identification: p.V600K identified as p.V600E and p.V600R identified as p.V600K.

Conclusion: Good concordance was observed for samples which had BRAF mutation frequencies ≥10%; RT-PCR technologies showed 100% concordance. BRAF mutation testing in melanoma is well established, however, the advancement of BRAF therapies in adjuvant and non-melanoma settings, will require more sensitive methods, especially to detect mutational allelic frequencies <5%.

PS-15-016

The search for markers of CIMP status in cervical cancer

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Background & Objective: Identification of DNA methylation-based markers of CIMP status in cervical cancer.

Method: The Cancer Genome Atlas (TCGA) data on expression level of genes and methylation level of CpG sites in 304 cervical tumours were analyzed with our CrossHub tool to reveal potential markers of CIMP status. Bisulfite sequencing technique was used for methylation studies in 20 primary cervical tumour samples.

Results: To identify promoter CpG sites which methylation level is associated with CIMP status in cervical cancer, we used TCGA data and CrossHub and developed the scoring function that takes into account methylation level of each CpG site and average methylation level of all promoter CpG sites in a sample, expression level of corresponding genes, and correlations between these parameters. Four genes revealed more than 4 promoter CpG sites with high rates: SALL1, KIAA1383, SOX17, ZNF880. SALL1 gene with a number of high-rated CpG sites was subjected to bisulfite sequencing in primary cervical tumour samples. Most CpG sites showed striking increase in methylation level in the majority of samples. However, for several CpG sites significantly diverse methylation levels were observed suggesting them the most promising as CIMP status markers.

Conclusion: The developed scoring function allowed us to suggest genes, namely SALL1, KIAA1383, SOX17, ZNF880, which CpG promoter methylation levels could be used as markers of CIMP status in cervical cancer. Further studies on representative sets of primary tumours are needed to check this.

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PS-15-018

Clinical responses to crizotinib and ceritinib in lung adenocarcinomas carrying distinct variants of ALK rearrangements

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Background & Objective: Multiple evidences indicate that distinct variants of ALK translocations differ in their responsiveness to ALK tyrosine kinase inhibitors (TKI). These data are supported by Asian clinical studies showing improved responses to crizotinib in non-small cell lung cancer (NSCLC) patients carrying particular variants of ALK translocation.
Method: This study retrospectively considered 64 Russian patients with ALK-rearranged NSCLC treated by crizotinib (n = 23), ceritinib (n = 39) or alectinib (n = 2). Fusion variants were genotyped by polymerase chain reaction (PCR).
Results: Median progression-free survival (PFS) approached to 18 and 21 months in subjects with "short" (v.3a/b, v.5a/b) vs. "long" (TAPE-domain containing) fusion variants (p = 0.783), respectively; similar data were obtained while comparing EML4/ALK variant 1 vs. other ALK translocations (19 and 21 months, respectively; p = 0.604). Objective response rates were strikingly similar in the above groups ("short": 88%, "long": 77%, p = 0.479; variant 1: 76%, other translocations: 81%, p = 0.753). Furthermore, ALK variants did not influence the disease outcomes when patients treated by crizotinib and ceritinib were analyzed separately. Ceritinib produced significantly longer PFS than crizotinib (p = 0.022).
Conclusion: This is the first non-Asian study evaluating the relationship between ALK fusion variants and response to ALK TKI. Although being larger than published data sets, it failed to confirm the role of the ALK translocation type in determining the treatment outcome.

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PS-15-019

Anchored multiplex PCR enables sensitive NGS-based mutation detection in the context of large primer panels

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Background & Objective: The mutational landscape of a vast array of paediatric and adult cancers is changing at a rapid pace, however targeted NGS assays typically lack the flexibility to adapt to changing mutational landscapes. For example, adding new targets to existing primer panels often requires redesign of the entire panel and expansion of panel size risks reducing the sensitivity of variant detection. Here, we describe a target enrichment method for NGS, Anchored Multiplex PCR (AMP™), which enables sensitive detection of variants regardless of panel size while permitting flexibility in panel design.
Method: AMP is a target enrichment strategy that uses unidirectional gene-specific primers and molecular barcoded (MBC) adapters ligated to DNA ends for amplification. We designed the Archer® VariantPlex® NGS assays to detect single nucleotide variants (SNVs), insertions and deletions (indels) and copy number variants (CNVs) with a customizable set of panel targets.
Results: We assess the performance of the VariantPlex Solid Tumour Focus panel using reference materials titrated from 50ng to 1ng total input. We show that this panel is able to detect CNVs, as well as SNVs and indels with allele frequencies down to 5%. Furthermore, we compare per variant sensitivity and CNV sensitivity across input amounts for this panel alone and in the context of additional content that substantially increases the total targeted genomic sequence. Our data show that these assays maintain similar abilities to detect variants in small and large panels.
Conclusion: Our results demonstrate that AMP-based NGS assays are sensitive while maintaining flexibility in panel design.

PS-15-020

Synchronous endometrioid endometrial and ovarian carcinomas – clonal origin: molecular study of 22 cases

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Background & Objective: Synchronous endometrial and ovarian carcinoma (SEO) occurs in about 5% of endometrial and 10-20% of ovarian carcinomas. The distinction between simultaneous independent primary carcinomas and metastasis from the ovary to the endometrium (or vice versa) is clinically significant. The criteria for this distinction are based on clinico-pathological features. However, a great benefit has been expected from molecular studies. Herein we present a molecular characterization of 22 SEOs.
Method: DNA was isolated from archived FFPE tissues. Samples for sequence capture NGS were prepared using the KAPA HyperPlus kit. Target sequences were enriched using hybridization probes (Nimblegen, Roche) of 73 genes or gene parts (219kbp).
Results: All SEOs shared nonsynonymous somatic mutation in at least one cancer driver gene (PTEN, AKT1, PIK3CA, KRAS, TP53). A total of 17/22 cases shared mutation in PTEN and 7/17 of those SEOs shared also ARID1A mutation; 2/22 shared ARID1A, AKT1 and PIK3CA while PTEN mutation was not detected; 2/22 shared only AKT1 mutation and 1/22 shared TP53 mutation.
Conclusion: SEOs are clonally related irrespectively of their clinico-pathological features and molecular profiling is not helpful in the staging of these tumours. Current approach based on assessing clinico-pathological features should continue to be used for the classification of these tumours. Nevertheless, molecular profiling of SEOs can be helpful for a better understanding of the pathogenesis and may have clinical impact with respect to its prognostic or predictive meaning.

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PS-15-021

The CIMP phenotype of colorectal cancer is associated with alterations in energy metabolism

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Background & Objective: In colorectal cancer (CRC), several factors might be associated with the strong hypermethylation of many promoter regions (CIMP-high phenotype), including a metabolic shift towards energy production via glycolysis. Bioinformatics analysis of the relationship between the activation of glycolysis and the CIMP-high phenotype was performed using The Cancer Genome Atlas data and qPCR verification in a Russian population.
Method: Methylation profiling and RNA-Seq data were analyzed using a modified CrossHub tool and R packages: DESeq2, clusterProfiler, and topGO. The mRNA level of glycolytic genes (20 CIMP-high and 20 non-CIMP) was evaluated using qPCR. This work was performed using the equipment of the EIMB RAS "Genome" Center and was funded by the Russian Science Foundation, grant 14–15-01083.
Results: Bioinformatics analysis revealed the upregulation of several glycolytic genes in CIMP-high tumours compared to that in non-CIMP samples. ENO2 showed a 3-fold increase in expression level, whereas PFKP, HK3, and PKM showed a 2-fold increase. Contrarily, the expression of genes involved in the Krebs cycle in CIMP-high tumours was altered slightly, except for the 8-fold decrease observed in OGDHL expression. Quantitative analysis of mRNA levels confirmed these results: CIMP-high CRC samples showed up to a 3-fold increase in ENO2, PFKP, HK3, and PKM mRNA levels and 7-fold decrease in OGDHL mRNA levels in the Russian population.
Conclusion: We thus identified an association between the CIMP phenotype and the activation of glycolytic genes in CRC samples.

This work was funded by the Russian Science Foundation, grant 14–15-01083.

PS-15-022

Site-to-site reproducibility of matrix-assisted laser desorption ionisation mass spectrometry imaging from formalin-fixed paraffin-embedded samples

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Background & Objective: Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry Imaging (MALDI-MSI) allows extraction of molecular information from tissue sections and can be used to create clinically relevant classification models, also known as tissue typing. For widespread clinical application, MALDI-MSI must be performed on Formalin-Fixed Paraffin-Embedded (FFPE) tissues. Our aim was to determine if MALDI-MSI of FFPE samples is reproducible when carried out at different sites.
Method: All sites used a standard operating procedure (SOP) which also covered instruments. FFPE tissues (3-5 μm; mouse intestine, tissue microarray of tumour entities sampled from three different sites) were prepared for MALDI-MSI. Samples were coated with trypsin using an automated sprayer then incubated in a humid environment. After digestion, alpha-cyano-4-hydroxycinnamic acid was deposited using the same sprayer and the section analyzed with a rapifleX MALDI Tissuetyper. After acquisition, statistical analysis and segmentation feature extraction was conducted.
Results: Mouse intestine was used to assess whether operators performing an idealized experiment at different sites can obtain similar results, while a TMA consisting of different tumour samples was used to investigate if different tissue sampling introduces variation. Eight measurements of the mouse intestine split over five sites and two time points showed reproducible delineation of the villi from underlying muscle. Measurements of the TMA indicated that tissue biology has a greater influence on the spectra than location of sample origin.
Conclusion: Preliminary results indicate that strict adherence to a SOP produces reproducible MALDI-MSI data from FFPE samples and that sampling site is not a major source of variation.

PS-15-023

Assessment of predictive biomarkers in cancer tissues using micro-immunohistochemistry followed by DNA sequencing

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Background & Objective: Limited access to cancer tissues strikes the need to combine on the same clinical specimen immunohistochemistry (IHC) and molecular profiling. Micro-IHC using the Microfluidic Tissue Processor (MTP) allows a fast and reliable staining that could be used for diagnostic evaluation on formalin-fixed paraffin-embedded (FFPE) sections of cancer tissues. This study aims at combining on a unique FFPE tissue section MTP-based micro-IHC and molecular analysis.
Method: FFPE tissue sections from BRAF V600E mutated cancers were immunohistochemically stained for pan-cytokeratin and BRAF V600E mutation using MTP at room temperature. Positively stained cells were scored, dissected, processed for DNA extraction and next generation sequencing (NGS).
Results: MTP-based micro-IHC was comparable to automated platform-based IHC. MTP-stained area displayed precise borders confining positive cells in a 17x17mm2 zone and gradient of positive- towards negative- stained area across 38.5±8 micrometers. Titration curve experiments by MTP indicated that H score evolution fitted to an exponential model and strong immunoreactivity required 4-minute incubation time with primary antibody. Sufficient amounts of DNA (from 4.34±1ng /cell block to 152±27ng /surgical specimen) allowed to detect BRAF V600E mutation by NGS.
Conclusion: MTP-based micro-IHC is a relevant approach to combine on a unique FFPE tissue section minute range IHC and NGS.

PS-15-024

Prospective study of intratumoural genetic heterogeneity of driver mutations in melanomas

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Background & Objective: 60-70% skin melanomas contain activating mutation in either BRAF or NRAS oncogenes. Intratumoural genetic heterogeneity of melanoma may compromise the results of molecular testing and administration of targeted therapies, and therefore deserves a detailed investigation.
Method: This study involved prospective collection of different tumour parts in 130 melanoma patients. 97 cases were evaluated for intratumoural heterogeneity in different areas of non-metastatic melanoma. Primary tumour and concurrently affected lymph nodes were analyzed in 17 subjects. In addition, 16 patients presented with non-metastatic melanoma at the time of initial diagnosis but were subjected to the 2nd surgery due to subsequent disease relapse in regional lymph nodes. All instances of apparent intratumoural genetic heterogeneity were validated by additional independent round of tumour cell microdissection and DNA analysis.
Results: BRAF mutation was detected in 61 (46.9%) melanomas, while NRAS oncogene was affected in 24 (18.4%) cases. Non-metastatic melanomas demonstrated intratumoural heterogeneity in 2/97 (2.1%) cases. Mutation status of lymph node metastases differed from the one in primary tumour in 3/16 (6.4%) instances of delayed lymphadenectomy but in none of 17 cases of simultaneous lymph node excisions. Heterogeneity was observed for BRAF V600E (n = 3), K601E (n = 1) and NRAS Q61L (n = 1) mutations. Heterogeneous BRAF V600E status was further confirmed by immunohistochemistry with BRAF mutation-specific antibodies.
Conclusion: Genetic heterogeneity for driver mutations, although being rare, does exist. It remains to be investigated how this phenomenon may affect clinical management of melanoma patients.

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PS-15-026

Change in the endothelial glycocalyx of placental terminal villi in the early- and late-onset foetal growth restriction

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Background & Objective: Today little is known about molecular changes of the feto-placental endothelium in fetal growth restriction (FGR). The aim of this study was to determine the histochemical characteristics of the endothelial glycocalyx (eGC) in the capillaries of placental terminal villi using a panel of biotinylated lectins with known specificity in healthy women and with FGR.
Method: Streptavidin-biotin-peroxidase labeling technique was used to localize the binding sites of Con A, UEA-I, ECL, VVL, GSL-II, MAL-II, SNA and DSL in 36 formalin-fixed paraffin-embedded samples of placental tissues in early-onset FGR (n=12), late-onset FGR (n=12) and normal pregnancy (n=12). Quantitative analysis of hystochemical reactions was performed by Nikon Eclipse E 80 computer program.

Results: A significant increase in the intensity of eGC staining with lectins UEA-I, VVL, GSL-II and MAL-II at early-onset FGR and lectins GSL-II and MAL-II at late-onset FGR was found in comparison with normal pregnancy. A significant reduction of the glycoconjugate sugar residues content was noted at early-onset FGR (staining by SNA, ECL) compared with normal pregnancy.
Conclusion: The most prominent alteration of the eGC composition was found in the capillary endothelium at early-onset FGR. It is likely that the modified glycome of capillary endothelium may play an important role in pathogenesis of FGR.

PS-15-027
A highly sensitive real-time PCR assay for detecting EGFR T790M mutation in liquid biopsy samples
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Background & Objective: Epidermal growth factor receptor (EGFR) mutations are found in 10-30% of non-small-cell lung cancer (NSCLC) patients. Patients with activating EGFR mutations usually benefit from tyrosine kinase inhibitor (TKI) therapy, but 50% of patients acquire resistance due to the T790M mutation. Osimertinib has recently been approved to treat T790M-positive NSCLC patients.
Method: We have developed a Taqman-based real-time PCR ("RealFast") assay for the detection of EGFR c.2369C>T (p.T790M) along with an endogenous control and including EGFR wild-type suppressor to facilitate mutant-enriched PCR. Fifty-six samples, including cfDNA from carcinoma patients and healthy donors, from EQA trials, commercial cfDNA reference standards (Horizon Dx), as well as NCI-H1975 cell line DNA and cloned T790M DNA spiked into wild-type DNA, have been used to validate assay perfomance.
Results: Out of 24 samples known to be positive for c.2369C>T, the RealFast assay detected 23 correctly. Mutation detection failed in one cfDNA reference sample (HD779, 0.1% T790M) when only 5 ng were used as template. Out of 32 samples negative in other tests, one positive result was obtained with the RealFast assay. Based on these preliminary data, a sensitivity of 91.7% and a specificity of 96.9% were calculated. The RealFast assay is capable of detecting 8 copies of c.2369C>T DNA in a minimum of 2.5 ng cfDNA.
Conclusion: The highly sensitive detection of EGFR c.2369C>T in low amounts of cfDNA make the EGFR T790M RealFast assay a useful tool for repeated testing of the T790M mutation status in liquid biopsy samples of NSCLC patients.

PS-15-028
Identification of altered molecular pathways in colorectal cancer with CpG island methylator phenotype (CIMP)
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Background & Objective: A set of molecular and signaling pathways are altered in CpG island methylator phenotype (CIMP)-high tumours. The CIMP-high phenotype is frequently associated with microsatellite instability, which is the surrogate marker for immunotherapy. Therefore, alterations in molecular pathways could potentially be caused by the heterogeneity of cell types in the tumour.
Method: Transcriptome and differential gene expression analysis was conducted in CIMP-high and non-CIMP colorectal tumours. Gene set enrichment analysis for genes differentially expressed in CIMP-high colorectal tumours was conducted (TCGA data). Thirty samples (15 CIMP-high and 15 non-CIMP) from a Russian population were used for qPCR validation.
Results: Hypermethylation in colorectal samples was accompanied by alterations in immune response, inflammation, TNF signaling, sphingolipoid metabolism and signaling pathways, glycolysis, cysteine, taurine and methionine metabolism, PPAR pathways, and deregulation of the cell cycle, MAPK cascade, p53, Hippo, HIF1A, cAMP-dependent pathways. Positive perturbations in immune-related pathways were consistent with the increased penetration of lymphocytes in CIMP-high tumours. Transcription factor binding site enrichment analysis for genes overexpressed in CIMP-high tumours suggested that the observed transcriptomic changes might be caused by beta-catenin, as well as transcription factors IRF1, SOX2, KLF4, STAT1/2, SP1, THRB, and CREB2. The role of miRNAs hsa-miR-130ab, 148ab, 152, 99ab, 100, and 221 was not excluded. Immunohistochemical staining revealed abundant tumour infiltrating lymphocytes in CIMP-high samples.
Conclusion: Sufficient changes in molecular pathways were observed in CIMP-high colorectal tumours. However, this may be associated with tumour infiltrating lymphocytes, rather than with tumour cell-specific alterations.

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PS-15-029
Identification of tumours with CpG island methylator phenotype based on genome-wide methylation profiling
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Background & Objective: Tumours with CpG island methylator phenotype (CIMP) represent a distinct subset of colorectal cancers (CRC) with an increased prevalence of DNA hypermethylation in gene promoter regions. However, traditional criteria for identifying CIMP-high tumours are not always accurate, even for colorectal cancers. Using the Cancer Genome Atlas (TCGA) data, we developed an approach to identify CIMP-high CRC tumours and CIMP-like tumours for other cancer types based on genome-wide methylation profiling.
Method: Our novel approach is based on evaluating median methylation levels of a specific subset of 'marker' CpG sites. Each 'marker' site should 1) be annotated in at least 2 of the 6 cell lines as a promoter, according to ENCODE data (ChromHMM/Segway) and 2) belong to the top 10% differentially methylated sites, according to TCGA data.
Results: This approach is universal in application; its modifications result in the identification of CIMP-like tumours in other types of cancer. Thus, we tested the approach on several tumour types such as prostate, bladder, breast, and lung cancer; 3–15% tumours were classified as CIMP-like for different localization, and approximately 15–20% CRC tumours were classified as CIMP-high according to this approach.
Conclusion: We developed a novel universal approach capable of distinguishing CIMP-high, CIMP-like tumours for different cancer types. This approach could be important for molecular diagnostics as well as for fundamental research.

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PS-15-030
Potential prognostic markers for locally advanced prostate cancer without lymphatic dissemination
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Background & Objective: Prostate cancer is the second most common cancer in men. Locally advanced prostate cancer (LAPC) is characterized by invasion of the prostatic capsule without evidence of nodular or distant metastatic spread. Patients with LAPC have different risks of recurrence. Our study is aimed at identifying prognostic biomarkers for locally advanced prostate cancer, which will lead to optimization of treatment and development of appropriate clinical recommendations.
Method: We performed bioinformatic analysis of The Cancer Genome Atlas (TCGA) project RNA-seq data in EIMB RAS "Genome" center, 130 samples (only Caucasians) of LAPC without lymphatic dissemination were divided into two groups: a favorable and unfavorable prognosis.
Results: The genes previously identified by published data as potential biomarkers of the prognosis were considered. Eight genes, characterized by differential expression as potential prognostic biomarkers, were identified. Increased expression of TWIST1, TUBB3, CHAT genes and decreased expression of CYP1B1, IGSF1, EDN3, MSMB, SERPINA3 was detected in the group of patients with unfavorable prognosis in comparison to the group of patients with favorable prognosis. Identified genes were associated with the key processes of carcinogenesis, such as angiogenesis, proliferation, migration of tumour cells and disturbance of regulation of signaling cascades.
Conclusion: Thus, we identified a number of genes as potential prognostic biomarkers associated with unfavorable prognosis of locally advanced prostate cancer without lymphatic dissemination.

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PS-15-031

Potential prognostic markers of locally advanced prostate cancer of the most common molecular subtype without lymphatic dissemination

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Background & Objective: Patients with locally advanced prostate cancer without lymphatic dissemination have different risks of disease recurrence. Identification of prognostic biomarkers for this cohort is necessary for optimizing treatment. However, panel of markers could depend on molecular subtype and particular stage of disease. Up to 40% of the cases are associated with the TMPRSS2-ERG fusion transcript
Method: Bioinformatics analysis of RNA-seq data from The Cancer Genome Atlas was performed in EIMB RAS "Genome" Center (http://www.eimb.ru/rus/ckp/ccu_genome_c.php). Fifty-one Caucasian patients with locally advanced prostate cancer without lymphatic dissemination and expressing the TMPRSS2-ERG fusion transcript were divided into two groups: favorable and unfavorable prognosis, according to recurrence data. Only the genes previously identified as potential prognostic biomarkers were considered in this study.
Results: Eight differentially expressed genes were identified as potential prognostic biomarkers. Increased expression of MAPK8IP2, LRFN2, CHGA, TUBB3, MYT1, and CHAT, and decreased expression of MYBPC1 and PAGE4 was detected in patients with unfavorable prognosis compared with that in patients with favorable prognosis. The identified genes are involved in key processes like intercellular interaction, regulation of signaling pathways, morphogenesis involved in neuronal differentiation, neuronal formation, secretion, and metabolism.
Conclusion: Thus, we identified several potential prognostic biomarker genes, associated with unfavorable prognosis of locally advanced prostate cancer without lymphatic dissemination but expressing the TMPRSS2-ERG fusion transcript. Such biomarkers could be important for instituting adjuvant therapy following radical treatment.

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PS-15-032

Patterns of somatic mutations and CD8+ lymphocyte infiltration in sporadic and Lynch syndrome-associated microsatellite-unstable colorectal carcinomas

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Background & Objective: Microsatellite instability (MSI) may occur both in sporadic and Lynch syndrome-associated colorectal carcinomas (CRCs). These two CRC entities display some differences with respect to clinical presentation and mechanisms underlying MSI phenotype, which warrants further comparison of their molecular and pathological features.
Method: Paired tumour and normal DNA from two sporadic and two hereditary MSI-positive CRC cases were subjected to whole exome sequencing. Intra- and peritumoural infiltration with CD8+ lymphocytes was evaluated in 14 MSI+ sporadic, 6 Lynch syndrome-associated and 28 MSI-negative CRCs.
Results: Whole exome analysis did not reveal differences in the total mutation burden (with sporadic tumours showing 836 and 228, and hereditary CRCs – 1921 and 650 nonsynonymous alterations, respectively), spectrum of nucleotide changes, share of insertions/deletions, number of mutations in MSI-target genes or in WNT, TGFbeta, PI3K, MAPK pathways between sporadic and hereditary MSI+ tumours. The mean number of intratumoural CD8+ cells per mm2 was significantly higher in all MSI-positive (228.8) vs. MSI-negative CRCs (28.0) (p=0.0003, T-test), while the levels of peritumoural lymphocytes did not differ between these groups (142.9 vs. 150.3, p=0.85). Hereditary MSI+ CRC demonstrated slightly lower mean levels of tumour-infiltrating lymphocytes (164.2 per mm2) compared to sporadic MSI+ CRC (256.4 per mm2) (p=0.21, T-test).
Conclusion: Patterns of somatic mutations and degree of tumour infiltration by CD8+ lymphocytes are similar in MSI-positive sporadic and hereditary CRC.

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PS-15-033

Differential expression of IL-17A gene with relation to KRAS mutation status and clinicopathologic characteristics of colorectal cancer patients

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Background & Objective: Largely produced by activated memory T lymphocytes (Th-17), IL-17A appears to be contributing greatly to colorectal cancer (CRC) development and progression. Aberrant KRAS signaling in CRC is involved in immunological responses and inflammation-driven tumourigenesis. Accordingly, we aimed to study the mRNA expression pattern of the IL-17A gene with regard to the KRAS mutation status in CRC patients from the Bulgarian population.
Method: TaqMan-based quantitative real-time PCR was performed for determining the relative quantity (RQ) of target genes from 52 fresh-frozen tissue specimens. Two reference genes (GAPDH and B2M) were used for normalization. KRAS mutations in exon 2, exon3 and exon 4 were studied with real-time assay based on allele-specific primers (KRAS Mutation Analysis Kit, EntroGen Inc, USA).
Results: mRNA levels in tumour tissues were up regulated compared to adjacent non-tumour tissue with mean RQ=3.26 (p=0.075). Differential

expression of the IL-17A gene was observed in stage-specific fashion: in 3rd and 4th TNM stage patients the target gene was significantly down regulated (p=0.040). Additionally, the IL-17A gene expression appeared to be age-related as in patients above the age of 70 years the target gene was significantly overexpressed (p<0.001). With respect to KRAS mutation status, our results indicate a significant down-regulation of the IL-17A gene in KRAS-positive cases (p<0.001).
Conclusion: Our preliminary results indicate that the IL-17A gene expression might be influenced by the ras-signaling pathway suggesting a molecular link between cytokine-driven tumourigenesis and cytokine expression profile in the tumour microenvironment.

PS-15-034
Expression level of potential CIMP-associated genes in breast cancer
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Background & Objective: Evaluation of expression of potential CIMP-associated genes, which were suggested by us previously on the basis of bioinformatics and methylation studies in breast cancer, and assessment of suitability of their expression levels as markers of CIMP-positive breast tumours.
Method: The set of 30 paired (tumour/normal) samples from patients diagnosed with stage I-III breast cancer was collected prior to radiation or chemotherapy. The evaluation of gene expression level was performed by qPCR with TaqMan probes. The data analysis was implemented using two reference genes (B2M and RPN1) and our ATG tool.
Results: We performed the expression analysis of CDO1, ALDH1L1, ALDOC, CLIP4, CYP11A1, ENPP2, GYPC, and PTGS2 genes, which methylation level of promoter CpG sites was previously shown by us to be correlated with CIMP status in breast cancer. Expression level of all 8 genes was strongly decreased in the majority of primary breast tumours compared to matched normal tissues. The frequency of downregulation varied from 70% (CLIP4 and GYPC genes) to 100% (ALDH1L1 gene). The median decrease of gene expression level was in the range from 5-fold (ALDOC, CLIP4, CYP11A1, and GYPC genes) to dozens-fold (CDO1 and ALDH1L1 genes).
Conclusion: Frequent and strong downregulation of CDO1, ALDH1L1, ALDOC, CLIP4, CYP11A1, ENPP2, GYPC, and PTGS2 genes in breast cancer allows us to suggest tumour suppressor function of these genes but also points to the unsuitability of their expression levels as markers of CIMP-positive breast tumours.

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PS-15-035
The relevance of precision epitope mapping for accurate oncologic diagnostic based on PTEN protein expression in tumours
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Background & Objective: Expression of protein markers, as detected by standard immunohistochemistry (IHC), together with the histologic analysis, constitute the first-line of diagnosis of most solid tumours. The heterogeneity of the proteome in tumour cells may encompass alternate marker variants which may hinder the accuracy of IHC in helping pathological diagnosis. PTEN is a major tumour suppressor protein. Here, we present evidence on the relevance of precision epitope mapping of anti-PTEN monoclonal antibodies (mAb) for an accurate IHC evaluation on the expression of PTEN protein in tumours.
Method: A set of six commercial anti-PTEN mAb potentially suitable for IHC was analyzed. Sensitivity and epitope recognition were monitored by immunoblot. Tissue microarrays (TMA) containing formalin-fixed, paraffin-embedded (FFPE) prostate carcinomas were analyzed by IHC and FISH techniques.
Results: Sensitivity and specificity assays showed important differences for the distinct anti-PTEN mAb, with two mAb (6H2.1 and SP218) displaying the overall best performance. Precision epitope mapping using recombinant PTEN variants revealed that all mAb recognized the PTEN C-terminus and identified the peptide sequences configuring the epitopes. Importantly, tumour-associated mutations found at PTEN C-terminus, and mutations mimicking phosphorylation, abrogated immunoreactivity in a mAb-dependent manner.
Conclusion: A preference for anti-PTEN mAb that recognize linear epitopes at the PTEN C-terminus is observed in the commercially available anti-PTEN mAb for IHC. Tumour-associated and phosphorylation-mimicking mutations targeting these epitopes affected the immunoreactivity of the mAb. Our analysis will contribute to the validation of anti-PTEN mAb as diagnosis tools in clinical oncology, facilitating a more reliable and accurate cancer diagnosis based on PTEN tumour expression.

PS-15-036
A comprehensive clinicopathological evaluation of the onco-suppressor microRNA-195 expression among breast tumours
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Background & Objective: MicroRNAs (miRNAs) have been considered as novel tumour markers because of their tissue specificity and association with clinicopathological parameters. The tumour suppressor miR-195 plays an important role in tumourigenesis. The aim of this study was to analyze the expression of miR-195 in 77 benign and 140 malignant breast tumours in order to explore its clinical value in breast cancer.
Method: Total RNA was extracted, polyadenylated, and reversely transcribed to cDNA from samples. Subsequently, a sensitive quantitative real-time PCR protocol was developed and miR-195 levels were then estimated by applying the 2-CT method by using RNU48 as a reference gene. The relative quantification units measured for miR-195 were finally subjected to comprehensive statistical analysis.
Results: The analysis indicated that miR-195 significantly downregulated in malignant compared to benign tumours, highlighting its value in discriminating these breast lesions (AUC: 0.633; 95% CI: 0.552–0.713; P=0.002). Moreover, the comparison of invasive ductal and lobular adenocarcinomas revealed a significant (P<0.001) increase in miR-195 levels of lobular tissues. Regarding the correlation of miR-195 expression with molecular subtypes, HER2 positive tissues displayed significantly more elevated expression of miR-195 (P=0.001) than those of luminal and even more than those of basal-like ones. A positive correlation was observed between miR-195 levels and primary tumour staging (P=0.001). In addition, miR-195 expression levels were increased in the samples with positive hormonal (P<0.001) and node status (P=0.031).
Conclusion: Overall these results recommended that miR-195 expression constitutes a promising molecular marker for the diagnosis, prognosis and classification of breast carcinomas.

PS-15-037
Transcription factor CBX3 is involved in the regulation of energy metabolism in colorectal cancer
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Background & Objective: A number of transcription factors (TF) can regulate the expression of genes involved in glucose metabolism. One of

them, CBX3, has been implicated in colorectal cancer according to our preliminary bioinformatics data.
Method: In order to evaluate the role of CBX3 in the regulation of energy metabolism, we performed a knockdown experiment. Using the free online resources (http://rnaidesigner.thermofisher.com/rnaiexpress/) and BLAST (http://blast.ncbi.nlm.nih.gov/Blast.cgi), shRNAs were designed to suppress the expression of CBX3 gene in RKO cell line with lentiviral vector pLSLP. The level of CBX3 expression was estimated using qPCR and western blot analysis, and expression of the predicted genes targeted by CBX3 was analyzed in this cell line. This work was performed using the equipment of the EIMB RAS "Genome" Center (http://www.eimb.ru/rus/ckp/ccu_genome_c.php) and was funded by the Russian Science Foundation, grant 14–15-01083.
Results: Up to two-fold decrease in G6PC3 and SLC37A4 expression levels and up to two-fold increase in that of PTK2B was observed. Key parameters of glycolysis were analyzed using a Seahorse XFe24 Analyzer (Agilent Technologies, USA); glycolytic capacity of CBX3 knockdown RKO cells was found to be lower than that in the controls. The value of extracellular acidification rate (ECAR) was decreased in CBX3 knockdown cells compared to that in the controls. Therefore, inhibition of CBX3 resulted in decreased anaerobic glycolysis rate.
Conclusion: Our data suggest that the transcription factor CBX3 may be involved in the regulation of anaerobic glycolysis in colorectal cancer cells.

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PS-15-038

Detection of ALK and Ros-1 gene rearrangement and c-met amplification with fluorescence in situ hybridisation in non-small cell lung carcinomas: our clinical experience and recommendations

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Background & Objective: The development of specific molecular targeted therapies have significantly changed the management of patients with metastatic non-small cell lung cancer (NSCLC). In this study we wanted to share our clinical experiences of ALK, Ros,1 and c-met molecular testings.
Method: We performed a retrospective pathology report analysis of patients diagnosed as NSCLC undergoing molecular analysis of ALK, Ros-1 and c-met status by fluorescence in situ hybridization test at a single center between 2014 and 2017
Results: ALK gene rearrangement was detected 22 (3,3%) of 665 cases with NSCLC while 142 (21,3%) of them were unable to evaluate because of technical problems. In 78 cases there were no signals and 64 cases had insufficient tumour cells. 398 patients with NSCLC were tested for Ros1 and 3(0,7%) of them were positive and 28 cases were lack of tumour cells and 107 cases had no optimal signals. C-met amplification were seen 3(2%) of 143 cases whereas 36 (25,1%) of them were unable to be evaluated.
Conclusion: The positivity ratios of ALK, Ros-1 and c-met were concordant with literature. Main reasons of indeterminate cases due to the technical problems were the lack of tumour cells, poor nuclei quality and/or quantity, and suboptimal time and/or type of fixation. Small specimens, using more than 2 immunohistochemical markers for diagnosis, embedding more than one piece of tissue in the same block were the main reasons of lack of tumour cells. Always must be kept in mind that taking extra care of small tissue fragments is important for molecular studies.

PS-15-039

EGFR and KRAS mutation testing on tissue and liquid biopsy at NSCLC. First experience in our country

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Background & Objective: Annually more than 3,000 new cases of lung cancer are registered in Kazakhstan, 24% of which are with inoperable form. Liquid biopsy enables to discover molecular genetic markers of tumour in such cases by the Circulating Tumoural DNA (ctDNA).
Method: EGFR test was performed for 267 patients with NSCLC. All EGFR negative samples were examined for KRAS mutations. EGFR tests by ctDNA were performed for 5 patients with progression on the background of target therapy. KRAS tests by ctDNA were performed for 2 patients.
Results: EGFR mutations were detected in 64 samples (23%). Exon19Deletion, L858R, Exon20Insertion, T970M, exon18 and complex mutation (T790M/L858R) were identified in 34(53%), 22(34%), 4(6%), 2(3%),1(1,5%) and 1(1,5%) cases, respectively. Patients harboring 19deletion and L858R mutations showed a tendency to have higher response rate for target therapy (TT) 71% and median progression-free survival of 11,5 months. Patients harboring Exon20Insertion, T970M and complex mutation showed resistance to TT, progression on the background of adjuvant chemotherapy for 6 months and a lethal outcome within two years. Primary EGFR mutations were detected in ctDNA in 3 out of 5 cases. Secondary EGFR mutations of resistance to first line TT were not revealed. KRAS mutations were detected in 26 samples. Two patients with a positive ctKRAS tests showed progression for 6 months.
Conclusion: Primary T790M, Exon20Insertion and complex mutations T790M/L858R are associated with resistance to TT and unfavorable prognosis Positive ctKRAS test can serve as a prognostic factor for early metastases Liquid biopsy as alternative monitor methods of treatments are recommended

PS-15-040

Tumour mutation burden assessment from FFPE research samples using a targeted next-generation sequencing assay

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Background & Objective: Tumour mutation burden (TMB) predicts durable benefit from immune checkpoint inhibitors in several cancer types. We demonstrate the ability of a targeted panel with fast turn-around time and low input needs to estimate TMB from research samples.
Method: We developed a single sample analysis workflow to estimate mutation burden (TMB; mutations/Mb) from FFPE tumour research samples. The assay utilizes a PCR-based targeted panel that covers 409 genes covering 1.7 Mb of genomic space. The workflow requires only 10 ng of input DNA and enables a 2.5-day turn-around time from sample to the final report. Sequencing is performed on semiconductor sequencing platform for high depth and accuracy. The workflow is tumour sample only and removes germ-line variants using population databases.
Results: In a preliminary comparison, whole exome sequencing (WES) was performed on 15 FFPE tumours (2 melanoma, 5 NSCLC, and 8 CRC) using hybrid capture on illumine through a service provider; germline filtering similar to TML was applied to tumour exomes, and TMB was calculated by normalizing mutations by number of covered bases. The targeted TML assay was ran on the same sample set and its TMB estimates were compared to that from WES to discover a strong positive correlation (r2=0.70) between two assays. TML assay was applied to 4 replicates of tumour positive cell line (HCC1143; expected TMB 6.76 mutations/Mb) to obtain high accuracy (median TMB at 8.28 mutations/Mb).
Conclusion: A simple analysis workflow for mutation burden has been developed to advance research in immuno-oncology.

PS-15-041

Targeted T-cell receptor beta immune repertoire sequencing in several FFPE tissue types – applications in profiling the tumour microenvironment

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Background & Objective: T cell receptor beta (TCRβ) immune repertoire analysis by next-generation sequencing is a valuable tool for studies of the tumour microenvironment and potential immune responses to cancer immunotherapy. Here we describe a TCRβ sequencing assay that leverages the low sample input requirements of AmpliSeq library preparation technology to extend the capability of targeted immune repertoire sequencing to include FFPE samples which can often be degraded and in short supply.
Method: This assay targets the highly diverse CDR3 region which allows for T cell clone identification and frequency measurement which, when combined, can provide a broad view of the immune landscape within archived tissue samples.
Results: To evaluate assay accuracy, we sequenced libraries including known amounts of 30 well-studied T cell lymphoma rearrangements, as well as samples comprised of sorted T cells. T cell repertoires were successfully evaluated from as low as 5ng to as large as 1ug of input from samples of varying T cell repertoire diversity, such as sorted T cells, peripheral blood leukocytes, fresh-frozen tissue, and FFPE tissue from a variety of normal and cancerous tissues including lung, colon, brain, spleen, lymph node, and thymus. In addition, we demonstrate use of a qPCR assay for quantification of sample T cell content to guide sample input for TCRβ immune repertoire sequencing experiments.
Conclusion: These data present a T cell immune repertoire sequencing solution for application in a wide range of sample types, in particular, challenging FFPE preserved samples. We find that the assay is capable of profiling repertoire metrics from FFPE samples over a large range of input amounts from several normal and tumour tissue types.

Tuesday, 11 September 2018, 09:30 - 10:30, Exhibition Hall I/II
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PS-16-001

Dysplastic cerebelar gangliocytoma: a case report

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Background & Objective: Dysplastic cerebellar gangliocytoma (DCG), or Lhermite-Duclos disease, is a rare lesion, characterized by enlarged cerebellar folia and replacement of internal granular layer by dysplastic ganglion cells. It is considered a WHO grade I tumour in the current WHO classification of CNS tumours, although some authors consider it to be a hamartomatous lesion. Clinically, the most common symptoms are due to increased intracranial pressure (nausea/vomiting, headaches, papilledema). Adult-onset DCG is considered pathognomonic for Cowden's syndrome (CS) - an autosomal dominant disorder caused by germline PTEN mutations, characterized by pathognomonic dermatological findings, multiple hamartomas, and a higher risk for development of breast, thyroid, and endometrial carcinomas. We herein report a case of a 36-year-old woman with previous thyroid surgery for a "nodule" in childhood and with a one-year history of headaches, vomiting and seizures. Magnetic resonance imaging showed a cerebellar vermis lesion, without contrast uptake, and compensated supratentorial hydrocephalus.
Method: Presentation of the clinical-pathological characteristics of a patient with GDC, and review of the literature with emphasize on histopathological features, pathogenetic considerations and clinical presentation of GDC.
Results: The lesion was excised and intraoperative cytologic examination (by imprint) showed numerous ganglion and granule cells in a glial background, and the preliminary diagnosis was a cerebellar gangliocytoma. The definitive histologic sections were consistent with DCG.
Conclusion: Given the high probability of this patient having CS, she was referenced to a genetic consultation in order to determine the PTEN mutation status. The genetic counseling is crucial for establishing a proper follow-up to detect or exclude concomitant malignancies.

PS-16-002

Abundant eosinophilic granular bodies in a case of cerebellar anaplastic ganglioglioma: a possible clue for malignant transformation of low-grade ganglioglioma

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Background & Objective: Gangliogliomas are rare brain neoplasms, which are usually located in the temporal lobe and rarely in the spinal cord, brain stem or posterior fossa (cerebellum). To date, there are less than 35 cases of cerebellar ganglioglioma described in the scientific literature, most of them being represented by low grade ganglioglioma affecting young adults.
Method: We report the case of a 60-year-old male who presented to our clinic with right dysmetria and ataxia. The MRI examination revealed an expansive process located in the cerebellum, which was compressing the fourth ventricle. The patient underwent complete surgical ablation and the tumour was sent to the Department of Pathology for investigation.
Results: Histopathological examination revealed an infiltrative neoplastic proliferation composed of anaplastic glial cells and dysplastic ganglion cells with striking mitotic activity. We were surprised to find abundant eosinophilic granular bodies as well as variable amounts of Rosenthal fibers. Areas of necrosis were also present. Immunostaining revealed neuronal positivity for synaptophysin, chromohgranin-A, CD56 and neurofilament, while glial cells were positive for GFAP. CD34 showed a focally distinct staining pattern limited to the neuronal cell bodies. The tumour featured a Ki-67 proliferative index of 15%.
Conclusion: Anaplastic gangliogliomas of the cerebellum rarely affect older patients and usually do not feature numerous eosinophilic granular bodies. The presence of the eosinophilic granular bodies is characteristic for slow-growing processes with extended course of evolution, which in our case may suggest a possible development from a low-grade neoplasm, such as a benign ganglioglioma.

PS-16-003

Fluorescence in situ hybridisation as a simple tool in the diagnosis of MN1-astroblastomas

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Background & Objective: The 2016 revision of the World Health Organization (WHO) Classification of Tumours of the Central Nervous System (CNS) defines astroblastoma as a rare form of glioma. Recently, MN1 fusions have been described in ex CNS-primitive neuroepithelial tumours (PNET) with astroblastic features and were designated as high-grade neuroepithelial tumours with MN1 alteration (HGNET-MN1). Thus, a sensitive and specific diagnostic tool that allows us to distinguish astroblastoma from its mimics would be useful. The main aim of this work was to validate the FISH MN1 as a diagnostic tool of the diagnosis of HGNET-MN1.
Method: We performed a MN1 FISH on 6 supra-tentorial tumours initially classified as ependymoma without RELA fusion and reclassified by the methyloma as HGNET-MN1. We performed also a histopathological review of cases and systematic immunohistochemical (GFAP, OliG2, EMA, Synpatophysin, CD34, MIB) and molecular analysis (hTERT mutations).

Results: All the 6 tumours presented anaplasia features and harbored a MN1 rearrangement by FISH. GFAP and EMA were expressed in all tumours (6/6) and Olig2 was variably expressed (3/6). Synaptophysin was never expressed (0/6). A CD34 expression was present in 2/6 cases. No mutation of hTERT was detected.
Conclusion: To conclude, MN1 FISH rearrangement has a sensitivity and specificity of 100% for a diagnosis of astroblastoma. Pathologists should look for MN1 rearrangement in tumours with astroblastic features and their mimics (particularly in supra-tentorial ependymoma-like tumours without RELA–fusion).

PS-16-004
Congenital rare form of ganglioglioma in an infant
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Background & Objective: Ganglioglioma is a rare benign primary tumour of the central nervous system (CNS), with a slow growth, affecting especially children and young adults, but up to 10% of them may become malignant. It is a well differentiated neuroepithelial tumour consisting of both neoplastic ganglion and glial cells.
Method: We present the case of a 2 months old male child, with a medical history of congenital thalamo-hipothalamic tumour, which was discovered during an imagistic investigation, a month after birth. Two months after birth, he died before surgery procedures, due to a community acquired desquamative interstitial pneumonia associated with extensive pulmonary atelectasis. The tissue samples were processed and examined with standard HE technique and special stains for nervous tissue such as Bielschowsky silver stain and Nissl. An indirect tristadial ABC-technique with NovoLink Polymer detection system was performed for GFAP, NFT, Nestin, Syn, Neu-N, P53, Ki-67.
Results: The autopsy revealed a subcortical localised tumour between thalamus and basal ganglia quite well determined, encapsulated, with firm consistency and 2 cm in diameter. Microscopically, a subcortical and subependymal astrocytic proliferation was noticed, consisting of two types of cells: medium tumour cells with a difuse pattern and large gemistocytic cells. Moreover, a reactive gliosis could also be observed. The aforementioned imunohistochemical markers were positive in rather numerous tumour cells.
Conclusion: The histopathology investigation and imunohistochemical tests confirmed the diagnosis of a congenital benign primary tumour of the CNS with malformative features, of ganglioglioma type.

PS-16-005
Skeletal muscle biopsy findings in the diagnosis of late-onset Pompe disease: report of a challenging case
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Background & Objective: Acid maltase deficiency, PD or glycogen storage disease type II is a rare condition caused by mutations in acid alpha-glucosidase gene GAA, leading to lysosomal glycogen accumulation, with very diverse clinical presentations. PD can mimic many disorders, especially limb-girdle or Becker muscular dystrophies, may associate unexplained early respiratory weakness and insufficiency or cardiac dysfunction. Genotype–phenotype correlations are difficult. We highlight the need to improve awareness of this devastating progressive disease.
Method: We performed a diagnostic open biopsy of the vastus lateralis muscle in a 29-year-old male patient diagnosed two years before with polymyositis and treated with steroids without improvement, revealing progressive pelvic limb weakness and pain, difficulty lifting from a seated position, frequent falls and elevated creatine kinase levels. Muscle cryosections served for histological, histochemical and histoenzimological stains. Electron microscopy was also performed.
Results: Muscle biopsy demonstrated marked variability in the fiber size and numerous vacuoles within many atrophic type I muscle fibers, containing PAS positive material, sensitive to diastase and rare necrotic fibers, suggesting PD. Ultrastructural examination showed myofiber disruption and deposits of free and membrane-bound glycogen, confirming the diagnosis.
Conclusion: The clinical diagnosis of PD is often delayed, therefore muscle biopsy is mandatory in patients with undefined limb-girdle myopathy or unexplained respiratory failure, even in whom PD was never suspected, with major impact on clinical management. PD is one of very few treatable muscular disorders using recombinant GAA therapy. The biopsy findings should always be corroborated with dry blood spot technique results and genetic testing.

PS-16-006
Epidemiologic and histologic characteristics of central nervous system lesions: a 20-year experience of a single institution
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Background & Objective: The overall incidence rate of all brain tumours is estimated to be 10.82 per 100 000 person-years. The aim of our study is to report the epidemiologic and histologic characteristics of these lesions in a Lebanese tertiary center.
Method: This is a retrospective study evaluating the characteristics of the CNS lesions diagnosed in 20 years in the Pathology Department of Hôtel Dieu de France Hospital of Beirut, Lebanon. Different variables were evaluated, from the samples types and epidemiologic characteristics, to the revealing symptoms and the histologic subtypes.
Results: 2474 samples of CNS lesions were interpreted in the Pathology Department. 25.4% of the samples were obtained by biopsy, 65% by surgical resection. 52.2% of the patients were men and 47.8% were women with a median age of 49 years. The most frequent revealing symptoms of these CNS lesions were epilepsy (22.5%), headache (20.6%) and motor impairment (19.9%). 90.7% of the tumoural lesions were primary CNS tumours and 9.3% were metastatic lesions, lung (35.6%) and breast (16.5%) being the two most frequent primaries. 46.2% of primary CNS tumours were glial, 42.5% non-glial, 3.5% mixed neuroglial and 6.4% mesenchymal. The two most frequent glial tumours were astrocytic (56.4%) and oligodendroglial (17.9%) tumours, while the two most frequent non-glial tumours were meningeal tumours (58%) and cranial nerve and paraspinal tumours (16.3%).
Conclusion: Determining the histologic and epidemiologic characteristics of CNS tumours in the Lebanese population is essential to develop further translational and prospective trials in this underexplored field in Lebanon.

PS-16-007
Interobserver variability of mitotic count in meningiomas
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Background & Objective: Meningiomas arise from the meninges-related arachnoidal cap cells and constitute about 15-30% of the intracranial masses. They are benign, slow-growing and World Health Organization (WHO) grade I tumours. Radiotherapy treatment is not attached after surgery for them. Atypical meningiomas WHO grade II represent a therapeutic challenge given their high recurrence rate and greater mortality compared with WHO grade I meningiomas. Traditionally, treatment has entailed attempts at gross total resection with radiation therapy reserved for residual disease or recurrences. The most

important criterion used to distinguish between grade 1 and 2 meningiomas is mitosis. The purpose of this study was the evaluation of interobserver discordance in the mitotic count of meningiomas.
Method: 141 cases with meningioma were taken from the archives. The number of mitosis in the tumour was re-evaluated using selected slides by 6 pathologists experienced in the field. They were blind to each other's grading and the original grading done at the time of reporting
Results: The results were interpreted statistically. The interobserver variability for the mitotic count was higher. Also, some meningiomas were classified different grade than previously.
Conclusion: The results of the present study indicate that there is interobserver variability in mitotic count from case to case. Moreover, there were differences in the grading of the cases. Postoperative radiotherapy for some grade 2 meningiomas will not be given to some patient due to downgrading. Should we evaluate mitotic count with a different method?

PS-16-008
Primary CNS lymphomas – 20-year-period evaluation study
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Background & Objective: Primary CNS lymphoma is an extra-nodal, non-Hodgkin lymphoma (NHL) confined to the cranio-spinal axis (brain, eye, meninges, spinal cord) without evidence of systemic involvement. Most prevalent form is Diffuse Large B-cell lymphoma (DLBCL). The aim of this study is to evaluate statistical features of this malignancy in Republic of Macedonia.
Method: This is a 20-year-period retrospective evaluation study (1998-2018) of 45 primary CNS limphoma cases operated in the University Neurosurgery Clinic, diagnosed at the Institute of Pathology, Medical Faculty-UKIM, Skopje, Macedonia using histological and immunohistochemical analyses (exclusion, diagnostic NHL and subtype-specific immunohistochemistry algorithms). Statistica for Windows 7 was used.
Results: From total 4929 cases of benign and malignant brain tumours, primary CNS lymphomas comprise 45 cases (0,91%); 24(53,3%) males (55,0±14,7 years), 21(46,7%) females (57,9±14,8 years), age 8 to 74 years (56,4±14,6 years); most common localization: cerebrum – 13(28,9%) cases. Age group distribution: most cases -15(33,3%) in 60-69 years group, only 1(2,2%) in 0-19 years group. DLBCL was diagnosed in 30(66,7%) cases, the rest subtypes in 15(33,3%) cases. There was no significant difference between the age of males and females diagnosed with primary CNS lymphoma (Mann-Whitney U test: Z=1,104; p=0,2695). There was no significant statistical difference between age groups and lymphoma subtypes (Kruskal-Wallis ANOVA: H=5,099; p=0,5311).
Conclusion: We found that DLBCL was diagnosed in 2/3 of the cases and no significant difference of lymphoma subtype between males and females.

PS-16-009
Not as easy as it looks! Difficulties of diagnosing pilocytic astrocytoma: histomolecular characterisation of a series of 156 cases
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Background & Objective: Pilocytic Astrocytoma (PA) is the most common paediatric brain tumour. Classified as a grade I tumour according to the 2016 WHO classification, its tumourigenesis is due to an alteration of the MAP-kinase pathway, most frequently a KIAA1549:BRAF fusion. Our goal was to report the histomolecular characteristics of a series of PAs diagnosed in Sainte Anne Hospital's neuropathology department and present the most frequent diagnostic difficulties.
Method: Between 01/04/2016 and 01/04/2018, 156 PAs were updated according to the 2016 WHO classification. First, a break-apart probe targeting the BRAF gene was used. If the result was negative, we looked for BRAF V600E mutations (by immunohistochemistry and/or molecular biology), NTRK2 rearrangements and FGFR1 mutations.
Results: 69% of PAs harbored a BRAF rearrangement with a duplication of the 3' end as classically described in the KIAA1549:BRAF fusion. 6% of PAs presented with another type of rearrangement signaling a fusion of BRAF with another partner than KIAA1549. In the cases without BRAF rearrangements, 3% presented a gain at the BRAF locus and 1% an FGFR1 mutation. No BRAF mutation or NTRK2 rearrangement were detected. In the remaining 20%, 3% presented in the context of type 1 neurofibromatosis.
Conclusion: FISH for BRAF is a robust diagnostic method which may comfort pathologists in the diagnosis of PA and allow them to avoid the diagnostic traps that this tumour may set.

PS-16-010
Analysis of Tau burden and distribution on the spectrum of PSP subtypes
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Background & Objective: Heterogeneous clinical presentations of Progressive supranuclear palsy (PSP) have been described. Their pathological basis is presumed to be the anatomical distribution of tau pathology. A few studies have related the tau burden and the disease duration showing an unclear relationship. Our aim was to assess the clinicopathological correlation in a series of 37 consecutive autopsied patients with pathological diagnoses of PSP coming from our centre.
Method: We studied the phenotypic spectrum of PSP by retrospective clinical records review, classified according to the recent Movement Society criteria. The distribution and severity of tau-related pathology (neuronal tangles, neuropil threads and glial tangles) were assessed in a 4 grades scale using AT8 immunostained sections in 20 brain regions examined.
Results: PSP-Richardson syndrome (PSP-RS) was the most represented 20 (54,1%). We founded more cortical tau pathology in cortical atypical subtypes (PSP-non-fluent progressive aphasia, PSP-frontotemporal dementia and PSP-corticobasal syndrome) than PSP-RS ($P<0,05$) and PSP-Parkinsonism ($p=0,065$). We founded a negative correlation ($p=-0,55$, $p<0,05$) between tau burden and survival in the group of atypical subtypes that was not present in PSP-RS.
Conclusion: PSP complies a broad spectrum of clinical and pathological subtypes. Cortical tau density could determine PSP clinical presentation and disease survival appears to be related to the Tau burden.

PS-16-011
Disseminated leptomeningeal glioneuronal tumour: clinicopathological, immunohistochemistry, and molecular evaluation of seven paediatric cases at a single institution
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Background & Objective: Diffuse leptomeningeal glioneuronal tumour (DLGT) is an entity recently incorporated into the current WHO classification. Our aim was to describe this entity in a paediatric series.
Method: Neuroimaging, morphology, immunohistochemistry (IHC), and molecular findings were evaluated in seven children seen between 2009 and 2017.
Results: Four patients were male; mean age at presentation was 8.7 years (5-15 years). MRI showed ventricular dilation and diffuse leptomeningeal

enhancement in all. Nodular images at the conus medullaris were observed in two, an intramedullary cystic lesion in one, a frontotemporal lesion in one, optic chiasm thickening in one, and no mass was observed at onset in two. Signs and symptoms were initially associated with an inflammatory process in all. Histology showed leptomeningeal infiltration by glial-like cells with oval, mildly hyperchromatic nuclei, and scant-to-clear eosinophilic cytoplasm. Parenchymal infiltration was seen in three, diagnosed with oligo-like-neurocytic/oligodendroglioma, diffuse optic-chiasm infiltrating glioma GIII, and spinal-cord low-grade glioma compatible with DLGT. IHC revealed positivity for GFAP (6/7), OLIG2 (3/4), SYN (3/5), and NeuN (1/5). V600E mutation by PCR was negative (4/4). A KIAA-BRAF fusion was found (1/3) in the case with optic-pathway involvement. FISH 1p deletion study was positive (1/4) and 19q deletion study was negative in 4/4. Despite different treatment schemes, disease progressed in all and three died.
Conclusion: DLGT is a rare paediatric cancer of largely unknown histogenesis. Pathological diagnosis is a challenge. Currently, the entity is probably underdiagnosed or misdiagnosed initially as an inflammatory process.

PS-16-013
p16 overexpression correlates with better survival in glioma patients: a single centre study
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Background & Objective: The World Health Organization (WHO) Classification of Tumours of the Central Nervous System (CNS) was revised in 2016, integrating molecular parameters. Determination of the mutation status of the isocitrate dehydrogenase (IDH) gene has become the standard of care with prognostic, therapeutic, and diagnostic relevance. Our aim is to determine the IDH mutation status and the expression of other molecular markers by immunohistochemistry (IHC) and to correlate them with survival in our series.
Method: We retrieved from our archives 207 cases previously diagnoses as gliomas from 2010 to 2017. A panel of IHC stains (IDH1mut, p53, p16, bcl-2, cyclin-D1, Sox11 and WT1) was performed on tissue microarrays of representative tumour sections. Cases were considered IDHmut or IDHwildtype according to IHC stain with IDH1mut. p16 results were classified as negative (staining< 10%) or positive (staining≥ 10%). The other markers were scored using histoscore (0/300; staining (1,2,3) x% of positive cells). Results were correlated with WHO grade and outcome. Statistics were performed using Chi-Square and Kaplan-Meier tests.
Results: As expected, according to the 2016 WHO classification, IDHmut gliomas (18) showed better survival than IDHwildtype gliomas (183) (p=0.009). p16 positivity was observed in 83 (40,1%) gliomas (66,7% of IDHmut gliomas; 39% of IDHwildtype gliomas), and it was correlated with IDH1mut group (p=0,002) and better survival in our series (p<0,001). These correlations were not significant when adjusted for age, sex and grade. The rest of markers did not show correlation with survival.
Conclusion: Our preliminary study supports an association between p16 positivity and survival. Further studies are required to confirm this finding.

PS-16-014
Saccular intracranial aneurysms - inflammation and macrophage imbalance as risk factors for rupture
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Background & Objective: The mechanisms leading to the rupture of saccular intracranial aneurysms (SIA) remain obscure. However, insight into these processes may lead to management strategies reducing the risk of rupture. In this study we quantified and compared the structural and inflammatory changes in the aneurysmal walls between unruptured and ruptured SIA.
Method: This study included 17 SIA resected after clipping - ruptured (n=6) and unruptured (n=11), and 11 control samples of analogous regions of the circle of Willis. The morphology of the aneurysmal walls, the presence of thrombosis, of neovascularisation, or alteration of the elastic membranes were evaluated in classical histological stains. Lymphocytes were quantified using anti-LCA immunohistochemistry. Macrophages were subtyped into M1 (pro-inflammatory) and M2 (anti-inflammatory and reparative) subsets by anti-HLA-DR and anti-CD163 immunohistochemistry, respectively, and the M1/M2 ratio was determined for each case.
Results: The absence or fragmentation of the internal elastic membrane and the thinning of the aneurysmal wall were observed in both aneurysms. The presence of organized laminar thrombus and neovascularisation was more frequently observed in ruptured SIA. The inflammatory infiltrate was significantly less severe and the M1 subset prevailed among the macrophages in unruptured SIA. In the ruptured SIA, there was significantly more intense lymphocytic infiltration; macrophages were also significantly increased in number with predominance of the M2 subset. Neither structural nor inflammatory changes were observed in controls.
Conclusion: Our findings suggest that chronic inflammation along with macrophage M1/M2 imbalance may play a role in the progression of cerebral aneurysms to rupture.

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PS-16-015
Isotope Ratio Mass Spectrometry as a new tool for investigation of fundamental problem of trigger mechanisms of cell migration and fate, and complex neural cell biology
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Background & Objective: Isotope ratio assessment is one of the most modern and the most precise analytical method. The evaluation of isotopic profile currently has become a highly specialized area of science able to reveal the differences not visible with the use of other techniques. We took this powerful approach to search for potential differences in isotopic composition reflected fate and biology of tumour cells in chosen neural crest derived tumours represent the ventrolateral migratory pathway controlled by the extracellular matrices surrounding the neural tube, and factors secreted by potential final destinations, the same as biology of prodigious number of tumours arising from them.
Method: Isotope ratios of carbon and nitrogen were assessed in 24 tissue samples from growing in vivo tumours (paraganglioma, pheochromocytoma, neurofibroma, and MPNST) with the use of Continuous Flow Isotope Ratio Mass Spectrometer and compared with literature data for neuroblastoma and ganglioneuroblastoma.
Results: Distinct differences in isotope ratios were found in tumour tissues with regard to location and malignant potential of neural crest derived tumours, clearly separating the examined entities, reaching as much as 3.88‰ for nitrogen, and 2.52‰ for carbon.
Conclusion: At this very early stage of isotopic research in oncology, it is very hard to draw firm conclusions concerning the exact, complex, processes behind our results; however, distinct differences captured in the studies suggest modified isotope fractionation patterns specific to tumour biology and that IRMS carries the potential to be harnessed for investigation of trigger mechanisms and pathways of cell fate and migration processes, as well as tumour-environment interactions.

PS-16-017

Primary central nervous system lymphoma: clinico-pathological correlation

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Background & Objective: Primary central nervous system lymphoma (PCNSL) is an extra nodal non-Hodgkin lymphoma conned to the brain, leptomeninges, spinal cord, or eyes, without systemic involvement. The typical radiological findings consist of a brain tumour that enhances homogeneously, multifocal and with incomplete ring enhancement. The differential diagnosis of PCNSL should consider other malignant tumours of the CNS such as glioblastomas or metastases. The goal of our study is to describe the histopathological characteristics and clinic-radiological correlation.
Method: Retrospective review of all the patients diagnosed of primary CNS tumours in our center in the last 10 years (2008-2018). We described PCNSL and collected clinical and radiological information such as age, sex, location and histological types. Survival and immunosuppression as well.
Results: We identified 15 patients, 4 women and 11 men with a mean age of 66 years old. 73,3% were located in the brain hemispheres, 13,3 % in the corpus callosum, 6,6 in the cerebellum and 6,6% in the brain stem. The last location present the shorter survival as well. Clinical pathology correlation was high, up to 80% of cases considered lymphoma within the differential diagnosis. The most frequent histological type was diffuse large B cell lymphoma (80%) and 13,3% patients were associated with immunosuppression.
Conclusion: Despite its low frequency LPSNC should be considered as a differential diagnosis within brain tumours. In our review the most frequent subtype of CNS lymphomas correspond to diffuse large B-cell lymphoma as it is described in the literature. Despite the high correlation with radiology, histological confirmation is still necessary.

PS-16-018

Prognostic value of immunohistochemical expression of EGFR in glioblastomas

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Background & Objective: Glioblastomas are the most prevalent primary brain malignancy and the prognosis is poor. Age, cognitive status, extent of surgical resection and adjuvant treatment are among the main prognostic factors. Some immunohistochemical markers seem to have a prognostic interest but the results are not unanimous and are sometimes contradictory. The aim of our study was to evaluate the prognostic value of EGFR antibody in glioblastomas and to find a statistically significant relationship between the expression of this antibody and the recurrence.
Method: Fifty-two cases of glioblastoma were identified in the Department of pathology of the Military Hospital of Tunis between 2005 and 2016. An immunohistochemical study was performed followed by a statistical analysis analysing the correlation with the recurrence and the overall survival.
Results: The average age of patients was 56 years old. The 1-year survival and 2-year survival were 33% and 4% respectively. The median progression-free survival was 26 weeks. The median survival was 35 weeks. There was Tumour recurrence in 37% of cases. EGFR was expressed in 87% of cases and had a percentage of marked cells of 100% in quarter of cases. EGFR labeling was intense in 38% of cases. EGFR had a statistically significant positive relationship with progression-free survival but it has no statistically significant relationship with overall survival.
Conclusion: Our study concluded that EGFR could have a role in prolonging progression-free survival. As the immunohistochemical expression of EGFR is inversely correlated with recurrence, it could intervene in the rhythm and frequency of postoperative controls in order to optimize the therapeutic management in time.

PS-16-019

Pleomorphic pineocytoma, a mimicker of a high grade lesion

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Background & Objective: Pineal parenchymal tumours (PPTs) account for <1% of all intracranial neoplasms and represent approximately 27% of pineal region neoplasms. Of these, pineocytomas (PCs) account for 20% and affect most frequently adults. A pleomorphic variant is encountered in some PCs, characterized by large ganglion cells and/or multinucleated giant cells with bizarre nuclei. The mitotic activity of this pattern is low, despite the worrisome nuclear features that may lead to an erroneous upgrading of the tumour.
Method: We report the case of a 72-year-old man with an episode of aphasia and fever. MRI showed supratentorial hydrocephalia due to a third ventricle solid mass of 1,3 cm, which enhanced slightly with gadolinium and lacked signs of necrosis. The patient underwent a ventriculostomy and biopsy.
Results: Two tissue fragments of 2 mm were analyzed and revealed a patternless neoplasia composed of ill-defined cells with variable cytoplasm and enlarged ovoid nuclei, with smooth outline, granular chromatin and prominent nucleoli. Intermixed with them, we found cells with marked nuclear pleomorphism and multinucleation. There was no significant mitotic activity. The immunohistochemical study confirmed the diagnosis of PC ruling out other options such as pleomorphic astrocytoma.
Conclusion: PC and PPT of intermediate differentiation are rare tumours which can present with marked pleomorphism, potentially leading to the misclassification and upgrading of these tumours. The lack of invasiveness and the low number of proliferating cells suggest a benign clinical course. This patient was then only biopsied to confirm the diagnosis and now follows regular MRI controls to decide whether surgery is necessary.

Tuesday, 11 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-17 | Other Topics II

PS-17-001

An integrative next-generation sequencing and cytogenetics solution for myeloid cancer research

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Background & Objective: Sanger sequencing and karyotyping are traditionally used to detect molecular alterations in myeloid cancer that inform diagnosis and treatment. Recently, new myeloid biomarkers have expanded the scope of molecular testing. To address the need for broader profiling, we developed a next-generation sequencing (NGS) assay to research alterations in 58 myeloid cancer genes and a cytogenetics assay to detect chromosomal alterations. Furthermore, we developed a reporting solution that integrates results from both platforms into a single report with curated evidence from published data sources.
Method: The NGS assay was developed on Ion Ampliseq targeted sequencing technology to detect DNA and RNA variants from 10ng of

input. The cytogenetics assay was developed on an Affymetrix platform with enriched coverage for cancer genes. Published evidence from drug labels (EMA, FDA), guidelines (ESMO, NCCN), and global clinical trials were identified using automated text searches and manual curation. A web application was developed to generate biomarker specific custom reports in 11 languages.
Results: The NGS assay detects single-nucleotide variants, insertion/deletions, and fusions in 58 genes with an average read depth of >2000 reads per amplicon and average uniformity of >95%. The cytogenetics assay contains 2.6 million markers for the detection of amplifications/deletions, LOH, and chromotripsis. The reporting solution integrates outputs from the two platforms to report relevant published evidence.
Conclusion: We developed two complementary platforms to detect mutations and chromosomal alterations in myeloid cancer research. Combined with an integrative reporting solution to provide the relevance of these biomarkers, we demonstrate a streamlined and robust sample-to-answer workflow.

PS-17-002
Integrated quality assurance (QA) for surgery and pathology from the EORTC-1420-HNCG-ROG "BEST OF" clinical trial
M. Urbanowicz*, C. Caballero, C. Fortpied, F. Zimmermann, P. Koivunen, D. Thurnher, T. Raveloarivahy, J. Bourhis, M. Evans, J. P. Klussmann, G. Spriano, C. R. Leemans, A. Dietz, C. Simon, K. Hunter
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Background & Objective: BEST OF is a phase III study assessing the "best of" radiotherapy (Intensity Modulated RadioTherapy, IMRT) compared to the "best of" surgery (Trans-Oral Surgery, TOS) in patients with T1-T2, N0 oropharyngeal squamous cell carcinoma (OPSCC). The aim of BEST OF (NCT02984410) is to assess and compare patient-reported swallowing function over the first year after randomization either to IMRT or TOS. The primary end-point is MD Anderson Dysphagia Inventory (MDADI) score reported by the patients at months 4.5, 6, 9, and 12 after randomization. An integrated QA for surgery and pathology was implemented to assess efficacy and standardize TOS.
Method: A panel of surgical and pathology experts established quality indicators and the QA process for BEST OF that includes pre-trial credentialing, standardization and central review. Pathology quality indicators are margin and lymph nodes status. Standardization of pathology assessment was based on the International Collaboration on Cancer Reporting Head and Neck Dataset (2018). Study specific guidelines for primary tumour HPV status by p16 IHC confirmed with ISH or PCR were developed. Central pathology review will be performed by independent pathologists using the macroscopic and microscopic digital photos from the first surgical resection specimen from each site. Precision of the QA strategy will be assessed after 10 patients will have undergone surgery.
Results: Twenty-four out of twenty-six sites from six countries have been credentialed for TOS.
Conclusion: An integrated surgery and pathology QA strategy is critical to assess efficacy in BEST OF. This can be a model for future EORTC head and neck cancer trials.

PS-17-003
Adaptation of a single institution's pathology service and other services involved, because new European regulation on classification, labeling and packaging of substances and mixtures with formaldehyde
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Background & Objective: Recently, EU regulation on classification, labeling and packaging of substances and mixtures with formaldehyde, changed classification of this product, going from category 2 (H351, suspect that causes cancer), to category 1B (H350, carcinogenic). This force pathology services to adapt.
Method: We were forced to adapt our facilities focusing on: centralizing formaldehyde use in properly qualified areas, develop multidisciplinary working groups in order to address the problem and evaluation of the state of formalin levels.
Results: Reduction of manipulation, on surgery, consultations and Primary Care, implementing formalin pre-filled packaging systems for small sample. Improving sample delivery, incorporating vacuum packaging systems in surgery areas, and later filling formaldehyde into the vacuum bags. Adaptation of hoods with formaldehyde dispensers and integrated disposal/inactivation system. Modification of grossing lab, with specific floor surface and automatic entry system, incorporating a negative pressure system and vacuum bell.
Conclusion: We reduced use of formaldehyde in areas without ventilation systems, improving risk control. Packaging/preservation has been improved, up to three days after its extraction, guaranteeing suitability for further immunohistochemical or molecular studies. Design and implementation new protocols for sample processing, adequate fixation and facilitate re-tapping avoiding overfixation. Reform of physical plant, with extraction systems and negative pressure environment, new tables and bells of carving with exposure control and adapted for ergonomics and occupational safety.

PS-17-006
Perception of Tunisian pathology training residents about their evaluation process: a national survey
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Background & Objective: A quality training program with adequate evaluation process will improve quality of future pathologists. In Tunisia, pathological residents take only one examination of both practical and theoretical knowledge in the end of the 4-year training period. A key question is what Tunisian training residents in pathology think about their examination system. We set out to an exhaustive survey study of training residents in pathology in Tunisia. The aim of this study was to assess their perceptions about their evaluation process.
Method: An online anonymous questionnaire prepared as a Google Forms survey asking resident's opinion concerning frequency of theoretical and practical evaluation was sent to all Tunisian pathology residents in January 2017.
Results: From the 36 residents invited, 28 entered the survey questionnaire. They were 22 women and 6 men belonging to one of the 4 Tunisian faculties of medicine. Twenty residents were not satisfied with the pace of evaluation of their theoretical knowledge. Ten of them thought that an annual evaluation would be more appropriate and 8 considered that semestrial evaluation would be more effective. The remaining preferred an examination after 2 and 4 yearstraining. Concerning the evaluation of practical knowledge, 22 residents were not satisfied with a unique evaluation in the end of training. Fifteen thought that a semestrial evaluation is more appropriate and six preferred an annual examination. The remaining preferred an examination after 2 and 4 years training.
Conclusion: Tunisian training residents in pathology are not satisfied with the pace of their evaluation. They are demanding of more frequent

theoretical and practical evaluations. These data support the need to develop the evaluation process of pathology residents in Tunisia

PS-17-007

Idiopathic systemic amyloidosis mimicking metastatic gastric cancer

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Background & Objective: Amyloidosis is a collection of pathophysiologically related disease entities caused by the progressive and irreversible extracellular deposition of abnormal fibrillar proteins called amyloid. Primary systemic amyloidosis involves many organs without any underlying disease and it usually affects young individuals compared with the secondary type.
Method: This report describes an uncommon case of idiopathic systemic amyloidosis mainly manifesting as a gastrointestinal disorder in a 36-year-old man. The pacient underwent surgery for a tumoural mass located in the stomach. Unfortunately, he died after the intervention due to systemic complications caused by multiorgan failure. Gross examination at autopsy identified numerous tumour-like lesions of variable size affecting many organs. The histopathologic autopsy report revealed many homogeneous and eosinophilic amorphous deposits associated with a granulomatous reaction, located in the vascular wall and interstitium of the lungs, heart, liver, kidney, pancreas, stomach, small intestine, thyroid and suprarenal glands. Amyloid material was confirmed by the Congo red stain and the subsequent apple-green birefringence under polarized light.
Results: Most of the tumoural masses thought to be metastases from a previous gastric cancer were, in fact, large amyloid deposits, as well as the stomach cancer itself.
Conclusion: This particular and unusual case raises concern about the rapid and massive amyloid infiltration which can lead to high morbidity and mortality through the disruption of normal tissue structure and misguiding the physician by leading to tumour-like masses.

PS-17-008

Malignant deciduoid mesothelioma: case presentation of an extremely rare variant and review of the literature

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Background & Objective: Malignant Deciduoid Mesothelioma (MDM) is a particular variant of epithelioid mesothelioma that appears extremely rare, being first described in the peritoneum of young females. The aim of this case report is to describe malignant deciduiod mesothelioma of the peritoneum and to discuss the differential diagnosis of this extremely rare variant of epitheloid mesothelioma.
Method: We report a case of malignant deciduoid mesothelioma that occurred in the peritoneal cavity of a 52 year-old man.
Results: A 52-year-old male patient, with no history of asbestos exposure, presented generalized abdominal tenderness and distension. Abdominal ultrasound examination showed moderate ascites. An exploratory laparotomy showed multiple gray white, firm nodules, infiltrating the peritoneal cavity. A biopsy was performed. We received multiple, gray white fragments. Microscopically, H&E stain showed nests of malignant cells, composed by pleomorphic epithelioid cells with abundant, eosinophilic cytoplasm, with central, irregular and vesicular nuclei, with small nucleoli. Focally, the tumour cells had the appearance of endometrial decidual cells. Neutrophilic intratumoural infiltration was moderate to dense. Immunohistochemistry tests revealed that tumoural cells were positive for CK5/6, WT1, D2-40, mesothelin, calretinin and Ki-67 in 10% of neoplasic cells and negative for CEA, BerEP4. The microscopic and immunohistochemical findings were compatible with deciduoid malignant mesothelioma. The patient received chemotherapy and he survived 3 years.
Conclusion: In summary, this case report highlights the clinical, histopathological, and immunohistochemical particularities of this extremely rare variant of epitheloid mesothelioma and review the literature reports.

PS-17-009

Sclerosing nodular angiomatoid transformation: a case report

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Background & Objective: Sclerosing angiomatoid nodular transformation (SANT) is a rare vascular lesion of spleen that recently described.
Method: We present a case of this rare entity discovered at a 60 years old woman who with abdominal pain.
Results: Abdominal computed tomography revealed a 58x58x62 mm diameter solid lesion in spleen and splenectomy had performed. In macroscopic examination a well defined, unencapsulated solid mass was described in spleen. In histologic examination, complex vascular structures formed with monomorphous endothelial cells with a collagen stroma and fibrin was seen.
Conclusion: We discuss the histopathologic and immunohistochemical findings and differential diagnosis of SANT with other lesions such as hamartomas, inflamation, pseudotumours and hemangiomas.

PS-17-010

Peritoneal splenosis mimicking carcinomatosis: a case report

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Background & Objective: Splenosis is an uncommon benign condition resulting from heterotopic autotransplantation of splenic tissues onto intra and extraperitoneal surfaces following splenic trauma and surgeries Our aim was to highlight the clinical-pathological features of this rare entity.
Method: We retrospectively studied clinical-pathological data of a case of peritoneal splenosis
Results: A 57-year-old woman presented to the gastroenterologist with chronic abdominal pain in the left iliac fossa. She had a past history of road side accident and splenic injury and underwent splenectomy for that. Computed tomography revealed multiple peritoneal nodules with ascites mimicking peritoneal carcinomatosis. Esogastroduodenal endoscopy and colonoscopy were made to search a primary tumour but were normal. Exploratory laparotomy found multiple brown dark nodules at the surface of the greater omentum. Histologic exam showed that these nodules correspond to normal splenic tissue. Diagnostic of peritoneal splenosis was made.
Conclusion: Splenosis can mimick peritoneal carcinomatosis on classic imaging investigation. This diagnosis should be kept in made if there is history of splenic trauma so unnecessary operations could be avoided.

PS-17-011

Association of KIBRA, CAMTA1 and BDNF genes polymorphisms with memory of Russian outstanding schoolboys

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Background & Objective: Episodic memory refers to memory for autobiographical episodes of a person's life. The primary information is first processed by the episodic memory system. We aimed to assess an association of the polymorphisms rs17070145 in the KIBRA gene, rs4908449 in the CAMTA1 gene and rs6265 in the BDNF gene with intellectual performance of talented school children of Kazan.
Method: The study implicated 22 schoolboys (16±1 years), prize winners of republican and All-Russian Olympiads. Children genotyping data was compared with the European population (1000Genomes). DNA was extracted from buccal epithelium. Gene polymorphisms were identified by real-time PCR. The

tests for cognitive abilities were obtained by the "NS-PsychoTest" software package.
Results: Genotypes frequencies for all SNPs was under Hardy-Weinberg equilibrium in our group (p>0.05) and wasn't significantly different from the European frequency distribution. T-allele carriers of the rs6265 took less time to complete the ability to generalize and to count tasks (Amthauer test) compared to the CC homozygotes (p=0.0002 and p=0.03, respectively). TT homozygotes rs17070145 had more correct answers in the "Mind awareness" task compared to the C-allele carriers (p=0.015) and fulfilled the task "Ability to Account" more quickly (p<0.0001). These results are consistent with the data of psychogenetic studies. It was revealed that T-carriers of rs4908449 showed less memory capacity in the "Memory for Numbers" task than non-carriers (p=0.002).
Conclusion: T-allele of rs17070145 and rs6265 is associated with high speed performance and in the case of rs17070145 also with higher mind awareness indicators. We report an association of C-allele of rs4908449 with better memory performance.

PS-17-012
Apolipoprotein A-1 deficiency differentially affects bone marrow osteoblasts and lipoblasts, resulting in the development of bone metastasis-friendly microenvironment
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Background & Objective: Increased bone marrow adiposity and disturbances in the lipid/lipoprotein metabolism affect bone homeostasis and result in metastases development. This study investigates the role of Apoliporotein A-1 (ApoA-1), vital component of HDL biosynthesis in bone marrow (BM) niche regulation and bone metastasis pathogenesis.
Method: We used control and ApoA-1 knock-out () male mice (10 mice/group). Quality/architecture of lumbar vertebra was evaluated histologically and histomorphometrically ([immunofluorescence (calcein-labeling), microCT tomography (Scanco vivaCT)]. Femora BM was flushed and the expression of osteoblastic (Runx2, Ostepontin), lipoblastic (ARγ, CEPBA, adiponectin, UCP-1, DIO2) and BM microenvironment (CXCR4, CLCX12, ANXA2, MAPK1, AKT, PI3K, MIF, NOTCH1, NOTCH2, JAGGED) regulators/effectors was evaluated applying RT-PCR, Western-Blotting and/or flow-cytometry.
Results: ApoA-1-/- mice had remarkably reduced bone mass and impaired osteoblastic function. The BM of ApoA-1-/- mice displayed greatly elevated adiposity compared to the control group. The osteoblastic regulators (RUNX2, Osteopontin) were significantly reduced, whereas the lipoblastic regulators (ARγ, CEPBA) were significantly elevated in the KO compared to the control mice. The white adipose tissue marker (adiponectin) was significantly reduced, in sharp contrast to the brown fat markers (UCP1, DIO2). The MIF-CXCR4-CLCX12-2 axis and the MARK, PI3/AKT, NOTCH1-2/JAGGED singling cascades that control bone metastases were remarkably deregulated, in the ApoA-1-/- mice.
Conclusion: ApoA-1 deficiency and hence reduced/impaired HDL, clearly affect BM microenvironment (osteoblastic niche) at both morphological and molecular level, leading to the activation of signal transduction pathways that favour bone metastasis.

Tuesday, 11 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-18 | Paediatric and Perinatal Pathology

PS-18-001
A difficult diagnosis in a child with renal mass: desmoplastic small round cell tumour of the kidney
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Background & Objective: Renal malignancies account for 7% of chilhood cancers, among which Wilms' tumour is the most common. However, a variety of other paediatric renal tumours can occur and enter into differential diagnosis histologically such as rhabdoid tumour, primitive neuroectodermal tumour (PNET), synovial sarcoma, renal cell carcinoma, etc.
Method: An 8-year-old girl who presented with abdominal pain was found to have a huge left renal mass. Needle biopsy diagnosis from the tumour in an outside center was PNET. Nephrectomy was performed after neoadjuvant chemotherapy and paraffin blocks were sent to our institution for consultation.
Results: Tumour was consisted of nests, cords, sheets of small round cells within desmoplastic stroma. There were frequent rosette-like structures, acantholytic areas with psedopapillary appearance and frequent rhadoid cells. FISH showed EWSR re-arrangement. However, neoplastic cells were negative for CD99, bcl-2, synaptophysin, chromogranin, S100, myo-D1, PAX8 and nuclear WT1 with intact INI1. Instead, they expressed distinctive paranuclear dot-like desmin, cytokeratin, EMA and CD56. As a result, the case was diagnosed as desmoplastic small round cell tumour (DSRCT) of the kidney. The child had a metastatic disease, was given adjuvan chemotherapy, but she died in the 30th month after surgery.
Conclusion: DSRCT in kidney is an aggressive, malignant tumour and has to be included in the differential diagnosis of Wilms tumour, PNET and other small round cell tumours as well as renal epitelial neoplasies. The diagnosis is particularly difficult in this location because of rarity. Immunohistochemistry in additon to cytogenetic and molecular studies are required for confirmation.

PS-18-002
Hyperplasia of Langerhans islands in Beckwith Wiedemann syndrome: a case report
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Background & Objective: In this study we describe a case of Beckwith Wiedemann syndrome (BWS) occurring in a preterm newborn died in the perinatal period. BWS is a rare genetic disorder: cardinal features include macroglossia, exomphalos, lateralized overgrowth, hyperinsulinism, adrenal cortex cytomegaly and pancreatic adenomatosis.
Method: A 26-year-old pregnant woman presented with pre-eclampsia, leading to preterm labor at the 27th week of gestation. Apgar index of the female newborn at birth was 5, with insurgence of a respiratory distress syndrome and hypoglicemia. The newborn died 44 hours after birth in the neonatal intensive care unit, and autopsy was performed. Tissue samples were formalin-fixed and routinely processed. Sections were stained with H&E, and pancreas specimens were immunostained with anti-synaptophysin and anti-Chromogranin antibodies.
Results: At autopsy, the newborn showed: anasarca; birthweight 2 standard deviation score above the mean values, macroglossia, generalized visceromegaly including lung, hearth, liver, pancreas and kidney, ectopic adrenal gland in a paraovarial site, exomphalos with incarcerated and ischemic intestinal loops. At histology, we observed cytomegaly of the adrenal cortex, hyaline membrane disease of the immature lungs, a marked hyperplasia of the Langerhans islands of the pancreas and increased hepatic haematopoiesis.
Conclusion: The case of BWS here reported is characterized by a dramatic clinical course. Hyperinsulinism and hypoglicemia should be considered a sign of poor prognosis, particularly when associated with preterm birth and immaturity. The marked hyperplasia of the endocrine

pancreas confirms that, in BWS infants with non-responsive marked hyperinsulinism, surgery with partial pancreatectomy should be considered.

PS-18-003
Intracardiac teratoma: a rare case of foetal hydrops
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Background & Objective: Congenital heart tumours are rare entities, with an incidence of 0.17-0.28% in fetal autopsies. The most frequent are rhabdomyomas (60%), followed by teratomas (25%) and fibromas (12%). These neoplasms may present with cardiomegaly and have hemodynamic repercussions of varying severity, according to their location, size and number, from slight alterations to severe cardiac insufficiency with hydrops and fetal/peri-natal death. We herein report a case of perinatal death of a hydropic 28-week-old newborn with a large intracardiac teratoma.
Method: Description and interpretation of the macro and microscopic findings at the autopsy, and literature review of intracardiac tumours in fetal period.
Results: Hydropic newborn with enlargement of the cardiac area, compression of the thymus, and remaining intrathoracic structures, and increase of the right atrium by a solid tumour of 3cm that, in section, was well delimited, white and firm, with cystic cavities without content. Histologically, the findings were consistent with teratoma.
Conclusion: Most cardiac tumours have an ultrasound diagnosis in the prenatal period and are referred for surgery after birth. However, in some cases, the diagnosis is only established during necropsy examination in the presence of unexpected fetal/perinatal death. The differential diagnosis of hydrops is extensive and includes cardiac neoplasms. Most of the teratomas in this area have an intrapericardial location. Intracardiac location is extremely rare, with less than 25 cases reported in the literature. This case confirms that the location and dimensions of the tumour are the main determinants for the prognosis of this type of neoplasm, although it has a histologically benign morphology.

PS-18-004
Nasal chondromesenchymal hamartoma in a 22 days newborn baby: case report
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Background & Objective: Nasal chondromsenchymal hamartoma is na extremely rare benign tumour, with less than 40 cases reported in the English literature, primarily diagnosed in young infants and children. It typically as a unilateral mass of the nasal cavity, exhibiting mixed mesenchymal elements. These lesions have been associated with de DICER1 tumours and maybe the herald tumour of this disease. Share the case of a rare tumour, which although benign may be associated with other tumours.
Method: Case report of a rare benign tumour including medical history, MRI, histologic features and its association with DICER1 Syndrome.
Results: We present a 22days newborn baby with nasal obstruction, tachypnea and peripheral cyanosis since birth. MRI demonstrated a partially calcified soft-tissue mass, with cystic areas obstructing the nasal cavity. The patient underwent endoscopic surgical excision. Histologic of the tumour was consistent with nasal chondromesenchymal hamartoma, exhibiting a mixed mesenchymal pattern of chondroid and osseous islands of tissue with a variably collagenous, mixoid or giant cell-rich stroma. The search for mutations in the DICER1 gene was made (by Polymerase Chain Reaction) and no clinically relevant variants or of uncertain significance were found.
Conclusion: Nasal chondromesenchymal hamartoma is a rare, benign tumour with good behavior and without history of recurrence after complete resection. Yet, it can be part of a syndrome associated with other paediatric neoplastic disease. In our case, the search for mutations in DICER1 genes was negative however the pathogenic variants of the DICER1 gene are found in only 65% of patients with pathologies associated with DICER1 Syndrome.

PS-18-005
Forensic and pathological aspects of a new born with anencephaly
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Background & Objective: Anencephaly represents a malformation of the central nervous system characterized by the failure of closure of the cephalic part of the neural tube. The frequency of this malformation is 0.012-0.62 ‰, the predominant affected sex being female, with F/M ratio between 3/1-7/1, which makes this abnormality a particular one.
Method: We present the case of a male newborn at term, originating from an unmonitored pregnancy. The newborn with Apgar 5, Sat O2=56%, AV=94, enters in cardio-respiratory arrest, shortly after birth. The case has become forensic due to home delivery.
Results: Following the necropsy exam, were highlighted the next aspects: the lungs were expanded, with positive Galen technique and partially breathed lungs (microscopically). At the cephalic extremity there was no cranial vault and the brain was transformed into an elastic membrane. The tissue samples from this area were stained with S100 antibody thus obtaining the identification of areas of nervous tissue among the dilatated blood vessels.
Conclusion: Following this malformation, the vault of the skull does not form, leaving the malformed brain exposed, which later will degenerate into a mass of necrotic tissue. The anomaly is more common in premature newborns, most of whom are born dead, the cases in which they live being rare, even for a short period of time. The authors support an active management of the pregnancy women and y this case report we wish to draw a warning sign about the drastic consequences of an unmonitored pregnancy by an obstetrician and the importance of pregnancy screening period.

PS-18-006
Port-A-Cath-related exsanguination in a child with hemophilia A: lessons learned from a fatal case
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Background & Objective: A Port-A-Cath is a small device that's surgically implanted under the skin, usually in the upper thoracic wall. These devices enable more frequent infusions (e.g. clotting factors) and more independence from medical staff. But they also have a high risk of developing an infection or a thrombosis. We will report a fatal case in a child with Hemophilia.
Method: A 10-month-old male baby with severe Hemophilia A was hospitalized for insertion of a right central venous catheter. During the postoperative period, active bleeding was observed at the puncture site. So the Paediatric Surgery Team decided for his hospitalization due to probable rupture with indication of substitution by a new one. Twenty hours after the surgery, death was verified and a clinical autopsy was requested.
Results: During the post-mortem we found a massive hemothorax and a retropulmonary blood clot (120g) that conditioned pulmonary atelectasis. After a careful dissection, we identified the distal end of the catheter in the lumen of the left subclavian vein and the free proximal end in the pleural cavity. In the preliminary report, drafted immediately after the autopsy, we wrote "Perforating lesion of the left subclavian vein."

Conclusion: Despite obvious potential risks with Port-A-Caths, they are useful in many cases. With this case we would like to highlight the importance of having good 1) anatomy knowledge 2) dissection skills 3) taking good photographs to perform high quality paediatric autopsies. Pathologists should always be aware that findings during an autopsy may trigger legal proceedings.

PS-18-007

Gaucher's disease diagnosed on bone marrow biopsy performed for suspicion of malignant hemopathy

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Background & Objective: Gaucher's disease (GD) is an autosomal recessive lipid storage disorder due to deficient or defective production of a lysosomal enzyme glucocerebrosidas. It is a rare genetic disorder. Here we report a case of a child in whom a blood cancer was suspected and the correct diagnosis of GD was based on bone marrow biopsy.
Method: This case was diagnosed at in our department of Pathology at of the University hospital of Monastir.
Results: A six-year-old female child with history of acute osteomyelitis of the distal extremity of the left femur presented with severe pain of the distal extremity of the right femur. On examination, the child had delayed milestones. The spleen was 11 cm palpable below the left costochondral margin. Haemoglobin was 8.2g/dl and Platelet count was 181,000/μL. An MRI of the right knee showed a diffuse infiltration of the bone marrow directing to a malignant hemopathy. A bone marrow biopsy was performed and showed sheets of Gaucher's cells seen as histiocytes with abundant granular and fibrillar cytoplasm. These cells had small eccentrically placed nuclei and had a crumpled tissue paper appearance. The diagnosis of GD was given and later confirmed by glucocerebrosidase levels estimation.
Conclusion: We report a patient with acute osteomyelitis as the single classical symptom, in whom Gaucher cells detected in bone marrow biopsy indicated the correct diagnosis of GD after clinical and radiological suspicion of malignant hemopathy. Our case might emphasize the utility of bone marrow study for GD, especially in cases where a blood cancer is suspected.

PS-18-008

Association between placental syncytiotrophoblast remodeling and angiogenic factor expression under hypoxia conditions

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Background & Objective: Gestation accompanied with maternal congenital heart disease (MCHD) is at risk with adverse pregnancy outcomes. We aimed to reveal the association of VEGF expression in placental syncytiotrophoblast (STB) and epithelial structural remodeling in cases of MCHD.
Method: 35 term placentas were divided into groups: I - 20 cases of MCHD and 15 cases of physiological pregnancy (control group). Chorionic villous morphology evaluated microscopically and by the computer morphometry. The standard immunohistochemical staining protocol with monoclonal mouse antibody to VEGF (RTU, Spring) for placental tissue samples has been developed. A standard single-stage protocol was performed with high-temperature antibody unmasking in 0.01 M citrate buffer (pH 7.6). Differences between groups' data were elucidated by non-parametric Wald-Wolfowitz test. Reliability established at $p<0.05$.
Results: Microscopic investigation revealed multiple foci of placental epithelial injury in cases of MCHD. Higher degree of pathologic changes discovered at peripheral and paracentral regions. Volume fractions of the terminal villi STB decreased in the central, paracentral and peripheral placental zones under MCHD conditions. These were accompanied with placental membrane thinning and higher expression of the VEGF within the epithelial layer.
Conclusion: The placental membrane thinning due to decreased STB volume fraction may accommodate fetal –maternal metabolism and gas exchange under hypoxia conditions in cases MCHD. The VEGF involvement in the control of fetal capillaries and syncytiotrophoblast remodeling discussed.

PS-18-009

Maternal factors and feto-placental remodeling in pregnancies with congenital heart disease

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Background & Objective: Number of pregnancies in women with cardiac disease is increasing worldwide. Heart distress during gestation always carries arduous challenge for physicians. The understanding of the adaptation mechanisms in 'mother-placenta-fetus' system may prevent maternal and fetal risk in pregnancy. To study maternal data, pregnancy outcomes and feto-placental peculiarities in operated vs non-operated cases of congenital heart disease (CHD) was the aim of present investigation.
Method: A total 39 patients of CHD were taken in this study. These were divided into two groups. Group 1- 20 patients who had no cardiac surgery and Group 2- 19- who had cardiac surgery to correct their cardiac defect before pregnancy. The control group (CG) included 15 cases of physiological gestation and childbirth. Medical records data, newborn - placental parameters, morphological and stereometric characteristics of placental villous chorion were compared in the two groups and CG using statistical analysis. Differences between groups' data were elucidated by non-parametric Wald-Wolfowitz test. Reliability established at $p<0.05$.
Results: Present study has shown that patients with CHD in pregnancy have a higher risk of obstetric complications. Mean newborns birth weight and body length, placental organometric parameters were smaller in cases of CHD. Cardiac pathology was accompanied with increased volume fraction of dystrophic processes in placental chorion structures. Nevertheless, the structural remodeling in placental fetal capillaries, villous membranes were very noticeable in operated vs non-operated cases of CHD.
Conclusion: Medical correction of hemodynamic disorders prevented placental insufficiency and thus contributed to successful maternal and fetal outcome of pregnancy.

PS-18-010

Features of the hidden immunodeficiency in a newborn baby whose mother suffered from leukemia

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Background & Objective: To study the features of the pathomorphological changes in the intestines, spleen and thymus gland in a baby with the hidden congenital immunodeficiency provoked by the BCG vaccination.
Method: We present a case of the death of the newborn baby (14 days of life), whose mother suffered from acute leukemia in youth. The baby was born without pathologies. Therefore, she was vaccinated against hepatitis B (Engerix-B) and tuberculosis (BCG) according to the immunizations schedule. In a week the state of health of the baby became worse, the disease progressed despite the pharmacological treatment and led to multiple organ failures that caused the death. During the postmortem examination the changes in the intestines, spleen and thymus gland were observed and were studied in detail by using the histological-immunohistological (CD3/CD79α/CK-pan) methods.

Results: The histological study of the intestines revealed the diffuse foci of necrosis, strong leukocyte infiltration and vascular congestion with multiple hemorrhages. Perivascular T-cells hypoplasia was observed in the spleen. Thymus lobules were reduced, cortex thickness (lymphocyte loss and reticular stroma collapse) and proliferation of the epithelial reticular cells were observed. Numerous Hassall's corpuscles, different in their size, were observed. The results of the immunohistochemical study of the spleen showed the absence of the perivascular T-cells and the follicular hyperplasia of B-lymphocytes at the same time. Small number of CD3/CD79a-positive cells was observed in the thymus gland, CK-pan - significantly expressed in epithelial-reticular cells. The abovementioned changes indicate the development of the congenital T-cells immunodeficiency that led to the ulcerous-necrotic enterocolitis.
Conclusion: This clinical case demonstrates the importance of early diagnosis of immune status in the newborns, whose parents have leukemia in anamnesis. BCG-vaccination against the background of T-cell immunodeficiency may lead to the dangerous complications that threaten baby's life.

PS-18-011
The effect of anemia and malaria on placental vascularisation; a stereological analysis to identify the most vulnerable time point in pregnancy

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Background & Objective: This study aimed at investigating how placental vascularization is affected by anemia and/or malaria during pregnancy to identify the most vulnerable timepoints.
Method: The placentae were sampled by Systematic Uniform Random sampling and further sectioned by Isotropic Uniform Random sampling. Stained slides were analyzed by 197 placentae were collected in Tanzania assessing the volume, length and surface area of the vessels. The placentae were categorized as either control, anemic (Hb≤9g/dL, 9g/dL<Hb≤11g/dL) or malaria positive. The effect on transport and diffusion vessels and villi were investigated in four different intervals in pregnancy by gestational age (GA)
Results: Anemia: Only anemia after a GA of 28 weeks influences placental angiogenesis. Mild anemia reduced length of diffusion vessels but increased the length of transport vessels. Surface and volume were increase for both vessel types. Malaria Malaria: before a GA of 14 weeks increased surface of diffusion vessels and decreased the length of diffusion and volume of transport vessels. Malaria after a GA of 28 weeks increased all measured indices of angiogenesis except for surface of diffusion vessels. Malaria and/or anemia at GA 14+1-27+6 did not affect placental angiogenesis
Conclusion: Only malaria in early pregnancy has an influence on placental development whereas both anemia and malaria in the late pregnancy have a significant effect on the placental angiogenesis. After a GA of 28 weeks the placental demands are high due to fetal growth spurt. Increased surface, length and volume could be an attempt to compensate for the decreased oxygen due to anemia and disturbed diffusion surface due to malaria.

PS-18-012
ICAM1 and VCAM1 gene expression level in women with insufficient miscarriage

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Background & Objective: The physiological course of pregnancy in addition to external factors depends largely on the functional state of the vascular system. Endothelial dysfunction is usually accompanied by a systemic inflammatory process. It is believed that in the early stages of endotheliosis adhesion molecules ICAM-1 is strongly expressed, and VCAM-1 appears in acute endothelial dysfunction. However, despite all available information, the role of ICAM-1 and VCAM-1 in the pathogenesis of insufficient miscarriage still unclear. To evaluate the ICAM-1 and VCAM-1 genes expression level in women with insufficient miscarriage.
Method: Gene expression was measured by qPCR based on TaqMan technology in venous blood samples from 29 women with uncompleted pregnancy (UP) (I-II trimester) and 79 physiologically pregnant women (PP) collected during 22-24th, 32-34th weeks of pregnancy, separately in primapara and multigravidas.
Results: The mean level of ICAM1 activity was much higher in third trimester in PP women (primapara and multigravidas) compared to non-pregnant women (RQ 4.11 and 3.89 respectively ($p<0.05$)) but in UP group we detected significant decrease of its activity (RQ 0.0144, p 0.0453). Moderate increasing of VCAM1 gene activity also detected in PP women during gestation ($p>0.05$) but in UP group we showed almost 6-fold increasing of its expression (RQ 6.57, $p=0.037$).
Conclusion: Measurement of gene activity adhesion molecules ICAM1, VCAM1 is necessary for understanding the mechanisms of obstetrical pathology in pregnant women complicated with varicose veins of the pelvis.

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PS-18-013
A new case of foetal fibrochondrogenesis – a diagnostic approach

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Background & Objective: Skeletal dysplasias are a rare and heterogeneous group of diseases that affects the development or growth of the chondro-osseous tissues. Presently, more than 450 skeletal dysplasias grouped by clinical, radiographic and molecular criteria are described. This work presents a case of a 21 weeks fetus with prenatal suspicion of skeletal dysplasia.
Method: Routine second trimester ultrasonography of an uncomplicated pregnancy revealed a male fetus with large head, frontal bossing and flat small nose. The long bones were short with normal echogenicity. The pregnancy was terminated due to the suspicion of skeletal dysplasia.
Results: The autopsy showed macrocephaly, prominent eyes with increased outer intercanthal distance and small nose. The most prominent feature was the markedly short limbs. Radiological examination confirmed rhyzomelic micromelia and showed metaphyseal flaring and methaphyseal spurs. The spine demonstrated platyspondyly and the ribs were short with metaphyseal cupping. Histophatological examination of the femur growth plate revealed a grossly disorganized hypercellular growth plate, with no demarcation between resting and proliferative zones. Chondrocytes of the resting zone were spindle shaped and intercellular matrix showed interwoven fibrous septae. Diaphyseal and metaphyseal trabecular bones were normal. Molecular studies identified one single mutation on gene COL11A1.
Conclusion: The evidence leads to the conclusion that the fetus had fibrochondrogenesis, a severe chondrodysplasia. A single mutation on gene COL11A1 is not sufficient to support the diagnosis of fibrochondrogenesis. However, the diagnosis is maintained by radiologic features and definitely confirmed by the unique histopathologic pattern. Genetic confirmation would however have been useful to improve genetic counselling.

PS-18-014
Adenoid cystic carcinoma of the lacrimal gland: a rare paediatric case

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Background & Objective: Adenoid cystic carcinoma (ACC) is the most common primary malignant tumour of the lacrimal gland. It generally presents in middle-aged adults with a mean age of 40 years. ACC of lacrimal gland is rare in children, however some cases of this tumour in children are described in literature.
Method: We reported an unusual case of lacrimal gland tumour for paediatric patient.
Results: A 12-year-old boy complained of nausea, vomiting, pain and tearing in right eye for the last three days, as well as exophthalmos for the last week. During physical examination the right eyelid was painful and exhibited a characteristic S -curve drooping like in case of dacryoadenitis. Magnetic resonance imaging revealed a smoothly contoured inhomogeneous, contrast enhancing mass lesion in the lateral corner of right orbit 3x2,2x2,5 cm in size. The radiological diagnosis was dermoid cyst, however radiologically diagnosis was not completely clear and histological investigation was recommended. Histological examination of surgically removed tumour showed cribriform (Swiss cheese) structures composed of basaloid cells with scant cytoplasm and small angulated hyperhromatic nuclei typical for adenoid cystic carcinoma. There was invasion of tumour cells in blood vessel wall and resection margins. The cells expressed CK7, CKAE1/AE3, S100, aktin, vimentin un GFAP according epithelial and myoepithelial differentiation of this tumour. The Ki67 labelling index was 30%
Conclusion: Although rarely, encountered ACC should be considered in the differential diagnosis of lacrimal gland neoplasms in paediatric patients. The correct diagnosis is especially important because of malignancy and high risk of intracranial extension of this tumours.

PS-18-015
Congenital syphilis resurgence: autopsy findings in the 21st century
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Background & Objective: A trend towards the resurgence of congenital syphilis (CS) has been noticed worldwide. Penicillin treatment is highly effective in the treatment of gestational syphilis, but lack of proper preventive measures, screening and treatment may occur, perpetuating CS in the 21st century. Furthermore, although CS is an ancient disease, detailed reports of its histopathological findings are still lacking, including the direct assessment of the pathogen provided by the novel immunohistochemical stains.
Method: Herein we describe a generalized interstitial inflammatory syndrome caused by Treponema pallidum, which was detected in high quantities in the affected organs.
Results: A premature female neonate with 32 weeks of gestational age was referred to the autopsy service of the University of São Paulo. The mother was 15 years-old and had a serum VDRL of 1:128. The neonate weighed 2100g, measured 40.0cm and had no gross malformations. There were petechiae in the skin and serosal surfaces, and the liver and the spleen were enlarged. Microscopic exam demonstrated a generalized interstitial inflammatory syndrome involving the lungs, liver, spleen, kidneys and bones. The liver presented loss of the lobular architecture, foci of hepatocyte necrosis and microabscesses. The lungs exhibited diffuse suppurative pneumonia. Immunohistochemical studies for Treponema demonstrated numerous spirochaete in the renal and pulmonary interstitium, osteochondral junction and splenic sinusoids. In the liver, the spirochaete were diffusely found in the sinusoids, with a higher concentration in microabscesses.
Conclusion: Congenital syphilis is resurging and should be included in the differential diagnosis of multiorgan inflammatory reaction observed in deceased concepts/neonates at the autopsy room.

PS-18-016
Alveolar capillary dysplasia in a newborn: a case study
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Background & Objective: Alveolar capillary dysplasia is diagnosed during an autopsy in 90% of cases, and the presence of malformations in other organs can help a pathologist with a diagnosis.
Method: We conducted a retrospective analysis of the undiagnosed alveolar capillary dysplasia in a newborn
Results: A full-term female newborn, weighing 3000 grams, with a body length of 50 cm, was born with an Apgar score of 7, 8. Two hours after birth, the child's condition has progressively worsened (from severe to extreme due to cyanosis). The patient started receiving artificial ventilation which was followed up by a cardiac arrest. The newborn lived for 27 hours and 55 minutes. The postmortem diagnosis included intraventricular hemorrhage (IVH)(?), congenital heart disease and defects(?), and congenital anomalies of the kidney and urinary tract (duplicated collecting system). Alveolar capillary dysplasia was diagnosed during the histological examination, as well as congenital lung malformations and congenital brain malformations. The autopsy allowed to confirm a duplicated collecting system.
Conclusion: Thus, the morphological study allowed to establish the cause of progressive respiratory failure and ineffectiveness of therapeutic measures. The peculiarities of the case include the congenital brain malformations found during the autopsy.

PS-18-017
Disturbancies in the balance of vasoconstrictors and vasodilatators in maternal blood plasma in the preeclampsia genesis
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Background & Objective: The aim was to estimate renin, angiotensin II(1-8), angiotensin(1-7) and copeptin (pre-vasopessin or arginine-vasopressin) in pathogenesis of early-(EPE) and late-onset preeclampsia(LPE)
Method: The study included 69 pregnant women of reproductive age at 28-40 gestation weeks (wg): 12 patients suffered from EPE, 17 women–LPE. The control groups consisted of 30 patients with normal pregnancy after 34 wg (NP); and 10 with preterm labor up to 33wg (PL).
Results: The vasoconstrictor angiotensin II (1-8) level in EPE group was significantly higher (23,8±5,1pg/ml) compare to PL group (9,7±1,2pg/ml;p<0,05). In LPE and NP groups angiotensin II (1-8) was (15,5±1,2pg/ml and 14,7±1,9pg/ml, respectively; p>0,05). Vasodilator angiotensin (1-7) level in EPE group was significantly lower than in PL (379,7±23,0 pg/ml, and 771,7±44,2 pg/ml, respectively;p=0,0001), but in cases of LPE and in NP angiotensin (1-7) level was 388,3±27,3pg/ml and 390,7 ±13,9pg/ml, respectively;p>0.05). Copeptin concentration was significantly higher in EPE group than in PL (365,6±73,5pg/ml and 96,3 ±15,3pg/ml, respectively; p=0,02) and it increased in LPE than in NP group (421,2±75,5pg/ml and 276,3±58,6pg/ml; p=0,04).
Conclusion: Thus, increase in angiotensin II (1-8) production and copeptin against of insufficient increase in angiotensin (1-7) production in cases of preeclampsia may be an important pathogenesis mechanism.

PS-18-018
Nefroblastoma: experience of a center, a retropsective study with clinical-pathological correlation
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Background & Objective: Nephroblastoma is a malignant embryonal neoplasm, that affects 1:8000 children, without sex predilection, and 90% are diagnosed before the age of 6years. Most cases are sporadic.
Method: Retrospective study of nephroblastomas diagnosed over a period of 12years (2004-2016): 13 patients, median age of 3.84years

(0months-20years), 7M:6F, being one case congenital. Nephroblastomas had a median size of 8.56cm (4.5-17), equally common in both kidneys, and 1 bilateral case. 11 patients were submitted to radical nephrectomy and 2 to partial. Patients were staged using Cancer Protocol from College of American Pathologists.
Results: After a median follow-up of 110.3 months, the overall survival (OS) was of 92.3% at 5-years, and a median disease-free survival (DFS) of 7.86years: one patient had local recurrence and two had pulmonary metastasis. 8 patients were submitted to adjuvant chemotherapy, 4 had neo ad adjuvant chemotherapy and only 1had no adjuvant therapy. 6 tumours were confined to the renal parenchyma, 4 extended to the renal capsule and 3 into adjacent organs. 7 cases had favourable histology, 2 had diffuse anaplasia, and regarding those with neoadjuvant therapy: 1 had low risk, 2 intermediate risk and 1 high risk. 10 cases had vascular invasion and only 1 had positive surgical margins. 7 patients were in stage I and 6 in III. 2 patients died during follow-up period.
Conclusion: Nephroblastomas are very sensitive to combined therapy, especially those of low stage. Although we have some cases with high stage, the OS remains high, as well as, the DFS, probably consequence of an adequate therapy.

PS-18-019
Chemokine expression is involved in the vascular neogenesis of Ewing sarcoma: the early stages of angiogenesis in three xenograft experiments
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Background & Objective: Ewing sarcoma (EWS) is the second most common bone cancer in paediatric patients. Angiogenesis is one of major factors for tumour growth and metastasis. Our aim was to carry out a histological, immunohistochemical and molecular characterization of the neovascularization established between xenotransplanted tumours and the host during the initial stages of growth in nude mice in three angiogenesis experiments (ES2, ES3 and ES4).
Method: The original human EWS were implanted subcutaneously on the backs of three nude mice. Tumour pieces 3-4 mm in size from early passages of Nu432, Nu495 and Nu471 were also implanted subcutaneously on the backs of three sets (ES2, ES3 and ES4) of athymic Balb-c nude mice (n=14 each). The animals were sacrificed 24, 48, and 96 hours; and 7, 14, 21 and 28 days after implantation to perform histological, immunohistochemical and molecular studies (neovascularization experiments).
Results: We studied histological, ultrastructural and immunohistochemical changes in the xenografted tumour at different times after implantation. Chemokine ligand expression peaked twice; once during the first 48h and again in the second week. We observed that tumour cells in contact with murine peritumoural stroma presented higher expression of chemokine ligands as well as more tumour cells around the capillary vessels.
Conclusion: Chemokines and other angiogenic factors have a relevant role in the angiogenic mechanism during tumour growth. This model could provide information on the early stages of the angiogenic process and could be a useful tool for using anti-angiogenic drugs for new therapeutic strategies in EWS.

PS-18-020
Post-transplant lymphoproliferative disorder in paediatric patients. Review of 20 cases diagnosed in a university hospital
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Background & Objective: Post-transplant lymphoproliferative disorder (PTLD) develops in solid organ (SOT) or bone marrow recipients (BMT). WHO 2017 classifies them into: non-destructive PTLD (plasmacytic hyperplasia (PH), mononucleosis-like (ML) and florid follicular hyperplasia), polymorphic PTLD, monomorphic PTLD and Classic Hodgkin lymphoma PTLD. PTLDs are associated with Epstein Barr virus infection (EBV). Monomorphics behave as lymphomas being monoclonal to B- or T-lymphocytes, while the others may be polyclonal or monoclonal.
Method: Vall d'Hebron University Hospital Paediatric PTLD's clinical histories and biopsies were reviewed.
Results: We found 20 cases (4 months-18 years old). 16/20 were found in SOT (7liver, 7kidney, 1lung and 1heart) and 4/20 in BMT. 10/20 were polymorphic, 7/20 monomorphic (diffuse large B-cell lymphoma (DLBCL)) and 3/20 non-destructive (1ML and 2PH). 11/20 have monoclonal B-cells: 2/10 polymorphic, all (7/7) DLBCL and 2/3 non-destructive (HP and ML). 14/20 were EBV+. 13/14 were diagnosed before 2 years post-transplant (2-23months). 6/10 polymorphic, 6/7 DLBCL and 2/3 non-destructive were EBV+. All EBV- were diagnosed later (3-13 years), 5/6 on kidney TOS. 1 polymorphic received no treatment and 4 required a decrease in immunosuppression: 3polymorphic and 1HP. 15 received rituximab: 6 polymorphic, all DLBCL and 2 non-destructive. Furthermore, 3 DLBCL needed chemotherapy. 1 DLBCL died of disease's dissemination.
Conclusion: In our series, PTLD developed mostly in TOS (80%) and polimorphic was the most frequent subtype (50%). Most were associated with EBV (70%) and developed early (<2 years post-transplant). Histological subtype define the best treatment.

PS-18-021
Paediatric non-Wilms kidney malignancies
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Background & Objective: Paediatric non-Wilms renal malignancies are rare and heterogeneous representing 7% of primary renal tumours in children. Our aim is to study clinical data and histopathological features of paediatric non-Wilms renal malignant tumours (NWRMT).
Method: Pathological reports of 13 cases of paediatric NWRMT diagnosed at our department between 2000 and 2015 were retrospectively reviewed.
Results: Our case series included 7 male and 6 female patients. Mean age was 5 years and 6 months [6 months-14 years old]. Tumour mean size was 73 mm. The final diagnosis was made in radical nephrectomy in 12 cases and in biopsy in one case. Histological groups included clear cell sarcoma (38%), renal cell carcinoma associated with Xp11 translocation (31%), rhabdoid tumour (23%) and Ewing sarcoma (8%). Distant synchronous metastases involving the liver, the ovaries, the bone and the nervous system were reported. Neo-adjuvant chemotherapy was administrated in 2 cases.
Conclusion: The most common NWRMT are clear cell sarcoma, rhabdoid tumour and renal cell carcinoma associated with Xp11 translocation. These categories have different peak incidences with renal cell carcinoma occurring in the late childhood and rhabdoid tumour usually occurring in infants under 1 year of age.

PS-18-022
A rare presentation of alveolar rhabdomyosarcoma with multiple subcutaneous nodules: a case report
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Background & Objective: Rhabdomyosarcoma (RMS) is a soft tissue neoplasm that usually arises in the head and neck region and genitourinary tract. Rarely, RMS may initially present as skin nodules or skin nodules metastases mostly in early years of life.

Method: A 15 months old male patient presented with pruritus and acholic gaita for one week. General physical examination was painful swelling in the left forearm and left thigh. Firstly, the mass in the arm was diagnosed as hemangioma by ultrasound. MRI showed heterogeneous multiple nodular lesions, involving skeletal muscles of all his body parts. A tru-cut biopsy was performed for histological analysis of the swelling on the left forearm.
Results: Histopathological examinations revealed the tumour composed of small, round, blue cells with clear cytoplasm, forming layers resembling pulmonary alveoli. Immunohistochemistry was diffusely positive for desmin, myogenin, and myo-D1, negative for leukocyte common antigen (LCA), CD99, chromogranin, CD34, S-100, confirming a diagnosis of alveolar rhabdomyosarcoma. Fluorescent in situ hybridization (FISH) analysis was performed on this biopsy confirmed the presence of FOXO1 gene rearrangement.
Conclusion: Primary cutaneous rhabdomyosarcoma or cutaneous manifestation of rhabdomyosarcoma is extremely rare. Clinically, these tumours can be mistaken for hemangiomas. The differential diagnosis includes other malignant small round cell tumours. Cases with multiple cutaneous lesions are extremely rare and associated with a grim prognosis.

PS-18-023
Gastrointestinal stromal tumours in paediatrics. A clinical, histological and molecular study

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Background & Objective: Paediatric gastrointestinal stromal tumours (GIST) are rare in children and adolescents. They arise from the interstitial cells of Cajal or their precursors. Adult GISTs are characterized by mutations involving genes KIT or PDGFRA. Seven cases of paediatric GIST were included (1987 to 2017) to analize the histological, immunohistochemical, and molecular features.
Method: DHPLC (Denaturizing High-Pressure Liquid Chromatography) and direct sequencing were performed searching for mutations in KIT (exons 9, 11, 13 and 17) and PDGFRA genes (exons 12, 14 and 18). Clinical charts were reviewed.
Results: There were three girls and four boys, age range: 5-188 months. Five tumours raised in the stomach and two in the jejunum. Sizes: 0.5 to 8 cm. The histological patterns were: spindle (2), epithelioid (2) and mixed (3). Immunostains were positive for SMA and CD34, and negative for S100. Five cases expressed CD117. SDH-B expression was negative in the only case it was performed. Six cases were wild type for mutations and 1 case had a deletion in exon 11 of the KIT gene. Clinical risk was assessed as: low (4), intermediate (1), and high (2). One patient was metastatic at diagnosis. The remaining six patients are free of disease with a follow-up of 1-18 years. One patient had a family history of achalasia and another one developed a pulmonary chondroma.
Conclusion: Accordingly, with reported literature this small series of paediatric GIST cases sustains the possibility of a syndrome association in a very infrequent tumour and supports the absence of usual genetic alterations.

PS-18-025
Nephrogenic adenoma of the urinary bladder in childhood: a rare lesion

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Background & Objective: Nephrogenic adenomas are benign tumourlike lesions within the urothelial mucosa of the urinary tract from the renal pelvis to urethra, with the highest frequency in urinary bladder. It is mostly seen in adults but approximately 10% of the nephrogenic adenomas were seen in children.
Method: A 5-year-old girl presented with recurrent urinary tract infections. Antireflux surgery at the age of 2 years was remarkable in medical history. Ultrasound scan of the urinary tract demonstrated small papillary lesions in bladder. Multiple small papillary tumours at the bladder base and the right lateral wall, were resected by cystoscopy.
Results: Histological section of biopsy of bladder lesions reveals broad papillary fronds with paucicellular stroma lined by layer of cuboidal epithelial cells with eosinophilic cytoplasm and uniform round nuclei. Immunohistochemistry was positive for pax-8, and pax-2, negative for gata-3. The histopathologic diagnosis was reported as a nephrogenic adenoma.
Conclusion: Nephrogenic adenoma is a rarely seen benign metaplastic lesion of the urinary tract, induced by chronic inflammation, irritation, and trauma. It is important to distinguish benign nephrogenic adenoma from other mimickers that commonly occur in the paediatric population, such as rhabdomyosarcoma, fibroepithelial polyp, papillary/polypoid cystitis, and urothelial neoplasms, in order of frequency.

PS-18-026
Ewing sarcoma with ERG gene rearrangements. Difficulties in detection using Fish techniques

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Background & Objective: Complex pattern of t (21;22) in Ewing Sarcoma (ES) constitute potential pitfalls on FISH. To analyze clinical, histological, and molecular features of ES with ERG gene rearrangements and to compare different strategies for using FISH techniques in the diagnosis.
Method: A retrospective study was conducted of 78 cases diagnosed as ES and confirmed by RT-PCR and sequencing in paraffin blocks over the past 27 years. Interphase FISH was performed to detect 22q12 (EWSR1) rearrangement. Cases that were negative but had a EWSR1-ERG gene fusion, were reassessed using FISH with a EWSR1-ERG dual-color break-apart probe.
Results: Among the 78 cases included in the study, EWSR1-ERG (12%) fusion transcripts were found in 10 by PCR. The FISH break-apart strategy detected EWSR1 rearrangements in 6/10, while the dual color, dual fusion strategy detected the rearrangements in all 10 cases. Six cases (6/10) were girls with a mean age of 6 years (range, 1-10 years) and the most common tumour location was in the bone (8/10). The histological findings showed patterns of nodular growth arranged in solid nests. In three cases mixoid stroma was observed. All cases showed diffuse positivity of the membrane with CD99.
Conclusion: Our results emphasize the possibility of false negatives in the search for EWSR1 gene rearrangements using FISH in ES with ERG rearrangements in tissue materials including paraffin blocks as the standard do not detect this type of complex rearrangements. These results suggest the need to add this type of probe to the diagnostic algorithm.

PS-18-027
16-year-old female with oesophageal and colorectal leiomyomatosis: a case report

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Background & Objective: We report a case of leiomyomatosis that involved the oesophagus and colon. Combined leiomyomatosis is very rare lesion, and we're required to have regard to the such cases in routine practice.
Method: 16-year-old girl from an early age suffered from constipation, with history of constipation during 7 days before hospitalization in 2016.

The study revealed tumour-like formation of the rectum with lesions throughout the circumference. The patient underwent colostomy, and biopsy showed leiomyomatosis of the colon wall. In 2017 the new symptoms appeared: indomitable vomiting, dysphagia and the patient had admitted in our hospital again. The examination revealed a sharp thickening of oesophagus wall throughout. It was decided to remove the oesophagus with subsequent plastic surgery. On gross examination, the oesophagus wall was irregularly thickened up to 4 cm. Histologically, the lesion was characterized by diffuse tumour masses that consisting of intricately arranged elongated cells in the location of the muscle layers.
Results: Immunohistochemical analysis showed diffuse positive staining with SMA, Desmin and negative S100, EMA, CD117, CK, Ki-67 less than 5%. Thus, we excluded GIST and confirmed leiomyomatosis.
Conclusion: By reviewing the literature, we found just a few reports, described diffuse leiomyomatosis of the oesophagus and the colon. This lesion is very rare, but in practice it's necessary to pay attention to young patients with prolonged unexplained constipation and remind about combination colon lesion with other parts of GI system.

PS-18-028
Review of generalised arterial calcification of infancy: about a case
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Background & Objective: Generalized Arterial Calcification of Infancy (GACI) is a rare neonatal genetic disorder which means a diagnostic and therapeutic challenge. The aim of the present poster is to make a review of it, including clinical, histological and molecular features.
Method: We present a case of a 35-36 week gestation newborn male child, with non-immune hydrops, widespread cyanosis, heart enlargement and no familiar pathological history. Complete necropsy was made. We studied paraffin-embedded tissue and mother´s blood was analyzed in order to correlate pathological and molecular findings.
Results: On microscopic examination, coronary arteries, aorta, pulmonary hilum and kidney main artery showed subendothelial calcification and fibrous intimal proliferation. Inflammation was not a prominent feature. The mother`s blood molecular study found mutation in ENPP1 gene. We are still waiting for the results in child`s paraffin-embedded tissue.
Conclusion: GACI is a rare autosomal recessive congenital disease which is usually related to mutations in ENPP1 gene (6q22-q23). It should be suspected when echogenic arterial calcification, cyanosis, non-immune hydrops and an association to a consanguineous partner is known. Autopsy study is the gold standard, which reveals foci of subendothelial calcification and fibrous intimal proliferation mainly in aorta and coronary arteries. Our case fits in with all the previous items.

PS-18-029
Mesoblastic nephromas - a short series of three cases
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Background & Objective: Mesoblastic nephroma was first described as a distinct entity by Bolande et al. in 1967, when they redefined the previously named leiomyomatous renal hamartoma and infirmed its relationship with Wilms's tumour. In spite of the rare occurrence (3 – 10% of all paediatric renal tumours), mesoblastic nephroma is the most common renal tumour diagnosed in newborns and infants.
Method: We analyzed 3 cases of mesoblastic nephromas diagnosed in the Pathology Department of Children's Emergency Hospital "St. Mary" Iasi, Romania, in the last 20 years (1999-2018).
Results: The 3 cases differed in age at presentation, imaging characteristics, and histological features. All children were males, aged between 1 and 4 months. All cases were clinically presented as malignant tumours. The macroscopic examination revealed tumour tissue with several areas of necrosis, hemorrhage and cystic changes. The histopathological examination showed a cellular type of mesoblastic nephroma in two cases (with more aggressive behavior), and a mixture between cellular and classic type in another case.
Conclusion: Mesoblastic nephroma is a rare and challenging diagnosis, due to its microscopic similarity with other stromal tumours of the kidney. The pathologic examination of the post-nephrectomy kidney specimens is compulsory for the final diagnosis that guides the appropriate treatment, according to the histological type.

PS-18-030
Malignant ossifying fibromyxoid tumour with multiple recurrences in a child
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Background & Objective: Ossifying fibromyxoid tumour (OFMT) is a rare mesenchymal neoplasm with possible long preoperative disease duration. It has a peak incidence in the fifth decade, with a wide age range including paediatric cases. The most common sites of involvement are shoulder, buttock, and thigh; less frequently head&neck, and trunk. OFMT has the potential for delayed recurrence (10-20 years after surgery). Rare malignant variants are defined by high nuclear grade or high cellularity and >2 mitosis per 50 HPFs. In Folpe series, 15% of cases (mainly atypical lesions) had metastases.
Method: We present the case of a 6-year-old boy with a posterior cervical mass that was resected and recurred four times during the following 2 years after initial surgery.
Results: We received five nodules immersed in subcutaneous soft tissues from 3 different surgeries. Their size ranged from 1 cm to 3,2 cm and most of them contacted with the resection borders. They appeared as well-circumscribed nodules with focal peripheral lamellar bone and partially lost fibrous capsule with more infiltrative growth. They were composed of uniform-appearing, small round to polygonal-shaped cells embedded in a myxohialine to collagenous matrix without recognizable pattern of distribution. There were highly cellular nodules with necrosis, hyperchromatic nuclei and 18 mitosis per 50 HPFs.
Conclusion: OFMT is a rare S100 protein-positive mesenchymal tumour that appears to have low-grade malignant potential with 27% local recurrence rate. Malignant OFMT should be identified due to its metastatic potential. The presented case is the only one collected in our laboratory in 20 years.

PS-18-031
Central nervous system pathology as a cause of legal termination of pregnancy
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Background & Objective: Letal terminations of pregnancy (LTP) are performed in our hospital due to fetal malformations detected by ultrasound or genetic testing, and clinical autopsy is requested to confirm the prenatal diagnosis. The cause of many of them is an involvement of the central nervous system (CNS), exclusively or in the context of a polymalformative syndrome.
Method: We reviewed the casuistry of our center in the last three years, collecting the LTP with CNS involvement.
Results: Between April 2014 and April 2017, 468 LTP were carried out in our center. In 122 of them (26%), CNS pathology was the cause. The most frequent pathologies were: neural tube defect (with or without

Arnold-Chiari malformation, including anencephaly, 37.7%), corpus callosum agenesia (13.1%), holoprosencephaly (8.2%), ventriculomegaly (7.4 %), Dandy-Walker complex (7.4%) and infections (cytomegalovirus, toxoplasma, 7.4%). In 6.5% of the autopsies the autolysis effect prevented a proper diagnosis and prenatal data could not be confirmed.
Conclusion: CNS pathology is a frequent cause of LTP, and the most prevalent pathology must be known. In a majority of cases the final diagnosis is macroscopic. However, the manipulation of these brains and together with the autolysis artifact prevent the confirmation of the prenatal imaging diagnosis.

PS-18-032
Perinatal lethal osteogenesis imperfecta (type 2) in a 18 weeks gestation: an autopsy findings and literature review
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Background & Objective: Osteogenesis Imperfecta (OI) is a group of clinical and genetically (disorder of collagen synthesis) heterogeneous diseases characterized by susceptibility to bone fractures with variable degree of severity. The incidence of different types of OI is approximately 1 in 15000-20000 birds, and 90% of patients with OI are heterozygous for mutations in the COL1A1 and COL1A2 genes.
Method: Fetus of 18 weeks gestation with ultrasonographic, macroscopic, microscopic and genetic findings, characteristic of OI and comparison of these with a normal fetus of the same gestational age.
Results: Fetus of anthropometric measurements inferior to gestational age, with shortening and widening of extremities and thoracic narrowing. Histologically, a serious defect of generalized ossification, fractures and alterations in osteocartilaginous joints is observed. In the genetic study performed by amniocentesis, a type 2 OI was diagnosed: lethal, and none of the parents were shown to be genetically carriers.
Conclusion: OI is a hereditary disease of type I collagen synthesis with an estimated incidence very low at birth. OI was classified into four groups (I-IV) with subgroups, according to criteria established by Sillence et al. based on clinical findings fundamentally. Nowadays, the OI is classified into 9 types according to genetic, clinical and histological parameters. Type two is the most serious and causes perinatal death. The recognition of the clinical and ultrasonographic findings is fundamental to guide an accurate diagnosis of the disease and the appropriate therapeutic attitudes according to the case

Tuesday, 11 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-19 | Soft Tissue and Bone Pathology

PS-19-001
KIT mutation status in gastrointestinal stromal tumours in Sudanese patients
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Background & Objective: Mutational analysis is highly important for definitive diagnosis and better treatment choice for Gastrointestinal Stromal Tumours' (GISTs) patients. This study aimed at determining the KIT mutation status of GISTs in Sudanese patients.
Method: A cross-sectional study conducted on all patients referred to GIST Clinic at (January 2014 to December 2015). Twenty-nine tissue blocks were examined - in a morphology-guided pattern- for the presence of mutations in the relevant host spot regions in the juxta-membrane domain of the KIT gene (exon 11). In addition, 21 were also examined for mutations in the extracellular domain (exon 9) using Polymerase Chain Reaction. Mutational analysis was performed using direct sequencing (pyrosequencing).
Results: KIT was successfully assessed in 23/29 cases; 48.3% were males (mean age, 53.72 ±12.86; range, 28-73). 14/19 cases (73.68%) were exon 11 mutation-positive and five were wild-type. Three out of the five exon 11 mutations that were examined for exon 9 mutations as well were wild type for exon 9 confirming mutually exclusive nature of these mutations. The majority of exon11 mutations clustered in the proximal region of the exon at codons 553-560 and only two tumours harbored a distally located mutation at L576del. Two exon 9 mutations have been detected in the sub cohort (19) with successful molecular testing (10.53%).
Conclusion: Sudanese patients with GIST do express mutations in line with the well-known mutually exclusive nature of exon 9 and exon 11 mutation in Imatinib-naive GISTs. The overall KIT mutation is 84.21%.

PS-19-002
Diagnostic value of TFE3 break-apart FISH assay for Xp11,2 translocation in alveolar soft part sarcoma
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Background & Objective: Alveolar soft part sarcoma (ASPS) is an uncommon neoplasm. ASPS has specific histological appearance, but unspecific immunophenotype. ASPS has ASPL-TFE3 gene fusion as a result of unbalanced translocation der (17) t(X;17) (p11;q25) or rarely a balanced translocate on t(X;17). Translocations involving TFE3 lead to characteristic overexpression in tumour cells, but this same gene fusion has been found in an unusual variant of paediatric renal cell carcinoma and MiTF subfamily of neoplasms. Aim: To exam diagnostic value of TFE3 break-a part FISH assay to confirm Xp11 translocation in ASPS.
Method: Twenty-three primary and metastatic ASPS were obtained from the Institute of pathology Medical faculty University Belgrade. All of them were immunohistohemically stained for TFE3. Nuclear staining was considered as positive. TFE3 FISH was performed using a dual-color break apart probe labeled in Texas Red and FITC.
Results: Immunohistochemical analysis showed 17/23 (74%) positive ASPS for TFE3, and 6 (26%) negative cases. All cases were evaluated for a TFE3 gene rearrangement. By FISH analysis 22/23 (96%) cases were positive for TFE3 rearrangement and 1 (4%) was negative. We confirmed correlation in 16 (70%) cases that were positive by both methods. Immunohistohemically negative cases were confirmed by FISH, and one case was FISH negative, but immunohistohemically positive for TFE3.
Conclusion: We confirmed a TFE3 break a part FISH assay as highly sensitive and specific test for detecting Xp11.2 translocation in ASPS. It can be utilized as an adjunct to morphology and immunohistochemistry to diagnose ASPS from other TFE3-positive neoplasms.

PS-19-003
Malignant transformation of a granular cell tumour of the hand
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Background & Objective: Granular cell tumours (GCT) are rare neoplasms of presumed neural origin, composed of cells with abundant granular cytoplasm. They are commonly found in skin and subcutaneous tissue of the head and neck region, being unusual in the extremities. GCTs are more frequent in women, presenting as solitary, slowly growing, painless nodules. Although they are usually benign, having excellent prognosis, approximately 0.5-2% have been reported as malignant, metastasizing in up to 50% of cases. Fanburg-Smith criteria have been used to classify GCTs as benign, atypical, or malignant.
Method: We present the case of a 71-year-old woman with an 85x75x70 mm soft tissue mass in her left hand.
Results: The mass had been first noticed in the year 2000; then, it was a 20x15x15 mm nodule. A biopsy was performed, obtaining a cylinder

with histological features suggestive of benign GCT. Follow-up was carried out for the next years, with no significant changes. 16 years later, the patient stated that the nodule had grown in the last two years; at that moment, it limited the second metacarpophalangeal joint flexion. Another biopsy was performed, with histological features suggestive of malignant GCT. After elective wrist disarticulation and local lymphadenectomy, pathology reported perineural and lymphovascular invasion, with lymph node metastases. Follow-up with full-body CT showed lung metastases, with fatal outcome nine months after surgery.
Conclusion: There are few published case reports describing the potential of benign GCTs for malignant transformation; we have not been able to find another case depicting this transformation in the extremities.

PS-19-004
Bone metastases – 10 years clinicopathologic experience
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Background & Objective: Bones are the third most frequent site of metastases which are radiologically characterized as osteolytic, osteosclerotic and mixed. The aim of this study was to make clinicopathologic characterization of the patients with bone metastasis (BM) and to correlate osteoblastic and osteoclastic activity with the metastasis type.
Method: We analyzed 80 patients with BM who underwent surgical therapy, for demographic data, radiological types, primary tumour, localization, pathological fracture and survival. Microscopically, we analyzed 10 high power fields of the densest metastatic deposition areas. We used semi-quantitative method to determine the density of bony trabeculae osteoblast rimming and the osteoclasts' density in Howship's lacunae, categorizing it as mild, moderate and high. Similarly, we determined the thickness of the trabeculae and osteoid.
Results: There were 55 osteolytic, 11 osteosclerotic and 14 mixed metastases. The commonest primary site for osteolytic metastases was the mammary gland and for osteosclerotic was the prostate gland. The most affected bone was the femur. Pathological fracture was present in 49 patients. The mean survival time was 16,42 months. The density of osteoclasts was significantly higher in osteolytic metastases ($p<0,01$), the density of osteoblastic rimming was non-significantly higher in osteosclerotic metastases, and the bony trabeculae and osteoid were non-significantly thicker in osteosclerotic metastases. Mixed MS showed prevalence of one or other type of activity without significant difference. There was significant correlation between the radiological and histological findings ($p<0,05$).
Conclusion: We found that the histological pattern of bone reaction correlates to the radiographical findings and the osteoclastic was the main activity in BM.

PS-19-005
Clinicopathological and immunohistochemical characterisation of liposarcomas – five years experience at a tertiary care centre
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Background & Objective: Liposarcoma is the most common soft-tissue malignancy (20%). They are divided into four subgroups exhibiting divergent clinical behaviour, morphology, genetic alterations, prognosis and management. This study aimed at analysing these differences along with immunohistochemical characteristics of various subtypes.
Method: Five years cross-sectional study was undertaken wherein cases diagnosed as liposarcoma were included. Details about clinical presentation, site, AJCC stage and radiological findings were collected. All cases were reviewed for identification of histomorphological features and FNCLCC grade. Immunohistochemical analysis was done using MDM2, S100 and Ki-67 immunostains. Statistical analysis of collected data was performed using SPSS-17 software.
Results: Among thirty cases studied, well-differentiated liposarcoma (WDLPS) was most common (n=13;43.3%), followed by myxoid liposarcoma (MLS) (n=7;23.3%), pleomorphic liposarcoma (PLS) (n=6;20%) and dedifferentiated liposarcoma (DDLPS) (n=4;13.4%). Mean age of patients was 55 years with equal gender distribution. Most patients (80%) presented with a mass, lower extremity was commonest site (40%) and mean duration of symptoms was 22.6 months. Nuclear pleomorphism, myxoid change, vascular pattern and dedifferentiation helped in histomorphological distinction. FNCLCC grade in most WDLPS cases was one, MLS was two and PLS and DDLPS was three. Tumour stage was lower (IA, IB) in WDLPS whereas higher (II onwards) in other subtypes. MDM2 was positive in WDLPS and DDLPS. S100 highlighted the lipoblasts and Ki-67 index was highest in PLS.
Conclusion: Careful analysis of histomorphology and correlation with immunohistochemistry (MDM2, S100 and Ki-67) is the key to distinguish liposarcoma subtypes and eliminate the differentials. WDLPS present with lower tumour stage and grade while other subtypes are more aggressive.

PS-19-006
Hybrid schwannoma/perineurioma is subclassified into mixed cellular and combined tumour types
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Background & Objective: Hybrid schwannoma/perineurioma is defined as a benign peripheral nerve sheath tumour with combined features of schwannoma and perineurioma. To further clarify the characteristics of this rare tumour, ten cases were pathologically studied.
Method: The ages of the ten patients ranged from 13 to 77 years and six were females. Seven tumours arose in the extremities, two in the trunk and limb girdle, and one in the mediastinum. The sizes ranged from 10 to 137 mm. Immunohistochemical studies were carried out using antibodies against S-100 protein, SOX10, EMA, claudin-1, GLUT1, CD34, neurofilament protein, and Ki-67. Double immunostaining for S-100 protein and EMA was also performed.
Results: The 10 cases of hybrid schwannoma/perineurioma were subdivided into two types: 1) mixed cellular type (nine cases) and 2) combined tumour type (one). The former demonstrated parallel, storiform, and whorl patterns, and was characterized by mixed proliferation of S-100 protein- and SOX10-positive Schwann cells, and EMA-, claudin-1-, and GLUT1-positive perineurial cells. The latter, a mediastinal tumour, had two distinct components: schwannoma and perineurioma. Nodular perineurioma areas characterized by onion bulb structures were included in schwannoma areas, which were a principal component. Immunostaining also supported the cellular lineage of each component.
Conclusion: There were two types of hybrid schwannoma/perineurioma: one with mixed proliferation of Schwann cells and perineurial cells, and a combined schwannoma and perineurioma tumour. It may be reasonable to designate the former as a hybrid Schwann cell/perineurial cell tumour, because they do not present typical schwannoma and perineurioma features.

PS-19-008
Retrospective study of bone tumours diagnosed as chondroblastomas: radiological diagnosis, histological confirmation and evolution over time
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Background & Objective: Chondroblastoma of the bone is a tumour classified as benign. It represents <1% of primary bone tumours and it has well-characterized radiographic and histologic features. We reviewed a

series of cases with the objective of knowing their characteristics at the time of the diagnosis, the index of recurrence and metastasis.
Method: Eight cases obtained from the database of the pathology departments of two spanish hospitals and diagnosed from 1993 to 2018.
Results: A total of 8 patients, 6 men and 2 women, aged between 11 and 57 years (average 29). All presented symptoms such as pain, joint effusion or mobility restriction, 3 were located in the femur; 3 with location unknown; 1 in the temporal and 1 in the first finger of the hand. Radiologically, they presented as lytic lesions with well defined sclerotic margins. The histological diagnosis was made in 5 excisional biopsies, 2 core needle biopsies and 1 unknown. All were composed of relatively undifferentiated, polygonal, pseudochondroblastic cells and multinucleated osteoclast cells were observed at the edges of the most differentiated areas. The treatment in all cases was curettage with bone grafting. In none of the cases has recurrence or metastasis been reported so far.
Conclusion: -In this series, the previously known clinical, radiological and histological characteristics are reaffirmed. -It is known that a small percentage could recur or metastasize at a distance, however, this was not observed in our series. -Chondromyxoid fibroma and giant cell tumour should be considered as the main differential diagnoses.

PS-19-009
Expression of fibroblast growth factor receptor1 (FGFR) in soft tissue sarcomas is associated with poor prognosis regardless of tumour subtypes
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Background & Objective: The oncogenic role of the fibroblast growth factor receptor (FGFR) has recognized and altered FGFR family members has emerged as therapeuric target in epithelial malignancy. In contrast, the role of FGFR family members (FGFRs) in soft tissue sarcoma has not been established. In this study, we observed the expression of FGFRs in numerous soft tissue sarcoma and evaluated the clinical significance by immunohistochemistry (IHC) and the new technique of multiplex tissue immunoblotting (MTI).
Method: Tissue microarray (TMA) was constructed using 249 cases of soft tissue sarcoma from 2000 to 2015 at single institute of the Asan Medical Center. MTI and IHC with TMAs, and western blotting with cell lines for FGFRs were performed and analyzed clinicopathologic parameters
Results: Myxoid liposarcoma (24.2 %, and 19.6 %) were most commonly positive for FGFR1 and FGFR3, repectively, dedifferentiated liposarcoma (17.4 %) was most commonly positive for FGFR2, and malignant pheripheral nerve sheath tumour (14.6 %) was positive for FGFR4. FGFR1 ($p < 0.001$) and FGFR3 ($p < 0.001$) protein expression were correlated between IHC and MTI, but FGFR2 ($p = 0.265$) and FGFR4 ($p = 0.234$) protein expression were not correlated between two methods. FGFR1 overexpression showed poor prognosis regardless of subtype of sarcomas ($p = 0.022$, log- rank)
Conclusion: FGFR family members were differently expressed according to sarcoma subtypes, suggesting selective FGFR inhibitors should be applied based on the tumour subtypes. FGFR1 protein expression is one of the prognostic markers for poor survival.

PS-19-010
Angiomatoid fibrous histiocytoma: a challenging diagnosis. Report of three new cases
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Background & Objective: Angiomatoid fibrous histiocytoma (AFH) is an uncommon low-grade tumour which diagnosis might be challenging. We report three cases in paediatric patients.
Method: We collected three cases of AFH. Paraffin sections were stained with haematoxylin and eosin and immunostained using the Envision method (Dako, Glostrup, Denmark). FISH analyses were performed using a EWSR1 break-apart probe (SureFISH, Agilent).
Results: In case 1, a 10-year-old girl presented with a deep subcutaneous mass in her right knee, measuring 1,4 cm. Histologically, a fibrous pseudocapsule was present, with a prominent peritumoural lymphoplasmacytic infiltrate. The tumour showed a solid pattern, with multiple nodules, stromal hyalinization, and myxoid areas. Neoplastic cells were histiocytoid and spindled-shaped and were positive for CD99, and desmin. In case 2, an 11-year-old girl debuted with a mass in her right thigh, measuring 9 cm. The tumour showed histiocytoid cells intermingled with a prominent lymphoid infiltrate, hemosiderin deposit, pseudoangiomatous spaces surrounded by neoplastic cells, and a fibrous pseudocapsule. EWSR1 rearrangement study by FISH was positive in both cases. In case 3, a 13-year-old girl presented with a subcutaneous mass on her scalp, with similar histological features than case 2. FISH studies were negative in this case.
Conclusion: Angiomatoid fibrous histiocytoma is a challenging diagnosis that may show overlapping histopathological features with other soft tissue tumours. AFH is characterized by EWSR1 rearrangement, reflecting the EWSR1-CREB1 fusion gene. However, other fusion genes can be found, including FUS-ATF1 and molecular testing of non-EWSR1 rearrangements might be useful in atypical cases.

PS-19-011
High-grade endometrial stromal sarcoma: a clinicopathologic and molecular analysis of 17 cases from a single institution
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Background & Objective: High-grade endometrial stromal sarcoma (HG-ESS) is a rare uterine malignancy harboring in most cases a t (10;17) (q22;p13) resulting in YWHAE-NUTM2 fusion. The clinicopathologic and molecular features of 17 cases of HG-ESS were reviewed.
Method: Seventeen cases were retrieved and analyzed morphologically, immunohistochemically (CD10; cyclin-D1, ER, PR and BCOR) and molecularly.
Results: Fifteen cases were primary, two metastatic. Six cases were hypercellular, composed of high-grade round cells without intervening stroma. Prominent vascularization and necrosis were seen. All tumours showed a destructive growth. Mitoses ranged from 10 to 62/10 HPF. Neoplastic cells expressed diffusely cyclin-D1 and BCOR, and focally CD10, ER and PR. Ten cases were moderately cellular, composed of round cells associated with a more prominent stroma. A low-grade spindle cell component was present in half of cases. Vascularization was not prominent and necrosis was present in 3 cases. The growth pattern was infiltrative but not destructive. Mitoses ranged between 5 and 50/10 HPF. Expression of CD10, ER and PR was more diffuse. In one case the low-grade spindle cell component was predominant with dispersed high-grade neoplastic cells. One case featured striking pleomorphism. Fifteen cases harbored a YWHAE-NUTM2 gene fusion. In 3 cases molecular analysis was not informative. FISH analysis did not show JAZF1 gene rearrangements in low-grade areas.
Conclusion: HG-ESS may include a predominant low-grade component to the extent that high-grade areas may be overlooked. The YWHAE-NUTM2 gene fusion is present independently from the presence of low-grade areas.

PS-19-012
Are pathologic diagnoses of chondrogenic tumours of long bones decisive for orthopaedic treatment? – proposal of pathologic term of low grade chondrogenic tumour covering both enchondroma and atypical cartilagenous tumour
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Background & Objective: Diagnoses of the chondrogenic tumours occurring in the long bones are often challenging. Atypical cartilagenous tumours (ACTs) are not common tumour, and therapeutic guidelines do not always coincide among clinicians. Aim of this study was to investigate the possibility whether the pathologic term of "low grade chondrogenic tumour" could be applied for the ambiguous cases.
Method: A total of 36 cases including enchondroma or ACTs diagnosed in the St. Vincent Hospital, The Catholic University of Korea from 2005 to 2016 were used for this study. This study was based on the retrospectively collected data of patients' clinical, radiological and pathologic results. This study was approved by the Institutional Review Board.
Results: Of the 36 cases of this study, enchondromas were 20 and ACTs were 12. The rest 4 were left undecided. Diagnoses were changed from enchondroma to ACT in second biopsy in some cases. Humerus, femur and tibia were most commonly affected. Pretreatment radiologic diagnoses were various but mostly as enchondroma versus ACT. Treatment modalities were diverse not only for enchondromas but also for ACTs, although more aggressive treatments were done in a few cases of ACTs. The most common form of treatment was curettage with allogenic bone graft.
Conclusion: It seems like that orthopedic treatment for the chondrogenic tumours of the long bones could be affected by various factors and the pathologic diagnoses were not decisive for the orthopedic treatments. Therefore, for the ambiguous cases, it may be plausible to propose the term of "low grade chondrogenic tumour" which covers both enchondroma and ACTs, and in these cases more intimate clinical, radiological and pathological correlations may be needed.

PS-19-013
Skeletal and extraskeletal angiomatosis with Kasabach-Merritt Syndrome. Report of a case
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Background & Objective: Angiomatosis is general term employed to describe a spectrum of rare pathologic conditions characterized diffuse infiltration of bone, soft tissue and viscera by vascular channels filled with lymph or blood. We describe a case of paediatric angiomatosis with extensive skeletal and extraskeletal involvement, and consumption coagulopathy type Kasabach-Merritt syndrome (KMS).
Method: A 3-year-old boy presented with a one-month history of left lower limb pain and swelling of the ipsilateral knee. At birth, multiple haemangioma of the soft tissues of the scalp were identified, and a lesion consistent with pulmonary sequestration was detected at chest CT scan. MRI studies revealed multiple lesions of the left femur, with soft tissue extension, of the left tibia and the right femur. A surgical biopsy was taken from the left femur, which was reported as non-diagnostic. One week later the mother reported bleeding from the site of the biopsy. Blood tests demonstrated anaemia, thrombocytopenia and both decreased and consumption of coagulation factors, consistent with KMS.
Results: A new biopsy of the femur showed a proliferation of thin-walled, dilated blood vessels, in between the bony trabeculae, as well as in the cortical bone and in the adjacent soft tissues. The endothelial lining was devoid of atypia, and immunoreactive for CD31 and CD34, while podoplanin and GLUT1 were negative.
Conclusion: Distinction of skeletal angiomatoses as discrete entities is difficult and has led to an array of confusing conditions with similar appearances at histology, with variable involvement of skeletal and extraskeletal sites.

PS-19-014
Giant cell tumours of bone treated with denosumab: histological changes and H3.3 G34W expression
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Background & Objective: Giant cell tumour of bone (GCTB) is a locally aggressive primary bone tumour. Denosumab offers a new treatment option for selected cases of GCTB and causes significant histological changes in treated tumours. Recently, a monoclonal antibody specific for H3.3 G34W was proposed to support the diagnosis of GCTB. Our aim was to evaluate the impact of denosumab treatment on histological features and H3.3 G34W expression in GCTB.
Method: H3.3 G34W antibody (clone RM263; RevMAb Biosciences, San Francisco, CA) was used with Leica Bond 3 fully automated immunohistochemistry stainer for analysis of 14 specimens from 6 patients: 7 pre-denosumab GCTB (5 primary and 2 recurrent), 6 curettage post-denosumab (5 primary and 1 secondary malignant) and 1 relapse after curettage post-denosumab.
Results: All 6 post-denosumab specimens showed histological changes such as ossification, giant cell depletion, stromal fibrosis and inflammatory response. In addition, one case underwent sarcomatous transformation. Diffuse strong nuclear staining for H3.3 G34W was present in 6/7 pre-denosumab biopsies. In contrast, except for one case, the staining pattern was focal and/or weak after neoadjuvant therapy, including the secondary malignant GCTB. Of note, cases with histologic diagnosis of pathological complete response showed H3.3 G34W positive cells. Interestingly, the single case that kept the diffuse strong pattern was the only one that relapsed.
Conclusion: H3.3 G34W antibody is a new helpful diagnostic tool for GCTB, even after denosumab treatment. Additionally, this marker is useful in treated tumours to highlight neoplastic cells that could be unnoticed with Haematoxylin and Eosin staining.

PS-19-015
Myxoid liposarcoma: comparison of the histological response between Trabectedin and other neoadjuvant therapies in a series of nineteen cases
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Background & Objective: Neoadjuvant therapies in patients with advanced myxoid liposarcoma lead to different histological changes in the tumour. A new preoperative treatment option is trabectedin, which has improved survival rate. The aim of this study is to evaluate the tumour response to trabectedin, describe the histological changes induced by this drug, compare these results with other neoadjuvant options and correlate the round cell percentage with the viable tumour.
Method: We analyzed nineteen cases of myxoid liposarcoma treated with neoadjuvant therapy. We evaluated the age, gender, localization, percentage of round cells, presence of rearrangement of DDIT3 by FISH in the diagnostic biopsy and the histological changes postneoadjuvant in the resected specimen.
Results: 11 patients received preoperative trabectedin, 6 ifosfamide-epirubicin and 2 radiotherapy. In the diagnostic biopsy the percentage of round cells ≥5% was 63%. Sixteen patients had DDIT3 and/or FUS rearrangement. The response of trabectedin was 81,8% of hyalinization/necrosis and 66.6% was mature adipocytes. In the other treatments the principal response was hyalinization/necrosis 87,5% and mature adipocytes 75%. The percentage of residual tumour in patients with round cell component ≥5% was 5,8% in 5 patients with trabectedin, 2,1% in 6 patients with ifosfamide-epirubicin and 70% in one patient with radiotherapy.
Conclusion: Trabectedin presented changes according to literature. Trabectedin and ifosfamide-epirubicin have similar histologic changes. The principal response was hyalinization/necrosis and secondarily mature adipocytic change.

Wednesday, 12 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-20 | Digestive Diseases Pathology - GI

PS-20-001
Various histologic patterns of terminal ileitis and their diagnostic significance
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Background & Objective: Identifying terminal ileitis (TI) is one of the most confusing and challenging issues in gastrointestinal pathology. In the present study, we carried out histologic pattern analysis in terminal ileal biopsies in association with patient diagnosis.
Method: A total of 193 patients with TI were reexamined using the criteria including cryptitis, crypt abscesses, focal activity, ulceration, crypt distortion, villous shortening, pyloric metaplasia to define patterns of active ileitis with or without ulceration and chronic ileitis. Histologic patterns were evaluated using Chi-square test and Fisher's exact test. A p value < 0.05 was considered significant.
Results: Of the 193 patients with TI, 176 (91.2%) had Crohn's Disease (CD), 11 (5.7%) had Ulcerative Colitis (UC) and 6 (3.1%) had Behcet's Disease (BD). Pattern analysis revealed 86 chronic ileitis, 23 ulcerated active ileitis and 84 active ileitis without ulceration. The dominant pattern was active ileitis without ulceration in both UC and BD (63.6%, 66.7%, respectively), while CD patients showed chronic ileitis as the dominant pattern (46%). Active ileitis without ulceration pattern correlated significantly with focal activity (34.5%) than the other patterns ($p < 0.05$). While diffuse activity was found in the majority of cases with UC and CD (63.6%, 60.8%, respectively), focal activity was more common in CD compared to UC (20.5% vs 9.1%). Ulceration (20.5%) and chronicity (46%) features were more frequently observed in CD.
Conclusion: Pattern analysis of TI suggests that more severe active TI and chronic TI are compatible with CD while UC and BD, when involved, present with milder patterns of TI.

PS-20-002
Lymphocytic gastritis: what is the underlying scenario?
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Background & Objective: Lymphocytic gastritis (LG) is defined as ≥25 intraepithelial lymphocytes (IEL) per 100 epithelial cells in gastric biopsies. LG is associated with a variety of conditions, including celiac disease (CD), *H. pylori* (HP) infection, Crohn's disease, hypertrophic gastropathy, HIV, and lymphoma, or it can be idiopathic. The aim of this study was to determine the background of LG in a Turkish cohort.
Method: H&E and CD3 sections of gastric and duodenal biopsies of 59 patients with LG were reviewed according to the presence of HP and CD. Statistical analysis was performed using Chi-square test. A p value < 0.05 was considered significant.
Results: The median age of 59 LG patients (12 males and 47 females) was 40 years ranging from 2 to 69 years. HP was positive in 19 cases (32.2%) while 33 cases (55.9%) were diagnosed as CD (2 Marsh 1, 9 Marsh 2, 22 Marsh 3), and the remaining 14 cases (23.7%) were considered as idiopathic. In 29 patients, both gastric antrum and corpus were diagnostic for LG and 19 of these (65.5%) showed IELosis in the duodenum. Presence of *H. pylori* in corpus biopsies with LG was significantly correlated with presence of *H. pylori* in antrum biopsies with LG ($p < 0.001$). While IELosis in the duodenum correlated with LG in the antrum mucosa ($p=0.038$), no such correlation was found for body mucosa ($p=0.483$).
Conclusion: Even in populations with high HP prevalence idiopathic LG is a diagnostic possibility, however, more common diseases should be eliminated before making this diagnosis.

PS-20-003
Histological factors selecting high-risk patients in colorectal cancer. Could they have a prognostic utility?
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Background & Objective: TNM system is the standard for staging colorectal cancer (CRC), even if it isn't precisely predicting the outcome in intermediate stages of the disease. Other factors, such as histologic type and grade of tumour, lympho-vascular and neural invasion, tumour budding (TB) and inflammatory infiltrate, should be taken into account to identify patients with higher risk of recurrence, who could benefit from additional therapeutic options. The aim of the study is to evaluate the association between histological findings and recurrences in our institution.
Method: We reviewed 112 patients (72males, 40females) with a median age of 72yo with T3N0-CRC diagnosed between 2015 and 2017 with R0 resection. Specimens were revised by two GI-pathologists. 16 recurrences were found during a median follow-up of 18months.
Results: Statistical analysis showed that recurrences were related to vascular invasion, TB and absence of Crohn's-like lymphoid aggregates in the invasive margin. Furthermore, we found a strong correlation between vascular invasion and TB and we observed that a low grade of TB is mostly associated with cases without vascular invasion ($p<0.05$ in all).
Conclusion: In T3N0 CRC, new histological parameters could be used to select those patients who would benefit from additional therapies. While some of them had already been associated with worse prognosis (such as vascular or neural invasion), new factors were related to higher risk of recurrence in our study. Interestingly, we found an important role of the inflammatory infiltrate that's not usually considered as a prognostic factor by oncologists.

PS-20-004
Serrated changes, lesions and adenocarcinoma in inflammatory bowel disease patients - single institution molecular and immunohistochemical study
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Background & Objective: Association of chronic inflammatory bowel diseases (IBD) with development of dysplasia and adenocarcinoma in a known event. Recently, the attention is drawn to specific epithelial changes including serrated lesions.
Method: Specimens of IBD patients examined at our department between years 2006 - 2016 were reviewed. Cases with available samples were stained immunohistochemically with MLH1, MSH2 and p53. Selected samples were tested for KRAS, NRAS and BRAF mutations.
Results: Generally, 309 cases, some with related endoscopic samples were reviewed. Overall 90 cases with 113 samples were eligible for immunohistochemistry and 53 cases with 78 samples were selected for molecular studies. Morphological patterns including serrated change, hypermucinous change, true serrated lesions as well as IBD-associated dysplasia and adenocarcinoma were described. Aberrant p53 staining was seen in 30 samples including IBD-related dysplasia, simple serrated change and goblet cell depletion. Similar findings were with MLH1 and MLH2 staining. There were 58 samples with proved KRAS, NRAS and/or BRAF mutation. There were 6 cases with both KRAS (and/or NRAS)

and BRAF mutations seen in their samples. There were 9 patients with adenocarcinoma with cases mutated in KRAS with wild-type BRAF status.
Conclusion: Immunohistochemical and molecular changes are detected in several types of morphological changes in IBD patients including goblet cell depletion, serrated change, serrated lesion and IBD-related dysplasia. Review of morphological findings regarded as dysplastic and potentially riskfull for development of adenocarcinoma is necessary. Further study of cases with both KRAS (NRAS) and BRAF mutations is desirable.

PS-20-005
Synchronous tumours in patients with GISTs
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Background & Objective: Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal tumours of the gastrointestinal tract. However, they represent a small amount of all the abdominal tumours that are diagnosed daily. The aim of this study was to evaluate how many of the patients with GIST presented a secondary tumour, the characteristics and correlations between these tumours.
Method: A retrospective study was performed on a seven-year long period of time (2011-2017) in order to identify patients with GISTs and other abdominal or pelvic tumours. We analyzed the morphological characteristics and the immunohistochemical profile of these tumours.
Results: We have identified 46 cases of patients with GISTs. Five of them presented synchronous tumours. They were diagnosed in our department with a secondary tumour such as: two patients with mixed-type gastric carcinoma, one with uterine leiomyoma, one with high grade pleomorphic sarcoma of the spleen and one with two synchronous GISTs.
Conclusion: Simultaneous occurrence of a GIST and another abdominal or pelvic tumour seems to be more common than it has been considered and it indicates that GISTs are and could be an incidental finding.

PS-20-006
Spheroid-type intestinal amyloidosis. A case report
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Background & Objective: Amyloid deposition in the gastrointestinal tract has been described in relation with many etiologies, resulting in an eosinophilic acellular deposition in the submucosa. Localized deposits without systemic amyloidosis are rare. This deposition may adopt a spheroid morphology simulating corpora amylacea although it has only been described in very few cases. We report a case of an 85-year-old woman with a malignant suspicious ulcerated mass in the duondenum without any previous diagnosis of amyloidosis.
Method: The patient presented gastrointestinal bleeding. She had past medical histories of hypertension, dyslipidemia, chronic atrial fibrillation treated and bile duct stenosis with an endoprosthesis., The gastroscopy evidenced four ulcerated masses in the second duodenal portion that were biopsied.
Results: Samples of the duodenum demonstrated multiple small-medium size spheroid depositions of pink, amorphous and acellular material in the submucosa with occasional concentric lamination simulating corpora amylacea. It affected the lamina propia ulcerating the mucosal epithelium without granulomatous or significant inflammatory reaction. This material was also seen in the vascular walls entrapped in the lesion and was positive for Congo red-stained technique showing green dichroism in polarized light. It was negative for A amyloid immunohistochemistry and kappa light chain and positive for lambda light chain, making the diagnosis of AL amyloid deposition spheroid-type.
Conclusion: Spheroid-type localized amyloidosis in the small bowel is a rare condition that can mimic other mass forming pathologies with gastrointestinal bleeding symptoms. Most cases described are lambda light chain positive and there is no evidence of progression to systemic disease in the literature reviewed.

PS-20-007
Early oesophageal adenocarcinoma: IMP3 expression in association with depth of invasion and lymphatic spread
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Background & Objective: The incidence of oesophageal adenocarcinoma (EAC) is increasing in the Western world. Endoscopic mucosal resection is preferable in early invasive tumours. However, risk of lymphatic invasion (LI) necessitates individual assessment. Insulin-like growth factor-II mRNA-binding protein 3 (IMP3) has been suggested as a predictive/ prognostic factor in cancers. The study aim was to evaluate the expression of IMP3 and presence of LI in early invasive EACs.
Method: In a retrospective study of 106 pT1 EACs, the invasion depth in 7 sublevels (m1-m4, sm1-sm3), tumour grade (G), LI and presence of lymph node metastasis (LNM) was evaluated. Expression of IMP3 was classified as negative, weak (low intensity of staining or moderate intensity in ≤30% of tumour) or strong (moderate intensity in >30% of tumour or any strong intensity).
Results: Among 106 early invasive EACs, there were 55 (51.9%) pT1a and 51 (48.1%) were pT1b tumours. The sublevel spectrum was following: m1/m2/m3/m4: 6/9/22/18 and sm1/sm2/sm3: 19/11/21. G2 tumours predominated: 69 (65.1%). LI was detected in 28 (26.4%) and LNMs in 10 (9.4%) cases. There were statistically significant correlations between invasion depth and LI (rs=0.512;p=0.0001), G (rs=0.517;p=0.0001) or pN (rs=0.356;p=0.0001), and between G and LI (rs=0.372;p=0.0001) or IMP3 expression (rs=0.433;p=0.0001). Significant differences in G and LI by IMP3 expression were found (p=0.001).
Conclusion: In early EAC, deeper invasion is significantly associated with LI, LNM and higher grade. Stronger IMP3 expression is associated with higher grade and LI. Thus, IMP3 could be useful predictive marker in early invasive EACs.

PS-20-008
Colorectal carcinomas and DNA mismatch repair status – a statistical analysis of 123 consecutive cases from a tertiary center
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Background & Objective: Colorectal cancer is the most frequent digestive tract tumour. The neoplastic pathway is represented by chromosomal or microsatellite instability mechanisms. Microsatellite instability (MSI) is observed in 15% of sporadic cancer and in Lynch syndrome. MSI carcinomas are commonly located in the right colon. Histologically, they are heterogeneous, with marked lymphocyte infiltration, Crohn-like reaction, reduced differentiation, medullary, mucinous or signet ring cell tumours.
Method: We analyzed a series of 123 colorectal carcinomas registered at 'Victor Babes' National Institute of Pathology between November 2016 – March 2018, according to clinical characteristics, morphopathological aspects and immunohistochemical reaction for MLH1, PMS2, MSH2, MSH6 (Automatic Ventana Benchmark).
Results: MSI was present in 27 (21.9%) cases. Most of the cases were adenocarcinomas (108), and 17 (15.7%) of them presented MSI. 6 (4.9%) cases were medullary, all with MSI. 8 (6.5%) cases were mucinous, only

3 of them with MSI and there was 1 undifferentiated carcinoma with MSI. Colorectal tumours were more frequent in men, with a male to female ratio of 1.16, but MSI tumours were observed with a higher frequency in female patients, with a female to male ratio of 2.4. Of the 123 cases, 67 were located on the left colon and 36 on the right. Although the tumours were more frequent on the left colon, MSI was more frequent in right colon tumours (16-right colon; 3-left colon).
Conclusion: MSI is a genetic pathway associated with a better prognosis and predictive treatment value. The histopathological aspect of tumours is not characteristic in all MSI tumours, rendering the conclusion that MSI testing should be performed irrespective of typical morphology.

PS-20-009
Sporadic duodenal gastrinoma with d418d polymorphism in exon 9 of men1 gene
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Background & Objective: Gastrinoma of the duodenum can arise sporadically or in the setting of multiple endocrine neoplasia syndrome type I(MEN1). The objective of the paper was to present a case of an apparently sporadic duodenal gastrinoma.
Method: A 65 years old male known with chronic peptic ulcer was hospitalized for abdominal pain, nausea, vomiting and sweating. Endoscopy reveals multiple erosions in the gastric body and duodenal bulb. In the biopsy specimens two G1 neuroendocrine islands and chronic gastritis were described. Gastroduodenal resection was performed.
Results: The gross analysis revealead no mucosa disorders, except erosions. Thickening of the duodenal bulb was noticed that proved microscopically to be hypertrophy of the muscularis propria. The full specimen was included for histopathological analysis. In the duodenum deep mucosa, without invasion of the deep layers, three neuroendocrine islets (0.5-2 cm in diameter) were identified. Based on their positivity for Chromogranin, Synaptophysin and Gastrin and low Ki67 index (below 5%), the lesion was diagnosed as G1 multicentric duodenal gastrinoma, developed on the background of endocrine hyperplasia, limited to mucosa, without angio-limphatic invasion. The MEN1 mutation analysis of exons 2-10 showed the polymorphism rs2071212(D418D) in exon 9 that was considered benign/likely benign.
Conclusion: Duodenal gastrinoma with hypertrophy of the muscularis propria and gastric ulcers may be developed on the background of chronic gastritis-induced endocrine cells hyperplasia, such in this case, or occurs in patients with MEN1 syndrome with associated germline menin gene mutations. The polymorphism rs2071212(D418D) is probably a non-pathogenic variant of MEN1 gene mutation.

PS-20-011
Microsatellite instability status in gastric cancer: why and how?
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Background & Objective: The molecular classification of gastric cancer (GC) recognises two subtypes prone for the immune checkpoint blockade: the microsatellite unstable, and the Epstein-barr virus (EBV) related tumours. MSI in GC has been associated to better outcome, and decreased response to fluorouracil-based chemotherapy. We aim to assess the concordance between immunohistochemistry (IHQ) and PCR for the MSI status evaluation, and to explore the value of MSI and EBV as predictive survival factors.
Method: We studied a series of 246 consecutive GC in all stages and evaluated the MSI status using IHQ for MMR proteins and PCR. EBV expression was studied trough in situ hybridization (ISH).
Results: In our series 45 (18%) cases were MSI, and 13 (6%) were positive for EBV. IMS-GC was associated to female sex, older age, distal location, and distal non-diffuse type of the modified Lauren´s classification (MLC). EBV expression was most frequent in proximal location and proximal non-diffuse type of the MLC. The clinical stage was not significantly associated to IMS or EVB expression. The sensitivity, specificity, positive predictive value and negative predictive value of the IHQ for the MSI status were: 91%, 98%, 91% and 98% respectively. Tumours with MSI have a more favourable disease-free survival than microsatellite stable tumours (HR=6.992, 95% CI: 1.62-30, p=0.02). EBV expression was not related to survival.
Conclusion: The MSI status in GC defines a different pathological entity with a better outcome and should be incorporated in the routine pathological report. For this purpose, IHQ is enough as it shows an excellent concordance with PCR.

PS-20-012
Impact of cancer associated fibroblasts in oesophageal adenocarcinomas
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Background & Objective: Oesophageal Adenocarcinomas (EAC) are very aggressive tumours with high rates of resistance to conventional anticancer treatment. Cancer-associated fibroblasts (CAFs) are an emerging target for cancer therapy as they promote tumour growth and metastatic potential. We investigated the impact of CAFs in oesophageal adenocarcinomas with a special focus on tumours treated with neoadjuvant therapy (nTX).
Method: Two case collections of oesophageal adenocarcinomas (total n=310) were investigated: 112 cases were primary resected carcinomas, 198 cases were resected after nTX. CAF markers COLL11A1, CD90 and SPARC, were detected by immunohistochemistry
Results: In primary resected EAC, the amount of CAFs was increased in advanced tumour stages and in tumours with aggressive phenotype, e.g. with a significant association with pT category ($p<0.02$; all markers), lymph node metastases ($p<0.005$ for COLL11A1 and CD90) and lymphatic vessel invasion ($p<0.02$ for all markers). Higher CAF counts were also associated with worse survival ($p=0.05$ for COLL11A1). In the nTX cohort similar significant associations between CAF markers and pathoclinical parameters were observed. The most striking finding, however, was the association between tumour regression and presence of CAFs: tumours with complete and subtotal regression had significantly lower CAF counts than those who did not substantially respond ($p<0.05$ for all markers), and CAFs were almost absent in the scars of completely regressive tumours.
Conclusion: Our results support the concept of CAFs as an important factor of tumour promotion and maintenance. They may serve as potential target for future therapeutic approaches for these highly aggressive tumours.

PS-20-013
Is revision of cut-off values needed when using immunohistochemical staining for CD3 lymphocytes in histopathological diagnosis of lymphocytic colitis?
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Background & Objective: The diagnostic criteria of lymphocytic colitis (LC) and lymphocytic colitis incomplete (LCi) are based on haematoxylin and eosin (HE) staining. Guidelines recommend using supplementary CD3 staining for highlighting the intraepithelial lymphocytes

(IELs) in borderline cases. This change in diagnostics may incorrectly lead to diagnosing patients with LC and LCi if the same diagnostic criteria are used on HE and CD3 staining.
Method: IELs were estimated independently by two pathologists and categorized in intervals of 0-4, 5-9, 10-19, 20-29, 30-39, 40-49 or > 50 per 100 epithelial cells based on HE vs. CD3. A single HE or CD3 stained slide was available.
Results: Patients with biopsies of normal colon mucosa (n = 19), colon mucosa with nonspecific reactive changes (n =24), LCi (n = 24) and LC (n = 40) were included. The number of IELs were unchanged in 28 cases (26%), higher in 78 cases (73%) and lower in 1 case (1%). In 53%, 79%, 79% and 75% of cases included as normal colonic mucosa, non-specific changes, LCi and LC, respectively, the number of IELs were estimated higher when using a CD3 stain.
Conclusion: Overall, we found significant higher numbers of IELs based on CD3 compared to HE staining. Using the same cut-off of IELs on HE and CD3 will lead to more individuals being diagnosed with LCi and LC. This may be correct in a number of cases while it will result in some cases being over diagnosed. Therefore, we believe that our data support increasing the cut-off values of CD3.

PS-20-014
Evaluation of the abnormal p53 protein expression as a predictor of colorectal neoplastic progression for patients with inflammatory bowel disease
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Background & Objective: Patients with inflammatory bowel disease (IBD) have an increased risk of developing colorectal cancer (CRC). Dysplasia is currently the best marker of risk for CRC in IBD. Abnormal p53 protein expression (overexpression or complete los of expression) could be useful for the diagnosis of dysplasia, and for risk stratification of progression to advanced neoplasia [high grade dysplasia (HGD) and adenocarcinoma (ADK)]. We thus have evaluated the frequency, the diagnostic and prognostic value of abnormal p53 protein expression in neoplastic colorectal lesions complicating IBD.
Method: P53 protein expression was determined by immunohistochemistry (clone DO-7) on a series of 308 neoplastic colorectal biopsies [low grade dysplasia (LGD), HGD, ADK and indefinite for dysplasia (IND)] developed in an area affected by IBD amongst 112 patients followed at saint-Antoine hospital between 01/01/2003 and 12/31/2015.
Results: Seventy-five (24.4%) lesions exhibited an abnormal p53 protein expression, mainly an overexpression of the protein rather than a complete loss of expression (78.7% versus 17.3%). This abnormal expression was significantly more frequently observed in HGD (versus IND and LGD) (p=8.15.10-16) and in all cases of ADK. A trend whereby the abnormal p53 protein expression in IND or LGD lesions would be correlated with the progression to an advanced neoplasia was observed (log-rank test, p=0.06).
Conclusion: The abnormal p53 protein expression is related to the severity of colorectal neoplastic lesions in IBD patients and may be useful to improve risk stratification in these patients.

PS-20-015
Alteration of claudin and microRNA expression in patients with both primary and metastatic colorectal cancer
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Background & Objective: Altered expression of tight junction proteins, including claudins, is related to carcinogenesis and tumour progression. MicroRNAs (miRs) might influence these processes through negative regulation. Our aims were to investigate expression of claudin-1, -3, -4, -7 and potential regulatory microRNAs (miR-22, -29b, -24, -27a, -155, -455-3p, -596, -149, -665 and -342-5p) in normal colon (COL), primary colorectal adenocarcinoma (CRC) and liver metastasis (CRLM) samples of the same patients and identify possible correlations.
Method: Claudin and miR expression was measured in COL, CRC and CRLM of surgical resection specimens of 47 patients. Claudin-1, -3, -4 and -7 immunohistochemistry was quantified through digital morphometry. Quantitative PCR was performed and relative expression of microRNAs was calculated using miR-345 as a reference. Wilcoxon tests were performed to compare sample groups. Immunohistochemistry and qPCR results were correlated with patient survival using Kaplain-Meier analysis. Exiqon miRCURY LNA Power Inhibitor treatment and Western blot analysis were performed in HT-29 cell lines to confirm the regulatory role of microRNAs in claudin expression.
Results: Claudin-4 expression remained unchanged. However, claudin-1, -3, and -7 expression showed significant ($p<0.001$) reduction in both CRC and CRLM in comparison to COL. MiR-455-3p was elevated in CRC and CRLM when compared with COL ($p<0.001$). MiR-455-3p inhibition in HT-29 cells resulted in two-fold increase of claudin-3 expression. No correlations were found between survival and claudin or microRNA expressions.
Conclusion: Expression of claudin-1, -3 and -7 was decreased in both CRC and CRLM when compared with COL. MiR-455-3p has a potential regulatory role in claudin-3 expression.

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PS-20-016
Correlation of mismatch repair proteins/microsatellite instability status with PDL1 expression in poorly differentiated colorectal carcinoma
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Background & Objective: Microsatellite instability-high (MSI-H) tumours are thought to have higher frequency of tumour-infiltrating lymphocytes compared with microsatellite stable (MSS) tumours. Data from previous studies have shown that MSI-H colorectal carcinomas (CRC) are potentially good candidates for immune-checkpoint immunotherapy.
Method: Formalin-fixed paraffin-embedded tissues obtained from surgical resection specimens of 31 patients with poorly differentiated CRC were stained using two different anti-PDL1 antibodies (clone 22C3, Dako; clone SP263, Ventana). PDL1 stain was scored as negative (<5%) or positive (≥5%) using both tumour progression score (tumour only) and combined positive score (tumour and infiltrating immune cells) methods. The MSI and MMR status of cases were also retrieved from intradepartmental files.
Results: Out of 31 total cases, 14 were identified as MMR deficient/MSI-H and 17 were identified as MMR preserved/MSS. Of the 14 MMR deficient/MSI-H cases, 13 (93%) expressed PDL1, while only 2 of the 17 (12%) MMR preserved/MSS cases expressed PDL1. PDL1 expression was restricted to the invasive tumour front in 8 of 15 (53%) PDL1-positive cases. There was 100% concordance between the positive vs. negative status of the tumours when comparing results of the two anti-PDL1 antibodies. The percentage of PDL1-positive cells, however, was slightly higher with the SP263 as compared to the 22C3 antibody, both among cancer cells and tumour-infiltrating immune cells. As expected, the percentage of tumours scores as PDL1-positive was higher when using the combined positive score.
Conclusion: In our study, majority (93%) of MMR deficient/MSI-H poorly differentiated CRC cases are associated with PDL1 expression.

PS-20-017

Presence of a high amount of stroma within BRAF-mutated colon cancer predicts for very poor survival

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Background & Objective: The tumour-stroma ratio (TSR) has a prognostic value for colon cancer patients, as does the KRAS- or BRAF-mutational status. In this study we investigated whether a combination of these parameters improves further outcome prediction.
Method: The primary tumour of 819 stage II/III colon cancer patients were analyzed for TSR and the presence of KRAS- and BRAF-mutations. Stroma-high (>50%) and stroma-low (≤50%) groups combined with mutational status were evaluated with respect to survival.
Results: Stroma-high and BRAF mutation were both independent prognosticators for worse overall survival (OS) and disease-free survival (DFS) after adjusting for age, gender, stage and lymphatic and vascular invasion (TSR: OS HR 1.42, 95%CI 1.03-1.96, p=0.03; DFS HR 1.41, 95%CI 1.06-1.87, p=0.01. BRAF: OS HR 1.75, 95%CI 1.19-2.58, p=0.004; DFS HR 1.49, 95%CI 1.05-2.13, p=0.03). Interestingly, combining stroma-high and BRAF mutation (N=38) resulted in poorer survival (OS HR 3.34, 95%CI 1.97-5.66, p<0.001; DFS HR 2.79, 95%CI 1.69-4.60, p<0.001). Five years survival rates in patients with stroma-high and BRAF mutation combined dropped compared to patients with only stroma-high or BRAF mutation (51% vs 74% and 69% respectively for OS and 49% vs 67% and 66% respectively for DFS). No such outcome pattern was found by combining TSR with KRAS mutation.
Conclusion: TSR and BRAF-mutational status are independent prognostic biomarkers in colon cancer. Both parameters combined selects for a group of patients with extremely poor outcome.

PS-20-018

Ulcerative colitis and lymphomas – a lethal combination with forerunner changes

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Background & Objective: Ulcerative colitis (UC) is a chronic disease that increases the risk for epithelial and lymphoid malignancies by multiple mechanisms, the most important being: prolonged inflammatory status, disease-induced immunosuppression, treatment-induced immunosuppression and mutations, increased exposure to viruses.
Method: We present a retrospective cohort study including 45 patients with UC that underwent repeated biopsies during their disease. All samples were routinely processed, diagnosed and then multiple immunohistochemical assays were performed, including lymphocyte markers (CD20, CD3, CD4, CD8 and CD7). Also, we present three cases of lymphoma in young patients with longstanding UC, preceded by an oligoclonal selection of B cells.
Results: In longstanding UC, there is an expansion of a T cell clone with special immunophenotype: CD3+/CD4+/CD7- (like in early HIV infection and mycosis fungoides). Also, the patients that developed lymphoma (2 men and one woman) had an expansion of an oligoclonal B cell population suspected on usual stain and confirmed with PCR. Oligoclonal B cells had modified morphology (larger cells, with more cytoplasm and slightly enlarged nuclei), indicating the cases in which PCR tests should be performed.
Conclusion: Since PCR tests are expensive and difficult, knowledge of pre-lymphoma changes in morphology and immunophenotype of lymph cells is very important in stratifying patients according their risk of lymphoid malignancy, considering that western societies are having and increasing number of young patients with longstanding UC.

PS-20-023

Tumour budding is predictive for lymph node metastasis and survival in patients with pT1b oesophageal adenocarcinoma

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Background & Objective: Clinical management of patients with oesophageal adenocarcinoma with submucosal invasion (pT1b EAC) is based on estimated risk for developing lymph node metastasis (LNM), which is inaccurate using current standard histological tumour characteristics. Tumour budding (TB) has been shown to be predictive of LNM in colorectal cancer, but its value for early EAC has not been established yet.
Method: In the present study we compared different manual TB scoring methods (described by Ueno, Ohike and Thies), as well as automated digital image evaluation, with the goal to select and validate the most reproducible and predictive TB scoring system for pT1b EAC patients.
Results: Therefore we first investigated 25 cases, demonstrating a good to excellent interobserver agreement for TB scoring using methods according to Ueno and Ohike. The validation cohort consisted of 103 pT1b EAC and TB scored according to Ohike method was predictive for LNM and survival in multivariable logistic regression analysis employing known histological risk factors (Odds Ratio LNM 3.51 (95% CI 1.05-11.68, p-value 0.041); Hazard Ratio Overall Survival 2.20 (95CI 1.17-4.12, p-value: 0.014); Hazard Ratio Disease Free Survival 2.99 (95% CI 1.22-7.35, p-value 0.017)). Pankeratin and desmin co-immunohistochemistry did not improve TB evaluation, both manually as well as digitally.
Conclusion: Our study shows that TB scoring according to Ohike is highly reproducible, and independently predictive of LNM and survival in pT1b EAC. TB is recommended to be implemented in the pathological assessment to improve prediction of LNM and adjustment of the therapeutic decision making of the patients with pT1b EAC.

PS-20-024

Standardising classification of PMP does not warrant standard interpretation: identifying the problem areas

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Background & Objective: A consensus classification of pseudomyxoma peritonei (PMP) was recently published after a modified Delphi process. This classification standardizes nomenclature and recognizes three categories of mucinous carcinoma peritonei: low-grade (DPAM), high-grade (PMCA) and high-grade with signet ring cells. We performed this study to explore the robustness of this scheme and its limits.
Method: Thirteen pathologists of the Peritoneal Surface Oncology Group International (PSOGI), as well as a reference group of 16 additional pathologists were asked to classify PMP cases using this three-tiered system. Each pathologist from the PSOGI submitted micrographs of 5 PMP cases, one example of each category and 2 cases that were difficult to classify. Images were circulated among the 13 PSOGI pathologists in 2 rounds, then reviewed by the reference pathologists.
Results: The PSOGI pathologists recognized a consensus diagnosis in 35/46(76%) cases in the first round, with unanimous agreement in 12(26%). The 35 consensus cases were again reviewed by the same group, who now achieved unanimous agreement in 74% of these cases; 16(46%) of these cases were also unanimously classified by the reference panel with a consensus diagnosis in 8 additional cases. In 9(26%) cases low/high-grade remained problematic, whereas in 4(11%) cases there was disagreement on the presence of signet ring cells.
Conclusion: The recently proposed three-tier classification criteria for PMP are readily applicable and consensus improves with practice. Distinction between low- and high-grade disease can be problematic, as

well as degenerated single cells simulating signet ring cells. Further investigation should be aimed at clarifying these issues.

PS-20-025

Lymphovascular invasion diagnostic rate variation and predictors assessed in 1,303 colorectal resections

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Background & Objective: Lymphovascular invasion (LVI) in colorectal cancer is a known independent predictor of outcome; however, pathologist diagnostic rate (PDR) is not routinely assessed and correlated with other pathologic parameters.
Method: All in house colorectal resections in 2011-2017 were extracted in two teaching institutions. Synoptic report parameters (LVI, perineural invasion (PNI), tumour stage(pT), nodal stage, presence of tumour deposits (TD)) were extracted to calculate PDRs and generate funnel plots/control charts (FP/CC) centered on the group median call rate (GMCR) using a custom program. Logistic regression (LR) was done with R.
Results: 1,426 colorectal resections could be extracted. Seventeen pathologists interpreted >25 specimens each and together assessed 1,303. Their LVI PDR mean|median|stdev|min-max was 35%|32%|19%|7to84% overall, 20%|11%|20%|0to79% for pN0 cases and 58%|58%|23%|6to89% in cases with a lymph node metastasis (LNM). FPs centered on the GMCR (32%) for the overall LVI PDR had 6of17 outliers (P<0.001). LR for LVI presence in a model demonstrated the following predictors: pathologist (P<0.0001), PNI (P<0.0005), LNM (P<0.0001), TD (P=0.03). Nonpredictive factors were surgeon and pT. A FP/CC suggests pN0 is called with more consistency, as only 1of17 pathologists was an outlier in relation to the GMCR of 58% (P<0.05) and 0of17 were outside the P<0.001 boundary. LR for pN0 suggests the pathologist is nonpredictive (P=0.06).
Conclusion: LVI call is subject to interpretative bias and varies with LNM. Separately assessing LVI PDRs in pN0 and LNM cases is warranted, and these PDRs could be calibrated by ancillary testing. Awareness and follow-up of PDRs may increase reproducibility in the context of statistical process management/Next Generation Quality.

PS-20-026

PD-L1 expression in EBV-negative gastric adenocarcinoma and clinicopathological analysis

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Background & Objective: Our research was to evaluate the prognostic value of PD-L1 and the association between PD-L1 expression and clinicopathological characteristics in gastric cancer.
Method: PD-L1(SP142) expression was carried out in 202 EBV-negative gastric adenocarcinoma by immunohistochemistry. The expressions of tumour cells and stromal cells were evaluated with a cutoff of 1%. The staining pattern of tumour cells was cytomembrane, whereas staining pattern of stromal cells was cytoplasm/cytomembrane. The relationship between PD-L1 expression and clinicopathologic characteristics or prognosis was analyzed via X2-tests, Kaplan-Meier method and Cox regression model.
Results: Of 202 gastric adenocarcinoma specimens, the median age of the patients at diagnosis was 62.4 years old. 13.86% had high PD-L1 expression in tumour cells and 42.08% was positive in stromal cells. There was no relationship between tumour cells PD-L1 expression and gender, age, pTNM stage, Lauren classification and histological subtypes. In stromal cells, PD-L1 expression was associated with Lauren classification and histological subtypes, which was more common in mixed subtype and papillary adenocarcinoma (P value=0.009 and 0.005, respectively). Moreover, distinct PL-L1 expression in stromal cells of infiltrating edge was discovered in 50% papillary adenocarcinoma. In univariate analysis, there was no significant difference in prognosis between tumour and stromal cells PD-L1 expression (P value=0.858 and 0.198, respectively).
Conclusion: In gastric adenocarcinoma, PD-L1 expression in the stromal cells was associated with histologic subtypes. Future studies are needed to investigate the value of PD-L1 in gastric adenocarcinoma.

PS-20-027

The correlation and upregulation of PD-L1 and CMTM6 in EB virus-associated gastric cancer

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Background & Objective: CKLF-like MARVEL transmembrane domain containing protein6 (CMTM6) is a ubiquitously expressed protein that binds PD-L1 and maintains its cell surface expression. In this study, we examined the expression of PD-L1 and CMTM6 in EBVaGC and analyzed the association between the expression status of these markers and the prognosis of patients.
Method: The expressions of PD-L1 and CMTM6 were detected by immunohistochemistry in 45 cases of gastric carcinoma (25 cases of EBV-positive GC, 9 MLH1-negative GC, 11 EBV-negative and MLH1-positive GC). The immunoreactivity of PD-L1 at cytomembrane in tumour cells and cytoplasm in stromal cells, and CMTM6 at cytoplasm/cytomembrane in tumour cells and cytoplasm in stromal cells was regarded as positive. Four score levels (P-scores) were classified according to the proportion of PD-L1 and CMTM6 positive cancer cells and stroma cells. The PD-L1 mRNA in situ hybridization (ISH) was performed with RNAscope assay according to the manufacturer's protocols.
Results: Expression of PD-L1 and CMTM6 was frequently detected in cancer cells of EBVaGC, with infiltration of PD-L1 and CMTM6-positive immune cells in tumour stroma. Moreover, there was a positive correlation of the expression status between PD-L1 and CMTM6 in EBVaGC (Kappa=0.644, P<0.01). In univariate analysis, PD-L1 expression in EBVaGC tumour cells and CMTM6 expression in EBVaGC immune cells were correlated with poor outcomes in overall survival (P=0.021 and 0.004, respectively).
Conclusion: The decreased expression of PD-L1 in EBVaGC tumour cells and CMTM6 in EBVaGC immune cells might contribute to the poor prognosis of EBVaGC, may be related to immune evasion.

PS-20-028

Hyperplastic polyp subtypes; morphomolecular study

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Background & Objective: The importance of hyperplastic polyps during colorectal carcinogenesis is appreciated related to the understanding of serrated pathway. The morphologic subtypes of hyperplastic polyps in carcinogenesis and the nomenculature of lesions with both hyperplastic and adenomatous areas are controversial. We aimed to reveal the molecular properties of hyperplastic polyp subtypes and the molecular changes in polyps containing both hyperplastic and adenomatous areas.
Method: 49 hyperplastic polyps [19 microvesicular (MVHP), 19 goblet-rich (GRHP) and 11 mucin-poor (MPHP)] and 10 mixed hyperplastic and adenomatous polyps were analysed. KRAS and BRAF mutations were analyzed in hyperplastic polyp subtypes and KRAS, BRAF mutation and MSI analyzes were separately performed in two areas of mixed polyps by real-time PCR.
Results: While 68% of MVHPs, 82% of MPHPs and 5% of GRHPs showed BRAF mutations, KRAS mutation was detected as 5%, 74%

and 18%, respectively. In 4 of mixed polyps, KRAS mutation was present in both adenomatous and hyperplastic segments, while BRAF mutation was not detected in both areas. All adenomatous parts of mixed polyps were determined as microsatellite stable. In the hyperplastic parts, 3 of polyps had low and 2 polyps had high frequency microsatellite instability.
Conclusion: MVHP and MPHP have frequently BRAF mutations and GRHPs show more frequently KRAS mutations. The presence of KRAS mutation and microsatellite instability in mixed adenomatous-hyperplastic polyps supports the fact that these polyps may be involved in carcinogenesis by the pathway of MGMT promoter methylation, an alternative pathway that has increased in importance in recent years.

PS-20-029

Characterising soluble E-cadherin and HER2 molecules compared to immunohistochemical expression in metastatic gastric cancer

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Background & Objective: CDH1 gene, coding for the E-cadherin (E-cad) and EGFR2 (HER2) is linked to gastric cancer (GC) invasion. Extracellular domain of both can be cleaved by metalloproteinases leading to an increase of serum E-cad (sEcad) and HER2 (sHER2). In vitro, sE-cad was able to bind HER2 and activated downstream signaling. sE-cad and sHER2 may reflect both E-cad and HER2 status of tumour load. We evaluate CDH1 haplotype, sE-cad and sHER2 revealed at diagnosis and E-cad and HER2 expression by immunohistochemistry with therapeutic results.
Method: DNA from PB of 59 patients (44males median60years), with metastatic GC was used for CDH1 haplotype analysis. We screened for germline mutation the promoter region, the 16 exons and splice junctions of the CDH1 gene. The allele and genotype frequencies were compared between HER2-positive and HER2-negative metastatic GCs. sE-cad and sHER2 levels were tested at diagnosis and after first/second cycle of therapy. E-cad and HER2 status was assessed by immunohistochemistry.
Results: An association between the HP7 CDH1-haplotype, including two polymorphisms (rs16260A-rs1801552T) and a subset of HER2-positive metastatic GC with better survival was observed. sE-cad level was found to increase with the presence of -285A polymorphism and a better OS. sHER2 level correlated with the HER2 expression evaluated by immunohistochemistry and CDH1-haplotype.
Conclusion: Although preliminary, our data demonstrated that CDH1 haplotypes may be useful to predict the OS of metastatic GC patients. CDH1-haplotype P7 showed the best response to treatment with trastuzumab. sHER2 and sE-cad may supplement tissue tests to identified patients HER2+.

PS-20-030

Nuclear farnesoid X receptor expression as indicator of progressive disease and poor prognosis for colorectal cancer patients

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Background & Objective: Farnesoid X receptor (FXR) has been implicated in several malignancies by either promoting or suppressing tumour growth. Our aim was to investigate its role in colorectal cancer.
Method: Seventy-seven patients with newly diagnosed colorectal cancer were included in this study. Immunohistochemical analysis (IHC) was performed on paraffin-embedded colorectal cancer tissue sections, to determine FXR expression. FXR positivity, extent of expression and intensity of immunoreactivity were assessed and combined to form a final score, used for associations with various clinicopathological parameters and patients' survival. Different colon cancer cell lines (CaCo2, HT29, HCT116, RKO, DLD-1, SW480, and Colo205) with differential tumour grade were used to assess FXR levels. Proteins from the whole cell, cytoplasmic and nuclear fractions were blotted for Western analysis.
Results: Nuclear FXR expression was found in 53 out of 77(68.8%) patients examined. High nuclear FXR expression was correlated with larger tumour size ($p = 0.0037$), presence of lymph node metastases ($p = 0.0037$) and advanced disease stage ($p=0.041$). High nuclear FXR expression proved as an independent prognostic factor of worse disease-specific survival ($p=0.001$) and relapse-free survival ($p=0.001$). Western Blot analysis revealed high FXR levels in a stage-dependent manner [CaCo2, HT29, HCT116 (stage II), <RKO (stage III), DLD-1 (stage high) < SW480 (stage III-IV), Colo205 (stage IV)]. FXR subcellular localization in colon cell lines showed mainly nuclear and barely cytoplasmic pattern of expression.
Conclusion: Our results indicate that FXR is correlated with colon cancer grade and stage. Further studies are urgently needed in order to verify its potential role in colon cancer patients' prognosis and management.

PS-20-031

The relationship between the immunohistochemical expression of WT-1, p16, p53 and the prognosis of gastrointestinal stromal tumours

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Background & Objective: The prognosis of gastrointestinal stromal tumours (GIST) is unpredictable. We aimed to show the prognostic significance of histopathological and morphological parameters and the expression of WT-1, p16, and p53.
Method: Total of 41 GIST cases included the study. Localization, tumour size, histopathologic variables retrospectively re-evaluated. The mean follow-up of the patients was 79,1±37,4 months (range, 12-152 months). We evaluated the cases regarding primary GIST risk assessment (RA) guidelines. All cases stained with CD117, SMA, Desmin, CD34, S100, Ki67 for diagnostic work-up. Additionally, WT-1, p16, p53 stained and results compared with variables.
Results: Stomach found the most frequently involved location (48,7%). The mean age at diagnosis was 65,1±14,7 (range, 39-94 years), while the male to female ratio was 15/26. The mean size of the tumours was 6,3±4,7 cm (range, 0,5-26 cm). We found a positive correlation with WT-1, p16, and p53 positivity and metastatic disease ($p<0.05$). RA found related to cell type, WT-1 expression, metastatic disease and, patient survival ($p<0.05$). The 5-year-survival was 100%, 85,7%, and 64,3% for patients with very low/low risk, intermediate, and high-risk groups, respectively.
Conclusion: We found that RA was the most important indicator for prognosis and immunohistochemical expression of WT-1, p16, and p53 has been shown to be safe to use for prognostic evaluation.

PS-20-032

SERPINB5 expression: association with CCRT response and prognostic value in rectal cancer

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Background & Objective: Due to the varying characteristics and conflicting outcomes on the overall survival of rectal cancer patients, many studies have been undertaken to determine various prognostic and predictive factors for the mainstay treatment of CCRT followed by surgery. Cancer cell motility contributes to tumour invasion, migration and eventually metastasis. However, the genes associated with cell motility (i.e., GO:0048870) have not been systemically evaluated in rectal cancers.
Method: A comparative analysis of gene expression profiles was applied to the transcriptomic dataset (GSE35452) with a focus on genes associated with cell motility (GO:0048870), where SERPINB5 was recognized as the most significantly up-regulated gene. Tumour samples from 172 primary rectal cancer patients who underwent neoadjuvant CCRT

followed by surgical resection were collected. Immunohistochemistry was used to semi-quantitatively assess the expression level of SERPINB5 protein. Statistical analyses of SERPINB5 expression and various clinicopathological features as well as survival were then performed.
Results: High immunoreactivity of SERPINB5 was significantly linked to pre- and post-CCRT advanced disease, lymphovascular invasion, and poor response to CCRT (all $P \leq 0.015$). SERPINB5 overexpression was not only negatively associated with disease-specific survival (DSS), local recurrence-free survival (LRFS) and metastasis-free survival (MeFS) rates in univariate analyses but also was an independent prognostic factor for DSS and MeFS in rectal cancer patients (all $P \leq 0.043$).
Conclusion: SERPINB5 may play an important role in rectal cancer progression and response to neoadjuvant CCRT and serve as a novel prognostic factor.

PS-20-033
Left and right are not the same: possible effects of tumour sidedness on tumour budding in colorectal cancer
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Background & Objective: Sidedness has recently been proposed to play an important role in tumour biology of colorectal cancer (CRC) with potential implications for treatment of advanced tumours. The aim of this study was to examine the effect of sidedness on tumour budding as an established marker of tumour progression in CRC.
Method: 298 patients with Stage I-IV CRC (161 left-sided, 137 right-sided) were entered into analysis for this study. Tumour budding was performed according to ITBCC 2016 recommendations and scored as Bd1, Bd2 or Bd3.
Results: There was no significant difference in Bd stage between right- and left sided cancers (p=0.5299). Right-sided tumours were more likely to be MMR-deficient (p<0.001). In Stage III tumours, right sided tumours were associated with poorer overall survival (OS) after adjusting for post-operative therapy (p=0.0455, HR 1.922, 95%CI: 1.013-3.647). High-grade tumour budding (Bd3) was significantly associated with shorter OS in left-sided tumours (p=0.0349), but not in right-sided tumours (p=0.3128).
Conclusion: Sidedness appears to be a prognostic indicator in advanced-stage CRC. Although right-sided cancers fare worse than their left-sided counterparts, our data indicate that the adverse effect of tumour budding might be diminished in these tumours and confounded by other factors. Further studies are required to examine potential antagonists of tumour buds in the tumour microenvironment in right-sided CRC.

PS-20-034
Characteristic Rb gene loss possibly relates to the poor prognosis of patients with primary small cell carcinoma of oesophagus
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Background & Objective: Primary oesophageal small cell carcinoma (SCC) is a rare entity with poor prognosis and unclear pathogenesis. The objective of this study was to determine the clinicopathologic and genetic features of SCC and compared with various differentiated oesophageal squamous cell carcinoma (SQCC).
Method: Surgical resected, formalin-fixed paraffin-embedded specimens of 20 primary oesophageal neuroendocrine carcinoma (NEC) with predominant small cell components (17 SCC, 3 mixed adenocarcinoma or SQCC components) were selected, compared with 10 poorly-differentiated and 10 moderate to well differentiated SQCC during the years 2015 to 2017 in our hospital. Neuroendocrine markers of CD56, chromogranin A, synaptophysin, squamous cell markers of CK5/6, P40 and glandular markers of CK8/18 were performed by immunostaining. The expression of Rb protein and alteration of RB gene were examined by immunohistochemistry and/or by single-probe FISH assay, respectively.
Results: Different expression of Rb protein was observed between the groups of SCC and mixed NEC or SQCC. Rb protein negatively expressed in all the cases of SCC. No statistical significance was found for the proportions of Rb positive tumour cells in the cases of mixed NEC and SQCC. Loss of heterozygosity of Rb gene was observed only in SCC by single-probe FISH assay. In SCC cases, the average survival time was 11 months, and the 2-year OS and DFS were 25% and 16.7%, respectively.
Conclusion: Rb gene loss may be a critical event and key potential contributor related to the poor prognosis of patients with primary SCC of oesophagus.

PS-20-035
Lipid metabolism genes expression are dysregulated in colorectal adenocarcinoma
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Background & Objective: Several lipid metabolism genes such as LPL, APOA1, APOB, APOE and CETP have been associated with Colorectal Adenocarcinoma (CRAC) development risk. All these genes are involved in several metabolic conditions and disorders, resulting in different levels of expression. This study aimed to determine APOA1, APOB, APOE, CETP, LPL and NPY expression in CRAC biopsies.
Method: Well-differentiated CRAC biopsies were submitted to the evaluation of APOA1, APOB, APOE, CETP and LPL genes expression levels, using Real Time PCR Sybergreen based, concerning 119 CRAC cases.
Results: Parallel upregulation of APOB, APOE, and CETP genes was verified amongst tumoural tissue, with a mean 15-fold increase (p<0.0005), while APOA1 and LPL genes were downregulated, with mean 5-fold decrease (p<0.005), when compared with optical normal colonic and rectal mucosae.
Conclusion: Our results showed that lipid metabolism was disrupted in CRAC, once tumour cells seem to have higher LDL concentration, consistent with APOE and APOB genes upregulation, and low levels of HDL, since CETP gene was upregulated while APOA1 and LPL were downregulated. These findings support the possible role of lipid metabolism disruption in CRAC development and progression and might be useful in tumoural screening.

PS-20-036
Macro and microglandular patterns of colorectal adenocarcinoma correlate with folate metabolism polymorphisms mthfr 1298c/mtr 2756g – mtrr 66g supporting hypomethilation in carcinogenesis/ progression
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Background & Objective: Folate metabolism is influenced by methylenetetrahydrofolate reductase (MTHFR), methionine synthase (MTR) and methionine synthase reductase (MTRR) enzymes. MTHFR, MTR, and MTRR common variants have been correlated with Colorectal Adenocarcinoma (CRAC) risk, which must affect histopathological differentiation. This work aimed to investigate MTHFR, MTR, and MTRR common polymorphisms impact in CRAC histopathological differentiation.

Method: Histopathological and morphological subtyping of 119 CRAC biopsies were interpreted and validated, according to WHO 2010 criteria. All biopsies were genotyped for MTHFR C677T, MTHFR A1298C, MTR A2756G, and MTRR A66G polymorphisms by PCR-SSP techniques.
Results: Among the 119 CRAC biopsies studied: 40 showed a Predominantly Microglandular Pattern (PMiP), 22 showed a Predominantly Macroglandular Pattern (PMaP) and 57 have a Mixed Pattern (MP). MTHFR 1298C mutant allele were associated with PMaP (57 % vs 39%; $p<0.05$), while MTR 2756G and MTRR 66G mutant alleles were prevalent among PMiP cases ($p<0.05$).
Conclusion: These findings provided insight into the potential influence of folate metabolism polymorphisms in CRAC development and differentiation. Hypomethylation, caused by MTHFR gene alterations, added to APC mutation can lead to high grade dysplasia associated with SMAD4 and TP53 conventional carcinogenesis pathway, showing a PMaP. Whereas MTR and MTRR mutations, showed in PMiP, commit with defects in DNA mismatch repair system / genes, causing Microsatellite Instability and affecting cell growth and differentiation genes, like BAX, BRAF, TCF-4, that promote cancer development in colon and rectum mucosa. Adenomas and preneoplastic lesions deserve also new insight to integrate these findings and certify its validity in carcinogenesis.

PS-20-037

Interobserver agreement study in gastric dysplasia using endoscopic biopsies

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Background & Objective: The diagnosis and grading of gastric dysplasia can be challenging for pathologists, especially when using small endoscopic biopsies. This study examines the interobserver and intraobserver agreement between pathologists for the diagnosis of gastric dysplasia, its grade and its most common subtype.
Method: We designed an interobserver study on gastric biopsies purported to have different grades of dysplasia and reactive changes. 32 lesions were reviewed by 31 pathologists using the Vienna classification, scoring the highest degree of dysplasia and most common type of dysplasia. Inter and intraobserver agreement were calculated by intra-class correlation coefficient. Pathologists were grouped as; international expert (IE n=2); IGIP pathologist experienced 10 years and more (n= 11); and those with less than 10 years experience (n = 18). Statistical analyses was performed for both highest score of dysplasia (HS) and most common subtype score (CS). The most common consensus diagnosis was used as the gold standard.
Results: For grade of dysplasia; the kappa values for interobserver agreement in the groups of IE; IGIP experienced and IGIP less experienced were 0.702, 0.680, and 0.593, respectively. For type of dysplasia, the kappa value of intraobsever agreement in the same groups were 0.499, 0.593 and 0.494 respectively. Interobserver score in all participants was 0.623 for highest score.
Conclusion: Intraobserver agreement for dysplasia was good. Interobserver agreement was good between experienced pathologists but moderate to poor in less experienced pathologist. Disagreement was higher in interpretating dysplasia subtypes. Experience in GI pathology is important but subtyping dysplasia may require immunohistochemistry, as H&E is relatively unreliable.

PS-20-038

Low Klintrup-Mäkinen score is an indicator of aggressive tumour behaviour and an independent prognostic factor in colorectal cancer

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Background & Objective: The Klintrup-Mäkinen (KM) score represents the density of peritumoural inflammatory infiltrate at the invasion front of colorectal cancers. The aim of this study was to determine whether the KM score is associated with clinicopathological features and clinical outcome.
Method: Surgically treated primary colorectal cancers (n=597) were retrospectively (cases 2002-2015) and prospectively (cases 2016-2017) analysed. Klintrup-Mäkinen (KM) score ranged from 0 to 3, with larger numbers indicating a higher density of infiltrate.
Results: A lower KM score was significantly associated with more advanced pT stage ($p=0.0132$), lymph node metastasis ($p=0.0048$), distant metastasis ($p<0.0001$), higher tumour grade ($p=0.0011$), lymphatic invasion ($p=0.0145$), venous invasion ($p=0.0003$), and perineural invasion ($p=0.02$). A strong inverse correlation between KM score and tumour budding (BD score) was observed ($p=0.0079$). Patients with KM scores 1-3 experienced similar outcomes but pronounced unfavorable overall survival was seen in patients when comparing KM score 0 versus 1-3 ($p<0.0001$). This difference was independent of tumour budding, TNM stage and postoperative therapy (HR=0.387 (95%CI 0.21-0.73); $p=0.003$).
Conclusion: The KM score contributes independent information on survival; low score is markedly associated with aggressive tumour-related features. The KM score is a simple measure of the inflammatory infiltrate and warrants comparison to other immune-related scoring systems.

PS-20-039

Long live polypoid dysplasia! A more rational approach to polypoid dysplasia in inflammatory bowel disease

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Background & Objective: It was previously thought that dysplasia-associated lesion or mass (DALM) related to inflammatory bowel disease (IBD) should be treated surgically due to a high risk of malignancy. However, the SCENIC consensus statement recommended continued surveillance instead of resection following the endoscopic removal of polypoid dysplasia based on consensus recommendation. Furthermore, it was suggested that standardized terminology replace DALM-related terms to reflect a more rational approach to dysplasia in IBD. Our aim was to determine the rate of colorectal cancer and dysplasia in patients with colonic IBD following the diagnosis of endoscopically resectable colonic polypoid dysplasia at our institution.
Method: A retrospective search of our database was conducted for patients with colonic IBD who had a first diagnosis of polypoid dysplasia treated by endoscopic resection between 2013-2017. Patients were included when the polypoid dysplasia occurred in colonic mucosa affected by IBD and if follow-up colonoscopy was performed. The incidence of invasive colorectal cancer and dysplasia on follow-up was determined.
Results: Sixteen patients (12 with ulcerative colitis and 4 with Crohn's disease) had a first diagnosis of low-grade polypoid dysplasia (21 polyps) treated with endoscopic resection during the study period. Active colitis in the adjacent colonic mucosa was present for 7 patients. Median follow-up was 28 months (range 5-48 months). No patient developed colorectal cancer. Two patients had low-grade polypoid dysplasia at 28 and 48 months, with one case occurring outside of colitic mucosa.
Conclusion: Endoscopic removal of polypoid dysplasia in patients with IBD is safe in our institution. A more rational approach to dysplasia in IBD should be embraced.

PS-20-042

Study of expression of calprotectin and myeloperoxidase in clinically diagnosed inflammatory bowel disease

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Background & Objective: Calprotectin and Myeloperoxidase have been employed as diagnostic fecal markers of inflammatory bowel disease (IBD). This study was performed to investigate the diagnostic role of calprotectin and myeloperoxidase immunohistochemical expression in colonic mucosal biopsies.
Method: Calprotectin and Myeloperoxidase immunostaining was performed in colonoscopic biopsies of 50 patients diagnosed clinically and/or endoscopically as IBD but with inconclusive diagnosis on histopathological examination. Also, 10 positive control cases proved clinically, endoscopically and histopathologically as IBD were similarly studied.
Results: Epithelial calprotectin expression was encountered in 38% and 60% of histopathologically inconclusive cases and positive control cases respectively. The image optical density (IOD) of calprotectin epithelial immunostaining showed no significant difference between confirmed IBD cases and histopathologically inconclusive cases (p=0.459). In addition, most of the values of IOD of the calprotectin epithelial immunostaining of the inconclusive cases fell within the range of the confirmed IBD cases. Myeloperoxidase score showed a significant difference between the two studied groups as a whole (p=0.001), whereas it showed no significant difference between the subset of cases demonstrating epithelial calprotectin staining in both groups (p=0.127) ; in which most of the values of myeloperoxidase score in the inconclusive cases fell within the range of the confirmed IBD cases.
Conclusion: Epithelial immunostaining of calprotectin in tissue biopsy was able to point to the cases with inconclusive histopathological diagnosis that showed agreement with the confirmed IBD cases, and thus would help in the diagnosis of IBD. Additional consideration of myeloperoxidase score, besides epithelial calprotectin, would further refine the diagnosis.

PS-20-043

The immune microenvironment of various histological types of EBV-associated gastric cancer

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Background & Objective: EBV-associated cancer is one of the molecular subtypes of gastric adenocarcinomas classified by mutation profile analysis. There is very few data on its IHC-characteristics and its immune microenvironment. The distribution of immune cells might appear to be an important diagnostic criterion of poor prognosis.
Method: Samples of 26 gastric adenocarcinomas (surgical material) were included in this study. IHC-staining for LMP-1 protein and IHC-staining for CD4, CD8, CD68, CD1a were used for EBV identification and immune cells detection, respectively. The tumour tissue and normal glands microenvironment was investigated separately.
Results: We identified 3 EBV-positive, 10 EBV-negative adenocarcinomas and 13 cases with significant expression of LMP-1 in normal glands of lamina propria. EBV-negative cancers had poorer prognosis than other two groups. CD68+ cells infiltration was significantly higher in tumour tissue in cases with EBV-positive normal glands than in EBV-negative and EBV-positive cases (p<0,05), but in normal glands microenvironment macrophages predominated in EBV-negative cases. We found out statistically significant differences in the number of dendritic cells: it prevailed in cases with EBV-positive normal glands (p<0,05) in the tumour tissue and normal glands microenvironment. In normal glands microenvironment significant correlation between the number of CD4+ cells in the signet ring cell carcinomas and in the highly differentiated adenocarcinomas (R=0,91) was found.
Conclusion: Immunological properties of tumour tissue and normal glands in gastric adenocarcinomas with EBV-positive normal glands of lamina propria differ significantly from EBV+ and EBV- cancers. We assume that these facts indicate a premalignant process in these glands different from the classical metaplasia-dysplasia-cancer pathway.

PS-20-044

STAT6 immunoexpression in samples from a metastatic model of colon adenocarcinomas to the liver reveals a group of patients with better prognosis

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Background & Objective: STAT6 protein plays a central role in exerting IL4 mediated biological responses. Moderate to strong cytoplasmic and nuclear staining was observed in most tumour cells, such as colon cancer cells. The main objective was to study the expression of STAT6 in samples of colon adenocarcinoma and in their respective hepatic metastases and to study their clinical relevance with survival rates.
Method: Fifty-two consecutive patients with colon cancer and subsequent hepatic metastasis surgically removed between 2007 and 2017 were studied. Tissue arrays were produced using a 2 mm diameter needle. Immunohistochemical studies were conducted, where the positivity was classified from 1 to 3 degrees and the extension was graded between 0 and 100%. A global score was obtained by multiplying both values. Statistical analysis of these findings was carried out using the SPSSv23; p<0.05 program.
Results: Almost all colon adenocarcinoma samples and 90% of metastatic samples showed different degrees of STAT6 positive immunoexpression. No significant differences in STAT6 immunoexpression were noted between primary tumours and their metastatic samples (74.41 vs 73.48 p=0.835). Interestingly, metastatic samples of colon adenocarcinomas with more than 100 points of STAT6 immunoexpression reveals a group of patients with significantly better overall survival, disease-free time and post metastatic survival (p=0,001; p=0,006; p=0,004 respectively).
Conclusion: No significant differences for STAT6 were found between primary and metastatic adenocarcinoma samples. Considering metastatic adenocarcinoma samples, those with more than 100 points of immunoexpression for STAT6 reveals a group of patients with better prognosis.

PS-20-045

STATB2 reveals a group of patients with better prognosis in a metastatic model of colon adenocarcinomas to the liver

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Background & Objective: The expression of SATB2 protein is primarily preserved in cancer cells of colorectal origin, indicating that SATB2 could function as a clinically useful diagnostic marker to distinguish colorectal cancers from others. To study the expression of SATB2 in samples of colon adenocarcinoma (52) and their respective hepatic metastases and to study their clinical relevance with survival rates.
Method: Fifty-two consecutive patients with colon cancer and subsequent hepatic metastasis surgically removed between 2007 and 2017 were studied. Tissue arrays were produced using a 2 mm diameter needle. Immunohistochemical studies were conducted, where the positivity was

classified from 1 to 3 degrees and the extension was graded between 0 and 100%. A global score was obtained by multiplying both values. Statistical analysis of these findings was carried out using he SPSSv23; p<0.05 program.
Results: More than 90% of colon adenocarcinoma samples and their respective metastatic tumours showed different degrees of SATB2 positive immunoexpression. A significant overexpression of SATB2 in the metastatic colon adenocarcinoma was noted (175,3 vs 125,0; p=0,009). Additionally, a significant inverse correlation between the number of positive regional lymph nodes and SATB2 expression was observed (r=-0,390; p=0,013). Finally, samples with more than 150 points of SATB2 immunoexpression reveals a group of patients with better overall survival, disease-free time and post metastasic survival (p=0,021; p=0,041; p=0,034 respectively).
Conclusion: Significant differences for SATB2 immunoexpression were noted between primary and metastatic adenocarcinoma samples. Colon adenocarcinomas with more than 150 points of SATB2 immunoexpression reveals a group of patients with better prognosis.

PS-20-046
The absence of COX2 immunoexpression in samples from a metastatic model of colon adenocarcinomas to the liver reveals a group of patients with poorer prognosis
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Background & Objective: COX-2 is an inducible enzyme, making it undetectable in the majority of tissues under basal conditions. The overexpression of COX-2, both in epithelial cells and in adjacent stroma, suggests that the derived prostaglandins may be promoting tumour development in the colon. To study the immunoexpression of COX-2 in samples of colon adenocarcinoma and their respective hepatic metastases and to study their clinical relevance with survival rates.
Method: Fifty-two consecutive patients with colon cancer and subsequent hepatic metastasis surgically removed between 2007 and 2017 were studied. Tissue arrays were produced using a 2 mm diameter needle. Immunohistochemical studies were conducted, where the positivity was classified from 1 to 3 degrees and the extension was graded between 0 and 100%. A global score was obtained by multiplying both values. Statistical analysis of these findings was carried out using the SPSSv23; p<0.05 program.
Results: Positive immunoexpression for COX-2 was detected in almost 80% of primary tumours and in 90% of their metastasis. A significant overexpression of COX-2 in the metastatic samples was noted (67,5 vs 40,16; p=0,019). Moreover, a positive correlation between the COX-2 expression and the disease-free time was found (r= 0,304; p=0,041). A negative expression of COX2 in the primary colon adenocarcinomas showed a group of patients with a significant lower overall survival, disease-free time and post-metastasic survival (p=0,01; p=0,006; p=0,016 respectively).
Conclusion: Significant differences for COX-2 were noted between primary and metastatic adenocarcinoma samples. The absence of COX2 expression reveals a group of patients with a poorer prognosis.

PS-20-047
Signet-ring cell carcinoma of the stomach: clinicopathological aspects and impact on prognosis
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Background & Objective: The prognostic implication of gastric signet-ring cell carcinoma (SRCC) remains a subject of debate. The findings of existing studies on this issue are inconsistent. The aim of this study was to analyze the clinicopathological characteristics of gastric SRCC and to assess its prognostic value.
Method: A total of 122 patients with gastric adenocarcinoma who underwent curative gastrectomy from 2001 to 2014 at Habib Thameur hospital in tunis were enrolled. The clinicopathological parameters and survival of SRCC were analyzed compared to non SRCC (NSRC).
Results: 61 patients (50%) had SRCC. SRCC patients were younger than those with NSRCC (p=0,001) with no difference in gender. Perineural invasion and desmoplastic stroma were more frequent in SRCC (respectively p=0.001 and p<0.001). Linitis plastica was observed in 15 patients with SRCC against 2 patients with NSRCC (p=0,001). Resection margins were more often positive in SRCC group (p=0.004). SRCC was more likely to be stage T4 (p=0.033), N3 (p<0.001) and have a higher metastatic lymph node ratio (p<0.001). Hepatic metastases were more frequent in NSRCC group (p=0.031). Peritoneal carcinomatosis was more common in SRCC group (p=0.004). There was no difference in recurrence between the 2 groups (p=0.348). 5-year survival was higher in NSRCC group but the difference was not significant. SRCC was not associated with high mortality at univariate and multivariate analyses. Multivariable analyses showed that advanced age, adjacent structure invasion and positive resection margins were a specific prognostic factor for SRCC.
Conclusion: Gastric SRCC is not associated with high mortality. It seems to have specific prognostic features.

PS-20-048
Giant desmoid tumours: two unusual cases without a history
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Background & Objective: Desmoid-type fibromatoses are rare diseases. Mainly they can be abdominal, intra-abdominal or extra-abdominal. Mesenteric fibromatoses are commonly located on the mesentery of the small bowel, ileocolic mesentery, gastrocolic ligament, omentum or retroperitoneum.
Method: We would like to share two case reports with unusual presentations.
Results: Case 1: A 31-year old woman presented with abdominal pain. She had no prior surgical history nor known diseases. CT scan was reported as a mass was found between the spleen and splenic flexura. Macroscopically the mass was measured as 10,5x9x7cm. It was attached to the gastric mucosa with a thin stalk and locally invaded the colon. Microscopically it was composed of uniform spindle-shaped cells with minimal atypia set in a variably cellular collagenous stroma. Case 2: A 22-year-old man presented with abdominal pain. CT revealed a mass on pancreatic tail extending to the left paracolic space. After the surgery, the mass was measured as 21x20x9cm, with a pseusodocapsule containing a 6 cm area of residue pancreas. Its' sections contained a 13x2 cm cystic degeneration field attached to the pancreas. Histopathologically there was a fibroblastic proliferation again set in a highly collagenous stroma. Immunohistochemically, both of the cases showed beta-catenin positivity and CD34 negativity. We diagnosed both cases as desmoid-type fibromatoses.
Conclusion: These tumours may overlap with other stromal tumours, especially with GIST and without a significant history like FAP or prior abdominal surgery, diagnosis can be challenging.

PS-20-049
Budget impact of molecular lymph node staging in colorectal carcinoma. Should we invest more in diagnosis?
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Background & Objective: Diagnosis of early-stage colorectal carcinoma (CRC) is a great achievement of CRC screening programs. The

likelihood of pN0 diagnosis with H&E is significant in this new scenario. Nodal stage (pN) determines CRC survival and the need of adjuvant therapy. Lymph node (LN) metastases not detected by H&E are associated with poor prognosis. Molecular LN analysis is more sensitive but more expensive than H&E. We aimed to evaluate the healthcare budget impact of incorporating the molecular one-step nucleic acid amplification (OSNA) assay for CRC LN analysis.

Method: Analysis of the total costs of actual clinical practice and with performing OSNA. The costs of the procedures and clinical impact are assessed at short and midterm. The economic data was obtained from the Spanish Health Costs Database (eSalud), from public websites-literature review and data from our institution.

Results: Conventional CRC H&E LN workout-pN stage costs 100 €/patient. pN0 patients do not receive chemotherapy, but 10-15% patients may recur with stage IV and first-second line chemotherapy; total costs 1,135,235€. Molecular LN analysis costs 500€/patient. Our stage II data: 80% negative patients at very low-risk or cured due to high NPV of the assay; 20% positive-stage III, only 6% with high OSNA results with stage IV progression; total cost 612,000€.

Conclusion: Clinical management of stage II CRC patients could become evidence-based by using more precise methods of LN diagnosis. The full benefits of early diagnosis and intervention could be seen through an initial investment in the diagnostic process and would lead to great savings than more costly later stage treatment.

PS-20-050

Bridging genomics and phenomics of gastric carcinoma

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Background & Objective: Genetic alterations are the starting point leading to numerous changes in clinical and pathologic features (phenotypes) of individual cancers; however, their inter-relationships in gastric cancer (GC) are not clear.

Method: We performed massive parallel sequencing of 6,839 exons from 381 cancer-related genes and introns from 23 genes in 330 GCs and compared the results with clinical, pathological, and immunohistochemical (IHC) findings.

Results: The most significantly mutated genes and respective prevalence of genetic alterations were as follows: TP53 (54%), ARID1A (22%), CDH1 (22%), ERBB2 (24%), APC (15%), PIK3CA (12%), RNF43 (10%), and KRAS (9%). We classified cases with ≥26 SNV/indels as the high-frequency mutation group (HMG). The HMG accounted for 11% of GCs and was most highly concentrated in MSI-H patients but also distributed throughout TP53 mutant and wild-type groups. HMG was associated with longer survival in MSS GC subtype (P=.024). Mutations of CDH1 (P=.004), ERBB3 (P=.011), and CARD11 (P=.037) were significantly associated with shortened overall survival, and poorly cohesive GC subtype/CDH1 combination showed the worst survival (P<.001). PTEN protein loss (22%) correlated well with underlying PTEN alterations (P<.001) and was closely associated with MSI-H, increased cellular immune response, and PD-L1 expression. For TP53, 68% of TP53 wild-type GC cases showed 0% p53 IHC but 9% showed 80-100% p53 positivity, resulting in high sensitivity (97.8%) and low (15.9%) specificity.

Conclusion: We correlated genetic alterations, clinical, and pathologic phenotypes of GC and found that phenotype and genotype were distinct and related independently.

PS-20-051

Mechanisms of genomic instability in human colorectal cancer: the role of signaling by Integrin-Linked-Kinase (ILK)

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Background & Objective: Genomic instability accounts for the majority of cases of colorectal cancer (CRC). Integrin-linked kinase (ILK), a focal adhesion protein, regulates cell proliferation, survival, cell adhesion and cell migration. Recently it was demonstrated that ILK is also localized at centrosomes and regulates microtubule dynamics and cell cycle progression. ILK has been also shown to regulate the DNA licensing factor Mcm7. Since errors in mitosis and DNA replication lead to genomic instability we assume that deregulation of ILK may be involved in mechanisms of genomic instability in human CRC.

Method: We studied the expression of ILK, in relation to p53 and DNA damage response markers (DDR) p-γH2Ax and p-ATM/ATR substrate using immunohistochemistry in 83 human CRC samples. To study the effects of ILK overexpression in mitosis and centrosomes, diploid HCT116 human colorectal cancer cell line was transiently transfected with ILK plasmid. Mitotic spindle morphology, centrosome number and mitotic count was evaluated in control transfectants and ILK overexpressing cells.

Results: ILK was overexpressed in human CRC and its expression correlated with stage and LN metastasis. DDR markers p-γH2Ax and p-ATM/ATR were overexpressed in CRC but there was no significant correlation with pathological parameters or ILK expression. ILK was efficiently overexpressed in transfectant cells and localized at centrosomes and mitotic spindles. Fewer mitotic cells were observed in ILK overexpressing cells after nocodazole treatment suggesting that ILK overexpressing cells override mitotic arrest upon mitotic poisons.

Conclusion: Further analyses are required to clarify the role of ILK overexpression in mitosis and mechanisms of genomic instability.

PS-20-052

Heterogeneity of KRAS, NRAS, PIK3CA and BRAF mutational status in primary tumour, lymph nodes and liver metastases in sporadic colorectal cancer

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Background & Objective: Mutations in KRAS and NRAS genes are associated with poor response to anti-EGFR therapies in patients with metastatic colorectal cancer. Also, approximately half of the patients with wild-type KRAS colorectal carcinoma do not respond to anti-EGFR. This could be because treatment decision is made based on the mutational profile of the primary tumour, regardless of the presence of tumour subclones harboring RAS mutations in lymph nodes or liver metastases.

Method: We analyzed KRAS, NRAS, BRAF and PI3KCA genes using low-density microarray technology in 26 paired primary tumours, 16 metastatic lymph nodes and 34 liver metastases samples from 26 untreated patients (76 samples).

Results: Overall, 37 mutations were detected (11 in primary tumours, 9 in lymph nodes and 17 in liver metastases). The most frequent mutation in PT was KRAS (15%), followed by PI3KCA (15%), NRAS (8%) and BRAF genes (4%). In the 16 lymph node metastases analyzed, 4 (25%) showed KRAS mutaions, 3 (19%) NRAS and 1 PI3KCA and BRAF (6%). The most prevalent mutation in liver metastases was KRAS (35%), followed by PI3KCA (9%) and BRAF (6%). 15 (58%) cases displayed an overall concordance in the mutation status in all samples, suggesting no clonal evolution. 11 patients (48%) showed different mutations among primary tumour and lymph node/liver samples, suggesting intertumoural clonal evolution.

Conclusion: We confirm the presence of different mutational profiles among prymary tumour, lymph node metastases and liver metastases. These results suggest the need of performing the mutational analysis prior to anti-EGFR treatment in all available tumour samples of the patient.

PS-20-053

Carditis: a relevant marker of gastrooesophageal reflux disease

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Background & Objective: Columnar-lined mucosa at the gastro-oesophageal junction may contain an inflammatory infiltrate, commonly referred to as carditis. Its etiology is not entirely clear since published data are conflicting. Some authors believe it is secondary to gastrooesophageal reflux disease (GERD) and others to *H. pylori* gastritis. This prospective study aimed at clarifying the relationship between carditis and the histological, clinical and endoscopic findings of GERD, in individuals negative for *H. pylori* infection.
Method: Biopsy material was systematically sampled from above and below the gastrooesophageal junction. Reflux-associated changes of the oesophageal squamous epithelium were assessed according to the Esohisto consensus guidelines. Grading of carditis was performed according to the Updated Sydney System.
Results: 873 individuals participated in the study. 590 (67.5%) had chronic carditis. Of these, 468 (53.6%) had mild chronic inflammation, with 321 individuals (68.6%) showing no or minimal changes on endoscopic examination. Chronic carditis was associated with GERD-related changes in the oesophageal squamous epithelium ($p<0.0001$). Data retained statistical significance even for individuals with mild chronic carditis and/or endoscopically normal mucosa. Chronic carditis was also associated with the presence of intestinal metaplasia ($p<0.0001$) and had a significant association with patients' symptoms of GERD ($p=0.0107$). This remained valid for mild chronic carditis in all patients ($p=0.0038$) and particularly in those with mild chronic carditis and normal endoscopic mucosa ($p=0.0217$).
Conclusion: In conclusion, chronic carditis appears to be the consequence of GERD, correlating with patients' symptoms and endoscopy. These results are valid in individuals with nonerosive reflux disease, which indicates a higher sensitivity of histological diagnosis.

PS-20-054

MAP1-LC3A expression in gastric cancer

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Background & Objective: In Autophagy, damaged proteins, membranes and organelles are engulfed into autophagosomes and, following fusion with lysosomes, the material is digested to simple molecules that are used by the cell for its metabolic demands. MAP1LC3A (LC3A) protein is a basic component of the autophagosome double membrane.
Method: Paraffin embedded material from 121 gastric cancer patients treated with surgery were analysed immunohistochemically for the expression of the LC3A protein. The proportion of cancer cells with strong LC3A cytoplasmic/perinuclear expression was recorded in all x200 optical fields and the mean value was used to score each case. Furthermore, we examined a cancer specific pattern of LC3A expression: Stone-like Structures (SLS) are recognized as large, rounded, densely stained, amorphous cytoplasmic material, enclosed within cytosolic LC3A+ vacuoles. Quite often these occupy the whole cytoplasm of cancer cells. The number of cells with SLS features was recorded in all x200 optical fields and the score was obtained by dividing the total number of SLS by the number of optical fields
Results: The median percentage of cancer cells with strong cytoplasmic LC3A expression was 30%. The median SLS score was 0.2 (range 0-1). A higher SLS score was noted in tumours of the gastro-oesophageal junction ($p=0.009$). High SLS score was significantly related with poor prognosis ($p=0.008$) and this persisted in multivariate analysis ($p=0.003$, hazard ratio 2.01).
Conclusion: Intense autophagic activity, as assessed with the LC3A immunostaining and SLS quantification, is a strong prognostic marker in gastric cancer and can be tested for clinical use.

PS-20-055

Distribution of SDHC methylation in neoplastic and non-neoplastic tissue in patients with Carney triad

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Background & Objective: Carney triad (CT) is a non-familial syndrome affecting young women, which manifests with multifocal gastric GISTs, paragangliomas and pulmonary chondroma. The CT-associated tumours are characterized by deficiency of mitochondrial succinate dehydrogenase (SDH) enzymatic complex. Recently, it was found out, that the deficiency results from SDHC gene promoter hypermethylation. To elucidate the topical distribution of SDHC promoter methylation in CT patients both neoplastic and available non-neoplastic tissue of 3 newly diagnosed patients with CT were tested for SDHC promoter hypermethylation.
Method: For SDHC promoter aberrant methylation analysis the tumour DNA samples were subjected to bisulfite conversion and methylation-specific PCR targeting the SDHC promoter.
Results: All 3 patients were females, mean age at the time of first presentation was 13.3 years. Epithelioid GISTs of the stomach were present in all cases. All investigated tumours were found to bear SDHC promoter hypermethylation. Non-neoplastic tissues of a perigastric lymph node and duodenum were unmethylated at the SDHC promoter site, whereas the non-neoplastic tissue of the stomach displayed SDHC promoter hypermethylation.
Conclusion: Lack of SDHC epigenetic silencing in the non-neoplastic lymphoid and duodenal tissue (i. e. tissues not involved in the development of CT-associated tumours) in association with the finding of SDHC promoter hypermethylation in non-neoplastic gastric wall favors the hypothesis of postzygotic somatic mosaicism as the biological background of CT, as well as it explains the multifocality of gastrointestinal stromal tumours of the stomach occurring in this scenario. However, precise mechanism responsible for the peculiar organ-specific distribution of CT-associated tumours is still unknown.

PS-20-056

Clinicopathological impact of the new American Joint Committee on Cancer (AJCC) classification of appendiceal mucinous neoplasms tumours in a series of 27 cases

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Background & Objective: The classification and nomenclature of mucinous neoplasm of the appendix is challenging and in continuous evolution. Last AJCC classification has implemented some relevant modifications. We focus on the disappearance of T1/T2 on low grade appendiceal mucinous neoplasms (LAMN) and on the evaluation of presence of cellular/acellular mucin involving the serosa/mesoappendix. We have retrospectively studied the impact of those changes in our cases.
Method: All mucinous appendiceal tumours collected at our institution during the last 12 years have been considered (n=27). All the slides have been reviewed and applying actual grading and staging diagnostic criteria have been reclassified.

Results: Twenty-four LAMN and three high grade appendiceal mucinous neoplasms (HAMN) have been diagnosed. According to stages we classified them as follows: 37.3 % pTis (all LAMN), 25.9% pT3 (four LAMN and the three HAMN) and 37.3% pT4a (all LAMN). Recurrences were not seen in 24 cases, but in three patients, peritoneal involvement was discovered during follow up and died of the disease. In addition, these cases were the only ones were cellular mucin was found in the deeper aspect of the tumour (whereas the rest was acellular mucin). Right hemicolectomy was performed in 3 cases to clear tumour margin but no residual tumour was found.
Conclusion: Novel staging classification of mucinous appendiceal tumours has had no impact at all in our cases, pT1 and pT2 tumours are extremely infrequent. Cellular mucin within mesoappendix or in the visceral peritoneum is suggested as a significant bad prognostic factor.

PS-20-057
Dynamics of morphological changes in the wall of the small intestine during developing enteral insufficiency
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Background & Objective: In abdominal surgery it's extremely important to determine the timing of the closure of small intestinal fistulas imposed for the purpose of unloading the small intestine (SI) due to acute intestinal obstruction and the syndrome of enteric insufficiency (EI). For this structural and functional changes in the intestinal should be studied.
Method: Fragments of resected parts of the SI (116 slides) of 24 patients (with age range from 56 to 64 years) with acute intestinal obstruction were examinated. The material was divided into 3 groups depending on the stage of EI: I - 9, II - 7, III - 8 patients. Histochemical and morphometric methods are applied.
Results: At first stage of EI, pronounced vascular hyperemia, edema of all layers of the intestinal wall and increased secretion without the formation of an inflammatory infiltrate, hyperplasia of the lymphoid tissue of the intestine, an increase in the number of intraepithelial lymphocytes were found. At the II stage of EI acute exudative purulent inflammation with desquamation and dystrophy of epithelial cells, a decrease in the volume of lymphoid tissue is expressed. In cases with stage III of EI purulent inflammation in all layers of the intestine was found, and lymphatic formations and intraepithelial lymphocytes almost were not detected.
Conclusion: Direct dependency between the degree of inflammation in the wall of the SI and the stage of EI in patients with intestinal obstruction was revealed, associated with the reduced reactive hyperplasia of the lymphoid tissue and the decrease in secretory activity of the mucosa.

PS-20-058
Histopathological study of the effects of antitumoural agent endoscopic placement in a murine model of colorectal cancer
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Background & Objective: Azoxymethane-induced colorectal cancer (CRC) in mice shares many clinical, histologic and molecular features with human CRC. Although direct administration of anti-CRC drugs in humans is not feasible, endoscopic targeted therapy of early invasive tumours with antitumoural agents may be a good strategy to minimize side effects compared to surgery. The aim of this study was to evaluate microscopic features in a murine model of azoxymethane-induced CRC after intratumoural injection with different combinations of antitumoural agents in a drug-eluting platform.
Method: Twenty Sprague-Dawley male rats (body weight, 100-125 g) developed azoxymethane-induced CRC with endoscopic follow-up at 3-35 weeks. Rats were divided into several therapeutic groups which were treated with irinotecan plus an anti-vascular endothelial growth factor receptor (anti-VEFR) agent (aflibercept®, bevacizumab®); irinotecan plus an anti-epidermal growth factor receptor (anti-EGFR) agent (panitumumab®, cetuximab®); or irinotecan alone. Total colon resection was performed 10 days after intratumoural injection of antitumoural drugs. Formalin-fixed, paraffin-embedded tissue sections were studied using haematoxylin-eosin stain.
Results: CRC development was achieved in all rats, five of which (25%) showed tumour multifocality. Average tumour size was 7.2 mm (6-8). All neoplasms induced were seen to be invasive adenocarcinomas. Tumour size reduction reached statistical significance only in animals treated with aflibercept® plus irinotecan, a combination that also resulted in total tumour necrosis.
Conclusion: Intratumoural injection of an anti-VEGF agent in a drug-eluting platform is able to produce tumour necrosis in an experimental model of CRC. This therapeutic approach may turn out to offer an effective tool for the treatment of human CRC.

PS-20-059
Complicated and uncomplicated appendicitis in surgical specimens: review of our experience
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Background & Objective: Appendicitis is typically managed by surgery, but recent studies have assessed the role of conservative management in selected patients. Our aims are to review all surgical appendices and to see how the rates of gangrenous, abscessified and perforated appendicitis vary over time.
Method: Retrospective study of all appendices surgically resected in our institution between 2008-2017 (n=3022). Clinicopathological data were collected and stratified by year of diagnosis.
Results: 55.9% of patients were male and age ranged between 0-98 years (mean:34.81). 74% of appendicitis were acute or suppurative (ASA), 10.3% gangrenous or perforated (GPA), 8.1% abscessified (AA) and 5.2% of all appendices showed no inflammation. Neuroendocrine tumours, low-grade mucinous neoplasms, high-grade mucinous neoplasms or carcinomas, and metastases were identified in 0.4%, 0.3%, 0.2% and 0.1% of all cases. These tumours occurred at different ages (mean:35.23, 64.38, 66.2 and 49.5). The rate of ASA diminished over time and the rates of GPA and AA increased considerably (peaking in 2015). ASA was more frequent in patients 11-20 and 21-40 years old, which showed the lower rate of GPA. The frequency of GPA is similar between patients 0-10 years old and >40 years old, and AA is more frequent in patients 0-10 years old. The rate of uninflamed appendices has been stable.
Conclusion: The rate of GPA has increased in the last years. This can be due to a change in the management protocols, and it can be associated with a higher rate of post-surgical complications and patient morbidity and mortality.

PS-20-060
FAK expression predicts poor response to neoadjuvant therapy in gastric carcinoma
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Background & Objective: Neoadjuvant therapy (NAT) is widely used in gastrointestinal neoplasms, including gastric carcinoma. However, some patients are unresponsive to this therapy and this can delay or make surgery impossible due to tumour progression during NAT. Our aim is

to analyze the potential role of focal adhesion kinase (FAK) expression to predict tumour regression in gastric carcinoma. This molecule is associated to the PTEN pathway for tumour development and progression.
Method: Retrospective multicenter study of patients with gastric carcinoma receiving NAT prior to surgical resection. Regression has been categorized according to modified Ryan/CAP criteria in four groups. We have analyzed demographic, tumour features and focal adhesion kinase (FAK) immunohistochemical expression to predict tumour regression.
Results: 57 patients have been enrolled in the present study. After NAT only 5.4% of the patients achieved a complete response and most patients showed a poor grade 3 one (59.4%). Our results show that FAK expression was found in 70.45% of the patients with poor regression as opposed to 52% of the patients with good regression. This association between FAK expression and poor response was significant with chi-squared test.
Conclusion: FAK is a tyrosine kinase, involved in growth signals regulation and overexpression has been associated in the literature to worse prognosis. In this series of NAT-treated patients we have confirmed that FAK immunohistochemical expression is a harbinger of poor response to therapy and can help choose a subgroup of patients that might be more adequate for direct surgical resection instead of NAT.

PS-20-061
High Yes-associated protein 1 with concomitant negative LATS1/2 expression is associated with poor prognosis of advanced gastric cancer
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Background & Objective: The Hippo pathway is one of the tumour-suppressive pathways and its inactivation is known to be associated with progression and metastasis of various cancers. LATS1/2 (large tumour suppressor homolog 1 and 2), YAP1 (Yes-associated protein 1), and TEAD4 (TEA domain-containing sequence-specific transcription factors 4) are core components of the Hippo pathway, and the specific roles of LATS1/2, YAP1 and TEAD4 have not been studied in advanced gastric cancer (AGC).
Method: A total of 318 surgically resected AGCs were retrieved. Immunolabeling for LATS1/2, YAP1 and TEAD4 was compared with clinicopathologic factors including patients' survival.
Results: High expression of YAP1 and TEAD4 was identified in 108 (34.0%) and 131 (41.2%) cases, respectively, and 223 (70.1%) cases were negative for LATS1/2 expression. High YAP1 expression was significantly correlated with presence of perineural invasion (p=0.032). High YAP1 and high TEAD4 expressions were significantly associated with poor overall survival (p<0.001 and p=0.003, respectively), and negative LATS1/2 expression was also associated with poor overall survival (p=0.002). Combined expression of YAPlowLATS1/2pos showed better overall survival while YAPhighLATS1/2neg expression showed worse overall survival than others (p<0.001). Expression of YAP1high (HR=2.938; 95% CI, 1.726-4.998; p<0.001), LATS1/2neg (HR=0.371; 95% CI, 0.181-0.758; p=0.007), and combined YAPhighLATS1/2neg (HR=13.785; 95% CI, 3.245-58.554; p<0.001) were independent poor prognostic factors of AGC patients.
Conclusion: Expression of YAP1, LATS1/2 and TEAD4 can be used as prognostic markers and has value to risk stratification of AGC patients.

PS-20-062
Colorectal cancer on pT1 polyps: our results and analysis of risk factors
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Background & Objective: The detection of colorectal cancer (CRC) in pT1 polyps has increased due to screening programs. Pathological risk factors predictive of lymph node (LN) metastasis are well known. Our aim is to analyse the association between risk factors and presence of LN metastasis.
Method: We retrospectively identified 61 malignant polyps diagnosed in the last 20 months. Tumour grade and size, lymphovascular invasion, depth of submucosal invasion, tumour budding and distance to the resection margin were reported. Outcome data was collected from surgical pathology reports. We analysed the predictive value of LN metastasis for each variable.
Results: Among 61 cases of pT1 CRC polyps diagnosed 29 underwent surgical intervention (47%) and 6 of them showed LN metastasis (21%). Multivariate analysis showed significant association between tumour budding and LN metastasis (OR= 4,67; CI= 1,12-19,02, p=0,001). Tumour grade and vascular invasion showed weaker risk association. Going further, we created a variable resulting from the sum of the number of risk factors. This new variable showed an OR=6,33 (CI=1,21-33,08, p=0,006) and a clear ascending trend in relation to the number of metastatic LN.
Conclusion: Tumour budding, as described previously, is a reliable predictor of LN metastasis in pT1 CRC. The size of this series is insufficient to draw meaningful conclusions but highlights one of the variables over the others (tumour budding) and suggests that the inclusion of the number of risk factors with a specific weight in a predictive model may provide greater affinity in the prediction of LN metastasis.

PS-20-063
Pathological features of total gastrectomy specimens from asymptomatic hereditary diffuse gastric cancer patients and implications for clinical management
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Background & Objective: Total gastrectomy (TG) is the treatment of choice for hereditary diffuse gastric cancer (HDGC) patients carrying a pathogenic CDH1 variant. In this study we aimed at understanding better HDGC syndrome, by exploring clinicopathological findings of TGs from asymptomatic HDGC patients.
Method: A comprehensive literature review was carried out, searching for TGs performed in asymptomatic HDGC patients. Fourteen unpublished cases, analysed in our institution, were also included.
Results: The series encompassed 174 cases. The mean age was 38 years and 56.9% (99/174) were women. Pre-operative endoscopic biopsies were positive in 20.7% (36/174). A macroscopic lesion was apparent in 6.3% (11/174) TGs. Histopathological analysis detected intraepithelial lesions in 33.3% (58/174) and/or intramucosal signet-ring-cell (SRC) carcinoma in 87.4% (152/174) TGs. When we explored the type of protocol used for specimen handling, we found that microscopic cancer foci were detected in 95.3% (122/128) TGs when a systematic, "research" protocol (assessment of the totality of gastric mucosa) was applied, and only in 62.5% (25/40) when no specific protocol was used (p<0.001). *Helicobacter pylori* infection was found in 23.8% cases. Alterations in non-neoplastic mucosa included chronic gastritis, tufting, globoid change/vacuolizazion/hyperplasia of the superficial foveolar epithelium, among other features.
Conclusion: TG is advised for asymptomatic HDGC patients, since surveillance by endoscopy has low sensitivity for the detection of early HDGC. In the setting of HDGC, the use of a "research" protocol for handling of TG specimens is of the utmost importance, for the detection of precursor and/or invasive lesions.

PS-20-064

Ki67 and CD44 as markers of colorectal cancer's carcinogenesis models

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Background & Objective: Hyperplastic polyps (HP), sessile serrated adenomas (SSA), adenomas tubular (AT), adenomas tubulovilluos (ATV) and traditional serrated adenomas (TSA) are considered to be possible colorectal cancer's precursors. There are two colorectal cancer`s carcinogenesis models: ascending and descending which are declared as alternative. However, there is no data about cancer's precursors and cancer`s carcinogenesis matching. CD44 is cell adhesion molecule, which is involved in many types of carcinogenesis including colon&rectum. Ki67 is protein of proliferative activity, reflecting the proliferating processes alterations in tumour.
Method: We assessed immunohistochemical expression of Ki67 and CD44 in 32 colorectal cancer and 83 colon and rectum polyps.
Results: In AT, ATV and TSA Ki67 and CD44 reactions were observable only in upper part of polyps and had a tendency to spread ("descent") downward. In HP and SSA groups reactions were detected in lower part of crypts with the spread to the middle crypt`s thirds. There was complete parallelism between Ki67 and CD44: in AT, ATV, and TSA groups they were both expressed in the upper parts of the polyp, in HP and SSA, on the contrary, in the basal sections ($p < 0.01$).
Conclusion: The described models of carcinogenesis are not alternative. AT, ATV and TSA are characterized by a "descending" model, for HP and SSA, on the contrary, "ascending". These circumstances indicate the fundamental difference between AT and ATV from HP and SSA.

PS-20-065

Expression of E-cadherin and p53 protein in colorectal tumours associated with tumour-associated macrophages density

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Background & Objective: Decreased expression of E-cadherin (E-cad) is a marker of tumour progression in colorectal cancer. This is due to the increase metastatic potential and the accumulation of mutant p53 protein in tumour cells. In addition, tumour-associated macrophages (TAMs) are always present in the tumour stroma, which produce a wide range of substances, including proteases that lysate E-cad. The aim of the study was to reveal the relationship between the E-cad and p53 protein expression and TAMs (CD68+ cells) density in colorectal tumours.
Method: A total of 70 patients with colorectal cancer were examined. In 19 patients (27,1%) was detected a normal expression of E-cad in the tumour (group 1), and a decrease in E-cad expression was found in 51 patients (72,9%) (group 2). The average percent p53+ cell in group 1 was 32,3%, and in group 2 - 59,8%.
Results: In group 1, the average density of TAMs was 645,1 ± 28,6 CD68 + cells per 10 field of view x400, and in group 2 the density of TAMs was 1,5 times higher – 1348,3 ± 14,8. There were found statistically significant inverse relationships between the level of E-cad expression and the accumulation of mutant p53 protein in tumour cells ($r = -0,373$, $p = 0,028$). Also, with an increase in the density of TAMs, the expression of E-cad decreased ($r = -0,401$, $p = 0,018$).
Conclusion: Thus, TAMs in colorectal cancers reduce intercellular adhesion and cause the accumulation of mutant p53 in tumour cells, increasing malignant and metastatic tumour potential.

PS-20-066

Assessment of the relation between the presence of tumour deposits and histopathologic parameters in resection specimens of colorectal adenocarcinomas

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Background & Objective: The aim of this study was to evaluate the relation between the presence of tumour deposits and histopathologic parameters in resection specimens of colorectal adenocarcinomas.
Method: A retrospective study was carried out in 278 patients, who underwent radical surgery with regional lymphadenectomy from 2014 to 2017.
Results: On univariate analysis, the presence of tumour deposits (TD) on resection specimens was significantly associated with tumour histology ($p = 0,025$) and lymphatic invasion (LI) ($p = 0,001$). Also, there was a marginal significance between the presence of TD and pT stage ($p = 0,058$).
Conclusion: The pathogenesis of tumour deposits still remains unclear but the significant association between TD and LI may suggest a potential role in pathogenesis of TDs. Further studies with a relatively larger number of cases are needed to establish the mechanisms for TD pathogenesis.

PS-20-067

Gastric myenteric plexus and *Helicobacter pylori* infection – is there a relationship?

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Background & Objective: Morphological assessment of gastric myenteric nerves in patients with *Helicobacter pylori* (*H. pylori*) infection has not been previously been performed. Our study aimed to investigate the relationship between *H. pylori*-associated gastritis and myenteric ganglia changes in the stomach.
Method: We evaluated the number and area of gastric myenteric plexus in full-thickness archival tissue samples obtained from 40 patients with *H. pylori* infection who underwent surgery for gastric cancer. Data were compared with findings on samples collected from 40 age- and sex-matched subjects without bacteria. All specimens were selected from gastric areas at least 5 cm away from macroscopically visible tumour and were analyzed immunohistochemically for S100 expression
Results: Both number and area of myenteric ganglia were significantly larger in patients with *H. pylori* infection compared to control group, thus revealing a correlation between the presence of bacteria in the stomach and hypertrophy and/or hyperplasia of myenteric plexus. However, we didn`t observe a relationship between the nervous enlargement level, on one hand, and *H. pylori* density, grade of gastritis activity or periganglionic inflammation grade, on the other hand.
Conclusion: The present study shows for the first time that *H. pylori* infection may induce structural alterations of gastric enteric nervous system, thereby providing a morphological basis for a better understanding of some still unclear aspects of pathogenesis of *H. pylori* infection.

PS-20-068

Neutrophil extracellular traps in colorectal cancer and their crosstalk with mast cells

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Background & Objective: Neutrophils are well-known mediators in tumour biology, and their role has been recently redefined by neutrophil extracellular traps (NETs), as they have been implicated in cancer growth,

metastasis and cancer associated thrombosis. Since they have never been studied in colorectal carcinoma (CRC), we sought to determine their presence in CRC surgical specimens. Moreover, based on a recent study demonstrating that platelet-derived inorganic polyphosphate (polyP) primes neutrophils to release NETs, we investigated on the same specimens the presence of polyP, as a possible NET inducer.
Method: Colectomy specimens were obtained from ten patients with CRC. NETs deposition and neutrophil presence as well as polyP expression were examined by immunohistochemistry and fluorescence staining. Biopsies with adenomas and other non-neoplastic conditions were used as controls.
Results: NETs and neutrophil localization were prominent in tumour sections and the respective metastatic lymph nodes. The presence of polyP was apparent, expressed by mast cells that were detected near tumour cells and neutrophils. Interestingly, in CRC and adenomas with high-grade dysplasia, a substantial number of mast cells, co-expressed intracellularly polyP with CD68 antigen (CD68+), but this was not the case in the other examined disorders.
Conclusion: These data support further the role of neutrophils and NETs in cancer biology. Moreover, they reveal a possible interplay between neutrophils and mast cells in CRC suggesting polyP-expressing mast cells among the stimuli which prime neutrophils to release NETs. Moreover, the detection of CD68+ polyP-expressing mast cells could represent a potential prognostic marker in CRC and adenomas.

PS-20-069
The clinicopathological and immunohistochemical study of gastrointestinal stromal tumours
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Background & Objective: The clinical behavior of gastrointestinal stromal tumours are divergent. The aim of the present study was to define the clinicopathological features that determine the patient's outcome.
Method: Sixty-five gastrointestinal stromal tumours were reviewed with their histological, immunohistochemical and clinical features and compared with their clinical outcome statistically.
Results: Tumours were located in the stomach (39, 60%), small intestine (22, 33.8%) and large intestine (4, 6.2%). Immunohistochemically, CD 117 positivity was found in 90.8%, whereas CD34, Smooth muscle actin, Desmin and S100 positivity was found in 73.3%, 61.7%, 11.7% and 28.3% of tumours respectively. All six ''CD 117-negative" cases expressed DOG-1. Mean Ki-67 proliferation index was 8.69%±12.76. Liver metastasis was detected in seven cases. Significant association was detected between decreased mean survival time and increased tumour size ($p<0.001$), mitosis ($p<0.001$), the presence of necrosis ($p=0.001$), metastasis ($p=0.033$), Ki-67 proliferation index ($p=0.002$) and risk category ($p<0.001$). CD 34 positivity was mostly seen in stomach ($p=0.001$), and CD 34 positive tumours had longer overall survival (92.85.±5.77 months versus 67.21±13.68 months) ($p=0.046$). Higher Ki-67 proliferation index (≥6%) was also correlated with the presence of metastases ($p=0.015$).
Conclusion: Our study indicates that increasing tumour size, high mitotic activity and Ki-67 proliferation index, the presence of necrosis, and metastasis were found to be related to shorter survival time.

PS-20-070
Which is the right assessment method for primary clarithromycin resistance? Resistance rates of eradication-naive and macrolide-naive *Helicobacter pylori* infected patients in a large scale study
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Background & Objective: Macrolide antibiotics are widely used in several indications in clinical practice. Any prior macrolide consumption can lead to development of clarithromycin resistance. Our aim was to compare primary and secondary resistance rates according to age and gender in a large cohort of Helicobacter-infected patients.
Method: 4,744 *H. pylori* positive patients (2708 females; 57%, 2036 males; 43%) were studied from the Central Hungarian Region. Gastric mucosal tissue slides were investigated by a bacterial rRNA-targeted FISH-test detecting clarithromycin-susceptible and -resistant *H. pylori* bacteria. Helicobacter eradication-related and -independent antibiotic consumption anamneses of patients were collected in cooperation with Hungarian National Health Insurance Fund.
Results: Overall clarithromycin resistance rate was 17% while eradication-naive and macrolide-naive resistance rates were 12% and 3% in the whole cohort, respectively. The same resistance rates in age groups 20-29, 30-39, 40-49, 50-59, 60-69 and 70+ of males were 13%_13%_4%, 15%_12%_4%, 14%_9%_2%, 12%_8%_2%, 15%_10%_2%, 13%_11%_4% and of females were 20%_19%_5%, 21%_16%_4%, 24%_14%_3%, 22%_14%_3%, 21%_15%_2% and 13%_9%_4%, respectively. Overall and eradication-naive resistance rates of females were significantly higher ($p=0.0018$ and $p=0.0249$, respectively) while no gender difference was found in macrolide-naive patients ($p=0.4383$). Macrolide-treated females exhibited more frequent exposition to macrolides in comparison with males (3.18 vs. 2.61 dispension/patient).
Conclusion: Great differences between macrolide-naive and eradication-naive clarithromycin-resistance rates suggest that not only eradication-related but any other prior macrolide treatment should be considered for assessment of primary resistance and choosing the right Helicobacter-eradication protocol. Higher prevalence of clarithromycin-resistance in females is closely related to increased exposition to macrolide antibiotics.

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PS-20-071
Amyloidosis in the gastrointestinal system biopsies: case series from a single center
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Background & Objective: Amyloidosis is a disorder of protein metabolism characterized by extracellular accumulation of normally soluble proteins and polypeptides in fibrillar form. The disease can be either inherited or acquired. In this case series, we aimed to show the different clinical presentations of amyloidosis.
Method: Sixty-two patients with a diagnosis of amyloidosis in gastrointestinal system biopsies evaluated between 2004 and 2018. Associated clinical and histopathological findings, primary diseases of the patients, accumulating amyloid noted.
Results: Of 62 patients, the male to female ratio was 36/26, and the mean age of the patients was 54,5±16,3 (range, 21-87 years). Approximately 30% of the biopsies collected from the stomach. Followed by rectum, colon, duodenum, and small bowel in decreasing frequency. Associated histopathological findings were as follows: Atrophic gastritis, CMV infection, dystrophic calcification, gastric mucosal calcinosis, duodenitis, ischemic colitis, tubular adenomas, perforation, and ulceration. Most of the patients had the end-stage renal disease and familial Mediterranean fever.
Conclusion: In Mediterranean countries, the finding of Amyloid AA deposits is well known, particularly in gastrointestinal biopsies. Concerning etiology, the importance if familial Mediterranean fewer in those patients has already been documented. Gastrointestinal biopsies have a great sensitivity to detect amyloid accumulation especially in patients who have a systemic disease with the tendency to the deposition.

PS-20-072

Colorectal Hodgkin lymphoma in a patient with ulcerative colitis

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Background & Objective: ExtranodalExtranodal primary malignant lymphoproliferative processes in the gastrointestinal tract is rare. Lymphomas only account for 0.2-0.6% of large bowel malignancies and primary HL involving the gastrointestinal tract is only reported in a limited number of case reports. Reviews in the literature suggest an association with inflammatory bowel disease plus treatment immunosuppression that may lead to its treatment.
Method: 36-year-old woman diagnosed with ulcerative colitis since 2009, with several hospital admissions and refractory to conventional treatment (corticosteroids and 5-ASA), starts treatment with azatriopine and etrolizumab. Subtotal colectomy was performed due to perforation complication in 2015. In 2016, the rectal stump is received.
Results: Microscopically, a complete destructuration of the rectal wall was observed with multiple pseudonodules composed of abundant mixed inflammatory cellularity (lymphocytes, plasmids, abundant eosinophils) together with large que atypical Stembergoid-like cells (CD15, CD30, EMA positive) with in situ hybridization for EBV positive. Diagnosis of classic Hodgkin lymphoma associated with EBV in the context of long-standing ulcerative colitis.
Conclusion: The pathogenesis is unknown, but many theories are postulated. Several risk factors have been demonstrated for the development of lymphoproliferative syndromes associated with inflammatory bowel disease: Long-term chronic inflammation; infection of EBV and treatment with drugs modifying the immune response (especially in the combined use of thiopurines and biological agents). It is important to have these entities in mind in cases of inflammatory bowel disease refractory to treatment and of long evolution.

PS-20-073

Accuracy of magnetic resonance imaging to evaluate the location and possible infiltration of the peritoneal reflection in rectal cancer - a pathological correlation

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Background & Objective: Rectal tumours located at the level of the peritoneal reflection (PR) may affect the peritoneal serosa (T4a) or the mesorectal fascia (MRC +) with therapeutic and prognostic implications. The objective of this study is to determine the accuracy of magnetic resonance imaging (MRI) for tumour localization with respect to the PR and its potential involvement.
Method: This is a prospective observational study (2016-2017) of patients diagnosed with rectal cancer. An expert pathologist analyzed the location of the tumour with respect to the PR by coloring the mesorectum with Indian ink and the serosa with orange ink.
Results: In the 97 rectal specimens analyzed, the tumour was located above the PR in 18 cases, at level of the PR in 39 cases and below the PR, in 40 cases. The preoperative MRI correctly located 72.2% (65/90) of the tumours in relation to the PR. Ten out of 39 tumours (25.5%) were located at the PR level , presented involvement of the radial margin: 7 at the orange dye level (T4a, MRC-), 2 at the orange dye and Indian ink level (T4a, MRC +) and, 1 – exclusively- at the level of Indian ink (T3, MRC +)Regarding the peritoneal involvement, MRI detected 68.4% (13/19) of the cases with peritoneal involvement (T4a), 8/13 and 5/6 were grades 3 and 4 of Shepherd, respectively.
Conclusion: The use of double dye is useful to differentiate the peritoneal involvement (T4a) or mesorectal fascia (MRC +). MRI is a reliable method to determine the infiltration of the peritoneum or the mesorectal fascia, and its possible therapeutic and prognostic implications.

PS-20-074

The impact of TGF-beta1 expression and -509C/T polymorphism in HER2 negative gastric cancer patients

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Background & Objective: Gastric cancer (GC) is one of the most common malignant tumours worldwide. To date many tumour-associated antigens either intracellular or on the cell surface have been identified. The aim of this study was to examine the expression of TGF-beta1 and HER2 and the impact of the TGF -509C/T single nucleotide polymorphism (SNP) and HER2 Ile/Val SNP in GC patients.
Method: Using immunohistochemistry we investigated 30 patients with GC for expression of TGF-beta1 and HER2. Consequently, RFLP-PCR was performed to analyze the presence of -509C/T polymorphism of the TGF-beta gene and HER2 Ile/Val polymorphism. The clinicopathological parameters and survival were analyzed retrospectively.
Results: All patients were HER2 negative immunohistochemicaly. Our data demonstrate a relationship between survival and -509C/T polymorphism of TGF-beta1. The median survival of TC-genotype patients was 28.1 months whereas the median survival of CC-genotype patients was 33.2 months (x2=8.21, p=0.016; log-rank test). Also, 58.4% from patients with TGF-beta1-positive status is in III-IV stage vs. 41.6% in I-II (x2=74.43, p=0.035).
Conclusion: In conclusion our results suggest that expression of TGF-beta1 and -509C/T SNP was related to survival time and rapid progression for gastric cancer patients.

PS-20-075

Evaluation of programmed death-ligand 1 (PD-L1) expression in gastric and gastrooesophageal junction cancer using paired resection and biopsy specimens

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Background & Objective: Immune checkpoint inhibitor targeting the programmed death-1 (PD-1) pathway has shown safety and efficacy in advanced gastric and gastrooesophageal junction cancer in the phase 2 clinical trial, recently. Our aim is to characterize the PD-L1 expression pattern by immunohistochemistry and to show both biopsy and resection specimens could represent the PD-L1 expression status for selecting patients.
Method: Formalin-fixed, paraffin-embedded 39 tissue samples, available for both biopsy and resection specimens, were analyzed. Immunohistochemistry was performed using PD-L1 22C3 pharmDx, and the expression was evaluated by the criteria used in the Pembrolizumab clinical trial for gastric and gastrooesophageal cancer. A Combined Positive Score (CPS) of greater than or equal to 1 was considered as a PD-L1 expression. We evaluated CPS of matched 39 cases and investigated the expression pattern and the correlation of PD-L1 expression status between paired biopsy and resection specimens.
Results: Of 39 resection specimens, 33 showed CPS≥1, only two of which showed diffuse expression, otherwise focal or patch, revealing that PD-L1 expression in gastric cancer tends to show heterogeneity. Of 33 PD-L1 positive resection cases, only 10 (30.3 %) showed CPS≥1 in paired biopsy specimen and 23 (69.7 %) showed CPS<1, 17 of which showed completely no expression; no significant correlation between biopsy and resection specimen.
Conclusion: Our study revealed the heterogeneity of PD-L1 expression in gastric and gastrooesophageal cancer and showed biopsy would not be appropriate to evaluate PD-L1 expression for selecting patients for anti-PD-1 immunotherapy. The evaluation should be done by resection specimens except in inoperable stage IV cases.

PS-20-076

Interhospital participation in the analysis of clear cell change in colonic polyps

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Background & Objective: Reed et al. reported the first case of clear cell change in colon adenoma (AD) in 1983. Clear cell change, usually results from glycogen accumulation, is a rare differentiation, being less than 1% of all AD.
Method: Due to the low frequency of this entity, we carried out a search involving three hospitals in the north of Spain: Cabueñes, Bidasoa and Valdecilla between 2012 and 2018.
Results: All lesions were apparently sporadic, and none of the patients presented relevant family data. Case of Cabueñes Hospital, Gijón. A 63-year-old woman admitted with rectal bleeding, and a polyp in the sigma that was removed. Case of Bidasoa Hospital, Hondarribia. A 57-year-old man with irrelevant clinical history, a resection of a sigma polyp is performed. Case of Valdecilla Hospital, Santander. A 78-year-old man in rectal cancer screening, polyp is seen in the left colon. Cells show vacuolated cytoplasm, for histochemistry characterization of the clear cell change, PAS was used and the clear cell change vacuolar component was negative. In the three cases, lesions were diagnosed like tubular adenoma with low-grade dysplasia and clear cell change.
Conclusion: The presence of clear cell change is a rare finding with few cases reported. As the PAS was negative, the clear appearance isn´t due to the accumulation of glycogen or mucin. There is a possibility that this change, after electron microscopy studies, could be to degenerative changes with cytoplasmatic lipid-like material accumulation. There are no studies that associate this change with greater incidence to adenocarcinoma than classical adenomas.

PS-20-077

Distribution of mature and proliferating cells in serrated colon lesions due to CK20 and Ki67 expression

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Background & Objective: According to the modern classification of premalignant colon lesions, hyperplastic polyps (HP) and sessile serrated adenomas/polyps (SSA/P) are considered to bepossible colorectal cancer's precursors. However, the nature of these lesionsis not still determined.
Method: We assessed immunohistochemical expression of CK20 and Ki67 in 28 colon and rectum HPs, 30 SSA/P and 88 intact mucosa as comparing group.
Results: There was no significant difference revealed either by the nature of cell distribution or by the intensity of CK20 and Ki67 staining between HP and SSA/P. In precursor lesions there was more diffuse and less intensive reaction in comparison with intact mucosa ($p<0,01$). The expression of Ki67 in the lower half of the dilated SSA/P crypts is significantly lower than in the lower half of the undilated SSA/P crypts and the lower half of HP ($p<0,01$). No significant difference was revealed by the level of Ki67 between lower half of the undilated SSA/P crypts and the lower half of HP ($p>0,05$).
Conclusion: The absence of significant differences in the distribution of pattern and intensity of CK20, the similar localization of Ki67between HP and SSA/P suggest the biological similarity of HP and SSA/P. In principle the distribution of proliferating and mature cells in HP and SSA/P indicates the preservation of the cellular compartmentalization of crypts, which casts doubt on the tumour nature of HP and SSA/P.

PS-20-078

Role of the neuroendocrine system of the stomach in chronic reflux gastritis accompanied by *Helicobacter pylori* infection

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Background & Objective: To test the hypothesis of possible protective (anti *Helicobacter pylori*) role of duodenogastric reflux (DGR) by assessment of gastrin-containing (G-) cells density and acid production in patients with primary reflux gastritis and *H. pylori* infection.
Method: 66 patients with reflux gastritis were examined (51 with DGR only and 17 with DGR combined with *H. pylori* infection), 15 persons made up a control group. Gastric biopsies were studied using histochemical and immunohistochemical (chromogranin, synaptophysin, gastrin, cytokeratin 20, villin, MUC2, CDX2, ki67) methods.
Results: The acidity in patients with DGR was higher (pH=3.55±2.3) compared to control group (pH=6.85±1.34). A negative relationship between the pH and the concentration of the bile acids ($r=-0.45$, $p=0.046$) was found, so higher acidity was associated with increased level of bile acids. Hyperplasia of G-cells in the antrum of stomach was detected in patients with DGR (29.0±4.0 vs 16.5±0.7 in the control, $p=0.006$). In patients with gastritis caused by combination of DGR and *H. pylori*, the density of G-cells did not differ from the control group ($p=0.776$) despite a higher acidity level (pH=1.4±0.6).
Conclusion: The data obtained in this study on G-cell hyperplasia does not support the assumption of protective function of the bile reflux. An increase in the density of G-cells leads to hypergastrinemia, followed by an increase in the production of acid, inflammatory and adaptive changes in the gastric mucosa.

PS-20-079

Diagnosis abetalipoproteinemia, before neurological disorders

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Background & Objective: Abetalipoproteinemia (ABL) is a rare autosomal recessive disorder at microsomal triglyceride transfer protein (MTTP) gene and has also known Bassen-Kornzweig Syndrome. Absence of apolipoprotein-B containing lipoproteins cause fatty acids in intestinal cells which can't be exported as chylomicrons. Fat malabsorption, steatorrhoea, acanthocytosis, hypocholesterolemia are characteristic symptoms which are seen in first years of life. Retinitis pigmentosa, coagulopaty, posterior column neuropaty, myopathy, ataxia are appeared subsequently because of deficiencies in fat soluble vitamins.
Method: Istanbul University Cerrahpaşa Medical Faculty Department of Pathology`s archive had researched retrospectively between 2000 and 2017. Thirty cases had detected that were taken duodenal biopsies with ABL suspicion. Three cases had diagnosed abetalipoproteinemia. Oil-red stain had performed at frozen section. All H&E slides had examined.
Results: All cases were diagnosed in childhood and average age was 2. Endoscopic findings were similar as diffuse white duodenal mucosa. The two patients were sisters, but one of them who was diagnosed at the five years old had epilepsy. All cases had similar histopathological findings in intestinal biopsies, that were vacuolated, fat filled enterocytes which were positive for oil-red stain at frozen sections. These vacuoles were PAS negative. Because of their similar microscopical appearance like vacuolated enterocytes, differential diagnosis were between Chylomicron retention disease, Megalobastic anemia, Coeliac disease, Tropical suprue.
Conclusion: ABL is a rare disease, because of it causes neurological disorders effects life quality negatively. These patients must have vitamin supplementation and special diets during all their lives.

PS-20-080

PDX1 expression identifies serrated pathway in precursor lesions of the colon

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Background & Objective: Expresion of PDX1 has been reported in polys of the colon with serrated morphology. Serrated polyps are premalignant lesions accounting 15% - 30% of colorectal cancers. A correct identification of serrated polyps has an important impact in the follow-up and clinical management of patients. We analyze PDX1 immunohistochemical (IHC) expression in polyps of the colon to assess the utility of PDX1 staining to differentiate between serrated and conventional Wnt pathway.
Method: 109 polips of the colon consisted of 42 sessile serrated adenomas (SSA), 32 SSA with low grade dysplasia, and 35 tubular adenomas (TA) was analyzed. Size of the lesions ranged from 2 to 23 mm (media 7.5 mm). According to colon location 58 polyps (53.2%) were located in the right side, 30 (27.5%) in the left, 18 (16.5%) in the rectum, and in 3 (2.8%) cases location were unknown. Immunohistochemistry was performed with anti-PDX1 rabbit monoclonal antibody. Pancreatic tissue was used as positive control. Positive criterion was the presence of a continuous nuclear staining of the crypt epithelium.
Results: PDX1 expression was observed in 75 (68.8%) of the 109 polyps analyzed. According to histology positive stain was shown in 38 (90.5%) of 42 SSA, in 26 (81.3%) of 32 SSA with dysplasia and in 11 (31.4%) of 35 TA. The results showed a strong statistical significant association between PDX1 positivity and serrated morphology (p=0.000).
Conclusion: Our results show that the PDX1 expression is useful to identify precursor lesions of the colon with serrated morphology and to differentiate them from conventional type polyps.

PS-20-081

Lobular breast carcinoma metastatic to the stomach: report of five cases with targeted deep sequencing results

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Background & Objective: The stomach is a rare site of breast cancer metastasis. It is difficult to distinguish a metastatic lobular carcinoma from a primary gastric carcinoma on the basis of clinical, endoscopic, and pathological findings.
Method: From 2010 to 2016, we experienced 5 cases of metastatic lobular carcinoma to the stomach in endoscopic biopsies. We reviewed electric medical records of all patients and got results of targeted deep sequencing.
Results: The endoscopic findings were early gastric carcinoma in 3 cases and advanced gastric carcinoma in 2 cases. Immunohistochemistry (IHC) of metastatic lobular carcinoma was all ER-positive and HER2-negative. At the time of gastric metastasis, all patients manifested with multiple metastases including bone in 3 cases (60%). Only one patient died of disease after 10 months of systemic chemotherapy and the remaining four patients are alive with disease ranging from 4 to 41 months. In 4 cases, we could get targeted deep sequencing results using more than 300 tumour-related genes. In three each case, mutations of NF1 and CDH1 gene were found. PIK3CA E453K and H1047R mutations were found in 2 cases. BRAF E586K, KRAS G12D, and FGFR1 amplification were found in one each case.
Conclusion: In patients with gastric tumour and a history of breast cancer, the possibility of metastasis from the lobular carcinoma should be considered and IHC analysis of both lesions is necessary. We found frequent mutations of NF1 and CDH1, suggesting that either germline or somatic alterations of NF1 and CDH1 may be involved in gastric metastasis of lobular breast cancer.

PS-20-083

Influence of Tachosil patches on the tissue response to hypoxia in a swine model of highrisk large bowel anastomosis

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Background & Objective: Anastomotic failure remains one of the most dreaded complications in gastrointestinal surgery. Recently fibrin patches have been proposed as a useful measure to avoid these leaks and improve prognosis. Our aim is to analyze the factors associated to tissue hypoxia in a high-risk anastomosis model and determine whether fibrin patches influence this expression.
Method: Experimental prospective randomized study with large white pigs, including 30 animals with induced mesenteric ischemia. Half of the animals were randomly allocated to the fibrin patch group and the others were considered controls. We analyzed the large bowel samples of the anastomotic site and performed immunohistochemical analysis of hypoxia induced factor (HIF) and nuclear-factor kappa beta (NF-λB).
Results: In the control group we observed a significant increase of HIF and NF-λB expression in the surgical bed compared to normal tissues. The use of the fibrin patch led to a significant reduction of the nuclear expression of HIF, with no changes in NF-λB expression. This increased HIF expression was significantly associated to a more intense polymorphonuclear inflammatory response, found more frequently in the fibrin patch group. The rate of anastomotic leaks significantly decreased in the fibrin patch group opposed to controls.
Conclusion: Fibrin patch seems to be associated to a more intense inflammatory reaction at the surgical bed. Despite this could lead to a delay in healing, the rate of anastomotic leaks significantly decreases, so we consider this effect is not detrimental for the whole healing process or the patients' outcome.

Wednesday, 12 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-21 | History of Pathology

PS-21-001

Pelvic phleboliths: an under-recognised condition in paleopathology

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Background & Objective: Phleboliths are calcifications representing the end product of venous thrombosis. They are frequently seen around bladder, prostate, uterus and rectum, but also in supra-pelvic organs and vascular tumours. Pelvic phleboliths are considered of no clinical significance, and actually neglected in modern radiology and histopathology reporting. They are common in people from economically developed countries, representing a marker of western pattern of diseases. Their presence has been described only incidentally in mummies. Aim of this study is to report phleboliths in 3 italian natural mummies and evaluate their significance in understanding biopathologic features of the subjects.
Method: The small series included two well-preserved females from Goriano Valli (Abruzzo) and from Scicli (Sicily) dating back to XX century and a well-preserved male from Modica (Sicily) dating back to XVIII century. All of them underwent radiology and CT scanning and in one subject histology was performed using autopsy samples.
Results: The age range was 50-80 years. Two of them showed evidence of high social class/good nutritional status, one had a pelvic mass of possible ovarian origin. Phleboliths were observed near the walls of pelvic organs, showing the classic concentric calcification pattern at microscopy.
Conclusion: These findings suggest that phleboliths are not uncommon in mummies, share pathogenesis and location with their modern counterparts, and can be easily distinguished from ureteral calculi or calcified lymph nodes by radiology, CT, and histology. Their search should be

improved in skeletal material as they represent a useful marker of age at death, social status, and a clue to the respective diseases.

PS-21-002

Breast pathology in mummies. Modern investigation methods applied to mummified mammary glands

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Background & Objective: Breast is often observed in mummies but only occasionally investigated, an issue in part explained by conservative purposes. A survey of paleopathological literature showed only one case of lactational changes, one fibroadenoma, and one carcinoma not confirmed by histology. We applied modern investigation methods to the breasts of three mummified women, aged at death 40-70, dating back to 15th, 16th, and 20th century, in order to find out pathological features and validate the approach.
Method: Radiography was performed in two subjects and computed tomography (CT) scanning in one. Samples from significant areas were rehydrated with Sandison solution, and routinely processed to obtain histological sections stained with haematoxylin-eosin, Masson's trichrome, periodic acid-Schiff, Van Gieson, von Kossa, and red alizarin stains.
Results: In two cases mammography showed diffuse microcalcifications of the outer breast quadrants, similar to those observed in modern patients affected by epithelial proliferative lesions. In the last subject CT scanning did not allow to detect significant alterations. In all cases histology displayed fibrous tissue with empty roundish spaces, possibly related to fibrocystic changes. In one subject a roundish, hyaline formation (0.8 cm in diameter) suggested a fibroadenoma. Microcalcifications appeared as scattered roundish structures with focal calcium deposits in a case, and as rounded basophilic granules with a sligthly eosinophilic center in the other one. Such findings were respectively attributed to taphonomic changes and true breast pathology.
Conclusion: Modern senology methods applied to mummified mammary glands disclose good morphological details and allow an effective approach to ancient breast pathology.

PS-21-003

Wax Cordis

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Background & Objective: Once upon a time, "wax models" of human normal and pathological tissues/organs were used for teaching purposes in Medical Schools and Hospitals. The authors decided to study and compare the wax heart collection of two historical museums.
Method: The heart models of two 19th century European Pathology Museums (n1=8; n2=10) were analysed and two recent routine cardiac specimens were used to compare anatomical and pathological accuracy.
Results: "Collection 1" presented congenital, infectious and inflammatory disorders. "Collection 2" displayed congenital, valvular, adaptative and degenerative pathology. The two recent autopsy heart specimens confirmed the resemblance between the original organs/lesions and the artificial models.
Conclusion: This joint study revisited cardiac pathology in the 19th century and emphasized the importance of Pathology Museums as well as of the wax models, namely when studying thee-dimension organs and lesions.

PS-21-004

Disease, death and embalming of Saint Giacomo della Marca (1393-1476)

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Background & Objective: Born Domenico Gangala in Monteprandone (central Italy), he graduated in Both Laws and joined Franciscan Order as Giacomo in 1420. With Bernardino da Siena and Giovanni da Capestrano, he represented a leading figure of the Franciscan Observance reformation movement. He was entrusted by Popes with inquisitional and diplomatic commissions and established the Mounts of Piety to lend money to the poor. At the age of 80 he was requested by the Aragonese King in Naples until his death, occurred on november 28, 1476.
Method: His body was moved back to Monteprandone in 2001 and underwent Canonic Recognition with computed tomography (CT) scanning in 2008.
Results: CT scanning evidenced edentulism, osteoarthritis, hypertrophic muscular insertions in lower limbs and a lesion of the first metatarsal. External inspection revealed a xipho-pubic incision sutured with brown thread stitches, performed to eviscerate abdomen and thorax via the diaphragm. A large defect of perineal skin suggested also pelvic evisceration. A posterior craniotomy appeared clearly evident as a circular sutured incision. Excerebration was confirmed at CT level by bone defect and intracranial packings. No defleshing incisions were noted in the limbs. Microanalysis of thoracic skin found traces of mercury.
Conclusion: These findings confirmed the strong walking activity and some pathologic conditions referred by historical descriptions, as edentulism and podagra, possibly related to gout or acute arthritis with fever. The embalming method appears similar to that performed at the Aragonese Court, without the complexity noticed in other Saints' bodies. Mercury might have been used for conservative purposes or as therapeutic ointment.

PS-21-005

Infectio & Infesto Hepaticus

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Background & Objective: Since in humans, the liver contains one-third of the reticuloendothelial system and receives both portal and systemic circulation, the effect of infections/infestations on it is of major importance, both locally and systemically. The pathogenic organisms may vary in time and throughout the globe. The authors decided to study the hepatic infections/infestations in specimens from an historical museum.
Method: Ten liquid-fixed liver specimens from a 19th century European Pathology Museum were analysed and compared to recent routine specimens from autopsy.
Results: Seven cases of bacterial infections and three of parasitic infestations were found. Some of the pathological patterns of involvement are no longer found, other are still observed in the recent routine specimens.
Conclusion: This study showed the type of liver infectious pathology in this European country in the 19th century and draw attention to the epidemiological investigation and teaching possibilities of medical students/residents that Pathology Museums present.

PS-21-006

Full member of the USSR academy of medical sciences: M. A. Skvortsov

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Background & Objective: The outstanding domestic pathologist Mikhail Aleksandrovich Skvortsov was born on October 2, 1876. In 1899 I have graduated from medical faculty of the Moscow university. Being a student of medical faculty he showed interest in pathological anatomy. Since 1911 until the end of life he worked as the pathologist of the Moscow Morozovsky children's hospital.

Method: Most of the scientific works of M.A.Skvortsov are devoted to children's pathology
Results: Analyzing morphological changes at infectious diseases, he has for the first time paid attention to features of reactivity of a children's organism. One of the first he have described therapeutic pathomorphosis at diphtheria. He drew attention to the great importance of a histological research in the analysis of children's autopsy material. He developed criteria for the morphological diagnosis of umbilical sepsis at children. Except infectious diseases, M.A. Skvortsov had great scientific and practical interest to rheumatism problems. So, he has for the first time described exydative myocarditis at rheumatism at children for which in 1938 he received the Gold Medal of the International anti-rheumatic committee. Analyzing oncological diseases of children's age, M.A. Skvortsov has established prevalence of their disontogenetic origin.
Conclusion: In 1945 according to the recommendation of the Academic council of 1 Moscow medical institute of I.M. Sechenov he has been elected the full member of the USSR Academy of Medical Sciences. M.A. Skvortsov's works on pathological anatomy of diseases of children's age have laid the foundation of the new scientific direction in national pathological anatomy – pathological anatomy of a paediatric profile.

PS-21-007
The history of development of pathology in Belgorod region
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Background & Objective: In 2018 the chair of pathology of the Belgorod State University will celebrate its 20th anniversary
Method: Work with archives of BSU and Belgorod region
Results: "The general regulation of hospitals" was published in 1735 in Russian Empire. According to this document the pathoanatomical autopsy of corpses was prescribed to be conducted. In 1830 the first city hospital was opened in Belgorod. In 1965 the autopsy room was updated. The autopsy was conducted in 65% of deceased. In 1954 during the USSR the Belgorod region, which earlier was as a part of Kursk province and then Kursk region, was formed. It was the basis for creation of hospitals with pathological departments. In 1989 the pathoanatomical bureau was organized. It became a clinical base for chair of pathology, which was opened in 1998 on medical faculty. The head of the chair is professor Pavlova T.V. The science work is conducted in next directions: gynaecological pathology, endocrine pathology, soft tissue and bone pathology, haematopathology, history of pathology, uropathology and other topics. Methods of raster and transmission electron microscopy, atomic power microscopy, confocal microscopy and immunohistochemistry are used. Conferences and congresses for pathologists from Russia and other countries are held on the chair. Seven monographies were published. Twenty-eight dissertations were defended.
Conclusion: Conclusion. The development of chair of pathology in The Belgorod State University contributes to improvement of quantity of health care in Belgorod region.

Wednesday, 12 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-22 | Infectious Diseases Pathology

PS-22-002
Diagnostic sensitivity and specificity of different mycobacterium tuberculosis detection platforms in a tertiary hospital setting
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Background & Objective: The Philippines has a mycobacterium tuberculosis (MTB) infection incidence of 324/100,000 population and MTB mortality of 13/100,000 population. Acid-fast bacilli smear (AFBS) and MTB culture (MTBC) remain to be the mainstay of detection method. More recently, the GenExpert MTB (MTBGX) real time polymerase chain reaction assay has been introduced into clinical practice. This study aims to determine comparability and limitations of all three methods.
Method: We reviewed 357 (231 pulmonary and 126 extrapulmonary) samples of patients with suspected tuberculosis infection. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of MTBGX and AFBS were calculated using MTBC as gold standard.
Results: Of 350 pulmonary cases and 124 extrapulmonary samples, where both MTBGX and MTBC were done, 39 (11.1%) and 17 (13.71%) of cases were positive on both methods, 28 (8%) and 6 (4.84%) were MTBGX-negative but MTBC-positive, and 22 (6.3%) and 10 (8%) were MTBGX-positive but MTBC-negative, respectively. Of 311 cases where both AFBS and MTBC were done, 18 (5.8%) cases were positive on both methods, 44 (14.1%) cases were MTBC-positive but AFBS-negative, 2 (0.6%) were AFBS-positive but MTBC-negative and 247 (79.4%) cases were negative on both methods. The overall sensitivity, specificity, PPV, NPV of MTBGX compared to MTBC are as follows: 58.2%, 92.2%, 63.9% and 90.3%. The sensitivity and specificity of AFB smears is 29% and 99.2%.
Conclusion: The MTBGX has an overall high specificity and acceptable sensitivity when compared to culture. It detected MTB infection in 37% of MTBC and AFBS negative cases.

PS-22-003
On dental pathology II: practical approaches
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Background & Objective: Philosophical problems of dental-medicine are discussed during World Congr Philos FISP-2013-Athens (Abstract Book p.766) followed by contribution "On Dental Pathology I: Theoretical Approaches" by Eva Neu et al. ESP-2018-Bilbao. Now are given practical approaches, esp. dental infections. IUM reported about clinical investigations on genito-urological & oncological patients during intern. congress genito-urology (SIU-2007-Paris: Urol. 70/suppl.3A:232-233), radiology/intraoperative therapy (IORT-2008-Pamplona: Rev.Cancer, 22:11-12/29-30), internal medicine (ISIM-2010-Melbourne, Int.Med.J., 40/Suppl 144-145).
Method: Clinical observations on patients
Results: Some persons (see introduction) are analyzed also about dental problems. Examples: 1. Patient (female, 45years) had parodontitis & gingivitis. After change of life (nutrition, sport, etc.) and antibiotic therapy the teeth are stabilized upto 95years. 2. Patient (female, 35years): Dentists recommended extraction of over 10 teeth (parodentitis). A prominent dentist and physician (Dr.med., Dr.med.dent.) applied combined therapy – all teeth are preserved! 3. Patient (male,30years) German odontological clinic (university) recommended extraction of teeth: dentist (see 2) preserved these. Later appeared dentalgia (pulpitis) and granuloma dentis: Dentists recommended treatment of radix dentis or extraction. Other dentists applied laser therapy (2940nm Erbium: YAG): caries dentium was annihilated without opening of cavum dentis!
Conclusion: These examples support proposals about ondotological projects (Neu et al. ESP-2018-Bilbao) on European-international level to prove better dental prophylactic & therapy in the future in context of UNO-Agenda 21 for better health-ecology-etc. on global level.

PS-22-004
The nature and severity of histopathological changes in African catfish, clarias gariepinus infected with ichthyophthiriasis
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Background & Objective: Ichthyophthiriasis, caused by a ciliate protozoan Ichthyophthirius multifilis, contributes to tissue dysfunctions in the gills and skin of wildfish and cultured fish. Histopathological changes in the gill and skin of Ich-infected Clarias gariepinus was studied
Method: A total of 180 apparently post juvenile Clarias gariepinus, were randomly distributed into three groups in 50 L plastic tank with 20 fish per replicate. The infective stage, theront of I. multifilis was obtained from wild infected fish as a parasite source and serial passage by cohabitation and amplification cycle was adopted. Approximately 24,000 theronts and 44,000 theronts were used to infect the fish for 14 days in group B and C, while group A was uninfected. The skin and gill tissues (n=3) were excised for histopathological analysis. Severity of the lesion was progressively classified in three stages of tissue damage.
Results: The skin and gill of uninfected fish showed normal skin morphology, intact chromatophores and intact primary and secondary lamellae. Significant lesion scores ($P<0.05$) were recorded between group B and C. The observed histopathological changes were aneurysm, edema, epithelial lifting with evidence of trophont accumulation, inflammation, distortion of lamellae while in the skin, hyperemia, abscess formation, edema and inflammatory responses observed between groups B and C recorded significant change ($P<0.05$)
Conclusion: I. multifilis can alter the functionality of the both tissues. Therefore, the need for proper sensitization of Ich infection and aquatic life safety is paramount.

PS-22-005
Visceral leishmaniosis and its presentation with hemophagocytic lymphohistiocytosis
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Background & Objective: Leishmaniosis is no longer tropical disease. Because of global warming, developing tourism and migrations, it could have potential for the spreading into a middle and northern part of Europe. Increased number of cases has been reported in France, Spain and Italy (also in northern parts). Sandflies as a main vector for Leishmanial transmission have already been proved not only in Slovenia, but also in Austria, Hungary, Germany, and Switzerland. Visceral leishmaniosis (VL) often triggers hemophagocytic lymphohistiocytosis (HLH) in immunocompetent patients. HLH is frequently fatal and underdiagnosed disease involving a final common pathway of hypercytokinemia, which can result in end-organ damage and death. Timely diagnosis and identification of the underlying cause is imperative.
Method: In the last two years three patients with VL have been identified in Slovenia, two presented with HLH. All three cases have been imported from the neighboring country. In two of them, morphological bone marrow examinations performed as one of initial diagnostic procedures were negative.
Results: Clinicopathological features together with diagnostic procedures and administered therapies are presented in Table 1.
Conclusion: Practicing pathologists not only in the southern part of Europe need to be aware of VL and HLH induced by it. High level of suspicion should be present in every person with typical clinical picture with history of traveling into (but not exclusively) endemic areas even in the case of negative bone marrow findings. High level of communication with clinicians as well as inclusion of other laboratory diagnostic procedures for Leishmania's infection evidence is mandatory.

PS-22-006
Herpes simplex infection as a factor provoking rheumatoid arthritis development and aggravating its activity
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Background & Objective: Rheumatoid arthritis (RA) pathogenesis is largely due to an inadequate immune response in genetically predisposed individuals to environmental challenges such as bacteria and viruses. Herpesvirus infection, in particular Herpes simplex virus (HSV) is widespread in population (60–95% in adults). However, the latency versus reactivation strategy of the Herpesviridae is defined by the ability of immune system to restrain pathogen proliferation. In recent study we studied the role of HSV reactivation in the RA provoking and aggravating its activity.
Method: In 335 early RA patients, 310 probands and 300 individuals with no autoimmune diseases in anamnesis we analyzed the annual incidence and duration of HSV exacerbations, the presence of viral DNA in the blood cell and buccal epithelium DNA samples, serum levels of antiviral antibodies and the links of these indexes with the generally accepted indexes of RA activity, severity and subclinical signs of joint symptom and laboratory inflammatory indexes and RA –associated serum autoantibody.
Results: The increased incidence and duration of the infectious episodes was revealed in probands and they were even higher in patients, that being in the reliable correlation with RA activity. The HSV reactivation episode history was associated with increased reactive oxygen production.
Conclusion: We suggest that HSV infection and inadequate immune system ability to its restrain play a key role in provoking RA development and aggravating its activity.

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Wednesday, 12 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-23 | Ophthalmic Pathology

PS-23-001
Clinicopathological study of eyelid tumours
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Background & Objective: In spite of being a small organ, the eyelid contains numerous histological elements that can be benign, precancerous and malignant lesions. Our aim is to report clinical features and histopathological diagnoses of eyelid tumours.
Method: We performed a retrospective study of eyelid tumours diagnosed at our department over a period of 19 years (1999-2017). Epidermoid cysts were excluded.
Results: A total of 146 patients were included with a mean age of 55 years old. The sex-ratio was 0.9. Tumours were mostly benign (65.1%) and located in the lower eyelid (52%). They were frequently of epidermal origin (73.3%). Adnexal (13%) and stromal (13%) tumours were less common. Nevi were the most common in benign group (26.3%) and basal cell carcinoma was the most common eyelid malignancy (78%). The most common benign epithelial tumour was squamous papilloma (55.3%). Apocrine hydrocystoma was the most common benign adnexal tumour (26.3%). All malignant adnexal tumours were sebaceous carcinoma. Hemangioma was the most common stromal tumour (73.7%). One case of metastatic micropapillary carcinoma was reported. Stromal tumours, mainly hemangioma and neurofibroma, occurred in the paediatric population while adults presented more with epidermal and adnexal tumours ($p<0.001$).
Conclusion: Eyelid tumours encompass a large spectrum of benign, precancerous and malignant lesions. Basal cell carcinoma has the highest incidence among malignant eyelid tumours. Hemangioma is the most common tumour in the paediatric population.

PS-23-002

Neuroendocrine cells associated with endocrine mucin-producing sweat gland carcinoma - a potential precursor lesion?

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Background & Objective: Herein, we describe a novel hyperplastic element of neuroendocrine (NE) cells in an endocrine mucin-producing sweat gland carcinoma (EMPSGC).
Method: A 51-year-old Japanese man had developed a mass in the left upper eyelid 4 years prior to the current presentation.
Results: The excised specimen contained a solid cystic tumour, histopathologically composed of solid growth of polygonal cancer cells with fine-granular cytoplasm and nuclei, sustained by highly vascular, fibrovascular cores. Immunohistochemical examinations revealed the cancer cells to be consistently reactive for chromogranin A, synaptophysin, cytokeratin 7 and estrogen receptor. Intriguingly, we noted non-neoplastic-looking NE cells demonstrating chromogranin A in adjacent sudoriferous ducts. Careful observation using serial sections, with immunohistochemical and H&E staining, revealed that these small NE cells were polygonal with slightly eosinophilic, fine-granular cytoplasm and ovoid nuclei without atypism.
Conclusion: We report this case to highlight the possibility of "NE cell hyperplasia" being associated with the histogenesis of EMPSGC as a premalignant condition, based on morphological resemblance to precursor NE cells showing an 'isolated/scattered pattern' in the background tissues of NE tumours, including NE ductal carcinoma in situ, a mammary neoplasm analogous to EMPSGC. (Pathology, in press)

PS-23-003

Patterns of CD44 and MMP9 expression in cornea with dry eye disease before and after injections of hyaluronic acid

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Background & Objective: Dry eye disease (DED) accompanies any other corneal pathology. In case of instillation therapy inefficacy, subconjunctival administration of 1% hyaluronic acid (HA) can be used. CD44 is a HA receptor, that can potentiate cell activation and regeneration. HA can also influence MMP9 levels, which participate in DED pathogenesis. The aim was to evaluate the changes of CD44 and MMP9 expression in cornea diseases after HA injections.
Method: The study was performed on the surgical material of 18 corneas (2—Keratitis outcomes, 4 – Keratoconus, 8 – endothelial-epithelial dystrophy, 2 – transplant disease, 2 – healthy corneas,). Expression was assessed by morphometric analysis of 5 eyeshots on every histological slide stained by immunohistochemistry with antibodies to CD44 and MMP9. Statistical differences between groups were assessed by Mann-Whitney analysis.
Results: Expression level of MMP9 was significantly higher in damaged cornea then in normal tissues ($p<0.005$). Only in keratitis stromal expression of MMP9 and CD44 was found. It was associated with stromal edema and descemetocele ($p<0.001$). In keratoconus the higher CD44 expression level was associated with stroma thickening ($p<0.001$). The staining was negative for both molecules in transplant disease. After HA administration CD44 expression level was higher than before administration ($p<0.001$), and MMP9 expression level was almost the same ($p<0.001$).
Conclusion: MMP9 can be used as a DED marker in different cornea diseases. Exogenous HA, administered subconjunctival, enhances CD44 expression and practically doesn't influence MMP's one.

Wednesday, 12 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-24 | Pathology in Favour of Developing Countries

PS-24-001

Pathological study of plasma cell neoplasms and evaluation of CD56

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Background & Objective: as there is a lack of studies on plasma cell neoplasms in Damascus University Hospitals and since Damascus hospitals receive hundreds of cases each year of plasma cell neoplasms coming from all over Syria, we had started our pathological study for the plasma cell neoplasms diagnosed at Al-Assad University Hospital and subtype it to multiple myeloma, Plasmacytoma, plasmacytosis then investigate positivity or negativity of CD56 on the tumour cells. our study is retrospective study, Cross sectional.
Method: 90 biopsies of plasma cell neoplasms from bone marrow or soft tissues had been sent to pathology department in Al-Assad university hospital between 2015 and 2016. Review H&E slides in addition to immunohistochemistry for CD138, CD20, Kappa, Lamda and special stains like Congo red and Masson, beside the patient's clinical history and radiological images to complete the diagnosis according to "WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues IARC, Lyon, France, 2008". Then we applied CD56 for all cases regarding that CD56 considered as a prognostic factor in many recent studies. We also applied CD56 on normal plasma cells in normal tissues from colon and lymph node as a control but we didn't involve them in statistics.
Results: Of 90 cases, 62% were females, the ages of the patients range between 21 and 85 years old. Average age for our patients was 58.686. 12%, 78%,1%, 9% of cases were diagnosed as plasmacytosis, multiple myeloma, osseous Plasmacytoma and extra osseous Plasmacytoma respectively. All the cases of Plasmacytoma and plasmacytosis were negative for CD56. normal plasma cells in normal tissues were negative for cd56. 51% of the cases of multiple myeloma were positive for CD56, Overall positivity (51%) is significantly lower when compared to recently published data from some other studies. Knowing that the percentage is 40 % from the total patients in our study. Of 70 cases of MM we found two cases with amyloid depositions that has red to green birefringence in polarizing microscope.
Conclusion: Prevalence rate of MM between age categories is similar to WHO reports and that was between 50 and 70 years old, where as its prevalence rate between males and females differs from WHO reports, because females with MM was more in our study. CD56 is negative in reactive and normal plasma cells and in cases of Plasmacytoma and plasmacytosis. The positivity of CD56 in MM cases in our study is approximates but lower than studies in other countries that may be caused by the lower sensitivity of the antibodies used. It was noticed that CD56 was positive in MM cases that contain high grade plasma cells CD56 is a prognostic factor in MM and is positive in neoplastic plasma cell.

Wednesday, 12 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-25 | Thymic and Mediastinal Pathology

PS-25-001

An atypical type AB thymoma – a clinicopathologic analysis of two cases and a proposal of a new histopathological variant of thymoma

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Background & Objective: AB thymoma is regarded as a low-grade malignancy with a good prognosis if totally resected. We present 2 cases

of AB thymomas that relapsed many years after surgery of primary tumours despite their low stage and complete resection.
Method: Case 1. A 66-year-old woman with an asymptomatic mediastinal tumour (13x8.5x6 cm) underwent thymectomy. The resection was complete. After surgery the patient received radiotherapy due to the tumour stage (II/Masaoka-Koga classification). Ten and 15 years after resection metastases occurred in the lung and brain, respectively. All metastases were resected. The patient died soon after neurosurgery due to the bilateral pneumonia. Case 2. A 67-year-old man with an asymptomatic mediastinal cystic tumour (5x4x4 cm) was admitted for tumour resection. The resection was complete. Due to the tumour stage (II) the patient received radiotherapy. Nine years later, multiple metastases were found in the chest wall, pleura and right lung. The patient received chemotherapy but died due to the progression of the disease.
Results: In both cases primary tumours were microscopically diagnosed as AB thymomas with A component of carcinoid-like/hemangiopericitoma-like morphology with foci of necrosis and increased mitotic activity. Neoplastic cells of this component revealed expression of AE1AE3 and p40 and in case 1 - GTF2I mutation; genetic analysis in case 2 was not performed. In both cases these components resembled the atypical variant of type A thymoma and they dominated in metastases.
Conclusion: Atypical A components in AB thymomas may indicate a more aggressive clinical course and, thus, should be noted in histopathological reports.

PS-25-003
Expression status of PD-1 and PD-L1 in thymic epithelial tumours: association with histologic subtypes
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Background & Objective: Programmed death-ligand1 (PD-L1) is an immune checkpoint protein and expressed in various human tumours. In this study, we aimed to examine PD-1 and PD-L1 expression status in thymic epithelial tumours (TETs) and evaluate clinicopathological characteristics of PD-1/PD-L1 positive tumours.
Method: We studied 369 cases of TET (32 type A, 92 type AB, 45 type B1, 67 type B2, 73 type B3, 60 type C/thymic carcinoma) arranged in tissue microarrays (TMAs). The TMA was stained with rabbit monoclonal antibody (clone E1L3N; Cell Signaling, Massachusetts, USA) to human PD-L1. The staining results were scored semiquantitively.
Results: PD-L1 expression was significantly correlated with WHO histologic subtypes ($p< 0.001$) as followings: B3 (62%; n = 45 of 73), C (34%; n = 20 of 60), B2 (24%; n = 16 of 67), A (16%; n = 5 of 32), B1 (11%; n = 5 of 45), and AB (7%; n = 6 of 92). PD-L1 scores were associated with Masaoka-Koga stage ($p = 0.006$) and capsular invasion ($p< 0.001$). TETs with simultaneous expression of PD-1 in TILs and PD-L1 in tumour cells were more frequently associated with aggressive histology ($p = 0.001$) and capsular invasion ($p< 0.001$).
Conclusion: In this study, PD-L1 high TETs were associated with more aggressive histology and can be a potential biomarker for anti-PD-L1 therapy. PD-1/PD-L1 co-expression in a tumour may reflect the selective suppression of cytotoxic lymphocytes in the tumour microenvironment and predict poor prognosis. Association with patients' outcome will be added.

Wednesday, 12 September 2018, 09:30 - 10:30, Exhibition Hall I/II
PS-26 | Uropathology

PS-26-001
The challenges of diagnosing testicular germ-cell tumours: revisiting a series of 166 tumours in light of the new WHO classification and AJCC staging system
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Background & Objective: Testicular germ-cell tumours (TGCTs) are highly heterogeneous, hence posing serious challenges for Pathologists. We aim to thoroughly revise a series of consecutively diagnosed TGCTs (2005-2016) in light of the new WHO and AJCC systems, discussing dilemmas faced routinely by Pathologists.
Method: All patients were treated at our Institution by the same multidisciplinary team. Clinical files and histological slides were reviewed. Follow-up was last updated on November/2017.
Results: 148(89.2%) TGCTs were germ-cell neoplasia in situ (GCNIS)-related, the most frequent being Seminomas (SEs,52%), followed by Mixed Tumours (MTs,38%). Median age at diagnosis was 30years. Non-Seminomatous Tumours (NSTs) showed more lymphovascular invasion (LVI), higher stage and poorer prognostic group than SEs ($p=0.001$, $p=0.007$, $p=0.038$). In MTs, the most common combinations were Embryonal Carcinoma (EC)+Yolk-sac Tumour (YST) (70.2%) and YST+ Teratoma (TE) (61.4%). However, we found no significant associations of co-occurrence between pairs of components. SEs with atypical features("anaplastic") were larger, showed more LVI and more extensive necrosis ($p<0.001$, $p=0.030$, $p=0.016$). LVI and >50%EC, but not rete testis invasion, associated with higher stage ($p<0.001$, $p=0.009$). Regarding SEs, larger size associated with higher stage and LVI ($p=0.004$, $p<0.001$), while mitotic count associated with LVI ($p<0.001$). Four patients showed change in stage when applying the AJCC 8thEdition system (all from IA to IB). Regarding the new subdivision of stage I SEs, pT1b tumours showed more rete testis invasion and extensive necrosis when compared to pT1a ($p=0.015$, $p=0.001$). In two cases tumour components in metastasectomy specimens were not present in the primary TGCT. Overall survival at 5 years was 98.6%.
Conclusion: TGCTs are challenging tumours and both Pathologists and Clinicians should be aware of recent updates in classification and staging for adequately tailoring treatment strategies.

PS-26-002
Utility of 34bE12 cytokeratin and ERG double immunostaining for the diagnosis of minimal adenocarcinoma in needle prostate biopsies
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Background & Objective: The diagnosis of adenocarcinoma measuring < 1 mm in needle prostate biopsies is a challenge. Immunohistochemistry plays an important role, using antibodies against basal cells and AMACR. However, AMACR staining pattern can be equivocal and is not completely sensitive or specific. ERG is a highly specific, not sensitive, marker of adenocarcinoma or HGPIN. We have analized if a 34betaE12 – ERG double immunostaining has advantages over the single 34betaE12 staining to diagnose these foci.
Method: Needle prostate biopsies with doubtful foci measuring < 1mm were immunostained with AMACR in one slide, and a double-staining method on another section with 34bE12 (immunoperoxidase: brown signal) and ERG (alkaline phosphatase: red signal). Every case has been classified comparing ERG with AMACR staining, determining if the adition of ERG to 34betaE12 staining was: (a) relevant for the diagnosis, (b) a complementary feature, or (c) did not add any information.
Results: 80 foci measuring 0.12-0.99 mm (mean: 0.48 mm) were reviewed, finally diagnosed as adenocarcinomas (45 cases), benign (25), ASAP (5 ERG+) and HGPIN (5 ERG+). 25 of the 45 adenocarcinomas were ERG+, 21 of them classified in group (a) and 4 in group (b). The negativity of ERG in the 25 benign cases was classified as (b).
Conclusion: Immunoreactivity for ERG has been useful for the diagnosis in the ERG+ minute adenocarcinomas. Negative ERG staining has been a complementary information for a benign diagnosis. More cases of ASAP

and HGPIN ERG+ should be investigated to obtain conclusions regarding these lesions.

PS-26-003

Adenocarcinoma of bulbourethral/Cowper's gland with survival of 20 years: a case report

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Background & Objective: Primary adenocarcinoma of the Cowper's gland is a very rare cancer with fewer than 10 recorded cases.
Method: A 45-year-old man presented with pain in the perineum and urinary difficulty. Imaging demonstrated an 8.9x7.4x6.3 cm locally infiltrative and centrally necrotic mass that had extensions to the root of the penis, anal canal, prostate gland, left adductor magnus muscle and left ischiopubic ramus with malignant nature. History revealed that the patient had first presented in 1999.
Results: Microscopically the tumour was composed of glandular, cribriform, tubulopapillary and solid patterns of growth. There was luminal mucin. Immunohistochemistry showed that the tumour was positive for cytokeratin 7, PAX2 and PAX8, while negative for cytokeratin 20, cytokeratin 5/6, CDX2, PSA, PSAP, AMACR, napsin, calretinin and estrogen receptor. P53 was positive in more than 50% of the cells. Ki67 index was 5%.
Conclusion: While little is known about the prognosis and natural history of adenocarcinoma of the bulbourethral/Cowper's gland, our case is reported to provide awareness and correct diagnosis of this tumour.

PS-26-004

Urothelial bladder carcinoma in young adults: a retrospective study of 23 cases

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Background & Objective: Urothelial bladder carcinoma (UBC) is very rare in young adults. However, we are witnessing an increasingly growing involvement of young people, certainly due to an influence of the environment and a change in lifestyle. The aim of this study was to reveal pathologic characteristics of UBC in young adults aged less than 40 years.
Method: We retrospectively analyzed the clinical and pathologic data of 23 patients, initially diagnosed and treated at our institution from 2008 to 2017. Histological confirmation of the diagnosis was obtained after endoscopic resection of the tumour or after cystectomy. Sex ratio, tumour grade, and stage were recorded.
Results: There were 17 men and 6 women with a sex ratio of 2,8. The mean age was 35 (range: 18–40) years. The pathological examination revealed 17 (73.9%) patients with non-muscle invasive urothelial bladder cancer, and 6 (26%) patients with muscle invasive urothelial bladder cancer. Initial cancer staging was: pTa with 15 patients (65.2%), pT1 with 2 patients (8.7%), pT2 with 4 patients (17.4%), and pT3 with 2 patients (8.7%). According to the distribution of grade, 15 (65.2%) tumours were of low grade and 8 (34.8%) tumours were of high grade.
Conclusion: Based on the results of our study, we conclude that UBC in young patients occurs more frequently in men, more frequently as low-grade tumours, and the disease at the time of diagnosis is more frequently at a low stage. Bladder cancer is a very rare condition in young patients; however, it is characterized by a relatively good prognosis.

PS-26-005

Primary angiossarcoma of the kidney, epithelioid variant: diagnostic pitfalls and review of the literature

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Background & Objective: Angiossarcoma is a highly aggressive rare neoplasm, accounting for <2% of sarcomas. About 1/3 occurs in soft tissue, 1/3 in skin and 1/3 in other sites, but rarely in the kidney. We aim to present a case of primary renal angiossarcoma, followed by a review of all cases reported in literature.
Method: A 61-year-old male currently being investigated for Crohn's disease underwent computed tomography, which revealed a 13cm complex cystic mass on the left kidney.
Results: Nephrectomy specimen showed a 15x13.5x11cm spongy, reddish mass, centered in the hilum. It was cystic and filled with blood and clots. On histological examination it was predominantly poorly formed, displaying solid sheets of bizarre epithelioid cells, with hyperchromatic, irregular nuclei and prominent nucleoli. There were focal hints of vasoformation, with evidence of tufting and intracytoplasmic lumina containing erythrocytes. There was extensive hemorrhage/hemosiderin and necrosis. The neoplasm infiltrated the perirenal adipose tissue. 7 mitosis/10HPF were depicted. Immunohistochemistry revealed positivity for vascular markers (CD31, CD34, FVIII, ERG) and also cytokeratins (AE1/AE3, CK8/18).
Conclusion: To the best of our knowledge this is only the 65th case of primary renal angiossarcoma reported in literature. Of cases with follow-up data, 36/47(77%) died of disease. Differential diagnosis includes other renal lesions, such as anastomosing hemangioma, which has a very different behavior. Epithelioid variant of angiossarcoma (as in our case) is even rarer, and mimics carcinoma or melanoma. Pathologists should be aware of this variant and use a panel of antibodies in order to avoid this pitfall.

PS-26-006

Radical prostatectomy with positive surgical margins: a clinicopathological review of 32 cases

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Background & Objective: Positive surgical margins (PSM) after radical prostatectomy (RP) are considered an adverse oncologic outcome, associated with biochemical recurrence, need for adjuvant therapy and progression of prostate cancer.
Method: A retrospective analysis of clinical data and histopathologic slides was performed on RP specimens from 2010 to 2013 of Hospital Pedro Hispano-Matosinhos.
Results: 144 RP were performed and 32 (22%) had positive margins, all Gleason (3+3) but one (4+3) on the margin. The length of PSM range from 0,1 to 15 mm. The most common location for PSM is the apex, followed by the postero-lateral edge of the prostate. The mean age was 64 years (50-75). Two men were Grade Group (GG) 1, 9 GG2, 17 GG3, 3 GG4 and 1 GG5. Seventeen men were stage pT2, 12 pT3a and 3 pT3b. All had perineural invasion. None had lymph node nor distant metastasis. Thirteen patients (41%) had biochemical recurrence (increasing Prostate Specific Antigen-PSA) and further treatment (radiotherapy or hormonetherapy), but still alive with no evidence of disease progression. 16 are alive and well, 2 were lost and 2 died from other causes. The mean follow-up was 75 months (55-98).
Conclusion: Although positive margins are a known prognostic parameter, there are other factors (staging, Gleason grade, extra-prostatic extension and seminal vesicle invasion) that influence the disease progression. Predictive value for metastasis and mortality are limited. Pathologists must measure and grade positive margins to help stratify patients who will benefit from adjuvant therapies, even though the management of these patients remain controversial.

PS-26-007

Correlation of expression of Tgf-ß, Mmp2 and Lmo2 between prostatic adenocarcinoma and adjacent unaffected parenchyma

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Background & Objective: LIM Domain Only 2 protein (LMO2) is a member of transcription factor family of proteins distinguished by their cysteine-rich, zinc-binding LIM domains. It is associated with prostatic adenocarcinoma prognosis and disease progression. Matrix Metallopeptidase 2 (MMP2) is endopeptidase that degrades extracellular matrix and is considered to be overexpressed in prostatic carcinoma with relation to its growth and aggressiveness. Transforming growth factor beta (TGF- β) is a peptide involved as a promoter in advanced prostate cancer. Also, both malignant stroma and epithelia have important role in tumour progression. Therefore, the aim was to investigate the expression of proteins TGF- β, MMP2 and LMO2 between both epithelia and stroma of prostatic adenocarcinoma and adjacent unaffected parenchyma.
Method: The intensity of TGF- β, MMP2 and LMO2 expression in epithelia and stroma of adenocarcinoma and adjacent unaffected parenchyma was analyzed in 83 specimens of prostatic adenocarcinoma by microarray-based immunohistochemistry.
Results: TGF- β and LMO2 were more expressed in malignant stroma than in non- malignant stroma (both P =0.000), while no statistical significance in case of MMP2 (P = 0.097) was found. LMO2 and MMP2 were more expressed in malignant epithelia than in non- malignant epithelia (both P =0.000), while no statistical significance in case of TGF- β (P = 0.096) was seen.
Conclusion: Study results demonstrate that both malignant stroma and epithelia have a role in tumour progression and support potential role of TGF- β, MMP2 and LMO2 in prostatic cancer progression.

PS-26-008
Expression of death receptors DR4 and DR5 in non-muscle-invasive bladder cancer
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Background & Objective: Cell death receptors induce extrinsic apoptotic pathway, following the activation by tumour necrosis factor-related apoptosis-inducing ligand. It has been found that high expression of death receptors in tumour cells of various cancers increases sensitivity to antineoplastic chemotherapeutic agents, nevertheless the investigation of their prognostic significance yielded varied results. The aim of this study was to analyze the expression of death receptors DR4 and DR5, and their prognostic impact in non-muscle-invasive bladder cancer.
Method: Immunohistochemical analysis of DR4 and DR5 expression comprised 496 non-muscle-invasive bladder cancer (202 pTa, and 294 pT1 tumours), incorporated in tissue microarrays. Expression status was correlated with clinicopathological and follow-up data. The median follow-up was 60 months (range, 23-96 months).
Results: High expression of DR4 and DR5 was detected in 73.6% and 71.2% of the tumours, respectively, and the majority of investigated samples (56.6%) showed intensive staining for both markers. Reduced DR4 expression in tumour cells was associated with high histologic grade, and tumour stage (p<0.001, respectively), while decreased DR5 correlated only with tumour stage (p=0.031). High DR4 expression was strongly associated with longer recurrence-free survival (p<0.001). However, patients with high DR5 expression did not have significantly longer recurrence-free rate compared to those with reduced DR5. There was no statistically significant association between death receptors' expression and patients' overall survival.
Conclusion: The expression of death receptors DR4 and DR5 may play a significant role in prediction of non-muscle-invasive bladder cancer prognosis. Moreover, assessment of death receptors expression may be of value in selection of patients who might benefit from adjuvant therapy.

PS-26-009
An immunohistochemical analysis of angiogenis in bladder cancer occuring in settlements linked with Balkan endemic nephropathy
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Background & Objective: Vascular endothelial factor (VEGF) and vascular endothelial growth factor receptor 1 (VEGFR1) are produced by bladder cancer cells that have undergone genetic changes and acquired more aggressive phenotype, irrespective of hypoxia status.
Method: Bladder cancer patients were divided into two groups: endemic (who were born and lived in settlements related to Balkan endemic nephropathy) and non-endemic. The angiogenic profile was estimated through immunohistochemical expressions of VEGF, and VEGFR1 in 640 bladder cancer samples incorporated in tissue microarrays. Exclusively, cytoplasmatic positiveness was considered significant and scored.
Results: Patients were followed for 47.12±32.94 months. Non-endemic patients had higher survival rate (p<0.05) and recurrence-free survival (p<0.05). Tissue samples obtained from endemic patients more expressed VEGF (p<0.01). This difference was observed only in male patients (p<0.05), primary tumours (p<0.05) and those without squamous differentiation (p<0.01), cystitis (p<0.01), carcinoma in situ (p<0.05) or exposition to known carcinogens (p<0.05). According to tumour stage, there was a significantly higher VEGF expression in T1 endemic tumours (p<0.05). Conversely, endemic T2 tumour samples expressed more VEGFR1 (p<0.05). Non-endemic patients with positive VEGFR1 had longer disease-free survival (p<0.01). Expression of both angiogenic markers did not have significant impact to overall survival rate and further outcome in patients from endemic settlements.
Conclusion: Present investigation has revealed that VEGF expression was more frequently altered in endemic T1 bladder cancer samples than in non-endemic tumours, vice versa endemic muscle invasive bladder tumours were more frequently immunopositive for VEGFR1, indicating that genetic factors interplay with the environmental factors.

PS-26-010
Urothelial carcinoma in radical nephroureterectomy: a clinicopathologic study of 53 cases
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Background & Objective: The aim is to investigate the clinicopathological features of patients with urothelial carcinoma of the upper urinary tract.
Method: Fiftythree patients undergoing radical nephroureterectomy were included in this study.
Results: The mean age of the patients was 70,8 years with a male to female ratio of 2.5:1. The major symptoms were gross hematuria and flank pain. Sixteen patients (30,2%) had diagnostic needle biopsies. One case was invasive UC (2%), 6 cases (11,3 %) were non-invasive low grade papillary UC, 14 cases (26,4 %) were invasive low grade papillary UC, 2 cases (3,8 %) were non-invasive high grade papillary UC and 18 cases (34 %) were invasive high grade papillary UC. Micropapillary growth pattern was present in 3 cases (5,7 %). Squamous differentiation was observed in 5 cases (9,4 %). Both squamous and glandular differentiation was present in 3 cases (5,7 %). One ureteral tumour (1,9 %) was giant cell UC type. Thirtyseven cases (69,8 %) were at advanced pathological stages (pT2-4) and 16 cases (30,1 %) were at lower stages (pTa-pT1). All of the UCs with variant morphology were at advanced stages. Clinical follow-up ranging from 1 to 124 months

was available in 37 patients; of these, 11 (29,7 %) has died of tumour with a mean survival of 33 months. Seven of the patients who died of cancers had an advanced stage tumour.
Conclusion: UCs of upper urinary tract is usually diagnosed at advanced ages and is more common in males. They are usually at advanced stages at the time of diagnosis.

PS-26-011
Chromophobe renal cell carcinoma in a tertiary centre hospital from 2007 to 2017: review of 54 cases
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Background & Objective: Chromophobe renal cell carcinoma (ChRCC) constitutes 5-7% of all renal cell carcinoma cases. Occurence peaks in the sixth decade and there is a slight male predilection. Our objective was to review the ChRCC cases in La Paz University Hospital between 2007-2017 and compare our results with the current literature.
Method: We reviewed retrospectively the pathology reports from our pathological records between 2007-2017. 51 patients from a cohort of 522 operated patients. Three cases had only a cytological diagnosis and the rest by biopsy.
Results: The mean age at diagnosis was 64 years old (37 - 84 years-old). 60% of the patients were men, 37% women, 2 cases unkown. Chromophobe renal cell carcinoma was 10% of all cases. Thirty-nine cases of the usual variant (typically arranged in a solid sheet-like pattern, with large pale cells with prominent cell membranes, and raisinoid nuclei), twelve had eosinophilic cytoplasm with poorly defined bordes (eosinophilic variant), one with a predominance of tubular áreas, another one with a papillary architecture; one had sarcomatoid features with squamous differentation and one was undifferentiated. Immunohistochemestry was performed in difficult cases.
Conclusion: We found that the epidemiology of our study (age at diagnostic and gender) is similar to the existing literature, our prevalence was slightly higher than currently described. It is important to recognise the different histological patterns of ChRCC to avoid misdiagnosis

PS-26-012
Prognostic role of microvascular density in clear cell renal cell carcinoma
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Background & Objective: The correlation between microvascular density (MVD; number of microvessels/mm2) and clinical behavior has been confirmed in several cancer types. However, the importance of MVD on patient outcome remains controversial in clear cell renal cell carcinoma (CRCC); hence the association between the MVD value and pathological features, as well as the survival rate was investigated in patients with CRCC.
Method: The morphological features and clinical data were recorded in 179 nephrectomies. Two cores with approximately 6 mm2 area were punctured from the highest ISUP grade area of the tumour. The capillaries were visualized by CD34 immunostaining, then the slides were digitalized, and the MVD value was calculated using the QuantCenter software package.
Results: Two prognostic groups were defined based on the mean of the MVD values measured. A high MVD value was characteristic for low-grade (ISUP grades 1 and 2) CRCC, while a low MVD value was observed in high-grade (ISUP grades 3 and 4) CRCC ($p<0.001$). The tumour size was larger for low MVD (73.8 mm vs 62.3 mm; $p=0.024$), but the MVD value seemed to have no influence on the pT stage. A low MVD was more frequently associated with local recurrence, lymphatic and distant metastasis ($p=0.005$). In multivariate analysis, a low MVD was independently associated with a lower survival rate ($p=0.016$).
Conclusion: In our cohort, the low MVD was associated with a high ISUP grade, an increased tumour size and an aggressive clinical course. Also, MVD was found to be an independent prognostic factor in CRCC patients.

PS-26-013
The peritumoural T-cell infiltrate in lymph node metastases of urothelial bladder cancer seems to be less effective than in primary tumours: a comparative study of the intra- and peritumoural immunarchitecture
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Background & Objective: Urothelial carcinoma is a common malignant tumour and 5-year survival rate for patients with metastatic disease is significantly worse (5-ys only 13%) compared with localized tumour disease. Lymphocytes and in particular CD8+/GranzymeB+ cells (CD8+GrB+) as cytotoxic effector T-cells are major players in tumour immunity. We analyzed the peritumoural immune cell architecture in metastasized bladder cancer patients in primary tumour (PT) and corresponding lymph node metastases (LNM) to evaluate significant changes in the IC infiltrate.
Method: 50 resection specimens from patients with metastasized urothelial bladder cancer were studied and immunostained for CD3/Ki67, CD8/GrB and for PD-L1, PD1 and CD4. Slides were digitized and evaluated for the number of intraepithelial and peritumoural IC.
Results: The number of CD3+ and CD8+ cells in the peritumoural stroma was significantly higher in LNM than in PT ($p=0.0001$), whereas the proportion of CD8+GrB+ to CD8+ cells as well as the proportion of CD8+ to CD3+ T-cells was higher in PT ($p=0.0001$). PD-L1 expression on TC of PT is significantly higher than in LNM ($p=0.037$) whereas no difference in the PD-L1 expression was found for the IC.
Conclusion: Although the total number of T-cells is higher in LNM, the ratio of CD8+GrB+ to CD8+ and of CD8+ to CD3+ is significantly lower than in the PT suggesting that the peritumoural immune cell architecture in lymph node metastases is less effective than in the PT which may add to the poor prognosis of these patients and possibly offer a perspective for immunoregulatory therapies.

PS-26-014
Renal cell carcinoma morphologically similar to fumarate hydratase deficient-RCC in a patient with BRCA2 germline mutation
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Background & Objective: Fumarate hydratase-deficient renal cell carcinoma (FHD- RCC) shows aggressive behavior, variable architectural patterns, presence of enlarged, viral-like nucleoli, and mutation of the FH gene. We describe an unusual RCC that although on morphology closely resembled FH-deficient RCC, occurred in a patient who did not have an FH mutation, but demonstrated germline BRCA2 mutation.
Method: Case report.
Results: A 56-year-old male, underwent laparoscopic radical nephrectomy for an incidental kidney tumour diagnosed during imaging studies. The tumour measured 6.3 cm with limited (5%) necrosis. It showed a predominant papillary and tubulopapillary growth. The cells exhibited eosinophilic cytoplasm and prominent eosinophilic nucleoli with perinucleolar clearing. The initial diagnosis was of a high grade, unclassified RCC, suggestive of FHD-RCC. The tumour cells expressed PAX8, AE1/AE3, CD10, AMACR, FH, INI-1, SDHB and focally for CA9, EMA, vimentin and cytokeratin 20. Negative stains included cytokeratins 7, cytokeratin 5/6, 34βE12, CD117, HMB45, Melan A, and cathepsin.

Next-generation sequencing on a peripheral blood sample with an extended gene panel covering familial syndromes (106 genes) did not detect mutations in the genes with known association with familial RCC. However, a heterozygous intronic variant chr13:32.945.092G>A (c.8488-1G>A) of the BRCA2 gene was detected. This variant interferes with the BRCA2 splicing and is related to the familial risk for breast/ovarian cancer. At 13-month follow-up, the patient was free of disease and without evidence of disease progression.
Conclusion: Some high-grade, unclassified RCC, demonstrating morphology similar to FHD-RCC may be related to BRCA2 germline mutations.

PS-26-015
Clinical significance of Farnesoid X Receptor expression in renal cell carcinoma
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Background & Objective: Farnesoid X Receptor (FXR), a member of nuclear receptor superfamily, is related with the bile acids, glucose and lipids metabolism and recently with cancer. The present study aimed to evaluate the clinical significance of FXR expression in renal cell carcinoma (RCC).
Method: FXR protein expression was assessed immunohistochemically on formalin fixed paraffin-embedded RCC tissue sections obtained from 80 patients and was statistically analyzed with tumour histological type and crucial clinicopathological parameters for patients' outcome.
Results: Cytoplasmic FXR immunostaining was noted in 34 (42.5%) and nuclear in 50 (62.5%) out of 80 RCC cases, respectively. High cytoplasmic FXR expression was noted in 23 (28.8%) and high nuclear FXR expression in 33 (41.3%) out of 80 RCC cases, respectively. High cytoplasmic FXR expression was more frequently observed in papillary and chromophobe compared to clear cell RCC (p=0.0165), as well as in female patients (p=0.0421). High cytoplasmic FXR expression was positively associated histological grade (p=0.0002). High nuclear FXR expression was not associated with any clinicopathological parameters examined.
Conclusion: This study reported for the first time that FXR is expressed in RCC and especially in papillary and chromophobe types, as well as in RCC cases of high histological grade.

PS-26-016
Assessment of transurethral resection of bladder specimens with pT1 high grade urothelial carcinoma for the predictor features of muscle invasion on radical cystectomy specimens
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Background & Objective: Some of the patients with disease limited to lamina propria on transurethral resection of bladder (TUR-B) develop muscle invasive or higher stage bladder carcinoma on radical cystectomy. We analysed the correlation between histopathologic parameters on TUR-B specimens with muscle invasion on radical cystectomy (RC) specimens.
Method: A retrospective study was carried out in 66 patients who underwent RC for non-muscle invasive high grade urothelial carcinoma diagnosed on TUR-B specimens.
Results: On univariate analysis; the presence of tumour necrosis on TUR-B specimens (p = 0,002) and pT1 substaging (p = 0,001) were significantly associated with muscle invasion on RC specimens (p = 0,002; p = 0,001 respectively). There was a marginal significance between variant histology and muscle invasion (p = 0,058). On multivariate logistic regression analysis, the presence of tumour necrosis and pT1 substaging on TUR-B specimens were independent predictors of muscle invasion on RC specimens (OR= 7,507, 95% CI=1,598-35,278, p = 0,011 and OR= 19,085, 95% CI=4,497-81,001, p = 0,001 respectively).
Conclusion: We suggest that the presence of the TN may be pointed on pathology reports of TUR-B specimens in addition to pT1 substaging. Further studies with larger number of cases are needed to establish whether the presence of TN and variant histology on TUR-B specimens may be considered as a predictor of muscle invasive disease on RC specimens.

PS-26-017
Kidney involvement in haematological neoplasms. Clinico-pathological study of 11 cases
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Background & Objective: Kidney injury can be a complication of haematopoietic neoplasia, and the pathology spectrum can be particularly wide. Infiltration by lymphoma/leukemia is diagnosed in late stages. Very few cases of lymphoma/leukemia diagnosed by percutaneous kidney biopsy have been reported.
Method: We reviewed the cases of renal biopsies with leukemia/lymphoma diagnosis between 1990-2017. Clinical data, biopsies, IHC and molecular results of each case were reviewed.
Results: 11 patients (6 male/5 female). Age: 25-81 years. Radical nephrectomy (3 cases) or needle biopsy (8 cases): 8 diffuse large B cell lymphomas (6 DLBCL NOS, 1 DLBCL T-cell rich and 1 intravascular DLBCL), 1 extranodal marginal, 1 T-cell lymphoblastic and 1 myeloid sarcoma. In 2 cases, lymphoma coexisted with renal carcinoma. Haematopoietic neoplasia represented 1.68% of renal neoplasms diagnosed. Radiologically, 5 patients: multiple intraparenchymal nodules, 4 single renal mass and 2 diffuse infiltration with increase in renal size. Four patients presented bilateral lesions. Five had a presumptive clinical diagnosis of renal carcinoma. Two patients had only nodal disease in addition to renal disease and 9 patients had multiple extranodal infiltration at staging. Follow-up: 7 died with disease (1-117 months, median 8 months), 3 were alive disease-free (7-102 months, median 64 months), and1 alive with disease (1 month).
Conclusion: Renal involvement due to haematopoietic neoplasias usually occurs in disseminated disease. Leukemia/lymphoma may show a renal disease with clinical and radiological findings mostly nonspecific. Percutaneous renal biopsy is essential to establish the correct diagnosis. B-cell lymphomas predominated, being LDCGB the most common subtype.

PS-26-019
Androgen-responsive PTPN1 immunostaining is associated to biochemical recurrence in prostate cancer
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Background & Objective: Abnormal regulation of tyrosine phosphorylation is important in many cancer types, including prostate cancer. The balance between tyrosine phosphorylation and dephosphorylation is finely tuned by the interplay between tyrosine kinases and tyrosine phosphatases. The protein tyrosine phosphatase PTPN1 (PTP1B) is upregulated in prostate cancer cells in response to androgens, and PTPN1 has been proposed as an important player in prostate cancer progression.
Method: We tested the expression of PTPN1 and androgen receptor (AR) by immunohistochemistry in a prospective prostate cancer cohort of 120 cases.
Results: PTPN1 was localized in the cytoplasm, while AR was localized within the nucleus. A positive correlation between AR and PTPN1 expression was found. AR expression associated with biochemical recurrence and disease-free survival, while PTPN1 expression associated with biochemical recurrence.

Conclusion: Our findings support the notion that expression of PTPN1 is associated with poor prognosis in prostate cancer. The therapeutic potential of PTN1 inhibition in prostate cancer deserves further studies.

PS-26-020

Sex cord-stromal tumours of the testis: an observational prospective review (2010-2018)

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Background & Objective: Sex cord-stromal tumours of the testis (SCSTs), that account for about 10% of the testicular neoplasms, include neoplasms of pure sex cord and pure stromal-type (Leydig, Sertoli and granulosa cell tumours), and an admixture of both. Account for about 2-5% of testicular neoplasms in adults but approximately 25% in children (in general, there is a wide age range for SCSTs, with ages in most of the series ranging between 14 and 87 years). The great majority of them are considered clinically benign but a minority are malignant, with atypical microscopic features. Our aim is to review the cases diagnosed in our institution since 2010.
Method: Our study is based on an observational prospective study of 10 patients diagnosed, treated and followed for SCST at the Universitary Hospital Miguel Servet in Spain, between 2010-2018.
Results: The average age of our patients is 37 years (range 4-72) at the moment of diagnostic. 94 testicular neoplasms were diagnosed and among them, 10 were diagnosed as SCST; 4 cases were diagnosed as Leydig cell tumour, with malignant transformation in one of them; 2 were diagnosed as Sertoli cell tumour; 3 were diagnosed as Granulosa cell tumour and one was diagnosed as Gonadal Estromal Fibroma. Only one patient did not survive; rest of the patients did not have any significative risk to develope a malignant transformation, based on atypical microscopic features.
Conclusion: Most SCST, that account for about 10% of the testicular neoplasms, are biologically benign, but about 10 % may show malignant behavior, usually having atypical microscopic features that are important to know.

PS-26-022

The UroVysion® Vysis FISH (UV-FISH) assay may not detect urothelial carcinoma (UC) due to the absence of the targeted molecular changes in some tumours

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Background & Objective: UV-FISH is a molecular-based test, applicable to urine specimens. Early studies suggested better test performance vs. urine cytology, but more recent studied have been less favourable. This study evaluates the performance of UV-FISH vs. Cytology with an analysis of reasons for discrepant results.
Method: 101 urine samples were prospectively collected and an aliquot each was processed for cytology and for UV-FISH. 12 were insufficient, leaving 89 for analysis. Sensitivity and specificity were determined, using biopsy results and long term clinical follow-up to determine the occurrence or not of UC. UC tissue, where available, was also evaluated by UV-FISH and correlated with cytology and urinary FISH.
Results: Sensitivity and specificity of urine cytology for the detection of UC were 48.39% and 83.33% and of urinary UV-FISH were 41.94% and 72.73%, respectively. FISH failed to detect 9 of 19 cases of biopsy proven high grade (HG) UC and 9 of 12 cases of low grade (LG) UC. UV-FISH analysis of the corresponding UC tissue showed an absence of the UV-FISH-detected abnormalities in the tumour in 5 of 9 HG UCs and 3 of 6 LG UCs.
Conclusion: UV-FISH fails to detect some HG and LG UC. In about half of those cases, this is due to an absence of UV-FISH-detected molecular changes in tumour cells. A negative UV-FISH test does not definitively exclude the presence of UC.

PS-26-023

Correlation of Cyclin D1, HER2 and AMACR with histologic grade in bladder tumours

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Background & Objective: Bladder tumours are the 9th most common type of cancer in the world. We aimed to investigate the relationship between tumour grade, lamina propria invasion, muscularis propria invasion, lymphovascular invasion and HER-2, Cyclin D1 and AMACR expressions in bladder tumours.
Method: A total of 72 cases of bladder tumours (noninvasive and invasive) reported between June 2011 and February 2017 at the Isparta State Hospital were selected. These cases were re-evaluated and classified according to the 2016 WHO classification. AMACR, HER-2, Cyclin D1 stained immunohistochemically.
Results: The cases were male in 80% (57) and female in 20% (15). The mean age of the patients was 68 years. Thirty five were noninvasive, and 37 were invasive urethelial carcinoma and 38 of them were low and 34 were high grade. Cyclin D1 showed a strong positive staining for 75% of tumours, 39% for AMACR, and 86% for HER-2. Strong Cyclin D1 and AMACR expression was observed in high grades ($p<0.05$, $p<0.005$ respectively). HER-2 expression (2 and 3 positive) was found at a high rate in low and high grades (84%, 88% respectively). AMACR and Cyclin D1 showed more staining in tumours with lamina propria invasion compared with tumours without lamina propria invasion.
Conclusion: Cyclin D1 and AMACR expressions were found to be significantly high in high grade tumours. HER-2 expression was found high in both low and high-grade tumours. These markers are may be important in determining the prognosis of tumours and may have a directing value for treatment options.

PS-26-024

Histopathological evoluation of multiparametric MRI targeted prostate biopsies

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Background & Objective: Multiparametric magnetic resonance (MR) imaging (mpMRI) is a widely used imaging technique to detect prostate cancer. Here we discuss the rate of prostate cancer detection in multiparametric MRI targeted biopsies.
Method: Formalin fixed, paraffin embadded, Haematoxylin eosin stained mpMRI targeted prostate needle biopsies from 45 men were histologically evaluated on light microscope.
Results: 45 patients were underwent mpMRI targeted prostate biopsy between 2016-2018 in our institution. 19 patient's targeted biopsies had prostatic adenocarcinoma and 26 patient's biopsy showed non-neoplastic findings. The rate of prostate cancer detection in mpMRI targeted biopsies was 42,2 %.
Conclusion: Multiparametric magnetic resonance imaging targeted biopsies showed 42,2% cancer detection rate on our 45 patient.

PS-26-025

Adenomatoid tumour of the testis. An unusual intratesticular tumour. Two case report

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Background & Objective: Intratesticular adenomatoid tumour is a rare tumour with aproximatly 12 cases described in the literature. By imaging is indistinguishable from a germ cell tumour derfor frozen section determined the final treatment. The objective is to report the clinicopathological findings of two cases of intratesticular adenomatoid tumour.
Method: All patients with an intratesticular mass diagnosed as adenomatoid tumour seen in the last 5 years at Viborg's Regions Hospital - Denmark were included. The clinical data, age, tumour markers, surgical treatment, pathological findings and the inmunhistochemical profile were evaluated.
Results: Two cases were studied. Patients age were 33 and 58. In both cases tumour markers were in normal range. Ultrasound reveleaded 20 and 10 mm. intratesticular tumour suspicious of malignancy. Frozen section were summited for diagnostic purposes. The first case was reported as non-germinal malignant tumour and posterior ochiectomy was performed, the second case was diagnosed as an adenomatoid tumour with no further procedure. Microscopic findings revealed a proliferation of neoplastic cells that grew in chains or pseudo-vascular spaces lined by flat and epithelioid cells with focal intracytoplasmatic vacuolization. Immunhistochemically tumours were reactive for mesothelial markers (calretinin, WT1), CK7 and negative for germinal and endothelial cell markers (CD30, OCT3/4, AFP, CD34).
Conclusion: Intratesticular adenomatoid tumour is a rare bening neoplasm that most probably arise from tunica albuginea or vaginalis. Ultrasoundly intraparenchymal and tunical tumours are difficult to differentiate from malignant tumours. Usually frozen section defines the posterior treatment. The histogenesis points toward a mesothelial oring and therefore surgical excision is therapeutic, without need for further intervention.

PS-26-026
Epidermal growth factor receptor (EGFR) and cyclin d1 in clear cell renal cell carcinoma (ccRCC)
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Background & Objective: Renal cell carcinoma is the most common solid tumour of the kidney with a mortality rate of more than 40% due to inefficient oncological therapy. The prognostic and therapeutic value of EGFR and cyclin D1 in RCC is still controversial and require further investigation. The aim was to determine the immunohistochemical expression of EGFR protein due to the localization in the cell (membrane and nuclear –mEGFR, nEGFR) and to establish the connection of EGFR and cyclin D1 immunoeexpression in the pathogenesis of ccRCC. The results were compared with nuclear grade (NG), Ki67 proliferation index, tumour size, pathological stage (pT) and 5- year survival of patients with ccRCC.
Method: We examined the protein expression of mEGFR, nEGFR, cyclin-D1 and Ki67 in 130 ccRCC obtained by nephrectomy by immunohistochemistry using tissue microarrays (TMA). Immunostainig mEGFR was expressed as a percentage and histoscor while other factors were quantified as a percentage of positive nuclei of tumour cells on the entire surface of the TMA.
Results: Protein expression of mEGFR as well as nuclear, showed positive correlation with patient survival. Multivariate analysis confirmed nEGFR and cyclinD1 as independent prognostic factors. Although the Cyclin-D1 is a major downstream target of EGFR-family-dependent signaling, we did not observe a statistically significant association to nEGFR but did observe an inverse correlation with m EGFR and cyclin-D1 expression.
Conclusion: Study showed that EGFR and cyclin D1 protein could affect the prognosis in patients with ccRCC.

PS-26-028
Clinicopathological profiling of LC3B, an autophagy marker, and ESRRA (estrogen-related receptor-alpha) in muscle-invasive bladder cancer
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Background & Objective: Microtubule-associated protein 1 light chain 3B (LC3B), an autophagy marker, has been used as a promising marker in various cancers. However, the expression of LC3B in muscle invasive bladder cancer (MIBC) and its prognostic significance have not been investigated. Recent studies pointed to the involvement of ESRRA in regulating autophagy via both transcriptional and post-translational control. In the current study, prognostic importance of LC3B and ESRRA in MIBC was investigated.
Method: We immunohistochemically studied the expression of LC3B and ESRRA in 56 MIBC samples.
Results: LC3B was stained high in 16 patients (28.6%) and low or negative in 40 patients (71.4%). ESRRA expression was high for 20 patients (35.7%) and low for 36 patients (64.3%). Both LC3B (p=0.003) and ESRRA (p=0.026) expression correlated significantly with disease-free survival rates. Patients with double-positive for LC3B and ESRRA correlates with poor overall survival (p=0.007) and disease-free survival (p=0.001) in MIBC patients.
Conclusion: LC3B and ESRRA might be a useful prognostic factor in patients with MIBC. The co-expression of LC3B and ESRRA might be a prognostic and therapeutic target for patients with bladder cancer.

PS-26-029
Degree of chromosomal abnormalities detected by UroVysion test predicts progression of non-muscle invasive bladder cancer
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Background & Objective: UroVysion fluorescence in situ hybridization test detects cytogenetic alterations characteristic for voided urothelial carcinoma (UCa) cells. Risk stratification based on conventional prognostic factors to predict the progression of non-muscle invasive UCas into muscle-invasive disease needs further improvement. Our aim was to predict progression of non-muscle invasive UCas to muscle invasive disease by assessing cytogenetic abnormality levels of tumours with a new UroVysion scoring system.
Method: Cytogenetic alterations were detected by UroVysion test from urine samples of 75 UCa patients from our prospectively maintained dataset. Cases were classified into five groups (UroVysion Score: UVS 0-I-II-III-IV) according to quantitatively assessed degree of UroVysion detected chromosomal abnormalities. The median follow-up was 68 months.
Results: UVS was proved to be an independent prognostic factor of overall survival (OS), progression-free survival (PFS) and time to progression (TTP). High risk (UVS III-IV) groups showed significantly worse prognosis when compared to UVS 0-II groups (UVS III-IV vs. 0-II: 34 vs. 92 months of median OS, p=0.0013; 32 vs. 87 months of median TTP, p<0.001). UVS predicted better the progression of non-muscle invasive UCas in comparison with the widely used risk stratification recommended by the European Association of Urology (EAU) guidelines (p<0.001 vs. p=0.134; TTP). Non-muscle invasive UCas with high risk UVS groups had a 31.93-fold increased hazard for progression to muscle-invasive cancer (TTP; 95% confidence interval 3.7-270.5, p=0.001).
Conclusion: UVS is a useful tool for assessing disease outcome. It provides better prediction of the progression of non-muscle invasive UCas into muscle-invasive disease.

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PS-26-030

Determination of PD-L1 expression in renal cell carcinoma (RCC) using immunohistochemical and PCR (polymerase chain reaction) methods

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Background & Objective: Renal cell carcinoma is revealed to have many features that suppress the host antitumour immunity. This made metastatic renal cell carcinomas which are unresponsive to conventional therapies, probable targets to the treatment with PD1/PD-L1 inhibitors.
Method: We determined PD-L1 expressions of 81 patients by using immunohistochemical (Anti PD-L1 antibody [28-8, ab205921], RabMAb, abcam) and quantitative real time PCR methods. We investigate the correlation between PD-L1 expression and prognostic features such as metastasis, stage and survival to contribute to the literature. Also, we aimed to evaluate convenient methods to guide patient selection for PD1/PD-L1 inhibitors treatment.
Results: Group consists of clear cell, chromophobe cell and papillary subtypes and PD-L1 expression rate is %19,75. We found a borderline statistic correlation between PD-L1 expression and metastasis (p=0,054). There was no significant relationship between PD-L1 and other clinical and prognostic parameters such as gender, age, mortality rates, histologic subtype, clinical stage, nuclear grade, sarcomatoid/rhabdoid differentiation, necrosis, tumour infiltration in kidney capsule, invasion into renal pelvis and hilar fat tissue, tumour size and survival. When we compared immunohistochemical testing with quantitative real time PCR method in determining the expression of PD-L1, we found that the sensitivity of immunohistochemistry is weak.
Conclusion: We found no statistically significant relationship between PD-L1 and prognostic parameters but we think PD-L1 expression can be used as a complementary diagnostic test in selecting patients for PD1/PD-L1 inhibitor treatment. We recommend using immunohistochemical and PCR methods together to eliminate the variations in the literature about staining and scoring interpretations for standardization.

PS-26-031

In search of IHC markers predicting urinary bladder cancer recurrence

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Background & Objective: To recognize IHC markers able to predict recurrence of urinary bladder tumours.
Method: Multivariate adaptive regression splines (MARS) was applied to IHC data evaluated independently by two pathologists. The MARS was used to predict the total number of recurrences by 9 IHC markers (EGFR, HER2, HER3, e-cadherin, Ki67, MLH1, MSH2, MSH6 and PMS2), among 33 patient (24 male and 9 female), aged 57-87 years, with primary urinary bladder cancer and one to six recurrences (a total of 113 tumour samples). Data were divided as initial tumours, the first and later recurrences, and as tumours that will relapse in 9 or >9 months. All markers were semiquantitatively classified in four groups.
Results: In predicting the total number of recurrences, the R2 value for all tumours was 0.423, for initial tumours 0.686, for the first recurrence 0.700, for later recurrences only 0.233. Key predictors for initial tumours were HER2 and MSH2, while for the first recurrence it was EGFR. For early recurrences, R2 was 0.474 with EGFR and HER3 as predictors, while for the late recurrences R2 was 0.640 due to EGFR and PMS2. The finding of E-cadherin was not found relevant by these MARS models.
Conclusion: The MARS results have associated multiple IHC markers with the number of recurrences and with Ki67 values. It is important that differences in predictive markers were found between the initial tumours and the first recurrences and between early and late recurrences, thus suggesting that tumour biology is different among these subgroups, regarding the total number of recurrences and Ki67 values.

PS-26-032

Comparative molecular pathological subtyping of bladder cancer by the age groups

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Background & Objective: Molecular profiling of bladder cancer, which was actively developed in the last decade, provides an additional prognostic and predictive information along with histology. We aimed to compare distribution of molecular subtypes in the age groups, taking into account the hypothesis about age dependent profile of urothelial bladder carcinoma.
Method: Ninety-two patients were included into investigation; 76 had non-muscle invasive (NMI) and 16 – muscle invasive urothelial cancers. Identification of molecular subtypes in our cohort was carried out using Lund algorithm with specific IHC panel. Log-rang test was used for recurrence-free survival analysis.
Results: The investigation revealed that all tumours in the most young group (20-29) were NMI Urothelial-like A subtype. Also, patients of this group had significantly longer recurrence-free survival period than elderly patient groups with same subtype (60-69, 70-79, 80-89), p<0,05. Frequency of Urothelial-like B, genomically unstable, basal/squamous-like, mesenchimal-like and small cell/neuroendocrine-like subtypes progressively increased with age.
Conclusion: Urothelial bladder carcinoma of young patients (20-29 years) tends to be of NMI Urothelial-like A molecular subtype and is associated with better outcome. It can be hypothesized that more aggressive molecular subtypes of bladder carcinoma appear and become more frequent with age.

PS-26-033

ERG positive PIN-like lesions without atypia: a retrograde colonisation of glands by invasive carcinoma instead of a preneoplasic lesion?

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Background & Objective: ERG is a highly specific immunohistochemical marker of prostate adenocarcinoma or high-grade prostatic intraepithelial neoplasia (HGPIN), a preneoplastic lesion. It has been proposed that some HGPIN cases could rather represent a ductal/acinar spreading of an invasive carcinoma. Our objective has been to investigate this hypothesis in a series of ERG-positive PIN cases.
Method: Needle prostate biopsies with ERG-positive HGPIN had been immunostained with AMACR in one slide, and a double-staining method on another tissue section with 34bE12 (using immunoperoxidase: brown signal) and ERG (clone EPR3864, with alkaline phosphatase: red nuclear signal). We have examined these cases searching for the presence of recognizable cytologically atypical cells in these PIN-like glands.
Results: Forty cores with foci diagnosed as ERG-positive HGPIN, with AMACR positivity and patched 34betaE12 positive cells, were evaluated. Seven of these glands (17.5%) were cytologically benign, although they contained intermingled ERG-positive cells: three of them were adjacent to <1 mm prostate adenocarcinomas, 2 were adjacent to ASAP and the other two cases were isolated findings.
Conclusion: HGPIN-like glands (positive for AMACR, ERG and 34betaE12) without atypical features can exist in the vicinity of adenocarcinomas and support the idea that they can represent colonization of benign glands by the carcinomas in a retrograde manner. As sometimes these changes can be adjacent to ASAP or may occur as isolate findings,

larger and prospective studies are needed to elucidate the predictive strength of this lesion for a malignant diagnosis in a future biopsy, which is expected to be higher than for usual HGPIN.

PS-26-034

Cancer stem cells as a new in vitro model to study metastatic prostate cancer

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Background & Objective: The gold standard therapy for metastasic Prostate Cancer (mPCa) is Androgen Deprivation Therapy (ADT) and docetaxel if resistance occurs. The therapeutic stress from ADT promotes the rise of neoplastic subsets of cells with abilities to survive the treatment. These cells that present at low levels in cultured cell lines (<3%), show characteristics of stem cells (CSCs) To identify the CSCs subpopulations the main objective was to enrich them by specific conditions that could favor their growth and to compare their expression profiles with the bulk tumour cells by RNA-sequencing.
Method: Two cellular models of androgen dependent AD and independent (AI) LNCaP cells; DU145 cells Docetaxel-Sensitive (DS), and Docetaxel-Resistant (DR) were used in order to confirm CSCs enrichment. 4 stemness markers were analysed by qPCR as well as the intrinsic resistance to chemotherapeutic agents used for PCa therapies. Finally, nude mice sub cutaneous xenograft injections of TICs were performed to confirm their tumour initiating abilities
Results: Androgen-independent (AI) cells enriched for expression of SOX2, ALDH1A1, CD133 and CD44 and compared to AD controls, confirming that the development of ADT induces the growth of CSCs subpopulations. Toxicity test with Docetaxel highlights that AI cells and spheres cultures are more resistant than AD parental cells.. In DU145 cells (DS and DR), sphere forming cells express stemness genes and show a higher survival to drugs compared to parental cells
Conclusion: A method to enrich CSCs subsets demonstrated that these cells are more resistant to chemotherapy than the bulk of the tumour. This method will allow to study CSCs RNA and protein profiles to find new specific targets to annihilate resistant prostate tumours.

PS-26-036

Paratesticular angiomyofibroblastoma-like tumour: pathological and immunohistochemical study of two cases

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Background & Objective: The angiomyofibroblastoma-like tumour (AMF) of the male genital tract is a rare benign tumour. A total of 34 cases have been reported in the literature. The aim of this study is to report two cases of this tumour in men arising as paratesticular masses of the scrotum and summarize the history of this tumour.
Method: We report two cases of AMF in males aged 78 and 39 years.
Results: Two men presented with painless inguinal and scrotal masses. Clinical examination revealed a testicular induration. Ultrasonography showed a paratesticular hypoechogenic mass. Treatement consisted in surgical resection. On gross examination, mean size, of the specimen, was 6,5 cm. The histological examination showed vessels with small caliber and turgidity of endothelial cells. These vessels were surrounded by clusters of epithelioid cells, sometimes having the appearance of giant cells. They were associated with spindle cells. Immunohistochemical (IHC) studies showed positive staining of the spindle cells for Desmin and smooth Muscle Actin. Endothelial cells and clusters of cells surrounding large vessels expressed CD34. Based on these histologic and IHC findings, the diagnosis of AMF was made.
Conclusion: AMF of the male genital tract is a benign often hormone-dependent tumour. Its histogenesis is still unclear. It has to be distinguished from aggressive angiomyxoma and myxofibrosarcoma.

PS-26-037

Pronostic group correlaction between needle biopsy and prostatectomy specimen, Gleason 3+4 with cribiform pattern

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Background & Objective: Gleason 4 has different architectural patterns, being the percentage of the Gleason 4, decisive for framing the patient in a prognostic group, in patients with Gleason 7 (3+4, or 4+3). The objective is to identify the potential association of the type of pattern in the needle biopsy with the results on radical prostatectomy.
Method: The prostate needle biopsies are reviewed from 2016 to the present date, with 150 biopsies, choosing from these, those with Gleason 3+4 and reviewing the pattern of grade 4.
Results: Of the 128 biopsies, 35 of them were Gleason 3+4. 13 biopsies showed cribiform pattern, 19 poorly formed glands and two glomeruloid. Subsequently, in the prostatectomy specimen, it was observed that, in the cribiform pattern, 61% (n=8) were pT3 stage, but the most striking, is that they increased the prognostic group in 62.5% of the cases. Thus, being the initial group prognostic grade 2, they passed to grade 3 in 37.5% and to grade 4 and 5 in 12.5% respectively. While, with a pattern of poorly formed glands only increased the degree in one case, assuming 5.3% versus 62.5% in the cribiform pattern.
Conclusion: Our data suggest that a cribiform pattern 4 is associated with a higher prognostic group in the prostatectomy specimen, than initially found in needle biopsy, so could mean to be an independent risk factor. Additional studies are being conducted in a larger cohort to expand these associations.

PS-26-038

Bladder cancer laser en-bloc resection – morphologist view

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Background & Objective: Background&objective: two surgical tactics by bladder cancer removal – "routine" transurethral resection (TUR) and "innovative" laser en-bloc resection (EBR) are used. Aim of study was to compare the intraoperative biopsies informative level.
Method: Material&methods: we investigated specimens obtained from 43–66 year old patients, 14 male and 1 female; 10 of them underwent thulium laser EBR, 5 (control group) – TUR. During the laser EBR the add-on material – circular margin of resection (around tumour base) and vertical margin (muscular layer fragment) – was taken. Light microscopy with haematoxylin/eosin staining was used.
Results: Results: TUR: scattered tumour papillae and bladder wall fragments were found; in two cases malignancy grade was difficult to identify (low-to-moderate); in four cases tumour was totally separated from adjacent bladder wall. In tumour base we found only submucosal layer and few muscular bundles in one biopsy. Laser EBR: well-structured tumour mass and its base – all-in-one with muscular layer were present in all specimens. Tumours were defined as papillary urothelial carcinomas with low grade of malignancy, in two patients grade was moderate. In two biopsies we detected cancer invasion into submucosal layer; muscular layer was always intact. Circular margin: once it was positive, once – foci

of perineural and perivascular invasion were present; dysplasia in lining urothelium was found twice. Vertical margin was everywhere negative.
Conclusion: Conclusion: tumour invasion into adjacent bladder wall, perivascular, perineural invasion is possible to identify in laser EBR-taken biopsies. Also we recommend to: expand the operation area, take circular and vertical tumour margins, include them into histological rating scale.

PS-26-040
Immunohistochemical expression of Annexin A5 in renal cell carcinomas
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Background & Objective: Renal Cell Carcinomas are neoplasms with high prevalence and mortality rates in Western countries. Annexin A5, a phospholipid binding protein, promotes proliferation and metastasis in RCC cell lines activating PI3K/Akt/mTOR pathways and regulating epithelial-to-mesenchymal transition processes and matrix metalloproteinase expression.
Method: A total of 135 renal carcinomas [clear cell (CCRCC, 100 cases), papillary (PRCC, 18 cases) and chromophobe (ChRCC, 17 cases)] were retrospectively selected for the analysis in a single institution (Pathology Department, University Hospital). A representative and well-preserved area of each tumour was selected and included in a tissue microarray (TMA) for immunohistochemical study. A commercially available anti-Annexin A5 antibody (Abcam, ab54775, working dilution 1:200, Dako Envision) was used.
Results: Annexin A5 was positive in 37% of CCRCC and in 87% of ChRCC while was negative in 100% of PRCC (Chi square test, $p<0.001$). Annexin A5 expression positively correlated with tumour diameter in CCRCC (Spearman Rho, $r=0.231$, $p<0.05$). Also, Annexin A5 expression was significantly higher in pT3/4 compared with pT1a CCRCC (Chi square test, $p<0.05$).
Conclusion: 1) Annexin A5 is consistently negative in PRCC, being a useful marker in the differential diagnosis of renal cell carcinomas, 2) Annexin A5 expression correlates with high tumour stages (pT3/4) in CCRCC, being a potential marker of tumour aggressiveness in these patients.

PS-26-041
Prognostic impact of Pirin expression in clear cell renal cell carcinoma. An immunohistochemical study of 100 cases with long term follow up
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Background & Objective: Pirin (PIR) is a newly identified nuclear protein that interacts with oncoprotein Bcl-3 regulating epithelial-to-mesenchymal transition processes and enhancing the development of cancer metastasis. The specific role of Pirin in clear cell renal cell carcinoma (CCRCC) has not been tested so far.
Method: A series of 100 CCRCC with at least 15 years of follow-up was retrospectively collected from the archival material of a single institution (Pathology Department, University Hospital). A representative and well-preserved tumour area has been selected in each case and included in a tissue microarray (TMA). A commercially available anti-Pirin antibody (ThermoFisher, PA5-29777, working dilution: 1:500, Dako Envision) was used in the study. Results were correlated with classic pathologic parameters and with overall survival.
Results: Pirin expression was correlated with tumour diameter (Spearman Rho, $p=0.039$). In addition, Pirin positive CCRCC had significantly shorter survivals after 15 years of follow up (univariate log-rank test, $p=0.007$; multivariate Cox regression, $p=0.028$).
Conclusion: The immunohistochemical expression of Pirin is an independent factor of bad prognosis in CCRCC patients. This finding suggests a role of this protein in the development and progression of CCRCC.

PS-26-043
Accuracy of ileum-obturator lymph nodes dissection in bladder tumours: predictive histological factors of ganglionic metastasis in a series of 68 cases
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Background & Objective: Bladder cancer is one of the most common cancers in men. In Tunisia, it represents the first urological cancer before prostate. The lymph node involvement is a major prognostic parameter. Our study aims to evaluate its frequency and to emphasize on the most histological predictive factors.
Method: This is a retrospective study of 68 pieces of radical cystectomy examined in the 3-year FH Sousse pathology department. The presence of lymph node metastasis has been studied in combinbation to other histological and macroscopic prognostic parameters
Results: Our series was made of 62 men and 6 women. The average age of our patients was 63 years. Tumours were classified as: urothelial carcinoma in 85% of cases, squamous cell carcinoma in 7.3%, carcinoma sarcomatoid in 3.4% of cases and in 1.5% in micropapillary carcinoma and mixed carcinoma. 54.4% of tumours in our series invaded the muscularis propria. Emboli and perineural invasion were observed respectively in 19% and 33.8%. an average of 6 lymph nodes was histologically examinated. Lymph node metastases were found in 16.2%. The correlation between ganglionic invasion, histological type, tumour size, vascular emboli, perineural invasion was studied. Only the presence of vascular emboli was significantly correlated with lymph node involvement ($p = 0.04$).
Conclusion: Our study suggests a significant association between the presence of vascular embolism and ganglionic invasion. This could lead to further management, particularly in patients treated with isolated cystectomy or in case of insufficient cleaning.

PS-26-044
Inflammatory myofibroblastic tumour / myofibroblastic proliferations of the urinary bladder presenting as a large obstructive tumour
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Background & Objective: Inflammatory myofibroblastic tumour (IMT) has fibroblastic and myofibroblastic origin. Different names have been used for identical cytologically benign myofibroblastic proliferations ie pseudosarcomatous myofibroblastic proliferation, IMT, pseudosarcomatous fibromyxoid tumour, postoperative spindle cell nodule. The urinary bladder is one of the most frequent sites of visceral involvement. Its ability to mimic malignancy poses a diagnostic challenge. A 35-year-old woman presented to our hospital with hematuria, dysuria and abdominal pain, with no previous medical history. Ultrasound revealed a large tumour at the bladder dome and the patient underwent cystoscopy and transurethral resection of the tumour.
Method: We received multiple grayish, solid, elastic tissue fragments measuring 9x6x1cm.
Results: Microscopically we observed fascicles of spindle-shaped cells with tapering nuclei distributed in a myxoid matrix, with slit-like vessels

and inflammatory background. The lesion infiltrated the bladder wall, but there were no significant atypia or pleomorphism. There were rare mitosis and focal necrosis. The surface epithelium had no dysplasia. The main differential diagnosis includes leiomyosarcoma, rhabdomyosarcoma, sarcomatoid urothelial carcinoma, fibromyxoid nephrogenic adenoma and myofibroblastic proliferations. The cells were immunopositive for CKAE1/AE3, Vimentin, Desmin, p16, ALK1 and focally for SMA and EMA.
Conclusion: It is crucial to distinguish IMT from malignant tumours for therapeutic and prognostic reasons. Treatment is complete surgical resection and close follow-up, as these tumours rarely metastasize and 25% recur after excision.

PS-26-045
Correlation between vascular density with metastasis and poor prognosis in clear cell renal cell carcinoma with venous tumour thrombus: review of 39 cases
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Background & Objective: Clear cell renal cell carcinoma is the most common type of malignancy of the adult kidney. The behavior of clear cell renal cell carcinoma is highly unpredictable. A correlation between microvessel density (MVD) and tumour aggressiveness has been established for several malignancies. We investigated the relationships between MVD, venous tumour thrombus, tumour size and prognosis.
Method: Tumour specimens from 39 patients with primary clear cell renal cell carcinoma and venous tumour thrombus were examined by immunohistochemycal staining for CD34 and CD31 were performed in three different areas of the tumour and two different thrombus areas.
Results: All the cases showed intense immunoreactivity for CD34 in both: the tumour and the renal vein thrombosis at least in one area. However only 18 cases showed positivity for CD31 especially in the vein thrombus. The high MVD and CD34 immunohistochemycal positivity were related with an bigger tumour size and also a worst prognosis.
Conclusion: This review showed a higher sensitivity of CD34 than CD31 to determine MVD suggesting that high MVD showed by the intense CD34 immunoreactivity may be associated with an bigger tumour size and worst prognosis. While low MVC it is related to a best prognosis.

PS-26-046
Clefting and the expression of E-cadherin and Lmo2 in prostatic adenocarcinoma
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Background & Objective: Periacinar retraction clefting is considered a reliable criterion for diagnosis of prostatic adenocarcinoma. E-cadherin is calcium- dependent cell adhesion molecule, while LIM Domain Only 2 protein (LMO2) belongs to transcription factor family of proteins characterized by their cysteine-rich, zinc-binding LIM domains. Aberant expression of both of these molecules is related to prostatic adenocarcinoma progression and prognostic outcome. In addition, malignant stroma and epithelia have a significant role in tumour progression. The aim of the study was to investigate the presence of periacinar clefting and the expression of E- cadherin and LMO2 in prostatic adenocarcinoma.
Method: Initially were 83 specimens haematoxylin and eosin stained and diagnosis of adenocarcinoma was established. Clefting was determined in the tumour and adjacent unaffected parenchyma. The intensity of E-cadherin expression in malignant and non- malignant epithelia and LMO2 expression in adenocarcinoma was then analyzed by microarray-based immunohistochemistry.
Results: LMO2 was more expressed in malignant epithelia than stroma (P= 0.000). Periacinar clefting was more expressed in prostatic adenocarcinoma then in adjacent unaffected parenchyma (P = 0.000), while no significant difference in expression of E- cadherin was demonstrated (P= 0.700). No statistically significant correlation between LMO2 expression in malignant epithelia or stroma and E- cadherin (P = 0.364; P = 0.615) was found. No significance when correlating clefting presence to LMO2 (epithelia, stroma) and E- cadherin expression in carcinoma (P = 0.882; P = 0.492, P = 0.299) was demonstrated.
Conclusion: We believe that these factors have a role in tumour progression, yet further investigation is needed.

PS-26-047
Correlation between biochemical prostate-specific antigen recurrence and histopathological parameters of prostatic adenocarcinomas in radical prostatectomy specimens
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Background & Objective: The aim of the study was to analyze the correlation between biochemical prostate-specific antigen recurrence (BCR) and histopathological parameters like tumour size, Gleason score (GS), radial length of extraprostatic extension (EPE), circumferential length of EPE, positive surgical margin, and extraprostatic seminal vesicle invasion in prostatic adenocarcinomas in radical prostatectomy (RP) specimens.
Method: A retrospective study was carried out in 445 patients, who underwent RP from 2009 to 2017. The mean follow-up duration was 65.03 months (range 6 - 109 months) after RP.
Results: In univariate analysis, significant differences included associations between BCR and tumour size (p=0.003), GS (p=0.001), radial length of EPE (p=0.001), circumferential length of EPE (p=0.001), positive surgical margin (p=0.001), extraprostatic seminal vesicle invasion (p=0.001), and preoperative prostate-specific antigen(p=0.001).
Conclusion: The results of our study showed that, in addition to the conventional Gleason grading system, tumour size, radial length of EPE, and circumferential length of EPE may useful prognostic parameters while evaluating long-term prognosis in prostatic adenocarcinoma.

PS-26-048
CEACAM1 expression in urothelial carcinoma – promising diagnosis and prognosis marker
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Background & Objective: CEACAM1 (carcinoembryonic antigen related cell adhesion molecule 1) encodes a protein with cell-cell adhesion role, found on leukocytes, epithelia, and endothelia. Our aim was to evaluate differences in CEACAM1 expression between non-infiltrative, low and high grade urothelial carcinomas (nIUC) and invasive urothelial carcinoma (IUC).
Method: We evaluate retrospectively all cases of urothelial carcinoma diagnosed on trans-urethral resection specimens in Colentina University Hospital in 2016: 46 nIUC and 76 IUC. IUC were in tumour stages pT1 and pT2. CEACAM1 was performed using positive and negative external controls. CEACAM1 expression was evaluated using a semi-quantitative scale with values between 0 (absent) and 2 (strong).
Results: CEACAM1 was strongly expressed in 100% of IUC and weak in 32.6% of nIUC. Large low-grade tumours with only small foci of invasion revealed both positive and negative areas.

Conclusion: CEACAM expression is related to tumour invasiveness in urothelial carcinomas and could be used in differentiation of IUC and nIUC. Further studies should be performed to evaluate the significance of CEACAM1 positivity in nIUC and its impact on patients' evolution.

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PS-26-049

Sarcomatoid carcinoma of the urinary bladder: a clinico-pathologic study of 15 cases and review

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Background & Objective: Sarcomatoid carcinoma of the bladder is an infrequent finding in daily practice (accounting for less than 1% of all bladder carcinomas) that has been reviewed in several studies to its better characterization. Our objective is to describe the clinical and pathological characteristics of the cases diagnosed in our center in the last 17 years.
Method: 15 cases were studied. Clinical information was recorded (age, gender, symptoms, procedure), as well as size, histologic description, heterologous component if there were, growth pattern, presence of carcinoma in situ, vascular invasion, pTNM and survival.
Results: Mean age found in our patients was 74 years (range:50-92). 12 were men (80%) and 3 women (20%). 12 patients had a history of smoking and all of them had clinical signs of hematuria. Mean tumour size was 68mm (30-120mm). In patients who underwent cystectomy (7), only one of them had no sarcomatoid component in the previous transurethral resection. The most frequent heterologous component identified was osteosarcoma (two patients), chondrosarcoma and rhabdomyosarcoma. In addition, neuroendocrine carcinoma was found in two patients. The mean postdiagnosis survival was 7.4 months (1-30 months), with 80% of patients less than 10 months. With regard to staging, 1 case was pT1(6,5%), 8 pT2(53%), 4 pT3(27%) and 2 pT4(13%). At diagnosis, 8 patients presented stage pT2, 1 patient was pT1 and 6 higher than pT2. All our findings agree with literature.
Conclusion: Sarcomatoid carcinomas of the bladder are frequently at advanced stage at time of diagnosis. Its poor survival (80% less than 10 months in our series) confers aggressive behavior and outcome.

PS-26-050

Expression of molecular biomarkers in prostate cancer at different stages of androgen deprivation therapy

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Background & Objective: Androgen-deprivation therapy (ADT) of prostate cancer (PCa) almost always leads to castration resistance prostate cancer (CRPCa) formation. The aim of the study was to establish expression patterns of ERG, p53, chromogranin A (ChrA), androgen (AR) and estrogens (ERa and Erß) receptors, aromatase (Arom), growth factors (TGF-ß, EGFR and VEGF), proliferation (Ki-67, CyclinD1, TopoIIα) and apoptotic (Bax, Bcl2) markers during ADT.
Method: Tissue samples of primary tumour, materials after adjuvant and neoadjuvant hormone therapy from 30 patients were analyzed. W-test was applied, $p<0.05$.
Results: Neoadjuvant therapy resulted in lower levels of p53, AR, Bax, Ki-67, CycD1), TopoIIα ($p<0,03$), and increased expression of ChrA and EGFR ($p<0,001$). At CRPCa, the expression of AR and Bax is significantly lower than in tumour after neoadjuvant deprivation ($p<0,001$). Also, the increasing of expression for ChrA, EGFR, Ki-67, CycD1, TopoIIα was found in CRPCa tumour ($p<0,01$). Comprising the primary tumour, CRPCa demonstrated decreased expression of AR, ERβ, Bax ($p<0,01$) and higher levels of ChrA, Arom, ERa, p53, EGFR, VEGF, TGF-β, Ki-67, CycD1, TopoIIα ($p<0,03$). In 33% of CRPCa the co-overexpression of AR and EGFR, TGF-β, VEGF was found.
Conclusion: Androgen suppression therapy leads to decreasing of p53, Ki-67, CycD1, TopoIIα levels after neoadjuvant therapy, unlike their expression increasing in CRPCa's. CRPCa is characterized by lower ERβ and higher Arom, ERa, EGFR, VEGF, TGF-β levels.

PS-26-051

Cystic renal neoplasms: a relook post 2016 WHO classification of tumours of kidney

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Background & Objective: Cystic neoplasms of the kidney are a diverse group of tumours with varying clinicopathalogical and radiological features. They include essentially different lesions which range from the benign cystic nephroma to renal cell carcinoma and its variants. Clear cell renal cell carcinomas frequently contain cysts and are usually degenerative in nature. The present study was performed to evaluate the clinicopathological features of those renal neoplasms which were predominantly cystic in nature.
Method: A retrospective study from January 2011 to December 2017 was conducted wherein all renal neoplasms were retrieved from the histopathology records of the Department of Pathology, Kasturba Medical College, Mangalore. Those cases which were described as cystic with minimal solid areas on gross examination were included in the study. The clinical, radiological details were obtained from the hospital files and the histopathology slides of these cases were reviewed.
Results: A total of 151 patients underwent nephrectomy for renal tumours during the study period. Of these, 25 were grossly cystic neoplasms. The age range of these patients varied from 19 to 68 years. Male: female ratio was 4:1. Five cases of cystic nephroma were seen in our study. There were 11 cases of cystic clear cell renal cell carcinoma, five cases of cystic papillary renal cell carcinoma and four of multilocular clear cell cystic neoplasm of low malignant potential.
Conclusion: Cystic neoplasms of the kidney can pose diagnostic conundrums. A combined clinicopathological and radiological approach with support from immunohistochemistry markers aids in arriving at a diagnosis. Multilocular clear cell cystic neoplasm of low malignant potential are uncommon and need to be recognised for their benign behaviour and favourable prognosis.

PS-26-052

Immunohistochemistry may avoid understaging of bladder cancer in surgical specimens with pT0 stage after trans-urethral resection

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Background & Objective: Trans-urethral resection (TUR) may determine complete removal of urothelial carcinoma and down-staging as pT0 in the following of bladder surgical specimen. In addition, it may lead to an inflammatory response which may obscure the presence of residual cancer. Herein we report the utility of immunohistochemistry to avoid understaging of bladder carcinoma in surgical specimens obtained shortly after TUR.
Method: Among 21 urinary bladders surgically resected for urothelial carcinoma over the last year, we observed cystis with giant cells or atypical mononuclear cells in a total of 4 (19%) cases. All were obtained from male patients who had been submitted to TUR of urinary bladder 1 to 2 months before surgery. None had received neo-adjuvant treatments. Since no residual tumour was seen in haematoxylin and eosin (H&E) slides we

performed immunohistochemistry against wide spectrum cytokeratin, GATA3 and p63, to identify residual cancer.
Results: Two cases had no cells positive for cytokeratin AE1, p63 and GATA3, apart from normal urothelium, and were classified as pT0. The other two cases were classified as pT3a due to the presence of aggregates or single tumour cells positive for cytokeratin, GATA3 and p63 in the muscularis propria, in the perivescical adipose tissue and in the vessels lumen, not identified in H&E slides.
Conclusion: Aggregates or single cancer cells may remain within the muscularis propria or in the adipose tissue after TUR. Immunohistochemistry against epithelial (CKAE1) and urothelial specific markers (GATA3 and p63) may be essential for their identification and to avoid pT understaging in the surgical specimen.

PS-26-053
Large cribriform growth pattern identifies men with aggressive Gleason score 3+4=7 prostate cancer
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Background & Objective: Cribriform architecture is associated with aggressive Gleason score (GS) 7 prostate cancer (PCa). However, the independent prognostic value of cribriform intraductal carcinoma (IDC-P) and invasive cribriform carcinoma is yet unclear. Our objective was to determine the prognostic value of IDC-P and invasive cribriform cancer subtypes in radical prostatectomies (RP).
Method: We reviewed 421 RPs with GS3+4=7 PCa, assessed percentages Gleason grade 4 and tertiary 5, and performed basal cell immunohistochemistry to distinguish IDC-P from invasive cribriform growth. Cribriform growth was dichotomized in small and large structures. Clinicopathological parameters and biochemical recurrence-free survival (BCRFS) were used as endpoints.
Results: Cribriform architecture was observed in 229 (54.4%) men: 195 (46.3%) showed small and 34 (8.1%) large cribriform growth. IDC-P was observed in 104 (24.7%) patients. GS3+4=7 PCa patients with large cribriform growth had higher prostate specific antigen (PSA) levels (P=0.003), higher pT-stage (P<0.001) and more frequent IDC-P (P=0.001), than those with small cribriform growth. Univariable analysis marked PSA, pT-stage, surgical margin status, IDC-P and invasive cribriform growth as significant predictors for BCRFS, but not grade 4, or tertiary grade 5. In multivariable analysis, pT-stage (HR1.64, 95%CI 1.02-2.63, P=0.04), positive surgical margin (HR3.28, 95%CI 2.06-5.23, P<0.001) and large cribriform growth (HR4.37, 95%CI 2.08-9.17, P<0.001) were independent predictors for BCRFS, while IDC-P and small cribriform growth were not.
Conclusion: In conclusion, large cribriform growth is an independent predictor for BCRFS in GS3+4=7 PCa, whereas small cribriform growth and IDC-P are not.

PS-26-054
TCEB1 wild type renal cell carcinoma with prominent (angio)leiomyomatous stroma
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Background & Objective: Renal cell carcinoma with prominent (angio)leiomyomatous stroma is currently classified as an emerging/provisional entity. Recently TCEB1 mutation has been found in neoplasms with these morphological features.
Method: A series of 10 renal cell carcinomas with prominent (angio)leiomyomatous stroma (5M, mean age: 70 years, mean size: 2 cm) were analyzed for the occurrence of TCEB1 deletion and/or mutation. TCEB1 gene Y79 and A100 hotspots were analyzed by Sanger sequencing. Fluorescent in situ hybridization (FISH) assay was performed using a break apart TCEB1 probe. Centromeric alpha-satellite specific for chromosome 8 (CEP8) and a dual fusion c-MYC probe were used as control probes on serial tissue sections.
Results: Mutation analysis and FISH assay did not detect TCEB1 mutation and/or deletion in any case.
Conclusion: In our series, renal cell carcinoma with prominent (angio)leiomyomatous stroma did not harbor TCEB1 mutation and/or deletion. Despite the identification of TCEB1- mutated renal cell carcinomas, this molecular alteration seems not to be the only pathway involved in tumours with prominent (angio)leiomyomatous stroma.

PS-26-055
Characterisation of large cell neuroencocrine carcinomas and comparison with small cell carcinomas of the urinary bladder. A European collaboration study
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Background & Objective: The primary large cell neuroendocrine carcinomas (LCNEC) of the urinary bladder are aggressive, rare tumours with only 54 cases described in the literature. Our aim is to evaluate the pathological features of LCNEC versus small cell neuroendocrine carcinomas (SCNEC) of the urinary bladder and the expression of some novel markers, GATA3, p16 and CD117, in these uncommon entities.
Method: We studied 10 cases of LCNEC from 6 different European Institutions from 2007 to 2018. The final diagnosis was confirmed following the score proposed by Gupta S. et al. The panel of immunohistochemistry included 4 neuroendocrine markers, cytokeratins, p63, TTF1 as well as GATA-3, p16 and CD117. The findings were compared to 7 SCNEC.
Results: 3 out of 10 LCNEC were mixed with other non-LCNEC tumour types. No significant immunohistochemical differences were noted between LCNEC and SCNEC, apart from a more frequent expression of cytokeratins in LCNEC. The most reliable neuroendocrine marker was Synaptophysin. GATA3 was expressed in 10%, p16 in 89% and CD117 in 40%. In the 2 mixed cases with urothelial component, the expression of CD117 in the non-LCNEC was 0%.
Conclusion: The recognition between LCNEC and SCNEC is purely morphologic, based on clear cytoarchitectural criteria. The knowledge of the LCNEC in this location is very limited and easily misdiagnosed as poorly differentiated urothelial carcinoma. In this sense GATA3 appears like a helpful marker in the differential diagnosis. The frequent positivity of p16 and CD117 remains unclear and suggests further research to determine the potential for utilizing targeted therapies.

PS-26-056
Neural density and perineural invasion in prostate cancer
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Background & Objective: Perineural invasion (PNI) is common in prostate cancer, being involved in tumour biology and neoplastic progression. New data show that neurogenesis occurs also in prostate cancer. Several mechanisms are involved in crosstalk between cancer cells and the nerves, including NPY signaling. The aim of this study was to assess nerve density and PNI in prostate cancer and to look for its significance.
Method: 73 radical prostatectomy cases were examined (tumour stage pT1b to pT3b) with grade group 1(12), 2(33), 3(13), 4(7), 5(8). PNI concerned 76% of cases. TMA were prepared, including 126 cancer and 14 benign cores. Additionally, 6 samples were analyzed in whole tumour/ prostate sections. Immunostaining for PGP 9.5, NPY and ERG was performed. Axonal density (AD) was specified as number of independent PGP 9.5

positive structures- dots/lines in 10 hot spots areas under 200x. NPY expression was assessed within the tumour and in PNI areas. ERG was examined in 0-1-2 scale. Olympus CellSense software was used for analysis.
Results: AD within the neoplastic tissue was higher than in benign prostate, but lower than in tumour surrounding border (250 vs 55 vs 450; $p<0.05$). The difference of AD between grade groups was not significant. Tumours with PNI and ERG- positive cases showed higher AD ($p<0.05$). High NPY tumours presented lower AD ($p<0.05$). NPY expression was stronger in PNI than in tumour mass and such cases had also higher AD.
Conclusion: Axonal density is increased in prostate cancer and correlates with PNI and expression of NPY and ERG.

E-Posters

Sunday, 9 September 2018 to Wednesday, 12 September 2018
09:00 - 17:15, Exhibition Hall I/II, E-Poster Terminals

E-PS-01 | Autopsy Pathology

E-PS-01-001
PET/CT with 18F-fluorodeoxyglucose (18F-FDG) revealed diffuse uptake in bilateral adrenal glands, resolved at autopsy

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Background & Objective: Adrenal glands have been traditionally imaged by either computed tomography (CT) scan or magnetic resonance imaging (MRI) but positron emission tomography (PET) imaging of the adrenal glands has been found useful in some situations, although this modality is not the initial test of choice.
Method: We present an 82-year-old woman, with a history of diffuse large B cell lymphoma in complete response after treatment, who had a progressive deterioration of the general condition in the last months. Laboratory analysis evidenced bicytopenia. PET/CT images showed a diffuse increased 18F-FDG metabolism involving bilateral adrenal glands, bone marrow, spleen and the pituitary gland. Finally, the patient died, and autopsy was requested to explain the meaning of unusual 18F-FDG uptake in adrenal glands.
Results: In the autopsy study, macroscopically we observed bilateral adrenal hyperplasia. In the microscopic study, we evidenced neoplastic lymphoid cells in the lumina of small vessels in: bone marrow, kidneys, adrenal glands, bladder and pancreas. Tumour cells were positive for B-cell associated antigens: CD20, CD79, and BCL2. The post-mortem diagnosis of intravascular large B-Cell lymphoma (IVLBCL) helped us to understand the cause of 18F-FDG PET/CT uptake involving adrenal glands.
Conclusion: The diagnosis of IVLBCL is made post-mortem in half of the cases. Hypermetabolism in adrenal glands was considered to be due to direct invasion of this highly vascular organ by neoplastic cells. We suggest that 18F- FDG PET/CT could be performed for early diagnosis of IVLBCL, which is important for effective therapeutic intervention.

E-PS-01-002
Intimal sarcoma of the abdominal aorta: an unexpected autopsy finding

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Background & Objective: Malignant neoplasms of the aorta are rare entities with poor prognosis and usually with metastatic disease. We present a case which diagnosis was only possible by autopsy.
Method: We present a 74-year-old woman with constitutional symptoms and uncontrolled hypertension for the last 6 months. She revealed renal insufficiency that evolved to anuria and conscience depression. PET scan unmasked a hypermetabolic lesion on the luminal surface of the abdominal aorta, which wasn't considered for any endovascular procedure due to its dimensions. An empirical course of corticosteroids was tried but patient died within a few days.
Results: Autopsy revealed a 10cm exophytic mass in the luminal surface of abdominal aorta, beginning downstream of the emergence of renal arteries, conditioning occlusion of the left renal artery. Histologically we observed a largely necrotic neoplasia, superficially with small aggregates of epitheliod cells. It was observed vascular invasion in lungs, adrenal glands, cecum, spleen, pancreas and liver. The immunohistochemical study revealed positivity of neoplastic cells for CK AE1/AE3, CK7, CD31, CD34, smooth muscle actin, FLI-1, INI-1, MDM2, CD117 and podoplanin and negativity for CK20, CK34BE12, GATA3, S100, desmin, HHV8 and HMB45. Patient died due to right heart failure and ischemic hepatitis.
Conclusion: In a typical case of intimal sarcoma, endotelial markers are negative, unless angiosarcomatous differentiation is present and nuclear expression of MDM2 can be observed in up to 70% of cases. It has an aggressive behaviour, poor outcome and mostly with metastatic disease. In most cases, diagnosis is established post-mortem or after emergency surgery for embolic complications.

E-PS-01-003
Leptomeningeal carcinomatosis and infiltration of the orbit mimicking a neurological paraneoplastic syndrome in a 51-year-old female with gastric adenocarcinoma

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Background & Objective: Gastric cancer is one of the most common malignancies worldwide. Metastases are usually located in the liver and peritoneum, while involvement of central nervous system is rare.
Method: We present a case of a massive dissemination, evidenced post-mortem, including infiltration of leptomeninges and orbits in a 51-year-old female with gastric adenocarcinoma presenting with complex neurological symptoms.
Results: The patient was admitted to the Department of Neurology, Wroclaw Medical University Hospital, after severe headache followed by impaired consciousness and generalized seizures. She gave history of acute headaches, strabismus and diplopia intensifying over the preceding three months. The patient had been treated for Graves' disease and had recently received 3 cycles of neoadjuvant chemotherapy for gastric adenocarcinoma, clinically staged T3N2M0. Neurological examination showed bilateral exophthalmos and ocular movement disorders, papilledema, right-sided facial sensory and motor deficits, ipsilateral tinnitus and hearing impairment. Head CT and MRI scans showed vague texture of the clivus and bilateral orbital infiltrates suggestive of sarcoidosis, pseudotumour or thyroid orbitopathy. The entire clinical picture raised suspicion of a paraneoplastc process. The patients' condition deteriorated quickly leading to rapid death. Autopsy and post-mortem histopathological examination revealed regionally advanced and massively disseminated gastric signet ring cell adenocarcinoma with diffuse infiltration of leptomeninges and orbits, including extraocular muscles. Metastases were also found in the clivus, heart and pulmonary hilar lymph nodes.
Conclusion: Central nervous system metastases should be always taken into account as a potential cause of neurological symptoms, especially in patients with known history of cancer.

E-PS-01-004

Influenza season 2017-2018 at a single institution: clinical, histologic and microbiological findings

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Background & Objective: Prospective/case series study of fatal Acute Influenza Virus (AIV) infections during the 2017-2018 epidemic at an academic institution.
Method: Autopsy cases were followed prospectively at UTMB during the 2017-2018 Influenza epidemic. Clinical, microbiological and histologic data were analyzed.
Results: A total of five fatal cases were identified. Complete autopsies were performed in all cases. Age ranged from 41-77 years. Three cases (60%) were females and two males (40%). All AIV infections were confirmed by PCR (three Influenza A [60%)] and two Influenza B cases [40%]). Four cases (80%) revealed superimposed acute bacterial bronchopneumonia. Bacterial cultures showed Methicillin-Resistant Staphylococcus aureus in two cases. Proteus mirabilis was isolated in one case while Streptococcus mitis was isolated in the 4th case. Two of the cases with acute bacterial bronchopneumonia also showed evidence of Diffuse Alveolar Damage (DAD). One case (20%) revealed DAD with no superimposed infections. Furthermore, all Influenza A cases revealed DAD while cases due to Influenza B only showed acute bacterial bronchopneumonia. All cases had co-morbidities including morbid obesity, COPD, diabetes mellitus, and congestive heart failure.
Conclusion: The 2017-2018 Influenza season was more active than recent influenza seasons. At UTMB, we performed five autopsies of fatal AIV infections during this season, as opposed to only one case in each of the two previous seasons. The presence of DAD only in cases of Influenza A infections strongly suggests that these infections are more severe than other Influenza viruses (B and C). However, Influenza B infections can also lead to superimposed pulmonary bacterial infections and subsequent sepsis and death.

E-PS-01-005

Reye-like syndrome in a patient with suspected medium-chain acyl-CoA dehydrogenase deficiency and two unaffected family members with an acyl-CoA dehydrogenase-mutation

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Background & Objective: Reye-like syndrome is a metabolic disorder characterized by rapid liver dysfunction such as hypoglycemia or a deteriorated coagulation.
Method: We report an autopsy case of a 24-year-old male who complained of severe headache to his friends before he collapsed. The patient was brought to our emergency department with ongoing cardiopulomonary resuscitation. Return of spontaneous circulation was established 56 minutes after collapse. The initial cranial CT scan showed a pronounced cerebral edema not explained by hypoxic encephalopathy alone. Laboratory testing revealed a severe dysfunction in coagulation with an international normalized ratio of 2.63 and a partial thromboplastin time of 86 s. Despite full neurocritical care and intracranial pressure management the patient died four days after admission from uncontrollable cerebral edema.
Results: The autopsy revealed a mild hepatomegaly of 1800 g and a severe microvesicular steatosis without recognizable fibrosis or inflammation. Electron microscopy showed dilated mitochondria without discernable cristae in hepatocytes. The examination of the brain showed a severe edema of the cerebrum and a pronounced necrosis of the cerebellar cortex.
Conclusion: The patient's past medical history revealed migraine since childhood with an episode medicated with ASS four days prior to admission as well as an episode with impaired coagulation nine months before. Thus, the diagnosis of a Reye-like syndrome was made and genetic counseling of the family members was proposed. The mother of the patient showed a heterozygous p.Y42H (199C>T) and the brother showed a heterozygous p.E18K (127A>G) mutation in the acyl-CoA dehydrogenase gene. Sequencing analysis of the patient's DNA is underway.

E-PS-01-006

Extranodal NK/T cell lymphoma/leukemia associated with hemophagocytic syndrome and spontaneous splenic rupture: a case report

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Background & Objective: Extranodal NK/T cell lymphoma/leukemia (ENKTCL) is an uncommon type of T-cell lymphoma associated with EBV which usually presents in the upper aerodigestive tract. Hepatosplenic involvement is exceedingly rare.
Method: We report the case of a patient who died due to ENKTCL associated with hemophagocytic syndrome and spontaneous splenic rupture.
Results: A 71-year-old man was admitted due to fever of unknown origin. The patient developed systemic inflammatory response syndrome and hemorrhagic shock during his hospitalization. He was diagnosed with hemoperitoneum due to spontaneous splenic rupture, was submitted to emergency splenectomy and died in the post-operative period. The autopsy's main findings were status-post splenectomy, pleural/peritoneal effusions, congestive lungs, multiple lymphadenopathies and hepatomegaly. Histologically, a population of intermediate to large lymphoid cells with irregular nuclei and scant cytoplasm could be seen infiltrating multiple organs, including the duodenum, ileocecal appendix, lungs, testis, pericardium, lymph nodes, bone marrow, liver and spleen (surgical specimen). The neoplastic cells were immunohistochemically positive for CD3, CD4, CD56, CD57 and granzyme. In situ hybridization for EBV (EBER) was also positive. The diagnosis of ENKTCL with multi-organ involvement was performed. Images of hemophagocytosis were also found in multiple organs.
Conclusion: Spontaneous splenic rupture is an extremely rare complication of lymphoproliferative diseases affecting the spleen. Association of ENKTCL and hemophagocytic syndrome correlates with a very poor prognosis.

E-PS-01-007

Autolytic changes due to formalin-fixation delay: a histomorphologic study

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Background & Objective: Autolysis may be a misleading factor when evaluating specimens exposed to delay in formalin-fixation, hampering morphological diagnosis and molecular study results. In this study we aimed to identify and characterize histomorphologic autolytic changes over time and at different storage conditions.
Method: We collected samples (n=187) of grossly normal tissues from surgical specimens (n=7), including colon, uterus, kidney, liver and adipose tissue. They were divided into 4 groups kept at different conditions: at room temperature and dry; at room temperature and immersed in saline; kept in refrigeration (4ºC) and dry; kept at refrigeration (4ºC) and immersed in saline. All the groups were exposed to predefined intervals of formalin-fixation delay (<15 minutes, 30 minutes, 1h, 2h, 4h, 8h, 24h, 48h, 72h and 96h). Histologic examination was made after formalin-fixation and routine haematoxylin and eosin staining.

Results: Earlier histomorphologic autolytic changes were observed at 30 minutes without formalin in kidney and liver, occurring later in the remaining tissues. Autolytic changes were first identified in tissues stored at room temperature and immersed in saline, being initially focal and later widespread throughout the fragments. Globally, the first autolytic changes consisted in disruption of tissue architecture, with structure shrinkage followed by isolated cellular discohesion; subsequently, there was cell disintegration with cytoplasm fragmentation, nuclear pyknosis and abnormal chromatin clumping.
Conclusion: Timing and extent of histomorphologic autolytic changes vary depending on type of tissue, temperature degree and moisture. This preliminary study indicates that architectural changes are evident earlier than cytologic changes.

E-PS-01-008
Nonbacterial thrombotic endocarditis: a silent cause of death revealed in autopsy

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Background & Objective: Nonbacterial thrombotic endocarditis (NBTE) was originally regarded as an unimportant finding in approximately 4% of autopsies. It results from vegetations associated with systemic processes.
Method: We present a 51 years-old woman with mitral valvular disease due to rheumatic fever. She was admitted in our institution for aetiological study of stroke due to afasia. Imagiological evaluation identified an apparent occlusion of both carotid arteries with a very marked commitment of the circulation of the territory of the left middle cerebral artery. Patient died few days later.
Results: Autopsy revealed multiple vegetations in mitral valve, the biggest one, nodular with a smooth surface, with 3x2.2x1.8cm, consisting of a whitish, laminated and elastic tissue. Histologically it corresponded to acelular, concentric layers of fibrin, preserving the valvular structure, without inflammation. It was also observed luminal occlusion of left carotid artery by thrombus and an area of cerebral softening in the convexity of the left fronto-parietal region and in the left temporal pole.
Conclusion: Cause of death was diffuse ischemic cerebral necrosis due to embolic occlusion of the left carotid artery in relation to NBTE. Noninfective vegetations can cause significant morbidity and mortality. Embolization from friable thrombi commonly causes systemic infarction. In autopsy studies, evidence of embolization was found in about 40% of cases, with renal infarction and stroke being the most common manifestations. Vegetations may also cause valvular dysfunction either by mechanical interference with valvular function or by valve distortion due to gradual fibrosis of the thrombus and underlying valvular tissue.

E-PS-01-009
Incidental chondroid chordoma – necroptic diagnosis

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Background & Objective: Incidental central nervous tumours are characteristic findings in forensic pathology, with a relative dominance of meningeal tumours, while brain and spinal cord tumours are relatively rare. The aim of our study is to report an incidental necroptic diagnosis of a chondroid chordoma, in a female, of 72 years old, from our files.
Method: The case has been investigated by routine haematoxylin-eosin staining, along with Alcian blue, and immunohistochemistry for S100 and CAM 5.2 cytokeratin.
Results: The gross findings were that of a whitish, cauliflower-like, subdural, relatively well-delimited, non-encapsulated tumour, with an elastic consistency, located in the optic chiasm region. The microscopy revealed cords of physaliphorous cells, with focal atypia, supported by a myxoid stroma exhibiting Alcian blue positive staining, associated with extensive areas of chondroid appearance. The histopathological findings in usual and special stainings, along with immunohistochemistry, certified the diagnosis of chondroid chordoma. Differential diagnosis with other primary or secondary tumours composed of vacuolated cells, along with myxoid and cartilaginous tumours have been considered.
Conclusion: Although incidental central nervous tumours are relatively frequent in forensic pathology, chordomas are rare. The diagnosis has to corroborate the medical history, along with gross findings, histopathological, and immunohistochemical features.

E-PS-01-010
Advanced urothelial carcinoma of renal pelvis with extremely high level of serum hCG

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Background & Objective: Some urothelial carcinomas can produce human chorionic gonadotropin (hCG). A higher rate of expression was found in the invasive stages of the disease. According to the previous investigations, such tumours have worse outcome and response to treatment.
Method: We present the autopsy case of Caucasian 53-year-old male with primary pelvic urothelial carcinoma and multiple lymph nodes, pulmonary and hepatic metastasis. A clinical diagnosis was retroperitoneal germ cell tumour, and was based on beta-hCG serum level, that was 245743 mIU/mL in five days before death. The patient received one course of chemotherapy with etoposid 180 mg.
Results: Gross examination revealed retroperitoneal masses, measures 23x19x7 cm, originate from left kidney pelvis, invaded through the kidney into perinephric fat, abdominal aorta, inferior vena cava, common bile duct. Multiple metastases in lungs, pelvis and distant lymph nodes (posterior mediastinal, pelvic) were found. Microscopical examination confirmed invasive high grade urothelial carcinoma. Small foci of syncytiotrophoblast-like cells were found in lymphnodes and lung metastases. Immunohistochemically: tumour cells were positive for Keratin 7, p63, GATA3, b-catenin, and negative for KRT20, S100, OKT3/4, D2-40, SOX-2 and CD3. Ki-67 level were 90%.
Conclusion: The presented case confirms the ability of high grade urothelial cancer to secrete hCG. Careful and complete investigation is crucial for avoid a discrepancy of postmortem clinical and pathological diagnosis.

E-PS-02 | Breast Pathology

E-PS-02-002
Microfluidic-based immunohistochemistry for molecular subtyping of breast cancer

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Background & Objective: Breast cancer is a highly heterogeneous disease. The differential diagnosis of the disease, as well as the efficacy of the therapeutic strategies, relay on the precise detection and quantification of specific molecular biomarkers by immunohistochemistry (IHC). Microfluidics is a promising innovative technology in the field of tissue diagnostic, enabling for rapid, reliable, and automated immunostaining. We previously reported microfluidic-based HER2 detection in breast carcinomas empowering for enhanced immunoreaction quality and reproducibility, resulting in greater repartition of negative versus positive cases with 90% decrease of ambiguous score and allowing HER2 gene copy

number prediction. Here, we aimed to develop a full panel of diagnostic biomarkers for fast and accurate microfluidic-based molecular subtyping of breast cancer.
Method: The microfluidic tissue processor device was used to perform IHC staining of formaldehyde-fixed paraffin-embedded (FFPE) breast tumour biopsies (n=50), in parallel with a standard automatized staining process routinely used in tumour diagnostics. All histological samples were stained for estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), proliferation factor Ki67 and cytokeratin (CK).
Results: IHC protocol for all tested markers was optimized to reach high staining quality comparable to standard procedure, while concomitantly shortening total process time to 16 minutes. High concordance/correlation coefficient was found for all markers assessed by microfluidic versus standard process. Importantly, HER2 genetic reflex test for all discordant cases confirmed the scores obtained by microfluidic.
Conclusion: Microfluidic-based IHC represents an effective alternative approach to standard chromogenic staining for rapid, precise and automated molecular subtyping of breast cancer.

E-PS-02-003
Using control charts to assess the consistency of breast cancer grading in 1,453 resections
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Background & Objective: The Nottingham grade is a predictor of breast cancer outcome; however, it is not assessed routinely from observational data with control charts and statistical process control (SPC)/Next Generation Quality (NGQ).
Method: All in house breast cancer resections with a synoptic report at two institutions (accessioned 2011-2017) were analyzed. Pathologist diagnostic rates (PDRs) for the Nottingham grade(G) and its components (tubular score (TS), nuclear score (NS), mitotic score (MS)) were calculated for pathologists interpreting >30 cases. Consistency was assessed using control charts centred on the group median diagnostic rate (GMDR) with control limits defined by +/-2 and +/-3 standard errors in relation to GMDR. PDRs were normed using (1) maximal cases read, and (2) the standard errors to the GMDR for each pathologist.
Results: The study period had 1,752 resections. Ten pathologists read 35-441 cases and together assessed 1,453. The PDR medians (normed ranges) were: G1_20%(17to25%), G2_47%(40to54%) and G3_26%(22to32%). The PDR component medians (normed ranges) were: TS1_8%(5to11%), TS2_22%(16to31%), TS3_67%(57to73%), NS1_6%(0to11%), NS2_57%(38to78%), NS3_33%(19to56%), MS1_54%(51to61%), MS2_20%(17to25%), MS3_19%(15to22%). The number of statistical outliers (P<0.05andP<0.001) to the GMDR, for the ten pathologists, were G1_2and0 (of 10), G2_5and1, G3_1and0, TS1_1and0, TS2_5and2, TS3_4and1, NS1_6and5, NS2_4and2, NS3_4and2, MS1_1and0, MS2_1and0, MS3_1and0.
Conclusion: The nuclear score and G2 had the most outliers. The intermediate score in a 3-tier system is expected to have the most variability; NS1 appears to be inconsistently used. The individual pathologist is a predictor of the Nottingham grade. SPC/NGQ could improve grading and may optimize resource allocation and facilitate improved patient outcomes.

E-PS-02-004
Routine biomarkers in preoperative biopsy and resected breast tumour - need for reassessment?
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Background & Objective: Breast cancer is a heterogeneous disease consisting of multiple subtypes and with a variation in prognosis and therapeutic response. Immunohistochemical (IHC) assessment of the therapy predictive biomarkers oestrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2) and the proliferation associated nuclear marker Ki67 is performed on all invasive breast tumours. To date, the variations in biomarker evaluations from core needle biopsy (CNB) and surgical resection has not been thoroughly investigated in Swedish breast pathology. The aim of this retrospective study was to investigate the concordance of biomarkers between CNB and consecutive surgically resected specimen.
Method: The study comprised 528 breast cancer cases with biomarker evaluations on CNB and consecutive surgical specimen without neoadjuvant therapy diagnosed at Karolinska University Laboratory, Sweden, in 2016-2017. Biomarkers and IHC based surrogate subtypes were compared in CNB and corresponding resected tumour.
Results: We identified a 98.6 % concordance for ER with almost perfect agreement (Cohen's kappa 0.917, p <0.001) and a 90.2% concordance for PR with a substantial agreement (Cohen's kappa 0.648, p <0.001). Importantly, HER2 IHC showed only a 75% concordance and moderate agreement (Cohen's kappa 0.456, p <0.001). Similar results were observed for Ki67 (78.5%, Cohen's kappa 0.523, p <0.001). IHC based subtypes showed a 72.6% concordance (Cohen's kappa 0.528, p <0.001).
Conclusion: We show a significant discordance for HER2 and Ki67 between CNB and consecutive surgical specimen. We recommend that biomarkers are re-assessed on surgical specimen in addition to CNB when planning tailored treatments.

E-PS-02-005
Prognostic value of clinicopathological features in a large cohort of triple negative breast cancer
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Background & Objective: Although much research has been done on prognosis of triple negative breast cancer (TNBC), only scattered information about the prognostic value of clinicopathological features is available. This study aims to obtain more insight in these clinicopathological features.
Method: A multicentre retrospective TNBC cohort was established using the Dutch National Cancer Registry. From 5 hospitals from Eastern-Netherlands, all patients between 2006 and 2014 were selected. Neoadjuvant treatment and stage IV disease at initial presentation were exclusion criteria. Clinical and follow-up data about overall survival (OS) and disease-free survival (DFS) were retrieved. Tissue blocks were collected and a central review of histological type and grade was performed.
Results: A total of 601 patients were included. Median follow-up was 60.2 months and median age 56.0 years. Of all patients 18.7% developed a recurrence, after which 78.5% died from metastatic disease. The most common histological subtype was invasive carcinoma of no special type (NST), followed by metaplastic carcinoma and lobular carcinoma. Special histological subtypes were associated with a worse DFS and OS compared to invasive carcinoma NST. In addition, higher tumour stage and not receiving adjuvant therapy were significantly associated with a worse DFS and OS.
Conclusion: In our stage I-III TNBC cohort, almost 1 out of 5 patients developed a recurrence with a subsequent high risk of dying from metastatic disease. Histological subtype was found to be an independent prognosticator for DFS and OS. This enables more personalized treatment and surveillance regimes for the different histological subtypes of TNBC.

E-PS-02-006
Breast leiomyosarcoma after breast reconstruction in a BRCA mutated (high risk) woman
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Background & Objective: Primary breast sarcoma is a rare tumour, accounting for less than 1% of all breast cancer.
Method: Case presentation: A BRCA1 mutated, 49 years-old Caucasian woman, underwent a left breast conservative surgery with SNB + RT, for invasive carcinoma NST. Eight years later, she had a high-grade DCIS recurrence, treated with left mastectomy and SNB. During lipofilling, an ultrasound examination evidenced a round mass with well-defined borders, firstly diagnosed as liponecrosis, that was core needle biopsied with a preliminary diagnosis of sarcoma.
Results: Neoplastic cells were immunopositive for vimentin, α-smooth muscle actin (α-SMA), Caldesmon, Ki-67+(10%). All other markers tested (Pankeratin, S-100, CD34, CD31, c-kit, HHF-35, calretinin) were negative, lending support to the diagnosis of a well-differentiated leiomyosarcoma.
Conclusion: After mastectomy for carcinoma, a mass in the subcutaneous fat may be due to neoplastic or non-neoplastic lesions. Even if the BRCA mutated status fitted more with malignancy, the final diagnosis of sarcoma has been obtained only after biopsy, excluding the differential diagnosis of liponecrosis secondary to lipofilling. Due to the peculiar histotype, we suppose no etiological role of adjuvant RT, and underline the need of a patient tailored diagnostic and therapeutic approach for the occurrence of tumours of unexpected malignant histotypes.

E-PS-02-007
Fluorimetry as a new approach for detection of proliferative activity and hormonal status of breast cancer

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Background & Objective: ICH is mandatory for administration of proper therapy for breast cancer (BC). As alternative the spectral techniques may be applied because of their high sensitivity and selectivity. Objective: to compare fluorescence spectra of hormone-positive and hormone-negative BC with different proliferative activity as a new approach for personalization of patients' treatment.
Method: Unstained histological sections from 30 cases of hormone-negative and 21 samples of hormone-positive BC with different proliferative activity were investigated. Expression of HER-2/neu in all the cases was absent, because presence of this receptors has strong impact in fluorescence spectra. Spectra of fluorescence excitation were measured. Wavelength of registration was 410 nm after its excitation in UV region.
Results: BC is hormone receptor-positive and needs hormonal therapy if at least 1% of its cells have hormonal receptors. The spectra of fluorescence excitation of triple-negative BC have three maxima in regions at 265, 305 and 335 nm which are characterized by present tryptophan-containing peptides collagen and elastin. Hormone-positive BC doesn't have maxima at 340 nm and the ratio intensity between the first two maxima is less then 1,0 as compare to hormone-positive BC. Different proliferative activity causes disproportion between the maxima in region at 265 and 305 nm and their shifting.
Conclusion: The cheap and quick method may be used for preliminary separation of BC samples before further thorough ICH examination.

E-PS-02-008
Primary diffuse large B-cell lymphoma of the breast: report of 8 cases

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Background & Objective: Primary breast lymphoma is a rare disease accounting for 0.4-0.5% of all breast malignancies. 90% are non-Hodgkin B-cell lymphomas and between them diffuse large B-cell lymphoma is the most common one. The clinical presentation of PBLs is usually no different from that of carcinoma. The behaviour of primary lymphoma of the breast is thought to be similar to that of lymphomas of the same histological types and stages arising at other sites.
Method: We discuss 8 patients with primary breast diffuse large B cell lymphoma who were diagnosed in our department in the past 5 years
Results: All of the cases reviewed had the same histopathologic, inmunohistochemical and molecular features that the same lymphoma arising at other sites (diffuse proliferation of large cells with mature B-cell phenotype). In that period of time 11 patients were diagnosed of primary breast lymphoma with an age range of 22-83 years. The results were: diffuse large B-cell lymphoma (8); follicular lymphoma (1); Hodgking lymphoma (1); marginal zone lymphoma (1)
Conclusion: Primary breast lymphoma (PBL) is a clinicopathological entity characterized by the appearance of a unilateral breast mass of months of evolution. The diagnosis, regardless of the clinical data provided by the patient and the exclusion of other entities, is established when a consistent histological pattern is demonstrated. The treatment options vary from surgical intervention to chemotherapy and/or radiotherapy, but mastectomy is not recommended because it offers no benefit as regards survival or recurrence risk.

E-PS-02-009
Hyperspectral optical imaging for intraoperative margin assessment during breast cancer surgery

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Background & Objective: Worldwide, up to 40% of the breast conserving surgeries result in additional operations due to positive resection margins. We propose to reduce this number by using hyperspectral optical imaging for intraoperative resection margin assessment.
Method: With a hyperspectral camera, we measure the optical properties of ex vivo breast tissue as diffuse reflectance spectra. These spectra are annotated with different tissue types, obtained from the pathologist. We included patients diagnosed with IDC, DCIS or both. Because the camera measures in the near-infrared wavelength range, we can measure tissue characteristics that are invisible for the human eye. Specifically, the amount of water, fat and collagen in the tissue can be visualized. Since tumour and healthy tissue are optically different in this wavelength range, we are able to differentiate them. For this, we use machine learning algorithms.
Results: On ex vivo tissue of 18 patients, we obtained > 25.000 spectra of four tissue types: IDC, DCIS, fat and connective tissue (containing glandular tissue). We could discriminate these tissue types with an accuracy of 91%. Furthermore, we could detect IDC and DCIS with a sensitivity and specificity of respectively 88%-98% and 74%-98%. This accuracy increases with the size of the tumour: IDC and DCIS larger than 2x2 mm are classified as malignant tissue in over 93%.
Conclusion: These results show that both IDC and DCIS can be differentiated from healthy tissue. These findings support the use of hyperspectral imaging as resection margin assessment technique intraoperatively, so that incomplete tumour removal can be prevented.

E-PS-02-010
Primary follicular lymphoma in a male breast: a case report with immunochemistry findings

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Background & Objective: Primary lymphoma of the breast is a rare occurrence; because of the paucity of lymphoid tissue in the breast; accounting for 0.04 -0.5 of all malignant tumours of the breast and is an even rarer entity in the male breast. Diffuse large B cell lymphoma is the

most common primary breast lymphoma while follicular lymphoma is less common. Furthermore, primary follicular lymphoma of the male breast is rarely reported. Our aim is to analyze clinical, pathological and immunohistochemical features of this rare entity.
Method: We present a 54-year-old man with no significant history presented a painless mass in the right breast who had multidisciplinary care at Salah Azaiez Institute.
Results: clinical examination objectified a palpable and mobile mass in the right breast and ipsilateral axillary lymphadenopathy. Ultrasound showed nodular gynaecomastia more marked on the right without suspicious lesions. At operation a 4*3*2 cm mass was excised and a frozen section demonstrated malignancy. Histological examination and immunohistochemical staining confronted to clinical findings established the diagnosis of primary follicular lymphoma.
Conclusion: The rarity of the breast primary follicular lymphoma, especially in men, and the problem related to therapeutic choices with these tumours require an early diagnosis based on histology and immunohistochemistry.

E-PS-02-011
The clinical outcomes regarding to tumour-infiltrating lymphocytes in the breast cancer patients treated with neoadjuvant chemotherapy
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Background & Objective: Host immune system is a new research area of breast cancer treatment. Tumour-infiltrating lymphocytes (TILs) as an immunologic marker may influence the patients clinical outcome. The aim of this study was to explore the prognostic and predictive roles of TILs in our breast cancer patients treated with neoadjuvant therapy and to determine its association with other clinicopathological parameters.
Method: Between 2011-2016, 89 patients were included in this study. The patients were categorized according to molecular subtypes as triple negative (TN), HER2 positive and luminal type. All patients' parafin sections were retrospectively evaluated and according to TILs value patients were distributed into two groups in each subtypes. The mean follow-up duration of all patients was 33.8 (15-84) months.
Results: HER2 positive patients had higher TILs value than others. No relationship was seen between TILs levels and presence of either locoregional recurrence or systemic metastasis. Both in survival outcomes and prediction of neoadjuvant therapy response no association was detected according to TILs value within all subtypes.
Conclusion: The relevance of TILs in small patient population is challenge. Although which level of TILs should be used to determine optimal treatment strategy for breast cancer patients has not been certain yet, many trials indicate that TILs of prognostic effect in long-term disease control and predictive effect of a better local response to treatment. But, further resaerchs are warrented before the utility ofTILs as an immune biomarker for routine clinical practise of breast cancer patients.

E-PS-02-013
A case of primary synchronous bilateral breast cancer with heterogenous hormone receptors and HER2 status
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Background & Objective: Incidence of the primary synchronous bilateral breast cancer (PSBBC) is between 0,3% and 12 %. We present a case of PSBBC with heterogeneous hormone receptors and HER2 status.
Method: A 64-y female patient with bilateral breast tumours after positive fine needle biopsy underwent quadrantectomy of the left breast and mastectomy of the right with sentinel lymph node dissection.
Results: Grossly the lesions measured 1 cm in the left and 1,5 cm in the right. Histologically both were invasive ductal carcinomas (G2). The left demonstrated weak (20%) ER/PR and strong (3+) HER 2 expression, while the right was strongly (75%) ER/PR positive and HER 2 negative (0).
Conclusion: PSBBC is rare condition with unclear etiology and uncertain biological behavior. Correct morphological diagnosis and IHC profiles are essential for the optimal treatment.

E-PS-02-014
Global DNA methylation in patients with benign and malignant breast lesions
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Background & Objective: Epigenetic changes in genome are well known to contribute to development of many disease processes. Methylation is the best-studied epigenetic change. In many conditions methylation level is found to be altered not only in affected cell groups, but also throughout other tissues. Based on this DNA methylation in blood is considered an early marker for detecting some disorders including breast cancer. We investigated global DNA methylation in patients with benign and malignant breast lesions and discussed the results in combination with the methylation data from previous studies.
Method: Patients undergoing breast surgery were involved in the study, blood was collected preoperatively. Based on the final pathology report each patient was included into one of the two study groups - benign tumour group or malignant tumour group. Global DNA methylation was studied in blood and tumour tissue using commercially available ELISA-based assay.
Results: Significant global DNA hypomethylation was found in breast cancer tissue compared to blood and tissues of benign breast lesions. Blood samples of patients with malignant tumours showed slightly lower methylation level than samples obtained from benign tumour group members, but this difference was not found to be statistically significant.
Conclusion: We can conclude, that global hypomethylation is a characteristic for tumour tissue. But epigenetic profile of blood DNA is not always representative of the methylation level in the cells of the lesion. Therefore DNA methylation in blood cannot be used as an independent marker for early cancer detection. Neither is it valid for determination of tumour behavior.

E-PS-02-015
A case of metaplastic matrix-producing breast carcinomas
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Background & Objective: Matrix-producing carcinomas (MPC) are an uncommon and specialized subtype of metaplastic breast carcinoma that constitutes less than 1% of all breast carcinomas. They are characterized by direct transition of carcinomatous component to cartilaginous/osseous matrix without an interspersed spindle cell sarcomatoid component.
Method: A 70-year-old female presented with a mass in the right breast. Both physical examination and radiological findings were consistent with malignancy. Core biopsy of the lesion indicated "invasive breast carcinoma," and radical mastectomy with axillary node dissection was performed. Grossly, the tumour was solid, gray-white in color, and 3.3×4.5 cm in size. Its center was looser than the periphery.
Results: Microscopically, the periphery of the tumour consisted of solid sheets of high-grade carcinoma cells. Tumour nests gradually diminished through the central chondromyxoid matrix with nests of ossification. No intervening spindle cell component was present. Immunostaining was negative for estrogen receptor, progesterone receptor, and Her2/neu

(triple negative). Other immunohistochemical staining results were as follow; pancytokeratin and protein S100 were diffuse positive, cytokeratin 5 was focally positive. The Ki-67 proliferation index was 25%. Lymph nodes were negative. The case was diagnosed as breast MPC due to its morphological features.
Conclusion: We report the case of matrix-producing metaplastic breast carcinoma for its rarity and difficulty in its recognition.

E-PS-02-017
Correlation between tumour angiogenesis and grade of breast invasive carcinoma of no special type
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Background & Objective: Activation of angiogenesis is one of the crucial points of tumour invasion and metastasis.
Method: We studied specimens of invasive carcinoma of no special type (IC NST) from 72 patients. Minimal tumour size was 1 cm, maximal – 8 cm with mean size 2,8±2,6 cm. Histological sections were 5-7 mkm thick and were stained with haematocsilin and eosin. For immunohistochemical study were used antibodies to CD44 (manufactured by Dako).
Results: Grade 1 tumours was detected in 16 (22,2%), grade 2 in 16 (22,2%), grade 3 in 40 (55,5%) cases. We found correlation between density of microvasculature and tumour grade. Higher grade correlated with higher microvessel density. At the same time there was no difference in vascularization between G1 and G2 tumours. There was reliable difference in microvasculature density between high and low grade specimens (p=0,019). Grade 1 and grade 3 tumours differed in number of microvessels in greatest degree (p=0,011).
Conclusion: Our study has shown that microvasculature density could be important for prognosis because angiogenesis is linked to ICNST grade and could be considered as additional morphological criterium.

E-PS-02-018
Invasive mucinous adenocarcinoma arising in an intracystic papillary carcinoma
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Background & Objective: Intracystic papillary carcinoma remains an uncommon subtype of breast cancer occurring almost exclusively in elderly females. Despite its excellent prognosis, its metastatic capacity and association with frankly invasive carcinoma has resulted in this lesion being regarded as a tumour in transition from an in-situ to an invasive component. Data on the nature of this lesion remains limited due to the rarity of cases. We report an exceptionally rare histologic variant of intracystic papillary carcinoma, associated with an invasive mucinous carcinoma with similar features.
Method: A 61-year-old female was diagnosed with a right breast lump detected during routine screening. Core biopsy revealed features of an intracystic papillary carcinoma.
Results: Wide local excision was performed and histological examination demonstrated a malignant papillary lesion with associated abundant extracellular mucin. Papillae were lined by uncharacteristically tall neoplastic cells with some features reminiscent of tall cell variant of papillary thyroid carcinoma. Intimately associated with the intracystic component was a focus of invasive mucinous carcinoma with tumour islands maintaining papillary architecture and unusual cytological features.
Conclusion: Intracystic papillary carcinoma remains an incompletely elucidated entity, which despite its excellent prognosis warrants further study to fully understand the true nature of these lesions.

E-PS-02-019
Liquid-based cytology and breast lesions: is there an alternative for traditional smear cytology?
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Background & Objective: Traditional smear cytology is an effective method for diagnostics of breast lesions. But in cases, when ancillary techniques (such as Immunocytochemistry, molecular testing, PCR) are needed, liquid-based cytology looks like the better possible method: good for ancillary techniques and for preserving a sample. Besides, in some cases it helps to obtain more cells from the syringe by washing a needle with the solution from the vial. The aim of our study was to investigate correlations between diagnoses of breast lesions reported by traditional smear cytology with Romanowsky-Giemsa staining and diagnoses reported by CellPrep Plus® (Biodyne) liquid-based cytology technique.
Method: In 2017 in our Centre 267 samples of breast lesions FNA were simultaneously studied by traditional smears (with Romanowsky-Giemsa staining) and by CellPrep Plus® liquid-based cytology (with Papanicolaou staining). In case of malignancy (62) diagnose was always approved by histology. In 52 cases immunocytochemistry with Estrogen, Progesterone, Her2neu and Ki67 markers was performed on the material of liquid-based cytology.
Results: CellPrep Plus® liquid-based cytology method keeps cell morphology and its cytology images resemble the traditional smears, that is good for habituation and training of cytopathologists. Reports coincided in 250 cases (93,6%). Discrepancies laid in the area of benign breast diseases (fibrocystic disease and fibroadenomas) and were due to different amount of cells in the sample. Immunocytochemistry data correlated with the results of Immunohistochemistry (performed on the surgical material) in 98% cases.
Conclusion: CellPrep Plus® data complement and correlate well with traditional smear cytology and gives additional facilities for investigating pathology diversity of breast lesions.

E-PS-02-020
Breast secretory carcinoma and adenoid cystic carcinoma: triple-negatives breast tumours with good prognosis. Presentation of 5 cases
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Background & Objective: Breast secretory carcinoma (SC) and adenoid cystic carcinoma (ACC) are extremely rare subtypes of triple negative invasive carcinoma representing less than 0.15% of all breast cancers. We present 5 cases with favorable prognosis.
Method: CASE 1: 32 years old woman. Total left simple mastectomy. 4 lesions between 0.5 and 2 cm in retroareolar zone and external quadrants. CASE 2: 70 years old woman. Right modified radical mastectomy. 4 cm tumour in the upper external quadrant. CASE 3: 60 years old woman. Lumpectomy from External lower quadrant breast of 7 cm with a cystic area of 4.5 cm. CASE 4: 86 years old woman. Left modified radical mastectomy. Tumour of 35 mm at the junction between the external quadrants. CASE 5: 55 years old woman. Lumpectomy of left breast of 7.8 cm with solid-cystic lesion with papillary areas.
Results: Cases 1-3 were SC. Case 1 was a multifocal type. They shows polygonal cells with eosinophilic or vacuolated cytoplasm and round nuclei, arranged in syncytial microcystic, solid, papillary, or tubular patterns associated with dense eosinophilic secretions. FISH ETV6-NTRK3: translocated in 2. Case 4 and 5 were ACC. They were solid-cystic tumour with proliferation of epithelial and myoepithelial cells arranged in solid or cribriform pattern. they form lights with basophilic material. CK7, P63, myosin and CD117: positive. All tumours were ER, PR and Herb2 Negatives.

Conclusion: SC and ACC , show distinctive histological, immunophenotypic and genomic characteristics with indolent clinical course, and an excellent long-term prognosis, with 5-year survival rates above 85-90 %, even the multicentric SC type, which is an extremely rare diagnosis.

E-PS-02-021

Analysis of the relevance between molecular subtypes and efficacy of neoadjuvant chemotherapy in breast cancer as well as its prognostic factors

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Background & Objective: Accurate pathological assessment of breast specimens after NACT is crucial. It is beneficial to determine the treatment efficacy and predict prognosis.
Method: Medical records of 264 patients with breast cancer who received neoadjuvant chemotherapy our Hospital. The relationship between molecular subtypes and neoadjuvant chemotherapy, and clinical pathological features were analyzed.
Results: The total pCR rate was 12.50% (33/264). The rate of pCR were 3.03% (1/33), 9.40% (14/149), 17.39% (8/46), 27.78% (10/36) in the subtype of Luminal A, Luminal B, HER2, and Basal-like, respectively. Which was predicted that The pCR rate associated with breast cancer molecular subtypes ($P<0.05$). Multiple factors analysis results show that: the independent impact factors of 5-year overall survival rate in neoadjuvant chemotherapy breast cancer patients were clinical stage, tumour size, chemotherapy regimens, lymph node metastasis, estrogen receptor status and pathological remission; the independent impact factors of 5-year disease free survival rate were tumour size, chemotherapy regimens, lymph node metastasis, estrogen receptor status, progesterone receptor status and pathological remission ($P<0.05$). Basal-like subtype breast cancer had shorter overall survival and disease-free survival ($P<0.05$).
Conclusion: The pCR was more frequently observed in HER2 and Basal-like subtypes breast cancer. That could achieve a higher rate of pCR on paclitaxel class joint anthracycline-based chemotherapy. But Basal-like subtype breast cancer were showed worse prognosis, so how to choose a more appropriate neoadjuvant chemotherapy regimens, we should need further research.

E-PS-02-022

Comparative evaluation of breast mammography, sonography, frozen section & permanent results from 2009-2013 in two hospitals

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Background & Objective: Breast cancer is the most cause of death among women in the world. Therefore, this study is done to determine the best and cost-effective method for early detection of breast cancer.
Method: This descriptive, cross-sectional study was undertaken among patients with breast mass during the period of 2008 to 2013. Finally, the histopathological results and outcome of resected breast specimens were analyzed. We reviewed their sonography, mammography, frozen section and surgical pathology results from the patient's hospital folders.
Results: There was 46.5% malignant and 53.5% benign lesions. Reports revealed the most age range was 50-59 years. 97.8% of patients were women and 2.2% were men. 46.8% of patients had mammography that 5.5% were benign and 26.5% were suspicious and 14.9% were malignant. 81.7% of patients had sonography that 43.8 % were benign and 34% were suspicious and 3.9% were malignant. 57.1% of patients had frozen section that 43.9% were malignant and 13.2% were benign. Agreement index for mammography with pathology was 88%, for sonography with pathology was 80%, for frozen section with pathology was 98% for mammography with sonography was 32%, for frozen section with sonography was 10% and for frozen section with mammography was 26%.
Conclusion: The common age range of breast masses were in patients between 50-59 years. The frozen section had the best agreement with pathology than mammography. Sonography with mammography, sonography with frozen section, and mammography with frozen section had not agreed. Keywords: breast, cancer, sonography, mammography, frozen section

E-PS-02-024

Apocrine encapsulated papillary carcinoma of the breast – a rare entity with more malignant potential than previously thought? First report on its association with invasive carcinoma

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Background & Objective: Encapsulated papillary carcinoma (EPC) of the breast with apocrine differentiation is a rare neoplasm with only ten published cases in the literature. While EPC by definition lacks the peripheral myoepithelial layer (MEC), the apocrine EPCs published to date were all clinically indolent, without a conventional invasive component.
Method: A 70-year-old lady was diagnosed with a palpable mass of the right breast. The lesion consisted of a cystic and an adjacent spiculated area indicative of an infiltrative part.
Results: Histologically the cystic component was surrounded by a thick fibrous capsule and filled by an intraluminal papillary-solid proliferation. The ill-defined element represented a no special type infiltrative carcinoma. Both parts showed a cytomorphology fulfilling the definition of apocrine differentiation, without any immunohistochemically detectable MECs.
Conclusion: Our case represents the first reported apocrine EPC with an infiltrative carcinoma component, pointing out the malignant potential of this entity. Although the malignant nature of apocrine EPC was previously questioned by some authors, based on the present case we propose that this entity is most probably only a morphological variant of conventional EPC with the same uncertain malignant potential as in non-apocrine cases.

E-PS-02-025

Diagnosis of invasive papillary carcinoma of the breast in core-needle biopsy: an analysis of 42 cases (2012-2017)

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Background & Objective: Papillary lesions, considered a diverse group of heterogeneus breast lesions, with hyperplastic and neoplastic entities, are defined as proliferative lesions characterized by the presence of fronds or finger-like projections and a fibro-vascular core layered by epithelium. Despite of the facility to identify a breast lesion as papillary, diagnosis of papillary breast lesions, in concrete invasive papillary carcinomas (an uncommon variant of breast carcinoma), especially in core biopsies, is challenging.
Method: Our study is based on an observational retrospective study of patients with diagnosis of papillary carcinoma of the breast in core biopsy at the Universitary Hospital Miguel Servet in Spain, between 2012-2017.
Results: Invasive papillary carcinoma of the breast is an uncommon variant of mammary carcinoma with an infiltrative growth pattern, with neoplastic ductal cells arranged around stromal papillary cores. In our casuistry, we have found 42 patients that were diagnosed of invasive papillary carcinoma of the breast through a core needle biopsy and confirmed after subsequent surgical excision, excluding the possibility of a metastasis.
Conclusion: Papillary lesions of the breast are a heterogeneus wide group of hyperplastic and neoplastic entities. Invasive papillary carcinoma, an unusual variant between them, are reported to be associated with a favorable prognosis.

E-PS-02-026

Pseudoangiomatous stromal hyperplasia of the female breast: a case report

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Background & Objective: Pseudoangiomatous stromal hyperplasia (PASH) is a benign myofibroblastic proliferation of the mammary gland, histologically characterized by interanastomosing slit-like lesions lined by spindle cells. Since its first description in 1986, less than 200 cases have been identified as tumour-forming PASH in the English literature. More frequently it localizes in the upper outer quadrant of the right breast. The aim of this study is to report a case of PASH in the axilla of a 20 year-old Caucasian woman.
Method: The clinical and ultrasound examination of the right axilla of the patient revealed a subcutaneous nodule of 25x5 mm. An excisional biopsy was performed.
Results: Macroscopically, the yellow-whitish nodule had a firm-rubbery consistence. The histological examination revealed spindle stromal cells lining thin empty spaces, without atypias or mitotic figures. There was not involvement of the surrounding adipose tissue. At immunohistochemistry, spindle cells were immunostained with vimentin, smooth muscle actin and CD34. Focal immunoreactivity for estrogen and progesterone receptors was also found, whereas stromal cells were negative for CK AE1/AE3/PCK26, desmin, CD31 and factor VIII. Ki-67 was positive in about 10% of proliferating spindle cells.
Conclusion: Tumour-like PASH in the axilla is a rare event. At the best of our knowledge, in women it has been described in five cases. PASH can mimic benign (fibroadenoma, myofibroblastoma, hamartoma) and malignant (phyllodes tumour, angiosarcoma) lesions. An accurate diagnosis is required in order to avoid overtreatment.

E-PS-02-028

GATA 3 expression in breast carcinoma. Correlation with prognostic factors

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Background & Objective: GATA3 is a member of the GATA family of transcription factors with a key role in cell differentiation, proliferation and movement. In the breast, GATA3 regulates the differentiation of luminal epithelial cells and impedes the transition between epithelial to mesenchymal phenotypes increasing metastatic tumour dissemination affecting the tumour-initiating capacity of luminal progenitor cells. It has also been engaged in a cross regulatory feedback loop with ER. The aim of our study was to correlate the expression of GATA3 with ER and PR status, Her2 amplification and other prognostic factors in breast carcinomas.
Method: We evaluated GATA3 expression in 69 tru-cut biopsies of invasive breast carcinomas (ductal, lobular and specific subtypes). We have also studied the protein's expression in some benign fibroepithelial lesions.
Results: GATA3 immunostaining was strongly correlated with ER expression ($p<0,001$). Weak-spotty labeling or loss of GATA3-expression was observed in ER, PR negative and in grade III neoplasm (for both correlations $p<0,001$). There was no significant association between the molecule' expression and Her2 amplification or Ki-67 expression. GATA3 was also expressed in fibroadenomas' epithelium.
Conclusion: Loss of GATA3 in ER and PR negative and grade III breast carcinomas suggest that this protein is engaged in cell cycle progression of ER-positive cells. GATA-3 loss is associated with the development of a more aggressive tumour phenotype and is a useful marker in the identification of metastatic carcinomas as it is mainly expressed in breast and bladder carcinomas. Its role as a prognostic factor in breast cancer needs to be further elucidated.

E-PS-02-029

A particularly uncommon primary sarcoma of the breast

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Background & Objective: Non-epithelial malignancies of the breast are known to be less than 1% of total breast tumours, the most common being malignant phyllodes tumour. Primary extraskeletal osteosarcomas have been reported throughout the body. Primary osteosarcoma of the breast (POB) represent 12.5% of all breast sarcomas and originates either from normal breast tissue or as metaplastic differentiation. Approximately 150 cases of POB have been reported in the literature since 1957.
Method: A 62-year-old woman presented with a hard, palpable breast mass. There were no pain, nipple discharge, skin involvement or palpable axillary lymph nodes. Ultrasound revealed, in the lower inner quadrant of the right breast, a heterogeneous hypoechoic solid mass measuring 5.5 cm in greatest diameter with calcifications, irregular margins and posterior shadowing. Contralateral breast without suspicious mass or calcifications. Sonographic features were deemed doubtful and biopsy was recommended.
Results: Ultrasound-guided biopsy was performed and microscopy showed a high-grade sarcoma with osseous differentiation. The differential considerations were given as primary breast sarcoma and malignant phyllodes tumour. Simple mastectomy was performed and confirmed the diagnosis of breast osteosarcoma.
Conclusion: POB should be diagnosed only after rule out the presence of an epithelial component. Therefore, it is essential to examine a larger number of tumour tissue blocks. Differential diagnosis involves metaplastic mammary carcinoma, malignant phyllodes tumour and metastatic osteosarcoma. After a pathologic diagnosis of osteosarcoma is made, bone scan should be performed to exclude a primary bone-forming malignancy elsewhere. The lack of bone lesions on whole body bone scan supported the diagnosis of POB.

E-PS-02-030

Modification of biomarkers and phenotype after neoadjuvant treatment in breast carcinoma: a study in a hospital complex

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Background & Objective: The assessment of estrogen receptor (ER), progesterone receptor (PR) or HER2 expression in breast cancer (BC) plays an important role in the choice of the neoadjuvant chemotherapy (NAC). There are no national guidelines regarding whether these biomarkers should be retested in the post-NAC residual tumour, what could be crucial for changes in the adjuvant therapy. The aim was to study the changes in the expression of biomarkers and phenotypes in a group of patients treated with NAC.
Method: We have evaluated the expression of the ER, PR, HER2 and Ki-67 and the phenotype (St Gallen 2013) in a group of 127 BC patients treated with NAC in our Hospital between 2011 and 2017.
Results: 35 (27.6%) of the 127 patients presented pathologic complete response (pCR) (Grade 5 in Miller-Payne). After NAC, 31 (36.5%), 18 (21.2%) and 13 (15.3%) cases were negative for ER, PR and HER2, respectively. There were 2 (2.3%), 6 (7.0%) and 6 (7.0%) tumours with de novo ER, PR and HER2 expression, respectively. These patients with de novo expression could benefit from hormonal and anti-HER2 therapy. 12 (14.3%) and 19 (22.6%) cases acquired a more and a less aggressive phenotype after NAC, respectively.
Conclusion: •We detected changes in the expression of ER, PR or HER2 biomarkers in 38.8%, 28.2% and 22.3% of the cases, respectively. •The phenotype before and after NAC changed in 36.9% of the cases. •9.0% of the patients displayed clinically actionable biomarkers after NAC. These changes suggest that is advisable to retest biomarkers after NAC.

E-PS-02-031

Cytology-biopsy correlation in 121 cases with spontaneous nipple discharge

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Background & Objective: To examine the cytology-biopsy correlation in cases with spontaneous nipple discharge.
Method: Between January 2011 and June 2017, 121 cases with cytological diagnosis for nipple discharge were re-examined, retrospectively. Cases with at least one biopsy proven for diagnosis were determined (n=41).
Results: Fourty-one out of 121 cases (41/121; 33.8%) had cytology and/or biopsy sampling 2 or more times. Twenty-one out of 41 cases were diagnosed cytologically previously as 'ductal ectasia' (21/41; 51.2%) and 8 cases as 'intraductal papilloma' (8/41; 19.5%). Malignancy was detected in biopsy/excision material in 7 cases (7/41; 17%). Two cases were diagnosed as intraductal papilloma with fluoride type hyperplasia without atypia, 1 case as complex sclerosing lesion and 1 case as sclerosing papilloma. The follow-up knowledge of 1 case could not obtained in our hospital database. From the 7 cases diagnosed as malignant in their biopsy/excisional materials, the initial cytological diagnosis was 'ductal ectasia' in 4 cases (4/7; 57.1%), 'papillary lesions / neoplasia' in 2 cases (2/7; 28.5%) and 'malignant cytology' in 1 case (1/7; 14.2%). The ratio for sensitivity was %14.3, the specificity %91.7, positive predictive value %50 and for negative predictive value % 73.
Conclusion: The malignancy could easily missed due to hypocellularity of smears. Moreover, malignant cells could be obscured by benign groups of cells in papillary lesions. The nipple discharge cytology has some limitations in routine pathology practice.

E-PS-02-032

The level of proliferation in cases of breast cancer with high and low maintenance of cancer stem cells

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Background & Objective: The aim of the research was to explore the level of proliferation in groups of breast cancer with high and low maintenance of cancer stem cells.
Method: The material of 110 cases of invasive breast cancer was explored. The immunohistochemical method was applied. The presence of ALDH1A1 protein was studied with use of Rabbit Monoclonal Anti-Human ALDH1A1 (EP168) antibodies (Epitomics, USA) for detection of cancer stem cells in tumour population. The level of ALDH1A1 expression was evaluated according to number of stained cancer cells: 3+ (the number of stained cells is ≥50%), 2+ (the number of stained cells is >10% but <50%), 1+ (the number of stained cells is ≤10%). For detection of level of proliferation expression of Ki-67 protein was explored with use of Rabbit Anti-KI-67 SP6 antibodies (Spring, USA).
Results: All the cases were divided into groups with low (0 and 1+) and high (2+ and 3+) level of ALDH1A1 expression – 97 and 13 cases respectively. The mean level of proliferation of all the cases was 39.3±2.4%. The level of proliferation in the group with low maintenance of cancer stem cells was 37.4±3.0%, in the group with high maintenance of cancer stem cells - 49,6±4,5%. The weak positive correlation (r=0,19) was found between ALDH1A1 and Ki-67 expression.
Conclusion: Cases of breast cancer with high maintenance of cancer stem cells have a higher proliferative activity in comparison with similar cases with low maintenance of cancer stem cells.

E-PS-02-033

Matrix producing breast carcinoma. Report of a case

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Background & Objective: Matrix-producing carcinoma (MPC) of the breast is a rare variant of metaplastic breast carcinoma (MBC) with 250 cases in the English literature. We present a case of MPC.
Method: A 65-year-old female patient with no previous history was admitted to the surgery department due to a palpable mass of the upper-outer quadrant of the left breast. Digital mammography revealed a BIRADS 5 lesion with a maximum diameter of 23mm. Frozen section was positive while sentinel lymph node biopsy was negative for malignancy. A mastectomy was performed.
Results: On gross examination the tumour was relatively well circumscribed, solid, and gray-white in color. On microscopic examination the tumour consisted of a solid areas, nests, cords as well as isolated single cells embedded in an extracellular myxoid matrix. Tumour cells were monotonous, had enlarged nuclei with distinct nucleoli. Focal areas of necrosis were present. An intervening spindle cell component, angiolymphatic invasion or peripheral lymphocytic infiltration were not identified. Immunostaining was negative for Her-2, estrogen and progesterone receptors, CK-5/6, P-63 and S-100. The Ki-67 proliferation index stained 60% of tumour nuclei. The final diagnosis was neoplasm consistent with matrix-producing carcinoma of the breast. The patient received adjuvant treatment and is alive without evidence of recurrence or distant metastasis 14 months after surgery.
Conclusion: MPC is a sub-variant of MBC having better 5year survival rate than other MBC, therefore deserves a separate position in tumour classification.

E-PS-02-035

Correlation between immunohistochemical findings and CISH evaluation in breast carcinomas' specimens

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Background & Objective: HER-2 oncogene is amplified in about 25% of breast carcinomas and has a prognostic and predictive role in breast cancer. HER-2 protein's overexpression which is also correlated with resistance to many chemotherapeutic agents, can be detected by immunohistochemistry while the gene amplification is evaluated using In Situ Hybridisation. The purpose of the present study was to correlate the results of immunohistochemistry and Chromogen In Situ Hybridisation (CISH) in breast cancer specimens
Method: 294 breast cancer specimens from our laboratory archives, were evaluated, in which both immunohistochemistry as well as CISH had been implemented. The results of both methods were correlated with each other.
Results: 50 of the 294 cases were positive for HER-2 gene amplification (17%). Of these, 45 (90%) had a 2+ score in immunohistochemistry while 5 (10%) had score1+. We also noticed that 3 specimens with 3+ score in immunohistochemistry gave a negative gene amplification result in CISH
Conclusion: Our findings indicate that CISH evaluation is necessary in indefinite results of immunohistochemistry. Moreover, women with advanced disease should have a further confirmation of HER-2 gene status in order to have the benefits of targeted therapy.

E-PS-02-036

E-cadherin (Clone 36) nuclear staining associates with adverse prognostic features in lobular breast carcinoma

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Background & Objective: E-Cadherin loss is a hallmark of lobular breast cancer (LBC). Primarily membraneous, E-Cadherin may be cleaved and translocate to the nucleus, affecting transcription and progression in various tumours. We compared immunostaining patterns among E-Cadherin clones, P-Cadherin and clinical outcome.
Method: Retrospective consecutive cohort of LBC (n=301, 1996-2011, female, HER2 negative) primarily treated with surgery. Immunohistochemistry for E-Cadherin (Clones 36 [Ventana], EP700Y [Ventana] and NCH38 [Dako]) and P-Cadherin (Clone 56C1 [Leica]) was performed on formalin-fixed paraffin-embedded tissue. Percentage of positive cells (membrane/perinuclear/nuclear) was assessed. Statistical associations were assessed by Chi-square test.
Results: Majority of tumours were grade 2 (78.3%), pT2 (42%) and pN0 (52.5%). 20.6% patients suffered distant events. Nuclear Clone36 immunoexpression was depicted in 107 (36%) tumours (over 30% of tumour cells in 47 cases). Nuclear staining with Clone EP700Y and NCH38 was only present in 3 and 9 cases respectively (<1% of tumour cells). P-Cadherin showed membrane, perinuclear and nuclear immunoexpression in 78, 145, and 1 case, respectively. There was an association between Clone36 nuclear staining and tumour grade, pT stage and distant events (p=0.017, p=0.003, p=0.011). 75% of grade 3 tumours showed Clone36 nuclear staining, whereas 77% of pT1 tumours and 69% of patients with no distant events showed negative Clone36 nuclear staining. No association was observed with hormonal status or pN stage.
Conclusion: E-Cadherin immunoexpression features varies according to antibody. Distinct nuclear staining of LBC with E-Cadherin Clone 36 associated with features of adverse outcome.

E-PS-02-037
Neuroendocrine breast carcinoma with apocrine phenotype: a case report
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Background & Objective: Primary neuroendocrine carcinomas of the breast are rare, with incidence under %0.1 from all breast carcinomas and under %1 from all neuroendocrine carcinomas. It has been demonstrated that about %50 of moderately and well-differentiated neuroendocrine breast carcinomas coexpressed the apocrine markers. We present a patient with well-differentiated neuroendocrine breast carcinoma with apocrine phenotype.
Method: The surgical specimens were formalin-fixed and parafin embedded. The sections were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 70-year-old female presented with a breast mass that had been growing for the last 6 months. Ultrasonographic examination revealed a nodular lesion approximately 22x16 mm in size in the left breast on the upper external quadrant. BI-RADS score was 4. Routine microscopic examination demonstrated that large cells with round nucleus and eosinophilic granular cytoplasm. The neoplastic cells were arranged in a nesting and trabecular pattern. Immunohistochemical study showed neuroendocrine markers (synaptophysin andchromogranin) were positive for all tumour cells and apocrine markers (GCDPF-15 and AR) were positive for more than 50% of tumour cells. Histopathological and immunhistochemical results were compatible well-differentiated neuroendocrine breast carsinoma with apocrine phenotype.
Conclusion: This case report is a rare and good example of multidirectional differentiation of breast tumours. These cells with coexist apocrine and neuroendocrine differentiation may support tumour is originated from a single stem cell with multidirectional differentiation.

E-PS-02-038
Pleomorphic adenoma of the breast
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Background & Objective: Pleomorphic adenoma (PA) of the breast is a rare tumour with mixed epithelial and myoepithelial cell differentiation. The nature and biology of similar tumours seen in the breast remains to be defined. Here in, we report a case of pleomorphic adenoma of the breast which was preoperatively thought to represent a fibroadenoma on clinical and radiological grounds.
Method: A 58-year-old postmenopausal woman presented with a non-tender, mobile, palpable lump, localised upper-outer quadrant in the left breast. Radiologically, a 2 cm, lobulated, hypoechoic solid mass with partially ill-defined borders was seen. Lesion was excized by surgeon sent to pathology labratory.
Results: We evaluated proliferating groups of epithelial cells in a hyalinised, partly myxochondroid matrix in histologic sections. The epithelial component was distributed as single cells, cordons, glandular/ductal structures. The inner cells of glandular foci showed eosinophilic cytoplasm with cuboidal or polygonal shape and small-medium sized ovoid nuclei. The outer layer was flattened, similar to a myoepithelial cell. Glandular structures including inner and/or outer layers of cells showed diffuse positive staining for cytokeratin 7, S-100 and vimentin while no immunostaining for smooth muscle actin (SMA), p63 was noted. There were no positivity for oestrogen and progesterone receptors. Ki-67 proliferation index was low (<5%).
Conclusion: These tumours share similar features with the salivary gland counterparts. The majority of mammary PAs have a benign behaviour, but local recurrence and development of carcinoma occur. Pathologists should keep these tumours with mixed epithelial and myoepithelial cell differentiation, such as pleomorphic adenoma, adenomyoepithelioma and adenoid cystic carcinoma in mind whenever a tumour with prominent myxochondroid appearance is encountered.

E-PS-02-039
Adenoid cystic carcinoma of the breast as unexpected find: case report and literature review
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Background & Objective: Adenoid cystic carcinoma (ACC) of the breast constitutes approximately 0.1% of all breast tumours. It is characterized by rare lymph node involvement and distant metastasis, and associated with a favorable prognosis with excellent survival, despite its triple-negative status.
Method: We describe the clinicopathological details of one case and review the frequency of these primary tumours in breast and its diagnostic and therapeutic implications.
Results: A 50 -year-old female patient presented a palpable mass in her left breast. Ultrasonography revealed a hypoechoic mass of 23 mm with ill-defined contours. Mammography revealed a 3 cm in diameter mass in the intersection of upper quadrants of the left breast, which was classified as BIRADS 5 (Breast Imaging Reporting and Data System). A core biopsy was performed and histologically showed a dual-cell population of luminal and myoepithelial-basal cells arranged in tubular and cribriform patterns consistent with an ACC. The patient underwent breast conserving surgery (BCS) and sentinel lymph node biopsy (SLNB) with uninvolved margins and a final stage classification of pT2N0. The patient received radiotherapy in the postoperative period and after one year there is no evidence of relapse.

Conclusion: ACC of the breast have very favorable biologic characteristics and, consistent with this, an excellent prognosis. SLNB can be used since axillary metastases are rare. Local recurrence and distant metastases are also very rare. Usually, BCS followed by radiotherapy is adequate to obtain local control. In selected patients with a poor prognosis, chemotherapy should be added to the treatment.

E-PS-02-040

Fixation conditions of mastectomy specimens: experience from a single institution

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Background & Objective: To ensure the preservation of specimens and the quality of pathology exam, the American Society of Clinical Oncologists (ASCO), and the College of American Pathologists (CAP) have established guidelines for breast specimens. The aim of this study was to assess fixation conditions of mastectomy specimens received in a department of pathology in Tunisia.
Method: Thirty-six mastectomy specimens were received in our department between January 2016 and December 2017 from 2 hospitals where departments of pathology were unavailable. Retrospectively, the date of intervention and date of reception in our department have been identified in specimen requisition. They were sent fixed in neutral-buffered formalin (10% vol/formalin in water; pH 7.4). The specimens weren't incised before their reception in our department. The time tissue removed in not mentioned in the specimen requisition.
Results: The mean delay of fixation was 3 days (0 to 5 days). In 2016, the mean delay fixation of the 14 mastectomy specimens was 3 days (6 to 1 day). In 2017 this delay was in mean 2 days (6 to 0 day). The time when the specimens were placed in formalin was never recorded on the requisition form. In one case the date of intervention was not recorded.
Conclusion: The mean delay of reception of mastectomy specimens in our department was between 2016 and 2017 of 3 days. This delayed formalin fixation would have a negative effect on morphological examination and immunohistochemical staining. Pathologists and surgeons have to work together to ensure a correct fixation of mastectomy specimens according to ASCO and CAP guidelines for an accurate assessment of diagnosis and prognostic factors.

E-PS-02-041

Influence of genetic polymorphism on circulating vitamin D level in patients with breast benign tumour

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Background & Objective: Circulating 25-hydroxy-vitamin (VD) deficiency may play a certain role in breast cancer. Several GWAS indicates that certain genes polymorphism (such as VDR, CYP2R1, GC, etc.) may influence VD level in healthy individuals. However, there is no evidence between VD level and its deficiency in breast benign tumour (BBT). The aim of this study was to determine the influence of genetic polymorphism on vitamin D level in BBT patients.
Method: SNP genotyping (rs2228570, rs2060793 and rs2282679 for VDR, CYP2R1 and GC genes respectively) performed in 247 DNA samples extracted from venous blood of unrelated women (mean age 36.14±0.91) with BBT (N=116) and control (N=131) by real-time PCR using TaqMan probes. VD level was determined by ELISA. Statistical analysis done with packet program SPSS Statistics v20.
Results: The VD level (ng/ml) was significantly lower in BBT women comparing to a healthy donors (20.6±0.71 and 29.8 ±0.97 respectively). Alleles and genotypes distribution for all studied SNPs were in accordance with HWE (p>0,05). In BBT we detected prevalence of TT genotype carriers of VDR gene polymorphism in women with deficiency of VD (<20 ng/μl) and no other associations were described. However, genotype CC carriers of CYP2R1 loci in BBT women but not in control group characterized by significantly lower VD level compared to other genotype (p=0,0276).
Conclusion: Our study confirmed that gene polymorphism can influence the vitamin D level and can serve as a marker to vitamin D insufficiency.

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E-PS-02-042

Features of tumoural and non-tumoural areas in invasive breast carcinomas including PASH (pseudoangiomatous stromal hyperplasia) areas within the tumour

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Background & Objective: To describe the features of tumoural and non-tumoural areas in invasive breast carcinomas including PASH areas.
Method: The HE stained sections of 200 consecutive surgical excision materials with invasive breast carcinoma were re-evaluated, retrospectively. PASH areas both in invasive tumour and non-tumoural areas were noted.
Results: PASH foci within invasive breast carcinoma were observed in 22 (%11) of 200 cases. Of these 22 cases, 1 was tubular, 2 was classic type lobular, 2 were mixed type (micropapillary + ductal), 17 were IDC, NOS. The extensivity of PASH areas in invasive tumour was ≥%50 of the tumour in 4 cases, %10-50 in 11, and %10 in 7. According to ER/PR/HER2 status of 19 cases, tumours showed molecular subtypes as; ER+/HER2-: 13, ER+/HER2 +: 5, ER-/HER2+: 0, ER-/HER2-: 1 In non-tumoural areas, PASH foci were detected in 4 cases (%18). Columnar cell changes were detected in 9 cases (%40), which were with atypia in 2 (%9) and no atypia in 7 cases (%31). The information of axillary lymph node metastasis were available for 21 patients and detected in 11 out of 21 cases (%52)
Conclusion: In surgical excision materials, PASH areas within invasive breast carcinoma were not uncommon. These tumours show mostly luminal phenotype. PASH and columnar cell changes were also accompanying in non-tumoural areas of these cases.

E-PS-02-043

Unusual metastatic pattern of lobular carcinoma: series of cases and review of the molecular basis of disease

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Background & Objective: Lobular carcinoma (LC) of the breast constitutes a threat, as it can remain silent for many years. We present a series of cases in which a correct diagnosis is imperative, as it would determine the correct management.
Method: In the first case, a cervical cytology was obtained from a 60-year-old woman, who presented with genital bleeding. Morphologically, uniform, round, monotonous cells arranged in single line were observed. After a thorough search, history of invasive LC 13 years ago was found. The second one consists of an endometrium biopsy from a woman on tamoxifen treatment. Microscopically, a highly dense area composed of diffuse signet ring cells was observed, the latter being suggestive of metastatic LC by immunohistochemistry. The last one, who had no history of interest, presented with peritoneal metastases of unknown origin with architectural and cytological features similar to the cases above. Therefore, a large immunohistochemical panel was performed and it proved to be a metastatic LC.
Results: In LC and low-grade breast disease there is loss of membranous expression of E-Cadherin due to inactivation of CDH1 gene at 16q22. This alteration decreases cellular adhesion, induces aberrant alternations of E-cadherin-associated signalling pathways involved in cell proliferation and favours epithelial-mesenchymal transition process.

Conclusion: LC exhibits a distinctive and different metastatic pattern compared to Ductal Carcinoma, being gastrointestinal, gynaecologic and peritoneum-retroperitoneum metastases markedly more prevalent in lobular carcinoma. This is why we consider being alert very important when facing with these specimens, even if the patient has been disease-free for several years.

E-PS-02-044

Adenomyoepithelioma of the breast: a tricky lesion in core needle biopsy

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Background & Objective: Breast adenomyoepithelioma is a rare epithelial-myoepithelial tumour of the breast. Malignant changes can occur in one or both cellular components. We present a series of adenomyoepitheliomas diagnosed in our institution between the years 2007 to 2017.
Method:
Results: Seven adenomyoepitheliomas were retrieved from the files of our Department and reviewed by a breast pathology consultant. The age range was 36–77 years old. On core needle biopsy, the cases were classified as: benign (n=3), of uncertain malignant potential (n=3) and malignant (n=1). In one case, previously classified by core needle biopsy as adenomyoepithelioma of uncertain malignant potential, the histopathological examination of the surgical specimen showed an intermediate-grade DCIS. In the malignant case both cellular components were malignant and the epithelial component displayed the features of low grade adenosquamous carcinoma. None of the cases recurred or metastasized during follow-up.
Conclusion: Breast adenomyoepithelioma is a rare neoplasia with unclear and unpredictable propensity for malignant transformation. It can constitute a diagnostic challenge in core needle biopsy.

E-PS-02-045

Correlation of mammaglobin and hormone receptors expression in a cohort of patients with primary breast carcinoma

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Background & Objective: Previous studies stated mammaglobin (Mmg) as a useful marker for peripheral metastases. Some primary breast carcinomas might be Mmg negative or possess cellular lines that no longer express it. This study evaluates Mmg, steroid hormone receptors and HER2 expression in primary breast cancer (BC) and the impact on patients` outcomes.
Method: We designed a cohort of 63 patients with similar background, who underwent surgery for operable, unilateral primary breast tumour. Previous diagnosis of carcinoma, distant metastases and neoadjuvant therapy were exclusion criteria.
Results: Significant correlation was found between high levels of Mmg and ER+, PR+, HER2 negative tumours (p=0,01); there was an inversely proportional association between Ki67 and Mmg levels - low Ki67 expression, Mmg+ tumours (71%) vs. high Ki67 levels, Mmg+ tumours (20%) - (p=0,025); no associations were found between Mmg expression and breast tumour grade.
Conclusion: High Mmg levels are associated with a favorable prognosis when assessed in primary breast tumours by being strongly related to steroid hormone receptors positivity and HER2 negative tumours as well as low Ki67 levels, so Mmg should be reported and taken into consideration when evaluating treatment responsiveness.

E-PS-02-046

Large cell neuroendocrine carcinoma of the breast showing triple negative, basal-like subtype

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Background & Objective: This is the first report describing a triple-negative neuroendocrine mammary neoplasm (large cell neuroendocrine carcinoma, LCNEC) with basal cell-like features.
Method: A mass in the outer portion of the right breast was detected by ultrasound examination in a 53-year-old postmenopausal Japanese woman.
Results: The mastectomy specimen contained an irregularly-shaped, grey-whitish tumour, measuring 10x8mm, histopathologically composed of medullary growth of polygonal or, occasionally, spindle-shaped cancer cells possessing fine-granular cytoplasm and large nuclei with granular chromatin and prominent nucleoli. Mitotic figures were numerous (108 per 10 high-power fields), with atypical mitoses. Macrometastases were identified in 5 of 8 dissected ipsilateral axillary lymph nodes. Immunohistochemical examinations revealed the cancer cells to be positive for synaptophysin, CD56 (NCAM), cytokeratin 5/6, CK7, CK14, c-kit and mammaglobin. Estrogen receptor (ER), progesterone receptor (PgR), HER1 and HER2 status were negative, and the Ki67 (MIB-1) labeling index was 75.2%.
Conclusion: Although, in the breast oncology field, the outcomes of NEC, mostly expressing ER and/or PgR, remain controversial, our present case with a primitive LCNEC developed multiple lymphogenic metastases (pN2) with extra-nodal invasion, even though the invasive foci were relatively small (pT1b) with tumour-infiltrating lymphocytes.

E-PS-02-047

Small-cell carcinoma of the breast with squamous differentiation

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Background & Objective: Small cell carcinoma of the breast is a rare neuroendocrine subtype, occasionally showing aggressive clinical behavior. Herein, we report an exceptionally rare small cell mammary carcinoma showing squamous differentiation.
Method: The patient, a 58-year-old postmenopausal woman, presented with a palpable mass in the right breast. Systemic CT detected no other suspicious lesions.
Results: The cut surface of the mastectomy specimen contained a lobulated gray-whitish tumour, measuring 45x40x40mm. Histologically, this invasive tumour was composed of solid and/or trabecular growths of densely-packed, small- to medium-sized cancer cells. Necrosis and hemorrhage were present. Cancer cells were polygonal or spindle-shaped, with scant cytoplasm and ovoid nuclei with fine-granular chromatin. Squamous differentiation, i.e. nest formation of polygonal cancer cells having abundant, eosinophilic cytoplasm and intercellular bridging with keratin pearls, was found. Mitotic figures were numerous. RT-PCR analysis revealed mRNA amplification of chromogranin A. The patient postoperatively received doxorubicin (60mg/m2) and cyclophosphamide (600mg/m2) every 4 weeks for 4 cycles as adjuvant chemotherapy.
Conclusion: Interestingly, our patient with a breast cancer showing both small cell and metaplastic features remains alive and well with neither recurrence nor metastasis 49 months after surgery (Histopathology, 2013 & 2015).

E-PS-02-048

Well-differentiated neuroendocrine tumour of the breast showing peculiar endovascular spread

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Background & Objective: Herein, we describe the first case of a mammary cancer [well-differentiated neuroendocrine tumour (NET)] with extensive intravenous spread.
Method: The patient, a 42-year-old premenopausal Thai woman, presented with a palpable mass in the subareolar portion of the left breast. Ultrasonography revealed a sharply marginated, hypoechoic left breast tumour showing heterogeneous internal echoes, with a cranially extending lumen-like structure filled with solid tumour with similar echoic findings. On MRI, these lesions appeared as an oval-shaped mass and a continuous intravenous occupying lesion, respectively, both of which were strongly enhanced during the early phases of the dynamic study. These images suggested an invasive cancer with a tumour thrombus.
Results: The cut surface of the lumpectomy specimen contained well-circumscribed, solid tumour nodules, measuring up to 17x15mm. Histologically, the tumour was composed of a medullary invasive growth of carcinoma cells with fine-granular cytoplasm and highly vascular stroma. Immunohistochemical examinations revealed carcinoma cells to be positive for chromogranin A and synaptophysin. Massive tumour embolization within prominently dilated veins, spreading from the primary focus, was confirmed by EVG and CD31. She has remained alive with multiple bone and liver metastases (36 and 47 months after surgery) and a marked chemotherapeutic effect for 87 months, to date, since surgery.
Conclusion: Our patient, who had a relatively small, well-differentiated NET with no nodal involvement and a low MIB-1 index (6.7%), followed a rather aggressive clinical course with distant metastases, probably related to the extraordinary tumour embolization in the breast (Histopathology, 2014).

E-PS-02-049

Can neoadjuvant chemotherapy change clinic pathological and survival parameters in HER-2 positive breast cancer patients?

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Background & Objective: HER-2 positive breast tumours are a group of invasive carcinomas with aggressive clinical behavior. The early set for metastasis is one of the factors that contribute to worse prognosis. The purpose of this study was to review if neoadjuvant treatment could change clinic pathological and survival parameters in a set of HER 2+, ER and PR(-) breast cancer(BC) cases
Method: We assessed retrospectively all HER2+ BCr, medical records (n=132) submitted to surgery and trastuzumab post-surgery, at IBCC (Intitute), from 2007 to 2013 with stages I-III, and divided into 2 groups: -1: treated with neoadjuvantand -2: without. Reports were compiled to retrieve tumour stage and LN status; and recurrence, death of disease and morbidity. IH for ER/PR and Ki-67. For statistical analysis, we used chi-square and student's t-test.
Results: The group 1 (n=54) of patients treated with neoadjuvant chemotherapy to the addition of trastuzumab was associated with reduced risk of recurrence (P=0.002), smaller primary tumour (T) (P=0.032) and reduced rate of death (P=0.022) and morbidity (46%); KI-67 rates (15% cut-off) were not statistically associated to treatment regimen; while group 2 (n=78) exhibited the highest morbidity (71%). Hormone receptors and Ki-67 expressions were not associated to neoadjuvant therapy in this subset of patients.
Conclusion: In conclusion, pour preliminary results confirm that neoadjuvant chemotherapy can change pathological and prognostic variables when used along with trastuzumab regimen The potential better prognosis must be considered as an opportunity to investigate new strategies for HER2-positive treatment.

E-PS-02-050

Dermatofibrosarcoma protuberans of the breast: a rare case

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Background & Objective: Dermatofibrosarcoma protuberans (DFSP) is a low-grade sarcoma of fibroblastic origin. It is usually localised on the trunk We, herein, represent a rare case with breast involvement.
Method: A forty-six-year old female patient was admitted to our hospital's general surgery department because of a solid, slow growing mass on her right breast. The physical examination revealed that the mass was fixed.
Results: An excisional biopsy of skin with underlying breast tissue specimen 5x3x3 cm in dimensions was evaluated. The microscopic examination revealed a diffuse infiltration of densely packed, cytologically bland and uniform spindle-shaped cells wich were positive for CD34, and negative for PANCK, estrogen, SMA, desmin and S-100 and the Ki67 proliferation index was <5%.
Conclusion: The differential diagnosis of spindle cell tumours of the breast is very important. Metaplastic carcinoma and sarcomatoid overgrowth of phyllodes tumour should always be considered as the main differential diagnosis of spindle cell proliferations of the breast. The lack of epithelial diffentiation eliminated spindle cell carcinoma and low Ki67 index exclude the sarcomatoid component of phyllodes tumour.

E-PS-02-052

Immunohistochemical evaluation of the expression of MAGE-C2 protein in breast cancer

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Background & Objective: Melanoma-associated-antigen-C2 protein belongs to the MAGE-C gene family and is included in the Cancer-Testis genes. It is not expressed in normal tissues, however, MAGE-C2's expression can be found positive in malignant tumours. Considering all of the above, as well as the fact that breast cancer is the main cause of women's death, we aimed to study the immunohistochemical expression of MAGE-C2 in breast cancer tissues and correlate it to clinicohistopathological parameters.
Method: During our experiments we used a sample pool of 29 human breast cancer specimens of different subtypes. Out of the 29 patients, 27 were females and 2 males. In these tissues, we conducted indirect immunohistochemistry, using the anti-MAGE-C2 antibody and then evaluated its expression to clinicohistopathological parameters.
Results: Our results showed that the mean age of patients was 59.2 years. Also, 27 of the specimens were of cancer grade 2/3. As far as the cancer type is concerned the sample pool consisted of 21 ductal carcinomas, 2 lobular, 2 in situ and 3 of other types. Out of the parameters measured, tumour grade and type showed statistically significant correlation with the expression of MAGE-C2 protein.
Conclusion: We concluded that MAGE-C2 may represent another efficient prognostic marker for breast cancer and can potentially be used as a possible therapeutic target. Due to the limited number of cases further studies on larger series are needed to confirm the present data.

E-PS-02-053

Primary breast, non-other-specified type, sarcoma with CD10 expression: a rare entity with features of myoepithelial differentiation

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Background & Objective: Sarcomas of the breast are a rare group of heterogeneous mesenchymal tumours accounting for less than 1% of all breast malignancies. The non-other specified (NOS) type sarcomas do not fit into any specific soft tissue sarcoma category and the immunophenotype of CD10 expression suggests that these neoplasms represent a sarcoma variant with myoepithelial features, which are extremely rare.
Method: We present the case of a 83-year –old woman who presented to our hospital due to a palpable tumour mass on her left breast, with subsequent inflammatory skin reaction, of 2 months duration and rapid growth. Mammography revealed a 7cm solid tumour and partial mastectomy was performed. Histological examination revealed a highly cellular spindle cell tumour with extensive necrosis. Mitotic count was 4/10hpf. On immunohistochemical examination there was a vimentin and CD10 positivity with partial SMA positivity, whereas desmin, calponin, pancytokeratin, CD34, caldesmon, ER/PR, p63 and high-molecular-weight cytokeratin were negative. Proliferation index ki-67/MIB-1 was 15%.
Results: Accordingly, the diagnosis of spindle cell sarcoma NOS with features of myoepithelial differentiation was favored. Staging imaging examinations with CT-scan were negative for metastatic disease. The patient received adjuvant chemotherapy and radiotherapy and six months later is on regular follow-up.
Conclusion: In conclusion, we present a very rare case of primary breast NOS-type sarcoma with features of myoepithelial differentiation. Histopathothological analysis along with an immunohistochemical panel are valuable in differential diagnosis from other breast tumours, including specific types of breast sarcomas, sarcomatoid carcinomas, metaplastic carcinoma. In these cases, early diagnosis and treatment are crucial for long-term survival.

E-PS-02-054

Breast cancer in men - about a series of 25 cases

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Background & Objective: Breast cancer in mens is a rare condition that accounts for 1% of breast cancers and less than 1% of cancers occurring in men. The etiology remains unknown given the rarity of this pathology.
Method: We report a retrospective study of 25 cases of breast cancer in men collected at the department of pathological anatomy and cytology of the CHU of Sidi Bel Abbes between 2005 and 2014.
Results: the mean age of our series is 52.5 years with extremes ranging from 30 years to 75 years and more than 32% of patients were 70 years old, the most common histological type was non-specific invasive carcinoma formerly infiltrating ductal carcinoma found in 76% of cases versus 12% of cases of invasive lobular carcinoma. The histological grade SBR was GIII in 20% of cases, GII in 72% of cases and GI in 08% of cases. An average of 3.33 cm for tumour size, the histopathological diagnosis was confirmed on total mastectomy piece in 52% and 48% on micro and macro biopsy. The immunohistochemical study was performed in 80% of cases, the hormone receptors were positive in 80% of cases and the overexpression of Her2 was found in 30% of cases.
Conclusion: Breast cancer in mens is a serious pathology and diagnosis is made at a later age than in women and at a later stage.

E-PS-02-055

Evaluation of HER2/neu status by immunohistochemistry and correlation with gene amplification by fluorescence in situ hybridisation assay in rare breast carcinoma case

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Background & Objective: Assessment of hormone receptor status and HER2/neu protein overexpression or amplification status is standard of care practice for the pathologic evaluation of breast carcinoma specimens. Traditionally, assessment of HER2/neu status has been performed by either immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH).
Method: A 43-year-old female patient was suspected of breast mass formation in a mammographic and magnetic resonance examination. After the diagnosis of carcinoma given biopsy, simple mastectomy was performed on the patient. invasive ductal carcinoma with apocrine differentiation was diagnosed as a result in our pathology laboratory. The majority of HER2 testing is performed using a combination of IHC screening followed by FISH.
Results: Immunohistochemical studies and fish studies for her2/neu gene were performed in areas of invasive ductal carsinoma with apocrine differentiation and pure invasive ductal carcinoma. According to the ASCO / CAP breast guide, her2 immunohistochemical study was scored as 3+ in area of apocrin diferantiation. Her2/neu amplification of this area was not detected in the FISH study In area of pure invasive ductal carsinoma her 2 immunohistochemical study was negative and non-amplified in the FISH study.
Conclusion: Correlation between immunohistochemical techniques and FISH is known to be imperfect. In our case, the first case of discordance between her2 FISH and immunohistochemical studies in invasive ductal carcinomas showing apocrine differentiation. As a result, both immunohistochemical and FISH studies should be performed for all areas in different morphological appearance to evaluate each amplification in breast carcinoma cases.

E-PS-02-056

Pleomorphic lobular carcinoma in situ: an unusual clinical and morphological variant

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Background & Objective: Recently, lobular carcinoma in situ (LCIS) has been segregated into 3 morphologically distinct variants (classic, pleomorphic and florid) which share some characteristics but vary in others. Pleomorphic LCIS (PLCIS) is an unusual variant of LCIS that exhibits histologic and molecular features analogous to those of ductal carcinoma in situ (DCIS).
Method: We present a case of a 75 years old-woman, who presented with an indurated mass in the right breast. Ecographically, there was a suspicious glandular hypoecoic area BIRADS-4. A core needle biopsy was performed, which showed an apocrine-type CIS.
Results: The patient was treated with ipsilateral mastectomy, which revealed a 55 mm mass showing lobular and ductal expansion by loosely cohesive cells, with eosinophilic cytoplasm, enlarged nuclei and prominent nucleoli. Necrosis and calcifications were frequent. After a careful study, invasive component was absent and margins free of disease.
Conclusion: Although the incidence of PLCIS is estimated to be between 2.7 and 4.4 % of all lobular neoplasias, the prevalence may be higher given the similarities of PLCIS to DCIS and probable misdiagnoses as such. Nowadays, LCIS has been established only as a risk factor for breast cancer. Therefore, surgical treatment is not necessary. Even though there is a lack of consensus, it has been suggested PLCIS treatment should

mirror that of DCIS rather than classic LCIS, as the risk of concurrent invasive or higher-grade disease in these cases has been estimated to be up to 65%. Nevertheless, further studies are needed to provide more information to establish evidence-based standard guidelines.

E-PS-02-057

Neuroendocrine tumour of the breast showing carcinomatous lymphangiosis

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Background & Objective: Herein, we describe, to our knowledge, the first case of a neuroendocrine (NE) neoplasm with extraordinary intralymphatic embolization in the breast.

Method: The patient, a 46-year-old premenopausal Japanese woman, presented with a mildly painful palpable mass in the upper outer quadrant of the left breast. Ultrasonography revealed an irregularly-shaped (geographic), hypoechoic left breast area and enlarged regional lymph nodes.

Results: The cut surface of the mastectomy specimen contained an ill-defined, grey-whitish solid tumour, measuring 23x22 mm. Histologically, the tumour was composed of a solid and/or trabecular invasive growth of carcinoma cells with highly vascular fibrovascular stroma. Polygonal carcinoma cells had finely granular cytoplasm and oval or irregularly-shaped nuclei with fine-granular chromatins and occasional conspicuous nucleoli. Immunohistochemical examinations revealed carcinoma cells to be consistently positive for synaptophysin and focally reactive for chromogranin A. Marked lymphatic permeation as well as vascular infiltration, confirmed by D2-40 and/or CD31 staining, were detected. Metastases were identified in 9 of 17 excised left axillary nodes, with extra-nodal invasion. The patient remains alive and well with neither recurrence nor metastasis, 3 months after surgery, receiving adjuvant chemotherapy.

Conclusion: Although it had long been considered that neuroendocrine mammary carcinomas show a less aggressive clinical behavior compared with unselected breast cancers, our present case had an unusual feature of lymphangitic carcinomatosis closely associated with nodal involvement as well as poor recurrence-free and overall survivals (Pathol Int, 2016).

E-PS-02-058

ER-/PR+ subset of invasive breast carcinoma (IBC): a distinct phenotype with good prognosis

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Background & Objective: The expression of the estrogen (ER) and progesterone (PR) receptors in IBC patients represents a well know prognostic and predictive factor. The existence of ER-/PR+ as a distinct phenotype however is controversial as well as its prognostic significance. The aim of the study was to assess the incidence and prognosis among patients with ER-/PR+ IBC.

Method: 112 patients with IBC were analyzed regarding ER/PR profile and survival. GraphPad prism 6 for Windows and Kaplan Mayer curve were used to determine overall survival (OS) and disease-free survival (DFS), with $p<0.05$ as statistically significant.

Results: Out of 112 IBC patients, 75% were ER+/PR-, 16.07% were ER-/PR-, 7.14% were ER+/PR- and only were 1.78% ER-/PR+. OS was 100% in ER-/PR+ group and 91.6% in the ER+/PR+ group. The lowest OS was found in the ER-/PR- group (72.2%). Regarding the DFS there was no statistically significant differences between the four groups ($p=0.11$), although the highest DFS was found in the ER-/PR+ group (100%) followed by ER+/PR+ group (83.3%), where local recurrences were found in 5.95% of cases, and 9.52% of these cases had distant metastasis. The lowest DFS rate was found in the ER+/PR- cases (50%).

Conclusion: Our results suggest that ER-/PR+ cases represent the rarest phenotype among IBC cases but its association with the best OS and DFS among other ER/PR phenotypes indicates an independent predictive value of PR for treatment considerations.

E-PS-02-059

Solid variant adenoid cystic carcinoma of the breast

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Background & Objective: The incidence of adenoid cystic carcinoma is less than 0.1% among all breast cancers. It is a low-grade tumour with histological features similar to adenoid cystic carcinoma of salivary glands.

Method: A 77-years old woman presented with mass lesion in breast over 2 months. On sonography, a hypoechogenic mass lesion (24 mm in diameter) with ill-defined margins was detected. The patient underwent fine-needle biopsy and the mass lesion was diagnosed as malignant tumour. Patient underwent breast-sparing mastectomy and sentinel lymph node biopsy.

Results: On histopathologic evaluation, tumour cells showed scanty cytoplasm with large nucleus and marked nucleolus, forming solid nests. Differential diagnosis should include collagenous spherulosis, invasive cribrifom carcinoma, small cell carcinoma and solid papillary carcinoma. On immunohistochemical analysis, diffuse CD117 expression was observed but no ER, PR and HER2 expression. The CK14 and p63 expression was observed around lumen. Mucin was detected within lumens of focal cribriform areas by Alcian Blue. Histomorphologic and immunohistochemical findings were suggestive for solid variant of adenoid cystic carcinoma.

Conclusion: Adenoid cystic carcinoma of breast is a slow growing tumour with rare metastasis. Although salivary gland tumour with solid growth pattern have poorer prognosis, this issue is controversial in breast.

E-PS-02-060

Breast carcinoma with choriocarcinomatous features: a case report and review of the literature

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Background & Objective: Breast carcinoma with choriocarcinomatous features (BCCF) is an exceptionally rare variant of breast cancer, characterized by evidence of choriocarcinomatous differentiation who express a human chorionic gonadotropin (HCG). Through our observation and literature we will illustrate the pathologicals characteristic of this tumour.

Method: A 76 years old women presented to the doctor with a well-defined lump in the super-inner quadrant of the right breast. Any family history of breast malignancies was denied. Mammography and echography was suggestive of malignancy. Fine needle aspiration biopsy was performed and showed diagnosis of invasive carcinoma was made. Mastectomy and axillary lymph node dissection was performed.

Results: Breast tissue specimen measuring 27 × 18 × 4 cm, partially covered with skin measuring 24 × 16 cm. The cut surface revealed a tumour mass measuring 4 cm in greatest diameter. The tumour tissue was of gray-white and hemorrhagic. Histopathologically, the tumour revealed an Invasive carcinoma of no special type with areas of choriocarcinomatous features with giant cells and intense atypia, that are positive for HCG in Immunohistochemical investigation. Histology examination of lymph nodes revealed 3 of 30 nodes positive for metastatic adenocarcinoma. A definitive histological exanimated was an Invasive carcinoma of no special type (NST) with choriocarcinomatous features. The tumour cells were negative for receptor of oestrogen and progesterone and Her2.

Conclusion: The optimal strategy of management of this tumour is the same of invasive carcinoma of NST. The prognosis is largely unknown, due to rarity of these neoplasms.

E-PS-02-062

Changes in the ER, PgR, Her-2 and Ki-67 biological markers between preoperative core needle biopsy and surgical excision specimen: A comparative study

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Background & Objective: The evaluation of estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor-2 (Her-2) and Ki67 status before surgical treatment is crucial when primary systemic therapy is a therapeutic option. The purpose of this study is to compare the results of core biopsy hormone receptor expression, and Her-2 status and also histologic type, histologic grade with those of excision specimens of patients.
Method: Data have been collected from 140 patients from Istanbul Medipol University Hospital, between January 2014 and August 2017. The conformity between molecular subtype classification was tested using kappa (k) test.
Results: Mean age was 50.99 years (range 26-86). There was concordance between the ER assessment on CNB and SS in 134 cases (95.7%). Concordance of the PgR assessment was observed in 128 cases (91.7%). Concordance of the Her-2 status was observed in 132 cases (94.3%). Concerning Ki-67 evaluation, we report a concordance rate of 93.6% (k=0.46). We found 88% concordance for histologic type, and 91.4% for histologic grade.
Conclusion: Our results demonstrated that CNB showed good accuracy preoperative diagnosis and management of the breast cancer treatment.

E-PS-02-063

Clinical impact of AJCC 8th edition on cancer prognostication in a tertiary hospital

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Background & Objective: The American Joint Commission on Cancer eight edition (AJCC 8th) introduced the prognostic staging for breast cancer for more accurate stratification of disease-specific survival compared to anatomic stage. A total of 123 consecutive Filipino patients with invasive breast carcinoma, in a tertiary care hospital, were analaysed for anatomic and prognostic stages, according to the AJCC 8th.
Method: A total of 123 consecutive Filipino patients with invasive breast carcinoma, in a tertiary care hospital, were analaysed for anatomic and prognostic stages, according to the AJCC 8th.
Results: According to anatomic stage, 28 (22%) cases were stage IA, 1 (0.01%) stage IB, 35 (28%) stage IIA, 23 (18.7%) stage IIB, 24 (19.5%) stage IIIA, 6 (4.9%) stage IIIB and 6 (4.9%) stage IIIC. A total of 88 (72%) patients' prognostic stages changed and compared with anatomic stage. Prognostic staging upstaged 32.14%, 40%, 30.43%, 20.83% and 50% of stages IA, IIA, IIB, IIIA and IIIB, respectively; and downstaged 45.7%, 69.6%, 52%, 16.7% and 16.7 of stages IIA, IIB, IIIA, IIIB and IIIC, respectively. The distribution of patients among prognostic groups was significantly different among the luminal and HER2 enriched subtypes of breast cancer (p=0.03)
Conclusion: Compared with the AJCC anatomic stages, the AJCC prognostic staging system upstaged 31 % of patients and downstaged 41% in our Filipino patient cohort. This pilot study warrants further validation in relation to disease-specific survival in a larger Filipino cohort.

E-PS-02-064

A logistic regression nomogram to predict axillary lymph node metastasis in early invasive breast cancer patients

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Background & Objective: The goal of this study is to develop an efficient model to identify the factors that might help in predicting the status of the axillary lymph nodes (ALN) before sentinel lymph node biopsy (SLNB) in early breast cancer patients.
Method: This cross-sectional study was performed between2015and2017in Mashhad University Hospital, Iran. All female patients with early invasive breast cancer (T1-3and N0-1), having positive axillary ultrasound findings, undergoing a successful SLNB were included. Age at diagnosis, menopausal status, tumour size, tumour location, histological type, ultrasonographic findings, status of estrogen receptor (ER), progesterone receptor (PR), HER2 and Ki-67 were recorded. Logistic regression was performed using SPSS.
Results: From171patients,136were randomly selected for the modeling group (82had ALN positive disease), while another 35 were assigned to the validation group. In the univariate analysis, factors that were significantly associated with ALN metastasis included ER (P=0.022), PR (P=0.004) and Ki-67 (P=0.015) positivity, absence of hilum (P<0.001), higher maximum cortical thickness (P<0.001) and maximum transverse diameter (P<0.001). To avoid omitting significant indicators, factors with P<0.25in univariate analysis were included in the multivariate analysis and predictive model. The model $(p/1-p)=-9.376-0.34\times a-0.88\times b+1.26\times c+0.76\times d+0.44\times e$, was generated (p=the probability of ALN metastasis;a=age at diagnosis>35years, b=post-menopausal status, c=absence of hilum, d=maximum cortical thickness of ALN as detected by ultrasound in mm and e=maximum transverse diameter) and showed good performance for evaluation of ALN metastasis in the validation group with an AUC of0.963. A cut-off value of7.75mm was found for cortical thickness in predicating ALN metastasis.
Conclusion: The predictive model presented here relies on readily available factors, indicating that it can be used to select patients who were more likely to have positive ALNs. However, this model should be applied prospectively to a large number of patients to verify its validity.

E-PS-02-065

Osseous metaplasia of breast: the experience of a hospital center

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Background & Objective: Osseous metaplasia is characterized by the presence of heterotopic bone tissue, which can occur in any soft tissue. Its appearance in the breast is rare and may be associated with benign or malignant neoplasms or less commonly, with no other associated breast pathology. The aim of this study was to understand the frequency of this entity and its association with other pathologies in our Hospital.
Method: Report the cases of breast osseous metaplasia in our Hospital in the last 19 years.
Results: Four cases were retrieved from our files. Two of them diagnosed on core needle biopsy, both with no other associated lesion. The other two cases, diagnosed on mastectomy specimen, were associated with carcinoma (Ductal carcinoma in situ/ invasive).
Conclusion: Osseous metaplasia has commonly been described in association with benign and malignant breast lesions. It is very rare to occur in the absence of any other breast pathology. To the best of our knowledge, we are describing the third and fourth case presented in the literature. The rare occurrence of osseous metaplasia alone should take us to search malignant features namely the presence of spindle cells in order to exclude the diagnosis of metaplastic breast carcinoma.

E-PS-02-066

The clinicopathologic features of primary invasive papillary carcinoma of the breast, single center experience

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Background & Objective: Invasive papillary carcinoma (IPC) of the breast is an uncommon histologic subtype with limited data in the literature. We aimed to present clinicopathological findings of IPC in our series.
Method: Between the years 2010 and 2018, we re-evaluated the HE sections of surgical excision specimens in patients with IPC, retrospectively.
Results: IPC were detected in 23 cases, of which 4 (17%) was in pure form and 19 (83%) in mixed histologic type. The other histologic types accompanying to IPC were IDC, NOS (19/19), micropapillary (4/19) and pleomorphic type lobular carcinoma (1/19). The ages ranged from 36 to 89 (median 58) and the tumour sizes from 8 to 70 mm (mean 22 mm). T stages were as; pT1: 13, pT2: 8, pT3: 0, pT4: 2. Lymphovascular invasion was noted in 9 cases (39%), perineural invasion in 2 (9%) and Ductal Carcinoma In Situ (DCIS) in 20 (87%). The DCIS patterns noted in decreasing order; cribriform (13/20), micropapillary (10/20), solid (8/20), papillary (7/20) and flat type (3/20). Comedonecrosis was seen in 17 of 20 cases (85%). Tumour associated microcalcification was seen in 10/23. Axillary lymph node status were as follows: pNx: 1, pN0: 11, pN1: 7, pN2: 2, pN3: 2. According to the values of ER, PR, HER-2 and Ki-67 index available for 22 cases, Luminal B phenotype determined in 15 (68%), Triple Negative in 6 (27%) and Luminal A in 1 case (5%).
Conclusion: IPC was determined mostly as an accompanying carcinoma to IDC, NOS and showed Luminal B molecular phenotype.

E-PS-02-068

Expression of Stathmin and tumour cell proliferation in association with the BRCA1 genotype and a basal-like phenotype in breast cancer

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Background & Objective: Previous studies have indicated that Stathmin expression is associated with PI3K activation in breast cancer, indicating that Stathmin staining might serve as a marker for stratification of patients for anti-PI3K therapy. Here, we studied Stathmin protein expression in breast cancer, with emphasis on associations with a basal-like phenotype (ER-, Her2-, CK5+), the triple negative category (ER-, PR-, Her2-), and a BRCA1-genotype. These tumours are associated with a poor prognosis and lack targeted therapies.
Method: The study included primary breast cancers from two independent patient cohorts (n=190/n=202). Immunohistochemical staining was performed on TMA slides, and evaluated using a semi-quantitative and subjective grading system. A staining index ≥ 6 was considered positive.
Results: Stathmin expression was associated with high histologic grade, tumour diameter, tumour cell proliferation (by Ki67 expression), p53 status and CK5 positivity (P≤0.036). Further, Stathmin predicted a basal-like profile, the triple-negative subgroup, and the BRCA1 genotype (OR≥ 4.0, P≤ 0.013). In a multiple logistic regression model, only p53 and Ki67 significantly predicted a basal-like phenotype, whereas no additional information was given by Stathmin. In contrast, Stathmin expression independently predicted the BRCA1 genotype (OR=4.6, 95% CI 1.0-21.7, p=0.024).
Conclusion: Our findings indicate that Stathmin expression is associated with proliferation (Ki67) and the BRCA1 genotype, rather than being an independent marker of a basal-like phenotype.

E-PS-02-069

Hypoxia up-regulates ID proteins in Luminal and HER2-positive breast cancer cell lines

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Background & Objective: Inhibitors of DNA binding (ID) proteins are a family of four transcriptional regulators involved in embryogenesis, stem cell homeostasis and tumour angiogenesis, an essential process for malignant growth and metastasis. Our aim was to assess if hypoxia induces the expression of ID proteins and activates the mechanisms of neoangiogenesis in breast cancer (BC) cell lines
Method: We included normal mammary epithelium (184A1) and BC cell lines of Luminal (MCF-7 and T47-D), HER2+ (SKBR3) and Triple Negative/Basal-like (MDA-MB231) phenotypes. Control cells were grown at 37ºC in 5% CO2 and 18% O2 atmosphere. For hypoxia, cells were at 37ºC, 5% CO2 and 5% O2 during 24h. We extracted and measured mRNA expression of ID1-4 and VEGF by qRT-PCR using TaqMan® assays. PUM1 and β-actin were the reference genes. Relative changes in gene expression were calculated as the fold change by the 2–Ct method. All experiments were done in duplicates.
Results: Overexpression, defined as increased levels of >150% compared to control, was seen for ID1 in T47-D (>300%) and slightly in MCF-7 (138%); for ID2 in MCF-7 (155%) and SKBR3 (157%); ID3 in T47-D (>300%), but ID4 was low and only in 184A1 (130%). VEGF was variably increased in all BC cell lines
Conclusion: Our results showed that under hypoxia, BC cell lines of the Luminal subtype overexpressed ID1, ID2 and ID3. Moreover, in HER+ only ID2 was up-regulated, as well as VEGF, supporting the role of IDs in angiogenesis.

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E-PS-03 | Cardiovascular Pathology

E-PS-03-001

Obesity paradox: if there genetics involved? Microarray study in morbidly obese decedent patients with severe and minimal atherosclerosis of the aorta

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Background & Objective: Atherosclerosis of the aorta is one of the major causes of death. We recently reported that there is a significant inverse correlation between body mass index (BMI) and atherosclerosis of the aortas of morbidly obese decedent patients with BMI >40 kg/m2. This obesity paradox was unexpected and the pathogenesis of these differences is still not known.
Method: Microarrays were performed on six aortas obtained from morbidly obese decedents. GeneChip® WT PICO Reagent Kit was used to generate ss-cDNA from the RNA. GeneChips Clariom D Human array chips were used. Data files were generated and processed with Transcriptome Analysis Console Software v. 3.0.
Results: Group 1 included three patients with moderate to severe atherosclerosis and Group 2 comprised three patients with mild atherosclerosis in the aorta. The patients in Groups 1 and 2 were matched by age and BMI. The microarray data showed significant (p<0.005) differential expression (>2 folds) of 1067 genes when compared between Groups 1 and 2, including 602 upregulated and 465 downregulated genes. Among those genes, there were 102 upregulated and 70 downregulated mRNAs, 11

upregulated and 10 downregulated small RNA genes, and 6 upregulated and 14 downregulated micro-RNA precursor genes.
Conclusion: Our data shows significantly differential gene signatures between morbidly obese decedent patients who have mild or severe atherosclerosis in the aorta. Further studies are needed to analyze protein expression in the aorta and detailed analysis, but these preliminary findings indicate role of aberrant gene regulation in the obesity paradox. Understanding the pathogenesis of obesity paradox may help in better understanding of the atherosclerosis in general and find therapies for this deadly disease.

E-PS-03-003
Infracentimetric capillary hemangioma of the artery. Report of 3 cases
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Background & Objective: Hemangiomas (HA) located in the arterial wall are rarely reported. We aimed to report 3 cases of capillary hemangiomas (HA) of the arterial wall.
Method: The lesions were detected incidentally at microscopy examination of cholecystectomy (2) and anal resection (1) specimens for cholecystitis and for anal squamous cell carcinoma recurrence after radiochemotherapy.
Results: The age ranged between 32 and 75 years, the gender ratio was 1:2 for women:men. The 3 HA were of capillary type, infra-millimetric, unique on the analysed specimens. Both gallbladder HA involved the arterial muscle layer (the internal elastic lamina/IEL being focally interrupted) as well as the adventitia for one of them. The colon HA was located in the intima (without IEL lesion). Perls-positive macrophages were detected only for the colon HA. The endothelial lining was normal in all 3 arteries.
Conclusion: In conclusion we report 3 cases of hemangiomas located in the arterial wall (gallbladder adventitia and mesocolon). This lesion-type, possibly an incipient stage to development of large, clinically relevant hemangiomas, should be acknowledged since possibly altering the vessel wall dynamics.

E-PS-03-005
Morphological features of peripheral thrombi in pulmonary embolism
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Background & Objective: Thromboembolism of the pulmonary artery is one of the most frequent unrecognizable causes of death in hospitalized patients. Almost 70% of cases the correct diagnosis is not established. Without treatment, mortality in PE is about 30%, due to recurrent thromboembolism.
Method: Histological slides obtained from autopsy material in the aspect of comparative morphology of blood clots in the veins of the lower limbs and thromboembols in various manifestations of pathology were examinated. Computer morphometric methods are applied.
Results: For the period from 2013 to 2017 1562 autopsies were performed, of which 112 cases were recorded as PE (7.2%) in middle-aged men (mean age 58 years) and women (mean age 70 years) in the elderly according to the WHO classification. Thrombi of the veins of the lower limbs at different stages of formation (fibrinous, with predominance of erythrocytes, with an admixture of leukocytes, organized with a different amount of collagen fibers, connective tissue cells, vessels, petrified, sometimes with crumbling lumps of lime, leading to foreign bodies embolus), as well as pulmonary thromboembols arteries and its branches.
Conclusion: Some features of the morphology of thrombi and thromboembolism, depending on gender and age of the patient, concomitant pathology have been identified.

E-PS-03-006
Primary cardiac lymphoma in immunocompetent patient: a case report
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Background & Objective: Primary cardiac lymphoma (PCL) represents an extremely rare entity of extranodal lymphomas with only 90 cases reported in literature. Frequently it is observed in immunodeficient persons. Nonspecific symptoms can delay the diagnosis and management with fatal end of the disease. We describe the clinical and pathological features of an autopsy case of an immunocompetent woman.
Method: A 72-year old woman is admitted to the emergency department for dyspnea, orthopnea, palpitations and syncope. CT scan revealed an intracardiac mass in the right atrium. Shortly after a biopsy of the mass was performed, the patient developed multi-organic failure that, despite the therapeutic measures dies. Necropsy study is requested.
Results: In the necropsy study, a right intraauricular polipoid mass of 4 x 3 cm was identified that infiltrate the interatrial septum, inferior vena cava and pericardium. Pleural effusion was present and lungs macroscopically without alterations. Histologically, the intracardiac mass corresponds to a large cell lymphoid proliferation, positive by immunohistochemistry for CD20, BCL2, BCL6, C-MYC (20%) and MUM1. Negative for CD10, CD23, CD30 and EBV. These findings were consistent with diffuse large cell lymphoma B type not germinal center. There was no evidence of disseminated disease.
Conclusion: Most PCL are of B-cell lineage, and they usually present as diffuse large B-cell lymphoma. PCL must be distinguished from secondary cardiac involvement of disseminated lymphomas. Polipoid morphology suggested a benign tumour in the differential diagnosis, nevertheless pathological study is mandatory to define prognosis of the disease. Most PCL affect right cardiac chambers and pericardium with high mortality.

E-PS-03-007
Wünderlich syndrome by iliac vein rupture, secondary to deep vein thrombosis
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Background & Objective: Wünderlich syndrome, or spontaneous retroperitoneal haematoma, secondary to spontaneous rupture of the iliac vein is an infrequent clinical entity and a medical emergency. It often occurs in middle-aged women. Habitually the etiology is difficult to identify and different hypotheses have been suggested, such as the presence of hormonal, inflammatory and/or mechanical factors. The association with the deep vein thrombosis has been described as an etiological factor.
Method: We present a case of a 46-year-old woman that admission in our hospital (HUMV), with lumbar pain and syncope. The exploration and the analytics, indicated the presence of a hypovolemic shock. In CT evidenced a voluminous retroperitoneal haematoma from de hypocondrium to the iliac fossa, and a thickening of the left iliac vein. The situation of shock progress, and finally the patient died. Autopsy study was requested.
Results: In the autopsy, the macroscopic study indentified the presence of a thrombus attached to the wall of the left iliac vein and dissection of the left iliac vein, confirmed by histological study. We evidenced the presence of rupture and infiltration of the wall by red blood cells using EVG histochemistry.
Conclusion: It is recommended to exclude Wünderlich syndrome in middle-aged women with clinical and analytical manifestations of hypovolemic shock. It may be important to evaluate the presence of a factor that triggered the deep vein thrombosis and secondary rupture of the iliac

vein and retroperitoneal haematoma. The literature shows better results with a conservative treatment versus a surgical alternative

E-PS-03-008

Papillary fibroelastoma of the aortic valve. A rare case report

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Background & Objective: Papillary fibroelastoma is a rare primary tumour of cardiac origin accounting for approximately 10% of all primary cardiac neoplasms.
Method: Here, we report our treatment of an aortic valve papillary fibroelastoma that was discovered incidentally, during routine intraoperative TEE, in a patient 36-year old woman. Due to a high thromboembolic risk, surgical excision is the mainstay of treatment in these patients and median sternotomy the most widely used approach.
Results: Macroscopically, the tumour (gr.dim.:1,2 cm) characterised by multiple frond-like fibrous projections creating a 'sea anemone' appearance when immersed in saline. Histologically, the tumour is comprised of an avascular fibroelastic core, made up of a hyalinised collagen matrix with a rim of smooth muscle cells and elastic fibres, lined by endocardial endothelium. Immunohistochemical characteristics include positive staining for factor VIII-related antigen, CD34 and Vimentin confirming a vascular endothelial cell lining, and multilayered type IV collagen elastic proliferation deep to the surface membrane.
Conclusion: The aetiology of PFE remains largely unknown. Recent hypotheses include fibroblast infiltration with organisation of mural thrombi, viral induced tumour growth, and an endothelial response to cardiac surgery, mechanical trauma or thoracic radiation. Historically, PFE has also been described as both a true neoplasm and a hamartomatous lesion, whereas some authors have suggested they are merely an overgrowth of Lambl's excrescences.

E-PS-03-009

Combined forms of amyloidosis (clinical and morphological observation)

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Background & Objective: In recent years, many views have significantly changed about amyloidosis. The aim of our study was to determine the clinical and morphological characteristics of combined forms of amyloidosis in patients with chronic heart failure (CHF).
Method: The material for the study was the myocardium obtained at autopsy of 89 years man, suffering from arterial hypertension and generalized atherosclerosis with the development of biventricular heart failure. A histological study was carried out with staining: haematoxylin and eosin, Congo-red with an estimate in a polarizing microscope, as well as immunohistochemical study was conducted with confocal laser microscopy using antibodies to Amyloid A (AA); Amyloid-P; IgG Lambda Light Chain (ATTR); Anti-Prealbumin.
Results: With a macroscopic assessment of heart its weight was 480.0 g, the thickness of the left ventricle wall was 1.6 cm, the right ventricle - 0.4 cm, and the heart index 0.008. The cavities of the heart are enlarged. Myocardium has a dense consistence of dark red color with diffuse interlayers of whitish dense tissue. Microscopically, amyloid is detected in the wall of coronary and intramyocardial vessels and also around vessels of different calibers and between thinned and overgrown cardiomyocytes. Immunohistochemical study revealed colocalization of AA and ATTR both in focal amyloid deposits located between cardiomyocytes and around intramyocardial vessels of different calibers. AA or ATTR was also determined in the wall of arterial vessels and cardiomyocytes.
Conclusion: In this observation, changes in the heart and vessels proceeded under the guise of HIHD. Amyloidosis has been revealed morphologically and the protein precursors were AA and ATTR without clinical and morphological features of the heart.

E-PS-04 | Cytopathology

E-PS-04-001

Diagnosis of atypical glandular epithelium in cervix cytology

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Background & Objective: Cervical cancer is the third most common type of cancer amongst women worldwide. Human Papilloma Virus (HPV) causes about 99% of the cases of cervical cancer. It is very important to discover and treat premalignant cell changes for prevent the development of cervical cancer and this is the main goal of the Norwegian national screening program.
Method: This report assessing cytology diagnosis Atypical Glandular cells of Undetermined Significance (AGUS) and Adenocarcinoma in Situ (ACIS) from 2011 to 2016 diagnosed at the Department of Pathology, Nordland Hospital (NLSH) and correlating it with subsequent histology. It was investigated 235 cases (214 AGUS and 21 ACIS). All the cases were studied and correlation of the results from cytology and histology was done. Positive predictive value (PPV) for both AGUS and ACIS were calculated based on histology-results.
Results: Benign histological findings that could explain the AGUS diagnosis include reactive and metaplastic glandular cells. Mild dysplasia (CIN1) were included in the category of benign diagnosis. Premalignant diagnosis includes high grade squamous dysplasia (CIN2/3) and ACIS. Malignant diagnosis includes adenocarcinoma and squamous cell carcinoma. 52% of all the cases had normal/benign histology, 43% had premalignant and 5% had malignant histology. 31% of AGUS cases with a premalignant diagnosis had high grade dysplasia in squamous epithelium (CIN2/3) histologically. PPV were calculated to be 42% for AGUS diagnosis and 100% for ACIS diagnosis.
Conclusion: AGUS diagnosis has a relative low PPV compared to ACIS. PPV of both entities is relatively high in NLSH.

E-PS-04-002

Cytological diagnosis of a solid-pseudopapillary tumour of the pancreas: a case report

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Background & Objective: Endoscopic ultrasound-guided fine-needle aspiration has become an essential pre-operative method to make accurate diagnosis of cystic and solid pancreatic lesions.
Method: We report here a case of a solid-pseudopapillary tumour of the pancreas, diagnosed by a fine-needle aspiration in a 70 years old female patient. She was a former smoker and had a history of invasive lobular carcinoma of the breast. A Positron Emission Tomography, performed to assess her breast cancer stage showed a hypermetabolic lesion of the pancreatic tail. Endoscopic ultrasound found a complex and multilocular cystic lesion with no evidence of connection to pancreatic ducts. Clinical context and radiological aspect were in favor of a cystic neuroendocrine lesion or a metastatic lesion of her breast carcinoma.
Results: Microscopically, fine-needle aspiration was very cellular and showed numerous papillary structures. They were characterized by a delicate fibrovascular core surrounded by a layer of monomorphic cells with round to oval nuclei, finely granular chromatin and small nucleoli. Many single cells with a similar aspect were also scattered in the background. Immunohistochemical study was performed on the cell block and showed positive staining for CD56, vimentin, CD10 and focally

synaptophysin. There was a cytoplasmic and nuclear staining for beta-catenin antibody. No immunoreactivity was observed for cytokeratin 19, 7 and 20, chromogranin, p53, mesothelin, Bcl10 and GATA3.
Conclusion: To conclude, cytological and immunochemistry studies allowed us to make the diagnosis of a solid-pseudopapillary tumour of the pancreas. We were able to eliminate a metastatic lesion of her breast carcinoma or other pancreatic cystic lesions.

E-PS-04-003
Cytological diagnosis of rare pancreatic involvement by multiple myeloma
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Background & Objective: Extramedullary plasmacytomas account for 5% of all plasma cell neoplasms. They are related to underlying multiple myeloma, a disease with peak incidence in the 6th and 7th decades of life. It results in anemia, hypercalcemia and lytic lesions on radiography. The most frequent sites of extramedullary plasmacytomas are the nasal fossae and other parts of the upper respiratory tract.
Method: We present a 44 years-old man with multiple myeloma, recently diagnosed, and multiple lytic bone lesions. Evaluation through endoscopic retrograde colangiopancreatography revealed three pancreatic nodules: hipoecogenic, heterogeneous and ill defined, dispersed in head and tail, with 25mm, 15mm and 27mm.
Results: Cytological smear was very celular, with amorphous background and sparse volumous cells of large cytoplasm and eccentric hyperchromatic nuclei. Cytoblock allowed immuno-histochemistry study and this cells were positive for CD138 and negative for LCA, CD56, synaptophysin and chromogranin.
Conclusion: Citopathological diagnosis was secondary localization of multiple myeloma. Although the majority of extramedullary plasmacytomas involve the upper respiratory tract, ten percent occur in the gastrointestinal tract, primarily the liver, spleen, or stomach. Most cases of pancreatic plasmacytoma had a history of multiple myeloma or related disease, suggesting that pancreatic involvement is a rare event at the time of diagnosis of myeloma. It is difficult to diagnose a pancreatic tumour without a history of such diseases due to the lack of typical features of pancreatic plasmacytoma on imagiology.

E-PS-04-004
Lymph node metastasis of the amphicrine variant of medullary thyroid carcinoma – a potential diagnostic pitfall
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Background & Objective: In medullary thyroid carcinoma, lymph node metastases are already present at diagnosis in 40-50% of cases. The amphicrine variant of medullary thyroid carcinoma is rare and metastasis can mimic adenocarcinoma.
Method: Case Report A 58-year-old man presented with right cervical lymphadenopathy, Cushing's syndrome (cortisol: 430μg/l) and extreme calcitonin levels (1821ng/l). Ultrasound-guided fine needle aspiration was performed. The smears were Papanicolaou stained.
Results: Cytology showed single cells and clusters of atypical epithelioid cells with enlarged, excentric located nuclei and granular chromatin. The cytoplasm displayed mucinous vacuoles. Immunocytochemistry revealed a positivity for calcitonin and synaptophysin. TTF-1 and PAX8 showed positive nuclear staining. Despite the unusual conventional cytology with vacuolated mucinous cytoplasm, the findings were consistent with a lymph node metastasis of medullary thyroid carcinoma. The patient underwent surgery with total thyroidectomy and bilateral lymphadenectomy. Histology confirmed the diagnosis of a multifocal amphicrine variant medullary thyroid carcinoma in the right thyroid lobe (max. diameter: 12mm) with angio- and perineural invasion, bilateral lymph node metastasis in nine of twenty lymph nodes, and focally positive margins. The primary tumour displayed areas of spindle cells, glandular formations, desmoplastic stroma and regressive calcifications. The prominent vacuolation with aspects of signet ring cells was highlighted in the lymph node metastasis. The patient sadly passed away three months after the operation, due to recurrent and insuppressible Cushing's syndrome, complicated by multiple nosocomial infections
Conclusion: Metastases of medullary thyroid cancer can be challenging in unusual morphologic variants. Metastasis of the amphicrine variant of medullary thyroid cancer is a potential diagnostic pitfall mimicking adenocarcinoma, especially when the clinical history including calcitonin levels is unknown.

E-PS-04-006
Endometrial adenocarcinoma: an accurate diagnosis is possible on routine liquid based cervical cytology
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Background & Objective: The detection of endometrial adenocarcinoma in a cervical sample is usually an incidental finding. The differential diagnosis includes other extra-uterine abnormalities like ovarian adenocarcinoma and metastatic tumours as breast carcinoma or gastric cancer. However, the cells of endometrial adenocarcinoma display some characteristic features that may allow an accurate diagnosis.
Method: Case Report A 77-year-old woman presented with postmenopausal bleeding in absence of any other specific symptoms. A cervical sample was taken and liquid-based cytology (Sure Path®) was performed (Papanicolaou staining).
Results: Cytology revealed small three-dimensional clusters of atypical cells. The enlarged and polymorphic nuclei had a coarse chromatin and were mostly situated at the outside margins in a berry cluster like architecture. The scant cytoplasm showed focal vacuolation and indigested polymorph neutrophils. Very few papilliform clusters were present. Due to the limited number of cells, the final diagnosis was based solely on cytomorphology without ancillary immunocytochemistry. The case was signed out as adenocarcinoma, consistent with endometrial adenocarcinoma. Consequently, an endometrial biopsy was taken, and histology confirmed the diagnosis of high-grade serous adenocarcinoma. Finally, the patient underwent surgery. Histology revealed a high-grade serous endometrial adenocarcinoma of the uterine corpus with deep myometrial invasion, confined to the uterus.
Conclusion: Although a relatively rare finding in routine cervical samples, an accurate diagnosis of endometrial adenocarcinoma is possible. Limitations occur when the number of tumour cells is low and the cytologist is not aware of this important differential diagnosis.

E-PS-04-007
The case of serous tubal intraepithelial carcinoma (STIC) with extended disease - the role of cytology in diagnosis and staging
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Background & Objective: To report a case of a patient with STIC, describe the presentation of disease, diagnostic pathway and the role of cytology in the detection and staging.
Method: A clinical assessment was performed on a 45-year-old woman, previously treated for Raynaud syndrome, to exclude paraneoplastic syndrome.
Results: A clinical assessment was performed on a 45-year-old woman, previously treated for Raynaud syndrome, to exclude paraneoplastic

syndrome. Abdominal ultrasound found bilateral inconspicuous ovarian cysts, additionally elevated serum CA 125, HE 4 and ROMA index. PET CT scan revealed pathological metabolism in multiple lymph nodes of supra and retroclavicular left region, paraaortic and pelvic region. Preoperative ultrasound-guided fine-needle aspiration (FNA) of supraclavicular lymph node was performed and cytology found metastatic adenocarcinoma with psammoma bodies. Immunocytochemical analysis on smears and cell blocks confirmed high grade serous carcinoma (HGCS) hence gynaecologic origin was suggested. Intraoperatively, bilateral follicular ovarian cysts were found, the rest of internal genitalia and peritoneal surfaces were macroscopically unremarkable. The peritoneal washing was positive for adenocarcinoma cells. Histological examination found STIC of the left fallopian tube with microscopic infiltration of the opposite fallopian tube and lymphovascular invasion in surrounding stroma. Four received pelvic lymph nodes were all infiltrated by HGSC. The patient received 6 cycles of chemotherapy and repeated PET CT scans revealed the residual disease only in the left renal artery region. During the second look surgery intraoperative cytology was used to detect exact location of the disease near aortic wall.

Conclusion: FNA, exfoliative and intraoperative cytological analysis combined with immunocytochemistry is a valuable method in detecting and monitoring of tumours with unusual clinical presentation.

E-PS-04-008

Small cell carcinoma of lung presented as soft tissue mass of gluteal region

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Background & Objective: Metastatic tumours presenting as soft tissue masses are relatively rare and can be the source of diagnostic pitfalls. We report a case of a 57-year-old male patient without significant medical history admitted to our hospital due to a painless, rapidly growing mass located subcutaneously at the left gluteal region.

Method: Clinical and radiological findings were indicative of a highly suspicious soft tissue tumour without known primary malignancy. Consequently, a fine needle aspiration (FNA) was performed. The aspirate material was processed using liquid-based cytology (ThinPrep). Immunocytochemical analysis was performed to establish the final diagnosis.

Results: Cytology revealed predominantly single, small-intermediate sized neoplastic cells arranged disperse, in a row or occasionally clustered with nuclear molding. Cells presented scant cytoplasm, fine "salt and pepper" chromatin and inconspicuous nucleoli. These features were indicative of a neoplasm, particularly a small cell carcinoma of neuroendocrine origin. Chromogranin, synaptophysin and CD56 were positive, confirming the cytological diagnosis. The patient underwent a full body CT scan that demonstrated a tumour at the left lower lobe of the lung with concomitant enlargement of multiple mediastinal lymph nodes and a metastatic site at the left adrenal gland.

Conclusion: Soft tissue initial metastasis is a rare occurrence for a lung cancer and is a finding that should always be included in our differential diagnosis panel. Furthermore, the incidence of soft tissue metastasis as the primary manifestation of a malignant neoplasm is considered approximately 0.8% and lung cancer is the most common primary neoplasm.

E-PS-04-009

A case of pancreas metastasis of small cell lung carcinoma in fine needle aspiration biopsy: the diagnostic role of cytomorphology and immunohistochemistry

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Background & Objective: Small-cell lung carcinoma represents a group of highly malignant tumours characterized by early and widespread metastais even at the time of diagnosis. However, the pancreas is a relatively infrequent site of metastasis by this neoplasm. Metastatic lesions of the pancreas are rare and account for approximately 2% of pancreatic malignancies.

Method: A 71-year-old male patient complained of abdominal pain, fatigue and weight loss. A 71-year-old male patient complained of abdominal pain, fatigue and weight loss. He was observed a mass lesion of 3,7x3,2 cm in size in the pancreas trunk at the ultrasound. Transabdominal ultrasonography-guided fine-needle aspiration biopsy (US-FNAB) performed on suspected pancreatic mass.

Results: Liquid based cytology was applied to the cytological material and stained with Papanicolaou stain (PAP) stain. Atypical cells with high nucleocytoplasmic ratios and thin chromatin nuclei were observed on the slide, with groups of cells forming nuclear crowds. Atypical cells showed diffuse staining with TTF-1, NSE and synaptophysin in immunohistochemical stain applied to cell block obtained from cytological material. The cytodiagnosis was reported as malign cytology. Positron emission tomography scan also showed a mass at the head of pancreas and the lesion at the left lung. Bronchoscopic biopsy was performed. Histological diagnosis was reported lung small cell carcinoma.

Conclusion: This case demonstrates that fine-needle aspiration biopsy is an important tool in the diagnosis of metastatic pancreatic neoplasms.

E-PS-04-010

Cytologic diagnosis of cooccurence of peritoneal high grade serous carcinoma and gastric gastrointestinal stromal tumour

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Background & Objective: Background: Herein we presented cytologic diagnosis of a case with concurrence of peritoneal high grade serous carcinoma and gastric gastrointestinal stromal tumour.

Method: A 70-years-old woman presented with gastric and pelvic pain with fullness. In physical examination ascites was present at left upper abdominal quadrant. A subsequent contrast-enhanced computed tomography scan demonstrated peritoneal carcinomatosis and a 30x27 mm submucosal mass with focal necrosis in the gastric minor curvatura. This finding was suggestive gastrointestinal stromal tumour versus tumour implant.

Results: We evaluated fresh ascitic fluid samples and fine needle aspiration material from gastric mass. Cytologic diagnosis of ascitic fluid was high-grade serous carcinoma suggesting peritoneal versus gynaecologic origin. Cytologic diagnosis of fine needle aspiration of gastric tumour was gastrointestinal stromal tumour (GIST). Histopathologic evaluation of gastric antrepylorectomy and total abdominal hysterectomy with bilateral salpingo-oophorectomy specimens showed primary tubal high-grade serous carcinoma and spindl cell GIST.

Conclusion: Coexistence of gastrointestinal stromal tumour and tubal high-grade serous carcinoma and gastric GIST was rare.

E-PS-04-011

Cytologic characteristics of secretory carcinoma of salivary gland: report of two cases

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Background & Objective: Secretory carcinoma (SC) is a newely introduced salivary gland tumour which shows similar characteristic features of secretory carcinoma of the breast. Histologically, SC is composed of microcystic/solid and tubular structure with uniform cells. There are abundant eiosinophilic homogeneous or bubbly secretion. SC carries identical ETV6-NTRK3 fusion gene. Only few cytopathological reports of SC are reported. We reviewed two cytology cases of SC in parotid gland confirmed as surgical resection.

Method: Two patients were 56-year-old male and 64-year-old female with mass at parotid gland. The diameter of the masses were 2.2 cm and 1 cm, respectively, and fine-needle aspirations were performed.
Results: Aspiration smears of two cases show relatively high cellularity. The nests of tumour cells show papillary or microglandular structure, floating in mucus-like secretion with scattered lymphocyte and macrophage. The nucleus of tumour cells shows round, smooth nuclear contour, distinct nucleolus and fine open chromatin. The tumour cells have multiple various sized cytoplasmic vacuoles. The singly scattered tumour cells frequently show binucleated eccentric nuclei with large cytoplasmic vacuole. The major differential diagnosis of SC is acinic cell carcinoma. Compared with acinic cell carcinoma, SC shows smaller nucleus, smooth nuclear membrane contour, and frequent vacuolated and singly scattered tumour cells at aspiration cytology.
Conclusion: Since SC is a recently described tumour, cytological features are not as well known. Although it is difficult to distinguish SC from cytology, close attention and knowledge of characteristic cytologic features of SC may be helpful for the accurate diagnosis.

E-PS-04-012
Malignant mesothelioma cells in sputum and bronchial aspirates. Report of one case of non-asbestos, chylous effusion cavities-related and review of the literature

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Background & Objective: To describe the difficulties of diagnosing malignant mesothelioma in the context of long-standing effusions secondary to previous non-neoplastic conditions when facing atypical cells in unusual anatomic samples.
Method: Case report: A 62-year-old male with chylous thoracoabdominal effusions due to recurrent thromboembolic events, Factor XII deficiency-related disease that resulted in stenosis of the left subclavia and cava veins and rupture of the thoracic duct consulted because of respiratory distress due to pleural effusion and ascites. Exfoliative samples of thoracoabdominal effusions, sputum and bronchial aspirates were evaluated with Papanicolaou and immunocytochemical stains. Two weeks after the initial consultation an enlarged right supraclavicular adenopathy was detected and underwent fine-needle aspiration cytology.
Results: In sputum and bronchial aspirates samples a discrete number of epithelioid cells with atypical, large vesicular eccentric nuclei with prominent nucleoli and vacuolated cytoplasm, single and in small tridimensional clusters, were identified. Previous pleuroperitoneal effusions consisted of mesothelial cell-rich, reactive-appearing specimens, also inconclusive for malignancy in biopsy.
Conclusion: Due to the unfrequent invasion of the bronchial tree by malignant mesothelioma, its diagnosis in sputum or bronchial exfoliative cytology is extremely difficult, moreover in the context of long-standing chylous thoracoabdominal effusions with mesothelial cell-rich samples previously interpreted as reactive by cytology and biopsy. Immunocytochemical markers are essential to confirm the mesothelial nature of the atypical cells. Since recurrent thromboembolic disease related to factor XII deficiency may result in anomalous pleuroplumonary lymph drainage connections, a definite diagnosis of malignancy may require demonstration of invasion and/or metastatic disease.

E-PS-04-013
Diagnosis of schistosoma haematobium is possible with urine cytology

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Background & Objective: Schistosomiasis is a parasitic disease caused by trematodes of the genus Schistosoma. The infection is contracted with activities related with infested waters. It is prevalent in tropical and subtropical regions. The clinical manifestations are due to the deposition of eggs, which cause an inflammatory response and histopathological changes. The symptoms range from initial cutaneous lesions to bilharzian uropathy: granulomatous inflammatory reaction and fibrous lesions. Schistosoma haematobium have been associated with squamous cell carcinoma of bladder. The diagnosis is made by detecting parasite eggs in stool or urine samples.
Method: To report a case of schistosoma haematobium, we describe the clinicopathological details and review the utility of urine cytology.
Results: We present the case of an immigrant 28-year-old male from Guinea, with long evolution hematuria, self-limited left supra pubic and lumbar pain. In the complementary tests, he presented eosinophilia in peripheral blood. In the imaging tests, a diffuse urothelial thickening of the left ureter was evidenced, and a defect of the intravenous urography re-collection. Urine cytology revealed an inflammatory smear with high proportion of eosinophils and Schistosoma eggs with a prominent terminal spine.
Conclusion: We must consider the diagnosis of schistosomiasis in immigrant patients or those who have travelled to exotic countries, with abdominal pain and macroscopic hematuria. The presence of eosinophils in urine, forces us to rule out a parasitic infection. Urinary cytology is considered the gold standard for diagnosis schistosomiasis, allowing us to make a diagnosis efficiently.

E-PS-04-014
Solid pancreatic pseudopapillary tumour diagnosed by fnab-eus-guided: a case report

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Background & Objective: Solid pancreatic pseudopapillary tumours are rare neoplasms, about 1-3% of all pancreatic neoplasms. This cancer mainly affects women between the third and fourth decade of life with low malignant potential.
Method: A 54 years old women reported history of upper abdominal pain for several days. Physical exam showed light abdominal pain at abdominal palpation. Ultrasound examination was performed and showed a 12,3x7x4cm pancreatic mass. An fnab-eus guided showed a tumour characterized by poorly cohesive uniform cells solid and pseudopapillary growth pattern. The patient underwent surgery.
Results: The histological examination showed a mass 12,3x7x4cm partially encapsulated constituted by solid and cystic areas with monomorphic proliferation of cells and capillary structures with ovoid nuclei, eosinophilic cytoplasm and granular chromatin and capillary structures. There are son areas with papillary structures and other with poorly cohesive pattern. Inmunohistochemical techniques showed positive staining for: CD10, ciclin-D1, beta-catenin, progesterone receptors and enolase and negative staining for: CK7, chromogranin y synaptophyicin; Ki67: 5%.
Conclusion: Solid pseudopapillary neoplasms of the pancreas usually has a favorable prognosis with just over 95% of patients reported as being disease-free after surgical resection with less than 2% of mortality and it rarely occurs in males or in paediatric people. The common localization is the tail of the pancreas following by head and body with metastasis in only 10-15% of cases.

E-PS-05 | Dermatopathology

E-PS-05-001

A stab in the back: an unusual case of cutaneous neural infiltration as a manifestation of chronic lymphoproliferative disorder of natural killer cells

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Background & Objective: A 52-year old woman with a background of Chronic Lymphoproliferative Disorder of Natural Killer cells (CLPDNK) was referred to dermatology with a rash affecting her face, upper arms, and back. Her main symptoms were severe burning pain, paresthesia and numbness in variable areas of the skin. On examination, she had skin tightness with faint dusky plaques affecting the back.
Method: Skin biopsies revealed a superficial and deep, primarily neurotropic atypical lymphoid infiltration. Results of immunohistochemistry studies showed CD4, CD7 and CD8 positivity. There were scattered weakly stained CD56 positive natural killer (NK) cells and strong staining for the cytotoxic marker Granzyme B and Perforin. Molecular genetic analysis for T cell receptor gene rearrangements was negative.
Results: Neurotropic lymphocytosis can be caused by several conditions, including viral infections, sarcoidosis, vasculitis and medications and by more atypical conditions such as neuroleukaemiosis (AML, CLL) and neurolymphomatosis (NHL, T-cell lymphoma and NK cell lymphoma). At initial presentation, our patient had presented with a CMV infection, we had postulated that this lymphocytosis may have been related however when comparing the immunophenotype of our patient's skin biopsy with her peripheral and bone marrow flow cytometry, they correlated favorably with her known diagnosis of CLPDNK.
Conclusion: Cutaneous findings in patients with CLPDNK have been reported, with one study demonstrating skin manifestations in 36% of patients. A large case series reported 3% of patients experiencing peripheral neuropathy. However, involvement of peripheral cutaneous nerves by NK cells seen on histopathology as described in our case has not been reported before.

E-PS-05-002

Postirradiation pseudosclerodermatous panniculitis: a case report

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Background & Objective: Postirradiation pseudosclerodermatous panniculitis is a rare panniculitic disorder induced by radiotherapy. We report a case of a patient with past medical history of breast invasive ductal carcinoma who presents an erythematous indurated plaque in the scar. The relevance of the case is based on its long latency period, the clinical suspicion of cancer relapse and the scarce number of reported cases.
Method: A 61- year-old female patient with medical history of breast invasive ductal carcinoma grade II treated with surgery, chemotherapy and external radiotherapy. 23 years later, she developed an indurated, erythematous, fibrous and ulcerated plaque in the scar. Due to its clinical suspicion of relapse, a skin punch biopsy was performed.
Results: The main findings were confined to the subcutaneous tissue and consisted of thickened, sclerotic septa combined with a lobular panniculitis characterized by centrally located adipocyte necrosis, lipophagic granulomas, lipophages, and scattered neutrophils and lymphocytes. We also found signs of chronic radiodermatitis like dermal sclerosis, superficial telangiectatic vasodilatation and hyaline sclerosis of vessel walls of the subcutaneous plexus. No evidence of carcinoma was found.
Conclusion: Postirradiation pseudosclerodermatous panniculitis is a rare panniculitic disorder induced by radiotherapy which can be found months or years later as an indurated plaque in the radiated area. It is important to make a proper differential diagnosis between this entity and a carcinoma recurrence since clinical manifestations may be similar while its treatment and prognosis are different.

E-PS-05-004

Cutaneous basal cell carcinoma with lymph node and pulmonary metastases

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Background & Objective: Basal cell carcinoma (BCC) is the most common skin cancer, generally associated with a good prognosis. Herein we present a case with node and lung metastases. The treatment option is also discussed.
Method: After a history of a slow-growing ulcerating tumour of the left forearm, a 55 years old patient was referred to our dermatology department. On initial presentation an 8x15 cm measuring wound on the left forearm and a 5x8 cm measuring and 3-4 cm deep ulceration of the left axilla could be observed. Moreover, multiple dark brown papules were seen on the left thoracic wall. Radiographic study revealed a pleural effusion in the right lung and several tumours-lesions in both lungs.
Results: At histological examination, both the lesions of the skin and also the biopsy of the lung were composed of BCC. After discussion of the case in the tumour-board, a treatment with hedgehog inhibitor molecule was performed, resulting in a short remission. Unfortunately, pulmonary metastases showed progression 9 months after starting the therapy, and the patient died for the cancer.
Conclusion: Metastatic BCC is an extraordinary rare finding, observed in only 0.5% of all cases. Because also BCCs can metastasize, an accurate multidisciplinary approach is mandatory.

E-PS-05-005

Squamomelanocytic tumours: any news or novelties?

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Background & Objective: Squamomelanocytic tumours (SMT) appear to have never enjoyed the spotlight, due to too recent discovery, underecognition or intrinsic rarity. Publicized cases are either outstanding singles or accompanied by few to form a series, be they humans or animals. We recently had the opportunity to diagnose SMT in parallel in two species that are friendly-related, though not personally.
Method: Advanced-aged female (88-year-old) underwent skin tumour excision of a cutaneous horn on face, right cheek area. The specimen received was remarkable for 3 cm outward projection of keratinaceous formation based on ulcerated area measuring 1x1.5 cm. Under microscope, the base of the lesion contained intimately admixed two discrete tissue types, namely malignant squamous and melanoma components with predominance of the later. Each part was subsequently verified by targeted immunohistochemistry (S100, HMB45, CK5/6).
Results: A 7-year-old female dog Cavalier King Charles Spaniel presented with rapidly growing, pigmented skin tumour on lateral abdominal wall that was surgically excised. Haematoxylin&Eosin stained slides, quite in reverse, demonstrated predominantly squamous and/or glandular-like areas of invasive malignancy, partially surrounded by pigment-rich atypical cells with some merging focci. Same immunohistochemistry was applied. First time, SOX 10 was employed on both available tumours with shared positivity on melanocytic and squamous components.
Conclusion: Our modest experience, based on a couple of cases, persuades us to give favor to the hypothesis for dual / divergent differentiation of a monoclonal cell population / pluripotent stem cells over the mechanistic collision theory.

E-PS-05-007

Trichilemmal carcinoma from proliferating trichilemmal cyst of the scalp: a case report

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Background & Objective: Trichilemmal cysts are common fluid-filled growths that arise from the isthmus of the hair follicle. They can form rapidly multiplying trichilemmal tumours, also called proliferating trichilemmal cysts, which are typically benign. Rarely, proliferating trichilemmal cysts can become cancerous known as proliferating trichilemmal cystic carcinoma of the scalp or malignant proliferating trichilemmal cyst which is a rare malignant tumour affecting elderly female. The aim of this case report was to discuss the nosological, pathogenic problems as well as the anatomo-clinical and evolutionary features of this tumour.
Method: We report a case of a 37-year-old woman with history of multiple simple trichilemmal cysts developed at the age of 13 years.
Results: clinical examination revealed multiple cystic and diffuse formations with firm or hard consistency of variable size between 1.5 and 8 cm of major axis (GA) and bleeding at the slightest trauma. Longtime, it was considered as a squamous cell carcinoma of the follicular cystic. A scalp resection with skin graft and bilateral lymph node excision were performed. We received at the department of pathology at "Salah Azaiez "institute the piece of resection of the scalp measuring 15 cm in diameter. It was traversed in its entirety by several cysts (more than a hundred) of variable size between 0.5 and 8 cm of GA. The definitive pathological diagnosis revealed trichilemmal carcinoma arising from a proliferating trichilemmal cysts.
Conclusion: malignant proliferating trichilemmal cyst is currently considered as a tumour derived from a pre-existing trichilemmal cyst. This clinical experience suggests that clinicians should consider the possibility of malignant changes when diagnosing and treating trichilemmal cysts.

E-PS-05-008

Atypical fibroxanthoma of the scalp with aberrant expression of HMB-45: a pitfall in dermatopathology

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Background & Objective: Atypical fibroxanthoma (AFX) most commonly occurs on sun-exposed skin in elderly individuals. It presents as a rapidly growing superficial nodule with a favorable prognosis. AFX still remains a diagnosis of exclusion and requires histological and immunohistochemical features. At histology, the tumour is composed of pleomorphic cells with hyperchromatic nuclei and abundant cytoplasm, commonly arranged in short fascicles. AFX shows a positive reactivity to vimentin, CD10, CD68 and sometimes SMA, while it is negative for CAM5.2, CD34, Melan-A, S100, HMB-45, cytokeratins.
Method: We report a case of a 89 year-old man, who presented with a recently growing nodular, ulcerated and bleeding lesion, measuring 2x1 cm, localized on the scalp.
Results: Histological examination revealed a dermal, nodular, ulcerated tumour with rich vascularization and pushing margins. Tumour cells were spindle, with abundant cytoplasm, arranged in short fascicles, with elongated nuclei. Mitoses and atypical cells were frequent. Immunhistochemistry showed reactivity of tumour cells for vimentin, CD10, CD68 and p53. Moreover, an aberrant diffuse and strong cytoplasmic expression of HMB45 was detected. S100, SOX10, cytokeratins, 34betaE12, SMA, desmin, p16, CD31, CD34, Melan-A, tyrosinase and mutation V600E of BRAF were negative. According to these findings, the diagnosis of AFX with aberrant expression of HMB-45 was performed.
Conclusion: The case here described is, at the best of our knowledge, the first report of a strong and diffuse immunostaining for HMB45 in AFX. This finding should be considered, in order to avoid a missing diagnosis of AFX and a wrong diagnosis of melanoma, when only based on HMB-45 immunostaining.

E-PS-05-009

Review of cutaneous plasmacytomas

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Background & Objective: Our aim was to review all the cutaneous plasmacytomas diagnosed in La Paz Hospital since 2003.
Method: We collected all the clinical information from our database of cutaneous plasmacytomas and reviewed all the slides from each case.
Results: We found four cases of cutaneous plasmacytoma sin our hospital. The four cases had similar morphology: sheets of cells circumscribed to the reticular dermis. The citology was of well differentiated plasma cells. Three cases expressed kappa light chains and one case lambda ones. The mean age was 74 years, with an age range from 70 to 84. Sex distribution was equal (two males and two females). Thorax was the preferential location (two cases). One case was found on the leg and other on the helix. Two of the cases (thorax and leg) were associated with a multiple mieloma, and one (the one on the helix) was considered a primary cutaneous plasmocytoma. The last case (located on the thorax) is still been evaluated for extracutaneus extension.
Conclusion: Cutaneous plasmocytoma is a very rare entity. It is most likely associated with multiple myeloma, but only 2-4% of multiple myeloma have cutaneous presentation. The differential diagnosis of cutaneous plasmacytoma is melanoma (plasmacytoid cells) and marginal zone lymphoma with plasmacytoid differentiation.

E-PS-05-010

Relationship between CEACAM1, E-cadherin and N-cadherin expression in thin melanoma of the skin

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Background & Objective: E-cadherin to N-cadherin switch in melanoma of the skin is believed to cause detachment of the tumour cells from the basal membrane, thus promoting both dermal and vascular invasion. Carcinoembryonic antigen-related cell adhesion molecule, CEACAM1, is a transmembrane protein capable of homophilic and heterophilic intercellular adhesion. In melanoma, CEACAM1 is facilitating the interaction between tumour cells and tumour-infiltrating lymphocytes (TILs), particularly NK and CD8+T lymphocytes, so that CEACAM1 upregulation causes resistance to TILs activity. Tumour progression takes place as a consequence of these two processes and we seek to see how these biomarkers are expressed in thin melanomas.
Method: We performed a retrospective study based on 20 consecutive cases of thin melanoma diagnosed in the Pathology Department of Colentina University Hospital. We studied the imunohistochemical expression of CEACAM1, E-cadherin and N-cadherin.
Results: We identified membrane positivity for CEACAM1 and E-cadherin in 100% of cases, while N-cadherin remained negative in 50% of cases. For CEACAM1 and N-cadherin there was a gradual growth of expression towards the invasion front, while E-cadherin showed decreased expression towards the dermis. 10% of cases showed strong positivity for E-cadherin at the tumour's periphery and a low expression at the center while being strongly positive for CEACAM1.

Conclusion: In thin melanomas, CEACAM1 and N-cadherin are better expressed at the invasion front, opposite to E-cadherin which is better expressed at epidermal and junctional level.

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E-PS-05-011

Progression of kerathoacanthoma and development of squamous cell carcinoma; an immunohistochemical study

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Background & Objective: Keratoacanthoma (KA) is a benign neoplasia originating from keratinocytes, located on sun-exposed areas of the skin. KA develops within 6-8 weeks and usually regresses after 3-6 months. It may show infiltrating growth and cytological atypia like squamous cell carcinomas (SCCs), and may be considered to be a precancerous lesion, since there are reports indicating that some may develop SCC (SCCexKA) KA has a life cycle reminiscent of the hair cycle, where activation of the Wnt signaling pathway is important for proliferation/regeneration in the anagen phase. An experimentally-induced murine KA model by Zito G et al showed activation of the Wnt signaling pathway during the proliferative phase. To test if this is true also for human KAs, we analyzed the expression of several downstream proteins of the Wnt pathway.
Method: Immunohistochemistry was done in our material that included young and old KA, SCC, and SCCexKA.
Results: Beta- catenin, Sox 9 and Lef-1 did not show increased expression levels in young KAs compared to older ones, in contrast to Cyclin D1 (p=0.003).
Conclusion: Since increased expression of Cyclin D1 may be induced via other pathways, our data do not necessarily support a role for Wnt signaling in KA progression. There were no differences in expression profiles of these proteins when comparing KAs developing SCC, and those that did not. SCCexKA, however, showed significantly higher Lef-1 values compared to ordinary SCC, suggesting differences in prognostic potential.

E-PS-05-012

Malignant melanoma: a tumour with increased incidence

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Background & Objective: To present the preliminary data regarding the clinicopathological aspects of malignant melanoma, in a university hospital from Tirgu-Mures, located in Transylvania, Romania.
Method: A retrospective analysis of the clinicopathological data regarding melanomas diagnosed in 2017 was performed. The obtained results were compared with our previous database comprising cases diagnosed between 2000-2009 (n=160). This work sampling intended to serve as a base for further molecular studies.
Results: There were 59 melanomas diagnosed in our university center in 2017, with a significantly increased number compared with 2000-2009 period (less than 20 cases per year). The M:F ratio was 1:1 in 2017 and 1:1.35 in the first period. From the 59 cases, 20 (33.89%) were melanoma metastases (lymph nodes, liver, gastrointestinal tract, brain) and 39 were primary tumours (66.1%). In the first period, 38/160 cases were metastases (23.75%), without significant differences (p=0.16). In both periods most of the cases were diagnosed in pT4 stage (55.69% - first period and 42.5% - second period) showing a median Breslow Index of 6.36 mm (mean values of 5.96 mm and 6.76 mm).
Conclusion: More than 3-fold overall increase in number of yearly diagnosed melanoma is noticed in the last period of time. The male and female patients tend to be equally involved and a significant number of cases are still diagnosed in advanced stage.

E-PS-05-014

The efficiency of skin biopsy in clinically unsuspected infectious diseases

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Background & Objective: We present four cases of skin biopsies whose previous clinical diagnostic orientations differed from the final histologic diagnosis.
Method: We examine microscopically four skin biopsies with H-E, special techniques such as PAS staining, inmunohistochemistry for spirochetes, herpes simplex type 1 and 2, and PCR for herpes virus.
Results: We diagnosed a case of primary syphilis with initial negative serology in a chancroid lesion of the penis, Majocchi granuloma in an inguinal vesicular and scabby injury previously oriented as a bullous dermatose and two herpetic infections remitted as basal cell carcinoma and eczema.
Conclusion: Serologic tests and culture techniques are two of the major diagnostic tools in dermatology. Occasionally, and specially when these former tests fail, it is the pathologic study which can clarify the truthfull nature of the diagnosis. The execution of simple and cheap histoquimic, immunhistoquimic and molecular tests, as much as the H-E inspection, allows performing a fast and accurate diagnosis in order to apply necessary treatment in a short time.

E-PS-05-015

Scrotal angiokeratomas: Fordyce angiokeratomas or Fabry disease?

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Background & Objective: Angiokeratomas are benign vascular lesions which occur solitarily, in clusters or streaks all over the body. Generalised forms are usually strongly associated with congenital disorders like Fabry's disease, an X-linked lysosomal storage disorder due to alpha galactosidase 'A' deficiency. The aim of this report is to differentiate between two rare clinical variants of angiokeratomas: Fordyce Angiokeratoma and angiokeratoma corporis diffusum (Fabry disease).
Method: We report a rare case of multiple angiokeratomas of Fordyce diagnosed in our department of pathology.
Results: A 12-year-old boy presented intermittent bleeding scrotal lesions. The patient had no history of medical problems. On physical examination, his abdomen was soft, with no masses palpable. Three small (1–5 mm) scrotal red purpuric papules of vascular appearance were seen. There were no intra-scrotal swellings and no varicocele or epididymal pathology. Histopathological examination of the papules revealed the presence of a dilated vascular lumen in the superficial dermis coated with non-atypical endothelium. The overlying epidermis was acanthotic and hyperkeratotic. These histological findings were consistent with angiokeratoma. A diagnosis of scrotal angiokeratoma of Fordyce was made and potential precipitants such as intra-abdominal masses, urinary tract tumours, varicoceles, hernias and angiokeratoma corporis diffusum (Fabry syndrome) were excluded. The patient was discharged with dermatology follow-up.
Conclusion: The important differential diagnosis of Fordyce angiokeratoma is angiokeratoma corporis diffusum (Fabry disease). Thus, the detection of angiokeratomas, regardless of their location or distribution, should alert the dermatopathologist to a possible diagnosis of Fabry disease and prompt the performance of relevant tests to confirm or rule out this serious, treatable disease.

E-PS-05-016

Papular acantholytic dyskeratosis of the genitocrural area

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Background & Objective: Papular Acantholytic Dyskeratosis (PAD) of the genitocrural area is an unusual clinicopathological entity, presenting as multiple small pink-white papules, more frequently in young women, although they can also be found in men. The papules are usually pruritic, keratinized on erythematous base, with fissures.
Method: We present two cases: a 71-year-old male with one genital wart in the frenulum; and a 56-year-old female with a single painful vulvar lesion.
Results: Microscopic examination on biopsies shows parakeratotic hyperkeratosis, irregular acanthosis, elongation of the interpapillary crests and acantholytic dyskeratosis, with suprabasal cleft formation. Direct and indirect immunofluorescence are usually negative. Clinical differential diagnosis includes condyloma acuminatum and lichen sclerosus; histological differential diagnosis includes Hailey-Hailey disease, Darier disease, pemphigus vulgaris, Grover disease and warty dyskeratoma.
Conclusion: It is essential to render an exhaustive clinical and pathological correlation in order to ensure a correct diagnosis, detailing location and chronology of the lesions, patient's age and symptoms.

E-PS-05-017

Skin limited Rosai-Dorfman disease with elevated IgG4 positive plasma cells

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Background & Objective: We report a rare case of exclusively cutaneous Rosai-Dorfman disease in a 61-years-old North-African man.
Method: The patient presented several well-circumscribed papular and nodular lesions on the skin of cervical, scapular and thoracic regions, that varied from 1,9 to 3 cm in maximum length. The lesion was excised and sent to our laboratory.
Results: Histology revealed polygonal S100 positive histiocytes showing abundant emperipolesis (intracytoplasmic lymphocytes, erythrocytes, plasma cells and neutrophils). The immunohistochemistry showed that the histiocytes were also variably positive for CD68 and CD163 and negative for CD1a. The specimen was rich in plasma cells that showed a >40% increase of the IgG4/IgG ratio.
Conclusion: Rosai-Dorfman disease is a benign, self-limited non-Langerhans cell histiocytosis of unknown etiology. Although most likely limited to the lymph nodes, over 40% of patients have extranodal involvement, with the skin being the most frequently affected site. Cutaneous disease without the presence of lymphadenopathy is extremely rare but has been reported. Although elevation of IgG4 plasma cells and association with the spectrum of IgG4-related sclerosing disease is described in many cases, it is unclear the diagnostic value of the IgG4/IgG ratio.

E-PS-05-018

Expression of mTOR pathway proteins in cutaneous squamous cell carcinomas developing in organ-transplant patients before and after conversion to mTOR-inhibitors

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Background & Objective: Inhibitors of the Mammalian Target of Rapamycin (mTORis) are drugs exerting both immunosuppressive and antitumour effects and are therefore used in organ-transplant recipients (OTR) as immunosuppressants able to reduce skin tumour burden in these patients. The aim of this study was to investigate the effects of mTORis on the expression of mTOR pathway proteins in cutaneous squamous-cell carcinomas (cSCC) developing in OTR, before and after conversion to mTORis.
Method: Formalin-fixed, paraffin-embedded specimens of 23 cSCC were retrieved from the archives of the Pathology Department, Ed. Herriot Hospital, Lyon, France. The tumours had been excised from a group of OTR with post-transplant cSCC, before (n: 12, 52%) and after (n: 11, 48%) conversion to mTORis, introduced in order to decrease the rate of cutaneous carcinogenesis. All tumours were immunostained with antibodies to pAKT, pmTOR and PI3KC, by using a standard streptavidin-biotin-immunoperoxidase technique on 4-μm thick sections.
Results: Expression of p-mTOR was found in 8/12 cSCC before switch and 8/11 cSCC after switch to mTORis (73%). The expression of pmTOR did not show significant correlation with cSCC differentiation. No differences were observed in pmTOR expression between pre- and post-switch cSCC. All but 2 tumours were positive for PI3KC, and all cases expressed pAKT.
Conclusion: There is no difference in pmTOR expression between pre- and post-switch cSCC. The observed PI3K and pAKT expression suggests that the molecular pathway is active in all cases. This may partially explain development of cSCC even after conversion to mTORis-based immunosuppression.

E-PS-05-019

Direct immunofluorescence on proteinase-digested formalin-fixed paraffin-embedded skin biopsies

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Background & Objective: Direct immunofluorescence (DIF) on formalin-fixed paraffin-embedded tissue (DIF-P) after antigen retrieval with Pronase has proven to be of value in renal pathology, not only as a salvage technique when frozen tissue is not available, but also to discover masked deposits. Its value in skin biopsies has been recently reported. The aim of this study is to compare the results of DIF-P and DIF in frozen sections (DIF-F) in skin pathology.
Method: We selected 37 skin biopsies in which both frozen and paraffin tissue was available, where histology and clinical findings were consistent with dermatitis herpetiformis (DH, 2 case), linear IgA dermatosis (LIgAD, 3 cases), discoid lupus (DL, 12 cases), pemphigus vulgaris (PV, 5 cases), bullous pemphigoid (BP, 9 cases) and Schönlein-Henoch vasculitis (SH, 6 cases). We compared the results of DIF-F with DIF-P for IgA, IgG and C3.
Results: IgA was positive in both DIF-F and DIF-P in cases of DH and SH, whereas LIgAD showed only positivity on DIF-F. IgG was always positive in DIF-P when DIF-F had been positive. Moreover, in 4 cases of DL, 1 case of PV and 2 cases of BP the DIF-P shows IgG positivity whereas it was negative by DIF-F. C3 showed poorer results, it was only detected by DIF-P in 20% of DIF-F positive cases.
Conclusion: This preliminary study shows that DIF-P may be useful for IgG detection in PV, BP and DL cases and for IgA detection in DH and SHV, when no frozen tissue is available, although not reliable for linear IgA dermatosis.

E-PS-05-020

Intraepithelial neoplasia in association with genital lichen sclerosus is likely to arise on the inflammatory stage of this dermatosis

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Background & Objective: The aim of the study was to determine the prevalence of certain intraepithelial neoplasia (IN) types in vulva and foreskin biopsies and to highlight whether the stage of the background lichen sclerosus (LS) was inflammatory ("early") or advanced one.
Method: All vulvar and penile biopsy cases (392 female and 196 male patients in 2012-2016) of the City Pathology Bureau in Minsk were revised for the presence of LS and IN without invasive squamous cell carcinoma. The diagnosis of advanced LS was based on the presence of basal cell vacuolization, band-like dermal homogenization and a variable dense lymphohistiocyte infiltrate beneath it. An inflammatory LS lesions were characterized by focal but evident homogenization along with the features above.
Results: LS was found in 70% (n=212) of vulvar and in 30% (n=89) of penile species. In the series of 212 vulvar biopsies with LS, VIN was observed in 4 cases (2%), 75% of which (n=3) were classified as uVIN and 25% (n=1) as dVIN. In these 89 penile species with LS, PeIN lesions were diagnosed in 8 cases (9%), among which uPeIN was observed in 50% (n=4), as was dPeIN. LS associated with VIN/PeIN was of the inflammatory stage in all the cases.
Conclusion: According to our data indeed VIN related to LS is rather undifferentiated. Penile IN associated with LS is likely to be of differentiated and undifferentiated types in equal parts. The risk of LS progression to PeIN is 4.5 times higher in comparison to VIN. VIN/PeIN coexisting with LS will rather develop on the inflammatory stage of LS lesions.

E-PS-05-021
Cutaneous glomus tumour of uncertain malignant potential presenting as a recurrent wrist hemangioma
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Background & Objective: We present a case of a recurrent cutaneous glomangioma of uncertain malignant potential formerly diagnosed as a hemangioma of the wrist region.
Method: On January 2016 a 64 years old male had a skin biopsy for a cutaneous hemangioma of the right wrist. One year later he presented again to plastic surgery department for a white/tan lesion at the same anatomic area.
Results: An elliptic skin biopsy was received in our department. Histologically, we observed a well circumscribed dermal lesion consisting of homogeneous oval or slightly spindle cells with mild to moderate nuclear atypia and 8 mitoses/10HPF. A glomus tumour with uncertain malignant potential was diagnosed based on morphology and immunohistochemistry.
Conclusion: Glomus tumours are generally considered benign lesions. The prognosis of glomangiomas with uncertain malignant potential is still unknown. This indicates a more careful follow-up due to the small number of cases described.

E-PS-05-022
Study of large B-cell lymphoma in skin biopsies. Experience in our institution during the last 18 years
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Background & Objective: According to the WHO classification of 2017, cutaneous B-cell lymphomas represent 20-25% of primary cutaneous lymphomas, of which, diffuse primary lymphoma of large cell B leg type (pcDLBCL-LT) represents only 10-20%. We have collected cases of cutaneous large B-cell lymphoma diagnosed in skin biopsy during the last 18 years.
Method: We reviewed 24 skin biopsies from 21 patients. 12 were male (57%) and 9 female (43%), with an average age of 75 years. The immunohistochemical techniques used were BCL2, MUM1, BCL6, CD10, C-MYC, cyclinD1, p63 and ki67.
Results: From 21 reviewed cases, 13 were cutaneous primary lymphomas (62%) and 8 secondary lymphomas (38%). All primary tumours were pcDLBCL-LT (BCL2+, MUM1+ and BCL6 +/-), five localized in leg and the rest in head, neck and trunk. These were also positive for C-MYC (61%), p63 (31%), CD10 (31%) and cyclinD1 (15%). The secondary lymphomas showed positivity for BCL2 (62.5%), CD10 (62.5%), C-MYC (50%), MUM1 (37.5%), BCL6 (37.5%), cyclinD1 (12.5%) and p63 (12.5%). We couldn't find any association between p63 expression and percentage of Ki67. From the cases of primary lymphomas, six patients died due to other causes, 6 had complete remission of the disease. From the secondary lymphomas three out of four died due to the disease itself.
Conclusion: 62% of the large B-cell lymphoma diagnosed by skin biopsy are cutaneous primaries. In our series, all cases were pcDLBCL-LT and the most frequent locations were legs. Other markers expressed in pcDLBCL-LT are CD10, C-MYC, cyclinD1 and p63, which are also related with other lymphomas.

E-PS-05-023
Genital lichen sclerosus with clusters of cytoid bodies: a study of 3 cases
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Background & Objective: Lichen sclerosus (LS) is a chronic idiopathic persistent inflammatory mucocutaneous dermatosis which affects predominantly the anogenital area. At times it may be difficult to distinguish LS and lichen planus (LP) on biopsies. Fung and LeBoit in 1998 reviewed 68 cases of vulvar LS and LP. They revealed cytoid bodies only in LP (0% LS, 100% LP). The aim of the study was to determine the presence of cytoid bodies in unequivocal LS lesions in vulva and penis.
Method: All vulvar and penile biopsy cases retrieved from the archive pathology files (2012–2016) of the City Pathology Bureau in Minsk, Belarus, were revised, firstly, for the presence of histologically diagnosed LS. Secondly, among these 301 biopsy specimens (212 women, 89 men) all early LS lesions were excluded so we examined only morphologically advanced ones. Thirdly, we looked for cytoid bodies, particularly in clusters.
Results: The diagnosis of late LS was based on the presence of wide dermal band of homogenization with a variable dense lymphohistiocyte infiltrate right beneath it, basal cell vacuolization and a variable degree of epidermal hyperplasia or atrophy. Cytoid bodies considered as round to oval, homogeneous, eosinophilic PAS-positive globules identifiable within the basal layer of epithelium and the papillary dermis. Late stage LS with clusters of cytoid bodies was observed in 3 cases (1%) only among males. The patients were 26, 77 and 79 years old.
Conclusion: In contrast to what was previously thought, to our data clusters of cytoid bodies cannot be a reliable feature in distinguishing LS and LP. These changes can sometimes be observed in non-doubtful lesions of LS.

E-PS-05-024
Lymphomatoid atypical fibroxanthoma: a new variant that may simulate a lymphoproliferative disorder
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Background & Objective: Atypical fibroxanthoma (AFX) in an uncommon skin in which different histopathological variants have been described. We report two cases of AFX with an atypical lymphomatoid infiltrate that may simulate lymphoproliferative disorders.

Method: We reviewed 133 AFX diagnosed at our institution. Paraffin sections were stained with haematoxylin and eosin, and sections were immunostained using the Envision method (Dako, Glostrup, Denmark) using a panel of antibodies. We found two cases with a prominent lymphoid infiltrate.
Results: Case 1: a 79-year old man debuted with a rapidly growing nodule on forehead. At histological examination the lesion showed a dermic celular proliferation composed of pleomorphic, spindled and epithelioid large cells, with a prominent intralesional atypical lymphoid infiltrate. Neoplastic cells showed CD10, CD99, CKAE1-AE3, EMA, vimentin, smooth muscle actin and desmin expression. The lymphoid infiltrate was positive for CD45, CD3, CD8 and TIA-1. Case 2, a 90-year old woman presented with an ulcerated nodule on the zygomatic arch. Histologically, it was composed of pleomorphic cells intermingled with an atypical infiltrate of lymphocytes, histiocytes, plasma cells and eosinophils. The pleomorphic cells were positive for CD10 and CD99. The lymphoid infiltrate showed a cytotoxic phenotype, and molecular studies demonstrated a monoclonal rearrangement of the TCR gene.
Conclusion: Many different variants of AFX have been described, pointing out stromal peculiarities: chondroid, myxoid and keloid changes. We describe two cases of AFX with an atypical lymphoid infiltrate. It´s been postulated this pattern may correspond to a regression of AFX, with scattered sclerosis. We emphasize the importance of recognizing this variant, and its differential diagnosis with a primary cutaneous lymphoproliferative disorder.

E-PS-05-025
Association study of proinflammatory cytokines genes polymorphism with psoriasis in cases from a single state

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Background & Objective: Psoriasis is a well-known chronic inflammatory skin disease with still uncertain etiology and very heterogeneous genetic background. Many studies showed that inflammation triggers psoriasis development but it is currently unclear whether genetic polymorphism of cytokines – main candidate genes – can be associated with psoriasis in the Tatar population. To determine the association of proinflammatory cytokines (TNFa, IL1b and Il6) genes polymorphism (rs1800629, rs16944 and rs1800795 respectively) with psoriasis in patients from Volga Tatar population (Republic of Tatarstan, Russia).
Method: SNP genotyping was performed by real-time PCR using TaqMan technology in 407 samples DNA extracted from venous blood (197 patients and 210 controls). Cytokines level was determined in 160 serum samples (80 patient and 80 controls) by ELISA. Statistical analysis performed by R studio packet program.
Results: All studied SNPs were in accordance with HWE in both studied groups ($p>0.05$). Compared to controls, cases showed significant higher frequency of certain genotypes including GG genotype of Il6 gene (OR=4.18, p=0.026), TT genotype of Il1b gene (OR=4.08, p=0.046) and GG genotype of TNFa gene (OR=3.4, p=0.037). Furthermore, patients with this genotypes characterized with higher cytokine level compared to other genotype carriers ($p<0.05$).
Conclusion: Our study confirmed previously obtained results from the association study of inflammatory genes polymorphism and psoriasis development in other populations and the certain genotype carriers must be paid close attention for preventing psoriasis.

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E-PS-05-026
Multinucleated giant cell angiohistiocitoma, a subtle pattern easy to miss

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Background & Objective: Multinucleated giant cell angiohistiocitoma is a benign vascular and fibrohistiocitic proliferation of unknown origin. They are usually multiple eritematoviolaceus papules in lower extremities, wrist or hands. Differences between histopathology (subtle vascular proliferation above some small multinucleated fibrohistiocites) and clinic (red papules or even small nodules) are striking yet need to be identified to proper treatment. Furthermore, we propose Pulsed dye laser (PDL) to do so, adding a new possibility to previous options.
Method: Four patients with multiple erytematous lesions in trunk, face, fingers and hands, were performed a punch biopsy which showed a dermal capilar proliferation of tiny vessels and presence of multinucleated fibroblast between collagen bundles in deep dermis. There was perivascular infiltrate of lymphocites. All of them were successively treated with PDL (2-6 cycles), in order to coagulate proliferated vessels.
Results: After 28 months, two of the patients had complete recovery from the lesions (face and hands), one persisted (trunk) and the fourth failed to come up to follow up.
Conclusion: Multinucleated giant cell angiohistiocitoma is usually asymptomatic but has an aesthetic demand for treatment. Pathologyst should be aware of the subtle vascular and multinucleated proliferation between normal collagen bundles that can be easily missed or wrongly assessed as non-specific.

E-PS-06 | Digestive Diseases Pathology - GI

E-PS-06-001
Tumour microenvironment in colorectal cancer

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Background & Objective: In recent studies, tumour microenvironment in colorectal cancer (CRC) has a growing interest as a prognostic factor. Immunoscore (IS) quantifies cytotoxic and memory T-cells both in the tumour core (CT) and in the invasive margin (IM), making a score with prognostic value in which a low IS is related to a worse prognosis. The aim of our study is to evaluate if there is a correlation between histological findings and IS score.
Method: 30 patients (pts)(17males, 13females) with a median age of 67yo with T3N0-CRC diagnosed in 2017, with R0 resection, were evaluated. No recurrences were found in a median follow up of 8 months. Each case was classified by IS with a percentile value and a score (0 to 4) and revised by two GI-pathologists.
Results: IS percentiles ranged between 4 and 91, classifying 2pts in IS 0, 8pts in 1, 15pts in 2 and 4pts in 3 (1case with extensive mucinous differentiation was excluded). Statistical analysis showed that a lower IS-percentile was related to higher-tumour-grade foci (p=0.035), while a higher IS-percentile was associated with a greater intensity of inflammation, Crohn's like lymphoid aggregates (CLA)($p<0.05$) and a tendency of incremented TILs (p=0.07).
Conclusion: In case of a lack of availability of IS, others parameters such as greater intensity of inflammation and CLA in the IM can be taken into account as a predictive value in CRC. We were not able to make a prognostic value regarding the risk of recurrence because all pts are free of disease nowadays.

E-PS-06-002

High-grade appendicular mucinous neoplasm

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Background & Objective: Mucinous neoplasms of the appendix cover a broad spectrum of tumours with distinct prognoses and is the most frequent cause of peritoneal pseudomyxoma. We report a case of high-grade appendicular mucinous neoplasm (HAMN).
Method: The clinical history, radiological exams, macroscopic and histological features were reviewed.
Results: An 86-year-old woman with a right inguinal hernia was seen in the Surgical Clinic. CT scan showed a poorly demarcated 80 mm lesion in the right lower abdomen extending from the cecum to the root of the mesentery, with water-like content and puctiform calcifications, suggesting the possibility of a mucocele or mesentery cystic lesion. The right ileocolectomy had an intact and dilated appendix 90 mm long with a 37 mm diameter, smooth surface, thin wall, mucinous content and smooth internal lining with vegetations, in the middle third. Histologically, there was marked fibrosis of the submucosa with loss of muscularis mucosae, flat or wavy neoplastic epithelium, with enlarged, hyperchromatic nuclei showing stratification and loss of polarity. Mitotic figures were seen. There was acellular mucin dissecting through the wall, characteristics of HAMN. Patient is well and under clinical surveillance (5 month follow-up).
Conclusion: HAMN shares the same architectural features as low grade appendicular mucinous neoplasm (LAMN) but has cytological features of high grade dysplasia. Despite the small number of cases studied, HAMN appears to have a more aggressive course and is more frequently associated with the presence of epithelial cells in extra-appendicular mucin, compared to LAMN. HAMN appears to have an intermediate prognosis between LAMN and mucinous adenocarcinoma.

E-PS-06-003

Results of the screening of colorectal carcinoma in a single institution

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Background & Objective: Colorectal carcinoma (CRC) is one of the most prevalent neoplastic diseases worldwide, so the introduction of a screening system for early detection is justified. We analyzed the histological and epidemiological characteristics of the colonoscopic findings of those patients with positive fecal occult blood test (SOH) at the General University Hospital of Ciudad Real (HGUCR) since its implantation, in September 2016, until August 2017.
Method: We studied the colonoscopic results of 371 patients aged 58-69 years. The variables studied were age, sex, type of injury, location and number of injuries.
Results: Lesions were found in 87% of the colonoscopies performed. The patients were more frequently males (3:1). 70% of the lesions were located in rectum-sigma. High-risk adenomas were more frequent in men and were located more frequently in the left colon and rectum. Likewise, multiple lesions were more frequent in males. One in ten patients had infiltrating CRC. 78% of the adenomas found were low risk, 27% medium risk and only 14% were high risk.
Conclusion: The descriptive results obtained in our hospital were similar to those of other Spanish hospitals. The screening system for the early detection of CRC is a relatively recent proposal that has allowed early detection and resection of premalignant lesions, decreasing the incidence of CRC in our population.

E-PS-06-004

Histopathological variables in liver metastases of patients with stage IV colorectal cancer: Potential prognostic relevance of poorly differentiated clusters

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Background & Objective: To evaluate the potential prognostic relevance of poorly differentiated clusters (PDC) in patients with stage IV colorectal cancer (CRC).
Method: We assessed PDC presence in the histological slides of surgically resected and synchronous liver metastases (LM) in 63 patients with CRC, who had been not submitted to any neo-adjuvant treatments. Then we analyzed its association with patients' cancer specific survival (CSS) or progression free survival (PFS).
Results: The presence of PDC (P= 0.016) and PDC localization at tumour edge of LM (P = 0.0004) were significantly associated with shorter CSS. PDC presence at the periphery of LM and positive resection margin were independent prognostic variables for CSS. PDC localization at the tumour edge of LM was a significant (P= .0079) and independent prognosticator of shorter PFS.
Conclusion: The prognosis of patients with colorectal LM is mostly established on clinical variables or on the anatomic extent of CRC. The number of PDC in primary CRC is associated with metastatic risk and bad prognosis, but PDC presence in LM has been scarcely analyzed thus far. Our data suggest that PDC presence and peripheral localization in LM maybe relevant to predict outcome and to make clinical decision inpatients with colorectal synchronous LM.

E-PS-06-005

De novo dedifferentiated heterologous gastrointestinal stromal tumour of the small intestine: a case report

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Background & Objective: Dedifferentiated heterologous gastrointestinal stromal tumour (GIST) is a rare tumour that occurs mainly after imatinib therapy. To date, only a few de novo dedifferentiated GISTs have been reported. We report the case of a 76-year-old man admitted for diffuse abdominal pain and absence of intestinal transit for 3 days associated with vomiting. Exploratory laparotomy revealed an intestinal intussusception, therefore enterectomy was performed.
Method: Tissue samples were routinely processed. HE stains and immunohistochemical tests were performed.
Results: Grossly, the intestinal fragment presented a nodular intramural tumour (12.5x7x6 cm) with heterogenous appearance on cut surface. Microscopically, the tumour presented 2 components with abrupt transition: one consisting of spindled cells with moderate pleomorphism, open nuclei with peripherally displaced chromatin, numerous mitoses, some atypical (15 mitosis/5mm2) and heterologous dedifferentiation (osseous metaplasia) with large areas of tumour necrosis. The second component was represented by a conventional GIST composed of spindled cells with fibrillary eosinophilic cytoplasm and elongated hyperchromatic nuclei with low mitotic activity. The GIST component was positive for DOG1, CD34, CD117 and negative for SMA, while the dedifferentiated area was negative for GIST markers and positive for SMA. Histopathological aspects and immunohistochemical pattern were consistent with de novo dedifferentiated heterologous GIST.
Conclusion: Even when there is no history of imatinib therapy, extensive sampling of an intestinal soft tissue tumour is mandatory in order to identify a dedifferentiated component which may change the prognostic group. Also, one should be aware of loss of expression of GIST markers which may lead to confusion with a collision tumour and misdiagnosis.

E-PS-06-006

Lipomatous polyposis of the colon: a case report

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Background & Objective: Lipomatous polyposis of the colon is an extremely rare condition first described in 1959 by Ling et al. There are less than 15 cases reported in literature of Lipomatous polyposis of the colon.
Method: We report a case of a 54-year old female that presented to the emergency room with sharp, sudden onset abdominal pain followed by gastrointestinal bleeding. Colonoscopic examination revealed multiple polyps throughout the entire colon. A right hemicolectomy was performed.
Results: Gross examination of the surgical specimen revealed approximately 27 submucosal sessile and pedunculated polyps ranging from 0.3 cm to 4.7 cm throughout the entire specimen. Cross section of the 4.7 cm-sized and pedunculated polyp, which was the largest one and almost completely obstructed the lumen, bore an appearance of yellow-colored fat tissue, compatible with a lipoma. Microscopic examination of the specimen showed many small-to-large polyps, composed of mature adipose tissue in the submucosa. Cellular atypia or mitosis were not seen. There was no dysplasia or malignancy in any of the polyps.
Conclusion: This rare entity can be confused with familial polyposis and mimicks malignancy, should be kept as a differential diagnosis of multiple colonic polyposis.

E-PS-06-007

Large polyp harboring a liposarcoma, exceptional finding in the oesophagus

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Background & Objective: Sarcomas arising in the gastrointestinal tract are infrequent, while oesophageal sarcomas represent less than 1% of all malignant oesophageal tumours. With leiomyosarcoma being the most frequent, liposarcoma is exceptional and can present either as a polypoid or a transmural lesion.
Method: A 61-years-old man with associated cardiac pathology presented to our hospital for dyspnea and sensation of intermittent asphyxia. An oesophagogastroduodenoscopy assisted by general anesthesia was performed. The operator described a polypoid, pedunculated lesion, demonstrating a long insertion base in the submucosal layer, in the region of the upper oesophageal sphincter.
Results: The lesion was endoscopically dissected at the level of the base, resulting in an intact 7,5 x 2,5 x 2 cm polyp, with clear gross margins. Macroscopically, the lesion had a soft consistency, a smooth surface, and heterogeneous aspect with lobulated, yellow-grey areas. The polyp was entirely processed and microscopy revealed a mesenchymal tumoural proliferation, composed of adipocytes with variation in size and shape, with focal nuclear hyperchromasia, separated into lobules by irregular fibrous bands or septa. Atypical stromal cells, myxoid changes, as well as a metaplastic ossification were noted. Lipoblasts were observed. The immunohistochemical panel showed positivity for S100, MDM2 and focally for CD34, while the Ki67 index was about 10%. The final diagnosis was well-differentiated liposarcoma.
Conclusion: Due to its rarity, there are only scattered case reports or short series of liposarcomas of the oesophagus. The management procedures such as imagistic studies, (neo) adjuvant therapy, surgical or endoscopic excision techniques, as well as the follow-up guidelines are scarce.

E-PS-06-008

Secondary tumours of the gastrointestinal tract - origin and histologic findings

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Background & Objective: Metastasis of the gastrointestinal tract are uncommon, patients often presenting with a dismal prognosis and in an advanced stage. Malignant melanoma, breast and pancreatic cancer represent the most common primaries. Metastatic tumours are more common in the small intestine than primary tumours. Metastases to the stomach are rare.
Method: We conducted a retrospective study of 20 consecutive cases of secondary tumours of the gastrointestinal tract, using for diagnosis, usual and special stains and immunohistochemical assays.
Results: There were 65% women and 35% men, with a median age of 65 years (range 35-85 years). The main localizations were colon (35%) and stomach (35%), followed by small intestine (30%). The most common primaries were represented by ovarian (30%), colonic (20%) and pancreatic (15%) cancers, while malignant melanoma (10%), uterine (10%), breast (5%) and scuamocelular (5%) cancers were the least frequent. Almost half (40%) of metastatic tumours were poorly differentiated carcinomas.
Conclusion: Although rare, gastrointestinal metastasis should be included in differential diagnosis of poorly differentiated carcinomas, in order to avoid misclassification and errors of staging and therapy. An appropriate panel of immunohistochemistry markers should be designed considering the most frequent malignancies that are metastazing in gastrointestinal tract.

E-PS-06-009

Eosinophils in the gastrointestinal tract: how much is normal?

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Background & Objective: The normal density of eosinophils in the digestive mucosa of children has been rarely addressed despite being important to provide baseline counts for the diagnosis of eosinophilic gastrointestinal disorders (EGID). Even though histopathological criteria for EGID remains undefined, there has been little consistency of results in different populations. We aimed to establish the eosinophil density of the normal digestive mucosa in a paediatric population submitted to endoscopic procedures that were reported as normal.
Method: Biopsies from endoscopies of 33 patients were evaluated. Quantification of eosinophils was performed manually. Review of the pathology reports confirmed absence of abnormality in the biopsy specimens. Counts were reported as mean±standard deviation eosinophils per mm^2.
Results: Oesophagus (n=33): eosinophils were uniformly absent in all biopsies. Stomach: fundus (n=14; 0.7±0.9), body (n=15; 0.3±0.6) and antrum (n=18; 0.6±1.5) revealed consistent values in the lamina propria. Small intestine: eosinophil counts revealed 17.8±16.6, 14.2±11.8, and 50.4±34.6 in the lamina propria of the bulb (n=13), second segment of duodenum (n=13) and ileum (n=16), respectively. Large intestine: the highest peak count was observed in the caecum (123; n=16) with a mean of 50.8±32.8. The eosinophil counts were lower in the ascending (n=16; 40.2±26.8), transverse (n=14; 33.6±21.5), descending (n=15; 39.2±26.1) and sigmoid (n=17; 25.3±17.4) colon and in the rectum (n=17; 13.6±9.9). Eosinophils were regularly absent in the surface epithelium or/and crypt epithelium.
Conclusion: These data provide a baseline count and distribution of eosinophils in the gastrointestinal tract of paediatric patients with normal histology, thus expanding the scarce published data.

E-PS-06-010

Malignancy arising in retrorectal cystic hamartomas (tailgut cyst)

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Background & Objective: Retrorectal cystic hamartomas (RCH) are rare congenital lesions. Malignant transformation is extremely rare with only case reports or small series described in the literature.

Method: We report two cases of malignancy arising in RCH, one adenocarcinoma and one neuroendocrine tumour. Literature review and differential diagnosis of retrorectal lesions are briefly explored.
Results: Case 1: 54-year-old female presented with a 5-month history of proctalgia. CT/MRI: 50mm right pre-sacral lobulated mass. Colonoscopy: rectal bulging lesion covered by grossly normal mucosa. Wide excision was performed and histology showed an infiltrative adenocarcinoma arising in a multicystic lesion covered by columnar epithelium with dysplasia. Due to positive surgical margins she was proposed to neoadjuvant CT/RT. Case 2: 56-year-old male presented with an incidental 82mm pre-sacral heterogeneous mass on CT. The lesion was palpable above the pectineal line at digital rectal examination. He was submitted to surgery and on microscopy an infiltrative neuroendocrine tumour was identified at the periphery of a multicystic lesion lined by stratified squamous, glandular and transitional epithelium. No additional therapy was performed and is alive without evidence of disease. In both cases, the multicystic lesions were morphologically consistent with RCH and involvement of the rectum wall was absent.
Conclusion: RCH is part of a heterogeneous group of retrorectal lesions. Malignant transformation is extremely rare and may be focal. A high degree of suspicion and a meticulous gross examination is necessary for adequate diagnosis and to prevent delay in treatment.

E-PS-06-011
Presentation of a case of mucinous adenocarcinoma on Crohn's disease
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Background & Objective: Primary adenocarcinoma of small bowel situated on the ileum is an extremely rare entity. However, it is been observed an increase risk in those patiens with Crohn's disease (CD) compared to healthy population. We proceed to present a case of mucinous adenocarcinoma over a CD.
Method: 73-year old man undergone ileocecal resection surgery due to a bowel perforation, with a presumptive diagnosis of CD. The surgical piece from the ileocecal resection was perforated and it had 62 cm long. It had a stenosed 45 cm long segment in the ileum, which showed a slightly friable mucosa with cobblestoned appereance and loss of the mucosal folds. It also showed a thickened, white and poorly circumscribed area on the wall, accompanied by mucinous material, which reached the muscle layer of the ileum.
Results: Microscopic examination showed a mucinous adenocarcinoma arised from an area with adenomatous features. The size of the tumour was 10 cm and it reached the subserosal layer. Furthermore, architectural alterations, fissures, transmural lymphoid follicles, piloric metaplasia and widespread fibrosis were found on the peritumoural area, in which the perforation ocurred.
Conclusion: Some population studies demostrated that risk of small bowel adenocarcinoma is increased 3-91 times in patiens diagnosed whit Crohn's disease, with higher incidence in those cases with severe inflamation and early onset. Another related risk factors are fistulous cronic disease, male gender and surgically excluded loop of small bowel. We have brought this case because is an infrequent entity, specially the mucinous variant, with a mortality rate near to 80%.

E-PS-06-012
Medullary carcinoma of the colon: clinical, histopathologic and immunohistochemical features, including MMR status – a series of 5 cases
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Background & Objective: Medullary carcinoma (MC) is a recently-recognised histologic subtype of colorectal carcinoma, characterised by poor gland formation and intratumoural lymphocytic infiltrate. The aim of this study is to discuss their anatomoclinical features, as well as immunohistochemical profile, especially the expression of microsatellites and calretinin.
Method: We selected a series of five consecutive cases, diagnosed between May 2016 and February 2018 as MC at Victor Babes National Institute of Pathology, Histopathology and Immunohistochemistry Department. They were evaluated according to age, sex, location, morphology and metastases. Immunohistochemical staining for CK7, CK20, CDX2, synaptophisin, chromogranin, MLH1, PMS2, MSH2, MLH6 and calretinin was performed.
Results: The mean age of the patients was 77-years-old (range, 62-94 years), and 4 out of 5 cases were women. All 5 cases of MC were localised on the proximal colon. Classic histologic features and an increased intratumoural CD8+ cytotoxic T cell infiltrate was observed in all cases. Only one out of 5 cases presented lymphatic invasion and lymph node dissemination. Neuroendocrine markers were negative or only focally positive. Microsatellite instability was present in all MCs from our study. Modified intestinal differentiation was suggested by the reduction or loss of expression of CK7, CK20 and CDX2. Calretinin was positive in 4 out of 5 cases (80%).
Conclusion: Even if the incidence of MC is very low, its proper diagnosis is important, given its favorable prognosis comparative to poorly differentiated carcinoma (undifferentiated carcinoma).

E-PS-06-013
A neuroendocrine small cell carcinoma of the oesophagus in a patient with longstanding primary achalasia
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Background & Objective: Neuroendocrine neoplasms of the oesophagus are very rare. Due to its poor prognosis the description of these cases is key to understand their clinical and histopathologic presentation in this location.
Method: All cases of oesophageal malignant neoplasms over a 10-year period were revised. Only one case of neuroendocrine neoplasm was found. We reviewed the clinical history and follow-up information of the patient in question.
Results: We analysed 114 cases of malignant neoplasms of the oesophagus, 13 surgical specimens with biopsy plus 101 biopsies. The type of neoplasia was as follows: 86 squamous cell carcinomas (75%), 18 adenocarcinomas (16%), 9 of other categories (0.08%) and 1 small cell neuroendocrine carcinoma (0.01%). The latter case was of a 62-year-old female patient with longstanding primary achalasia who presented with peripheral and central oedema. The subsequent study revealed a 2 cm endoluminal polipoid mass of the distal oesophagus with adjacent lymphadenopathies and metastatic hepatomegaly with no pulmonary or gastric lesions. Histological analysis of the biopsy specimen revealed an infiltrative neoplasm, composed of small atypical cells with hyperchromatic and molding nuclei and scanty cytoplasm sparing the surface epithelium. The neoplastic cells were immunorreactive for keratins, NSE, and synaptophysin. One month after the diagnosis the patient died of hepatic failure.
Conclusion: This case is an example of the poor prognosis of neuroendocrine carcinomas of the oesophagus and illustrates some of their typical histopathological characteristics. Although rare, association of achalasia with oesophageal neuroendocrine carcinoma has been previously reported.

E-PS-06-014
Gastrointestinal stromal tumour diagnosed during donor procurement: experience of two institutions and review of the literature
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Background & Objective: Gastrointestinal stromal tumours (GISTs) are rare neoplasms, accounting for 5% of all sarcomas. Yet, they represent the most common mesenchymal tumours within the gastrointestinal (GI) tract. GISTs occur throughout the GI tract, the stomach being the most frequent site of origin.
Method: Herein, we describe 10 cases of GISTs diagnosed during donor procurement from 2010 and 2017. Frozen sections of the tumours were highly suspicious for GISTs, and mitotic count evaluation was also performed. However, the definitive diagnosis and risk assessment required immunohistochemical staining for CD117 and DOG-1 together with the mitotic count performed on permanent sections. Molecular detection of KIT, PDGFRA, KRAS, NRAS, PIK3CA and BRAF gene mutational analyses was also performed in all tumours.
Results: From our ten donors, 2 kidneys and 3 livers were transplanted with no evidence of donor transmitted neoplasia of at least 18 months.
Conclusion: So we described 9 cases of GISTs with no risk of progressive disease and 1 case with very low risk. In accordance with the latest guidelines of The European Committee on Organ Transplantation, only donors with small gastric GIST are accepted for liver and renal transplant.

E-PS-06-015
Does size matter? Prognostic impact of pT3 colon cancer according to the degree of tumour infiltration in mesocolic fat
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Background & Objective: Relate the prognostic implications of tumour invasión degree in mesocolic fat in patients with pT3 colon tumours.
Method: Retrospective analysis of a prospective database of patients with pT3 colon cancer without metastatic disease at diagnosis time, operated with curative intention. The histological sections were reviewed by a pathologist and a colorectal surgeon to determine the extension in millimeters (mm) of the tumour infiltration in the mesocolic fat. The relation between mesocolic fat infiltration and oncological results was analyzed. A ROC curve was used to show the best cut-off point of the study variable.
Results: 548 patients pT3M0 in total. In 356 patients it was <5 mm, in 158 between 5 and 10 mm and in 34> 10 mm. The median follow-up was 62.0 months. In the multivariate analysis, infiltration of mesocolic fat was an independent risk factor for local recurrence ($p = 0.39$, OR 1.10 per mm), worse disease-free survival ($p < 0.0001$, OR 1, 10 per mm) and worse overall survival ($p = 0.004$, OR 1.06 per mm), but not of carcinomatosis ($p = 0.15$, OR 1.10 per mm). The value in mm of the infiltration of the tumour in the mesocolic fat that best predicted local recurrence, systemic recurrence and mortality was 5 mm.
Conclusion: In pT3M0 colon cancer, the depth of tumour penetration in the mesocolon fat can stratify the risk of recurrence and survival and therefore it should be a factor to consider when determining the oncological prognosis and indicating adjuvant treatment.

E-PS-06-016
The variability of local peritoneal involvement according to Shepherd´s classification: does it determine the prognosis in patients with colon cancer?
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Background & Objective: Assessing the prognosis of advanced colon cancer in relation to the different degrees of serosa infiltration according to Shepherd's classification.
Method: Retrospective analysis of a prospective database (1993-2016) of patients with locally advanced colon cancer, without metastasis at the time of diagnosis and operated with curative intention. The histological sections were reviewed by a pathologist and a colorectal surgeon, classifying the tumours according to Shepherd's classification (4 types). Demographic, surgical and pathological data were also analyzed. Finally, the association of peritoneal infiltration according to Shepherd with the oncological results was evaluated.
Results: 716 patients colon cáncer operated pT3-pT4aM0, were stratified according to Shepherd: 274 (38.2%) type I, 258 (36.0%) type II, 124 (17.3%) type III and 61 (8.5%) type IV. 429 patients were pN0, 197 pN1 and 91 pN2. The median follow-up was 53.0 months. The actuarial rate at 5 years of local recurrence was 8.5%, including carcinomatosis, which was 3.9%. Disease-free survival and overall survival were 76.5% and 64.4%, respectively. In the univariate analysis, Shepherd's grades were not associated with local recurrence ($p = 0.08$), nor with carcinomatosis ($p = 0.12$), but with disease-free survival ($p = 0.001$) and overall survival ($p = 0.18$). $p = 0.047$). On the other hand, in the multivariate analysis, Shepherd´s classification was not an independent risk factor in any of the oncological results analyzed (p minimum: 0.36).
Conclusion: Peritoneal involvement according to Shepherd's classification did not prove to have prognostic relevance after curative resection for colon cancer in the analyzed sample.

E-PS-06-019
Microsatellite instability and tumour deposits in colorectal cancer
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Background & Objective: Microsatellite instabilty (MSI) and tumour deposits are evaluated in a series of colorectal carcinomas.
Method: Colorectal carcinoma cases with immunohistochemistry MSI results were selected. Morphomolecular features were retrieved from the pathology reports along with BAT25, BAT26, NR21, NR24 and mono-27 MSI analysis with real-time PCR. Frequency of MSI biomarkers were evaluated and pathological features of MSI positive and negative cases were compared.
Results: Loss of MLH1, MSH2, MSH6, PMS2 expressions were observed in 46(10,43%), 10(2,27%), 34(7,94%), 49(11,11%) of the 441 cases respectively. At least one of the MSI markers was lost in 76(17,23%) cases; of these, 50 cases had RT-PCR results; 3(6%) were MSI-low and 31(62%) were MSI high. Intratumoural, peritumoural inflammation, mucinous, medullary and poorly differentiation were significantly more in MSI(+) cases, but T stage, lymphatic, vascular, perineural invasion and budding was not different. pN stage was significantly lower in MSI(+) cases. Tumour deposits were less frequent in MSI(+) cases (18,2% versus 29.4%), but this was not statistically significant. Three cases without IHC markers but family history and suspicious morphology were also MSI(+).
Conclusion: With a stepwise approach, including morphology, IHC and RT-PCR for providing information about MSI status of colorectal carcinoma cases, like lymph node metastasis, tumour deposit formation may be less frequent in MSI(+) colorectal carcinoma cases.

E-PS-06-020
Study of MUC5AC, C-MET and SOX9 immunoexpression in a metastatic model of colon adenocarcinomas to the liver
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Background & Objective: MUC5AC is a protein usually absent in normal colon and colorectal adenocarcinomas (CRC). C-MET is

overexpressed in primary CRC and it is described as an important prognostic marker for early stage invasion and regional metastatic disease. Finally, SOX-9 is described as an independent adverse prognosticator in CRC. The main objective was to study the expression of MUC5AC, C-MET and SOX9 in samples of colon adenocarcinoma (52) and their respective hepatic metastases.
Method: Fifty-two consecutive patients with colon cancer and subsequent hepatic metastasis surgically removed between 2007 and 2017 were studied. Tissue arrays were produced using a 2 mm diameter needle. Immunohistochemical studies were conducted, where the positivity was classified from 1 to 3 degrees and the extension was graded between 0 and 100%. A global score was obtained by multiplying both values. Statistical analysis of these findings was carried out using he SPSSv23; $p<0.05$ program.
Results: Positive immunoexpression was noted in almost 35% of colon adenocarcinoma samples for MUC5AC, 37% for C-MET and more than 95% for SOX-9. In comparison, 25% of their respective metastatic tumours showed positivity for MUC5AC, up to 70% for C-MET and 100% for SOX-9. Furthermore, a significant overexpression of MUC5AC in primary adenocarcinomas was found (26.77 vs 5.77; p=0,045), while a significant overexpression of C-MET (35.03 vs 15,44; p=0,07) and SOX-9 (284.76 vs 253.75; p=0,039) was observed in metastatic adenocarcinomas.
Conclusion: Significant differences for MUC5AC, C-MET and SOX-9 were found between primary colon adenocarcinomas and their respective liver metastasis.

E-PS-06-022
Atypical mycobacterial infection of the duodenum: a histological Whipple's disease mimic in a renal allograft recipient
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Background & Objective: Renal transplantation (RT) being the definitive approach for treatment of end-stage kidney disease; is nevertheless, fraught with perils, with infections being an important cause of morbidity and mortality post transplantation. Atypical mycobacterial lesions are infrequent in renal transplant recipients, but they can cause serious morbidity. Our aim is to demostrate and discuss the pathology of atypical mycobacterial infection of the duodenum resembling Whipple's disease – in a RT patient.
Method: A 70-year-old man, post cadaveric RT 5 years , presented with nausea, vomiting and diarrhea of a month's duration. The underlying cause of end-stage kidney disease was hypertension. Endoscopic examination revealed white irregular areas on the mucosa of second part of duodenum.
Results: The endoscopic biopsy consisted of 4 bits, measuring 0,2 cc in aggregate. Histology revealed massive infiltration of, periodic acid-Schiff positive macrophages in the lamina propria, resembling Whipple's disease macrophages. Ziehl-Neelsen staining demostrated acid resistant pink bacilli within the macrophages.
Conclusion: Atypical mycobacterial infection of duodenum has histology similar to Whipple's disease. The presence of PAS positive macrophages is a feature common between these two diseases. ZN staining is required for discrimination between the two, this despite PAS positivity. Immunocompromised patients are candidates for this infection, as was our patient. This illustrates that, if histology from from irregular, shaggy duodenal mucosal lesions reveals PAS highlighted macrophages - ZN staining and culture should be mandatory

E-PS-06-023
The value of the assessment of type III intestinal metaplasia for the risk stratification of the gastric cancer
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Background & Objective: The aim of our study was to analyze the prevalence of intestinal metaplasia subtypes in three different countries-Latvia, Kazakhstan and Russian Siberia. In addition, we aimed to assess the inter-observer agreement in reporting intestinal metaplasia subtypes between three GI pathologists.
Method: The patients from Latvia (n=1012), Kazakhstan (n=115) and Russian Siberia (n=525) were prospectively enrolled in the study. Altogether, five biopsy samples were obtained from each patient:two from the antrum, one from the incisura and two from the corpus. 4 microns-thick sections were stained with haematoxylin and eosin, alcian blue and high iron diamine-alcian blue for the subtyping of intestinal metaplasia.
Results: The prevalence of intestinal metaplasia in Latvia, Kazakhstan and Siberia population was found 21%, 32% and 29.5%, respectively. In Latvia the incomplete intestinal metaplasia was observed in 24% of cases (type II in 16.0% and type III in 8.0%). However, among subjects carrying metaplasia in Siberia, the incomplete intestinal metaplasia was present in 36.0% of cases (type II in 22.0% and type III in 12.0%), whereas in Kazakhstan incomplete intestinal metaplasia was present in 48.0% of cases (type II in 22.0% and type III in 26.0%). The inter-observer agreement for detecting type I, type II and type III intestinal metaplasia was 94%, 82% and 88%, respectively.
Conclusion: To conclude, the prevalence of type III intestinal metaplasia correlated with high incidence of gastric cancer in the corresponded country. The inter-observer agreement for detection of intestinal metaplasia subtypes was almost perfect between the pathologists. The intestinal metaplasia subtyping was important for the risk stratification of gastric cancer.

E-PS-06-024
Relation between VEGF expression and CD1a-positive dendritic cells in development of gastric cancer
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Background & Objective: Vascular endothelial growth factor (VEGF) is secreted from a variety of tumour cells of epithelial origin. In cancers VEGF has been investigated mainly in connection with tumour neoangiogenesis. Although the clinical significance of immature CD1a-positve dendritic cells (DCs) has been investigated in a variety of human cancers, few studies have focused on the distribution of these cells and determine the relationship with the other clinico-pathological data in gastric cancer. The aim of the study was to analyze the significance of CD1a+ DC and VEGF expression gastric cancer patients' development.
Method: We evaluated 50 gastric cancers for expression of VEGF and the presence of CD1a+DC using immunohistochemistry. The clinicopathological parameters were analyzed retrospectively.
Results: VEGF positive staining was observed in both membrane and cytoplasm of gastric cancer tumour cells, whereas weak positive staining was observed in the normal epithelium. VEGF over-expression was observed in 14 (28%) out of the 50 cases, whereas VEGF low- and non-expression was observed in 36 cases (72%). Expression of VEGF was significantly associated with the presence of distant metastases ($\chi2=3.937$, $p = 0.041$). In addition the low number of CD1a+DCs in tumour border was correlated with positive lymph node metastases ($\chi2=6,64$; p=0,036).
Conclusion: Our results suggest that tumour infiltration with CD1a+DCs may be of great importance in initiating the primary anti-tumour immune response and VEGF may play an important role in local recurrence and metastasis through induction of angiogenesis in gastric cancer.

E-PS-06-025
Microvillous inclusion disease (Davidson's Disease)
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Background & Objective: Microvillous inclusion disease (MID) is a rare autosomal recessive congenital enteropathy characterized by intractable secretory diarrhea. The goal was the in vitro and posthumous diagnosis MID.
Method: The diagnosis was carried out in two different-sex full-term children from the same family with the usage of morphological examination of the jejunum and molecular genetic expertise. Morphological research of the jejunum was performed using haematoxylin-eosin, PAS, Villin and CD10 staining.
Results: Full-term children from the first and second pregnancy. Since birth, sibs have had similar clinical disease manifestation: diarrhea, dehydration, abnormal loss of weight, intestinal paresis, increase of glucose-galactose malabsorption and protein-energy deficiency. Further development of bilateral destructive pneumonia which was the cause of the death of 6 months old sister, the brother at the age of 1month. Molecular genetic research: MYO5B (OMIM 251850). During the in vitro and posthumous examination of the jejunum atrophy of the villi, epithelium desquamation of the individual villi. The surface of enterocytes in uneven, in the apical departments the cytoplasm vacuolization. With Pas weak irregular staining of the brush border, mostly in apical enterocytes and Pas-positive reaction in the enterocytes cytoplasm. In enterocytes is determined Villin-positive intracytoplasmic microvesicles. The expression of CD 10 in enterocytes with the sharp shading of the brush border and intracellular accumulation in apical cells in determined.
Conclusion: MID diagnostic is based on a typical clinical symptoms, family medical history, morphological research of the jejunum biopsy with the usage of immunohistochemical methods. Decisive in the diagnosis the medical genetic expertise of the child and his parents.

E-PS-06-026
Serosal squamous metaplasia of the vermiform appendix: report of 6 cases
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Background & Objective: Squamous cell metaplasia (SCM) of the vermiform appendix serosa is rare. The clinical relevance resides in the differential diagnosis with other serosal lesions, benign or malignant. We aimed to report characteristics of these lesions in a series of 6 cases.
Method: Appendectomy specimens were selected as based on microscopy findings of cystic or solid foci of squamous cell metaplasia. Immunohistochemistries (IHC) for CK5/6, p63, CD138 and Bcl2 were performed. Morphological features were analysed with regard to clinical features.
Results: All cases showed cystic SCM (age ranging between 30-60 years, gender ratio 2:1 woman:men). The appendixes showed acute inflammation (5/6) or subacute (1/6). Peritonitis was diagnosed for 4 specimens, in 3 of which also at the SCM site. Solid SCM was detected in 2 of the cases. Cystic SCM sized between infra-millimetric and 3 mm. IHCs for CK5/6 and p63 were positive in the 3 cases with available lesions on the slides. IHCs were also positive for CD138 and Bcl2 (2 and 1 cases with available lesion on the slides, respectively).
Conclusion: Appendix serosal SCM, occurring in both women and men, may present as cystic or solid lesions, incidentally detected at microscopy examination. Acute appendicitis with peritonitis is more frequently encountered. Immunohistochemistries for CK5/6 and p63 confirm the diagnosis while those for CD138 and Bcl2 may give new insights for the histogenesis of these rare lesions in the appendix.

E-PS-06-027
Stromal inflammation in colorectal adenomas. Relevance for dysplasia and relationships to PTEN protein
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Background & Objective: Colorectal adenomas (CRA) are the most frequent precarcinomatous gastrointestinal lesions. The evaluation of dysplasia is made in an effort to differentiate the benign lesions from those prone to transform into carcinoma. We aimed to evaluate the relationships of stromal inflammation to dysplasia degree in CRAs.
Method: A series of 127 CRAs were analysed for baseline features (age, gender, size, architecture, dysplasia degree, presence of cystic glands) as well as for stroma-related features (amount of stromal component, presence of lymphocytic inflammation, of stromal/extracellular mucus). The Kendall's rank correlation test and logistic regression models (for dysplasia) were used for statistical analysis (MedCalc, Belgium).
Results: Stromal inflammation correlated to low grade dysplasia ($p<0.01$/tau=-0.215) as well as to the extent of stromal component ($p=0.02$/tau=0.132) and to the presence of stromal mucus ($p=0.02$/tau=0.143). On logistic regression analysis, stromal inflammation predicted low grade dysplasia independently of age, gender and adenoma size, however with a decreased statistical significance than size ($p=0.02$ versus <0.01) Stromal inflammation also correlated to presence of cystic adenomatous glands ($p<0.01$/tau=0.201) as well as to epithelial Ki67 ($p=0.04$/tau=0.184) and to nuclear PTEN ($p=0.02$/tau=0.176). Stromal mucus correlated to adenoma size ($p<0.01$/tau=0.197) and to presence of cystic glands ($p<0.01$/tau=0.201).
Conclusion: The results of this study indicating that stromal inflammation correlated to low grade dysplasia as well to degenerative lesions such as stromal/extracellular mucus suggest a dual role, both in tumour immunity (neoplasia immunoprotection) and in reactive change to degeneration.

E-PS-06-028
Metastatic clear cell renal cell carcinoma to the stomach: differential diagnosis of poorly differentiated gastric adenocarcinomas
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Background & Objective: The stomach is an unusual site of metastasis. Clinical findings are usually unspecific, and metastatic tumours to the stomach may resemble primary gastric adenocarcinomas in gross and microscopic findings.
Method: Herein we report the differential diagnosis of a poorly differentiated adenocarcinoma in the stomach.
Results: A 72-year old male patient with history of clear cell renal cell carcinoma (CCRC) was submitted to endoscopic biopsy of an elevated lesion in the gastric corpus. Microscopy demonstrated an ulcerated and infiltrative lesion constituted of poorly cohesive cells with abundant clear cytoplasm and nuclear atypia. The patient was diagnosed with an invasive adenocarcinoma and the diagnostic hypothesis of poorly cohesive signet ring carcinoma was investigated. Immunohistochemical studies showed diffuse positivity for PAX8 and pan-cytokeratin (AE1/AE3). Therefore, considering the histological characteristics of this neoplasm as well as clinical data, the patient was diagnosed with RCC metastatic to the stomach.
Conclusion: Metastatic tumours to the stomach are uncommon, with an estimated prevalence of up to 2.6% of all gastric neoplasms. Of note, only 37 cases of metastatic CCRC have been reported so far. Clinical findings are unspecific, but the presence of a mural nodule resembling a submucosal tumour with a central depression (known as "volcano-like lesion") may be suggestive of secondary disease. Microscopically, the neoplasm is usually centered in the submucosa/muscularis propria. Nevertheless, these findings are not constant. Therefore, a high degree of suspicion is necessary for the diagnosis of metastasis to the stomach, which represents a diagnostic pitfall in the evaluation of poorly differentiated gastric adenocarcinomas.

E-PS-06-029

Folate genes expression is downregulated in colorectal adenocarcinoma

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Background & Objective: Folate metabolism influences the synthesis of purines and the methylation level of the global DNA. These processes are described to be usually associated with Colorectal Adenocarcinoma (CRAC) development risk. This study aimed to determine MTHFR, MTR and MTRR genes expression levels in CRAC biopsies.
Method: A series of 119 CRAC biopsies of well-differentiated Adenocarcinomas, was studied to determinate expression levels of MTHFR, MTR and MTRR genes by Real Time PCR Sybergreen based.
Results: It was verified that MTHFR, MTR and MTRR genes were downregulated in tumoural cDNA, with a mean 10-fold decrease among tumoural tissues ($p<0.005$). MTHFR presented the lowest expression levels, with a mean 15-fold decrease, while MTRR only showed a mean 5-fold decrease.
Conclusion: Our results corroborate the potential role of folate metabolism in CRAC development/progression and emphasise the potential role of MTHFR, MTR and MTRR enzymes in CRAC for early-staging. Furthermore, downregulation of folate metabolism genes might be important in colon and rectum tumour cells proliferation capacity.

E-PS-06-030

Antral/pyloric type hyperplastic polyp with prominent myoglandular features: a distinct subtype of gastric polyps

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Background & Objective: Some of gastric protrusions which are readily identified as "polyps" endoscopically cannot be easily or reproducibly classified histologically. Here we describe a gastric polyp characterized by "almost-normal appearing mucosa with antral/pyloric type glandular hyperplasia and thickened, irregular muscularis mucosa".
Method: We analyzed 54 polipectomy samples of 28 cases.
Results: All polyps were located in antrum, were non-pedunculated and dome-shaped, with a mean diameter of 1.1±0.62 cm (Range: 0.5-3.5 cm). The mean age at diagnosis was 59±14 years-old (Range: 31-80 y.o). Female/male ratio was 1.33. The most common and "diagnostic" findings were marked antral/pyloric type glandular hyperplasia (100%), thick and irregular muscularis mucosa (100%) and mild to prominent eosinophilic infiltration in 38%. Inflammation was absent (29%) or mild (64.3%). Although larger polyps showed superficial erosion and inflammation, no *Helicobacter pylori* colonization was observed. The polyps were mostly solitary (53.6%). "Hyperplastic" or "prolapse polyp-like polyps" were observed either concominantly or subsequently in 25% cases during 10 years of follow-up.
Conclusion: "Antral/pyloric type hyperplastic polyp with myoglandular features" is divergent from so-called "mucosal prolapse polyp" by lack of clinical prolapsus, thick arborizing smooth muscle bundles or large vessels at the polyp base or from "polypoid focal foveolar hyperplasia" which shows more pronounced foveolar elongation and from "typical hyperplastic polyp" as it lacks branching foveolar/cystic glandular changes and edematous inflammatory stroma. It appears to be a distinct lesion, but an etiological link to hyperplastic or prolapse-polyp should also be considered.

E-PS-06-031

The role of neurogenesis in colorectal cancer, morphometric comparison of neural densities in normal and tumoural tissue

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Background & Objective: Perineural invasion (PNI) is a well-known prognostic factor for colorectal cancer (CRC), however whether the tumour itself induce a "neo-neural" tissue development or not, is not studied comprehensively. We evaluated the correlation between neurogenesis and CRC prognostic factors.
Method: Representative tumoural and non-tumoural areas of 80 cases diagnosed between 2008-2010 years were stained with S100 and photographed. The largest nerve diameter, the number of nerve sections per unit area and nerve density were measured morphometrically (Axio-Vision LE, Rel.4.8) and statistically compared with nonparametric tests.
Results: Tumour stage (pT) was T3-T4 in 95% and pN was N0-N1 in %78.8. PNI was found in 38.8% and 39% died in 5 years' period. PNI was associated with pT ($p=0.017$), pN ($p=0.008$), lymphovascular invasion ($p=0.000$), satellite nodules ($p=0.025$), tumour budding ($p=0.005$), dirty necrosis ($p=0.009$) and survival ($p=0.018$). Largest nerve diameter was 2.4 fold (mean:123.45 μm±109.85, range:22-799 μm vs 52.06 μm±24.61, range:15-156 μm; $p<0.001$), the number of nerve sections per one unit area was 1.3 fold (6.36±3.32, range: 2-17 vs 4.84±2.55, range: 1-12; $p=0.001$) and nerve density was 6.1 fold (104948.7 μm2/x4 HPF±212497, range: 1190-1799254 vs 17153 ±23593 μm2/x4 HPF, range: 819-190771; $p<0.001$) higher in tumoural areas compared with nontumoural areas. Increased nerve diameter and nerve density was correlated with shorter overall survival ($p=0.023$ and $p=0.005$, respectively).
Conclusion: Our results show that neural tissue is more intense in tumoural areas than normal bowel wall therefore "tumour-related neurogenesis" can be a potential prognostic factor or therapeutic target in CRC. However, further molecular studies are needed to elucidate tumourogenesis-neurogenesis interaction.

E-PS-06-032

Immunohistochemical assessment of CD30+ lymphocytes in the intestinal mucosa facilitates diagnosis of paediatric ulcerative colitis

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Background & Objective: Diagnosis of paediatric inflammatory bowel diseases (IBD) remains a challenging issue. In the inflammatory infiltrate, certain T helper lymphocyte subpopulations in IBD may express antigen CD30. We aimed at the evaluation of the value of immunohistochemical assessment of CD30+ lymphocytes in the intestinal mucosa in differential diagnosis between paediatric Crohn's disease (CD) and ulcerative colitis (UC) and its utility as a predictor of future differentiation in patients with IBD unclassified (IBDU).
Method: 74 treatment naive paediatric patients with IBD (33 CD, 30 UC and 11 IBDU) were enrolled into the study. Biopsy samples from six different standardized regions were immunohistochemically stained with anti-CD30 antibody and number of positive cells was quantified.
Results: Significant differences between CD and UC were found when compared total counts of CD30+ cells in median numbers, mean values and maximal numbers and also for separate counts in terminal ileum, transverse colon, descending colon and rectum. The most profound difference was shown for total median values of CD30+ cells and for the values in rectal localization. The difference was independent on the intensity of inflammation. A cut-off value of 2.5 CD30+ cells with sensitivity 83% and specificity 90% was found for the rectal localization. There was no difference between patients with CD and IBDU, but a marked difference between UC and IBDU patients was revealed.
Conclusion: Histopathological assessment of biopsy with rectal CD30+ count represents a reliable and simple method that could help in differential diagnosis among IBD subtypes in children with IBD.

E-PS-06-033

Mucosal Schwann cell hamartomas do occur the gastric mucosa – report of two cases mimicking fundic gland polyps

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Background & Objective: Mucosal Schwann cell hamartomas (MSCHs) is a recently characterized benign spindle cell lesion of the colon and rectum. There is only one report of MSCH in the stomach (antrum). We present herein the first reports of MSCH occurring in fundic mucosa as lesions that endoscopic mimicked an usual fundic gland polyp.
Method: Case reports
Results: Case 1. A 56-year old woman sought medical attention due to epigastric pain. The patient underwent antral and corporal biopsies which showed chronic active gastritis associated with *Helicobacter pylori* infection. A small polypoid lesion in fundic mucosa was removed with endoscopic impression of fundic gland polypoid. Case 2. A 66 year-oldman sought medical attention due to epigastric pain. The patient underwent antral and corporal biopsies which showed mild non-active gastritis without *Helicobacter pylori* infection. Small polypoid lesions in fundic mucosa were seen and one was removed with endoscopic impression of fundic gland polypoid. At microscopy, both lesions were entirely intramucosal, ill-defined spindle cell aggregations suggesting a fascicular growth pattern. No nuclear atypia was seen. The lesions measured 0.6 mm in case 1 and 2.2 mm in case 2. In case 2, the lesions permeated gastric glands. Both lesions were strongly and diffusely positive for S100 and negative for all other tested markers (EMA, CD117, CD34 and neuroendocrine markers).
Conclusion: MSCHs do occur in gastric mucosa. Awareness of this lesion is relevant to avoid the diagnosis of other benign spindled cell lesions that are associated with familial syndromes.

E-PS-06-035

Clinicopathological evaluation of the lymph node involvement frequency in patients with oesophageal squamous cell carcinoma and their survival rate

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Background & Objective: Oesophageal cancer is a common cancer of the gastrointestinal tract. In oesophagectomy operation in recent years, lymph nodes around the oesophagus are removed. All cases of oesophagectomy in a ten-year study were investigated.
Method: This study is a retrospective analytic cross-sectional study. The study population consist of 170 patients with oesophageal cancer who had oesophagectomy and referred to pathological center of Yazd during the years 2006-2016. the required information included: age, sex, anatomical location of the involvement, the distance between the tumour and the surgical incision, the number of post-operative relapses, type of treatment (chemotherapy, radiotherapy) were recorded. The collected data were entered into SPSS version 18 software and were analyzed by statistical tests.
Results: The result showed that the mean age of participants was 60.30 ± 14.60 years. The mean survival time was 28.03 ± 2.64 months and the mean relapse period was 34.40 ± 3.62. There was a significant relationship between the mean survival time according to the number of dissected lymph nodes and age, and duration of recurrence in patients according to their age (P-value < 0.05). Also, the result of Cox model showed that two variables of age and number of lymph nodes were effective on survival risk and age variable was effective on the risk of recurrence.
Conclusion: According to the results, with increasing the number of removed lymph nodes and age increasing, the survival rate decreases in patients with oesophageal cancer that has oesophagectomy operation.
Keywords: oesophagectomy, lymph nodes, survival rate, recurrence rate

E-PS-06-036

Unsuspected synchronous mucinous adenocarcinoma in transverse colon and low rectum arising from longstanding severe ulcerative colitis

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Background & Objective: Active inflammatory bowel disease often renders endoscopic and radiological assessments challenging in the context of suspicious malignancy.
Method: A 60-year old gentleman with 24-year history of poorly controlled ulcerative colitis, presented with rectal bleeding. Sigmoidoscopy showed a tumour at the dentate line and biopsies showed an adenocarcinoma arising from surface high and low-grade dysplasia. Pelvic MRI showed a 4.5cm polypoid tumour, above the anal verge (cT1sm1/sm2N0M0, EMVI-) but no other tumours identified in the colon. Further biopsies from the region with abnormal MRI signals showed active chronic proctitis only. He went to have a panproctocolectomy.
Results: Macroscopic assessment revealed an ulcerating tumour in the transverse colon merging with the diffuse inflammatory appearance, alongside the rectal tumour. Both were mucinous adenocarcinomata. The unsuspected tumour was diagnosed at a higher stage (pT3N0, EMVI+) than the distal tumour (pT2N0, EMVI-). Mismatch repair immunohistochemistry is normal.
Conclusion: This case highlights the diagnostic complexity in such scenarios where endoscopic features are subtle and imaging findings non-specific. This also raises the question whether the incidence of early stage adenocarcinoma is underestimated in this patient population.

E-PS-06-037

Comparison of immunohistochemical mismatch repair (MMR) protein expression in colon adenocarcinomas with clinicopathologic features

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Background & Objective: Microsatellit instability pathway caused by loss in "Mismatch repair genes (MMR)" is responsible of Lynch Syndrome related tumours and 10-15% of sporadical colorectal cancers. Although MSI-test is regarded as the golden standart for detection of "Lynch Syndrome-related tumours", there are increasing evidence on similar analitic sensitivity of immunhistochemical evaluation.
Method: We retrospectively evaluated 1002 colorectal tumours diagnosed between 2002-2011 years for loss of MMR protein (MLH1, PMS2, MSH2, MSH6) immunhistochemically. The results were correlated with clinicopathological features and MSI-H related histological parameters.
Results: MMR protein expression loss was observed in 9.8% of the cases as well as mucinous (10.5%), medullary differentiation(5%), tumour invading lymphocytes(10.4%), Crohn-like lymphocytic reaction(38.4%). MLH1-PMS2 loss (%53,2) was the most common loss followed by MSH2-MSH6(31,6%), isolated PMS2(12%) and isolated MSH6(2%) losses. MMR loss was more frequent under 50 years-old(p<0,0001), in right colon tumours(p<0,0001), poorly differentiated tumours(p<0,0001) and tumours with tumour infiltrating lymphocytes(p<0,0001), mucinous(p=0,001) and medullary components(p<0,0001) and less frequent in tumours with tumour budding(p=0,001) and dirty necrosis(p<0,0001). The 5 years-survival rate was 55.7%. No correlation was found with MMR loss and survival.
Conclusion: MMR protein loss was observed in 9.8% of the cases with distinct clinicopathological features. The results were consistant with previous studies. Immunhistochemical evaluation appeares to valuable as a first screening method for selection of cases for MSI-test.

E-PS-06-038

Lymphoid neoplasias of the gastrointestinal tract and background of gastrointestinal inflammatory pathology. Experience of a single institution's surgery department

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Background & Objective: Study the antecedent of inflammatory pathology in the B and T lymphomas of the gastrointestinal tract (GIL) detected in our pathology department in the last 10 years to establish a relationship.
Method: We reviewed the history of endoscopic biopsies with previous gastrointestinal specific (SIP) and nonspecific (NIP) inflammatory pathology in each patient.
Results: 18 cases in Stomach. 11 were high-grade B-cell lymphomas (HGBCL), 5 of MALT lymphomas, 1 of Burkitt's lymphoma (BL) and 1 of peripheral T-cell lymphoma (PTL). In HGBCL, the SIP was found in 4 cases, 2 with H. Pilory (HP) and 2 with inflammatory bowel disease (IBD). We found with NIP, 7cases; 3 of follicular lymphoid hyperplasia (FLH) and 4 with nonspecific ulcer (NU). MALT, 1 with SIP (H.P.) and 4 with NIP (2 FLH and 2 NU). In small intestine, 4 cases with a history of PI were identified. 1 case of HGBCL with NIP (NU). A chronic high-grade lymphoproliferative process (suggestive NK) with SIP (IBD). A T lymphoma associated with enteropathy with Celiac disease. In Colon, 7 cases of GIL. 2 of HGBCL, 1 with microscopic colitis (MC) as a SIP and 1 with chronic non-specific colitis (CNC) as NIP. 1 case of BL with a SIP of MC. 1 case of PTL with SIP of ischemic colitis and 1 case of mantle lymphoma, with a SIP of chronic atrophic gastritis.
Conclusion: The most frequent location was the stomach and the most frequent was HGBCL. 50% had previous inflammatory pathology. 30.76% had a history of NIP and FLH was the most frequent. HP and IBD were in SIP (21.15%).

E-PS-06-040

Significance of sex hormones in cancerogenesis of signet ring cell gastric carcinoma

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Background & Objective: Comparative analysis of Estrogen and Progesteron expression in gastric mucosa (GM) of the pa-tients with signet ring cell carcinoma (SRC) depending on sex and age.
Method: 486 GM specimens of 43 patients with gastric carcinoma of both intestinal and diffuse types aged 26-87 years were examined histologically and immunohistochemically (IHC). IHC profile consisting of estrogen (ERs) and progesterone (PR) receptors was investigated in tumour, perifocal zone and intact GM.
Results: Groups of patients were formed according to the histological type of tumour. Group I – pure SRC: n=12 (males 4, females 8), Group II – poorly differentiated adenocarcinoma with SRC: n=15 (males 7, females 8). Group III – adenocarcinoma of various tissue differentiation degree: n=16 (males 11, fe-males 5). In males with SCR increased activity of PR (>3 times) and ERs (>3.5 times) was detected. In females activity of ERs was increased more significant (>4 times) but PR – slightly less (<3 times). The average age of women was 45±3, males 64±4. Changes in hormone activity in other groups were not so indicative.
Conclusion: SCR is a special kind of tumour which characterized by significant changes in ERs and PR expres-sion in GM, depending on sex and age. It more commonly develops either in females of 35-50 years of age or in older man (60-70).

E-PS-06-041

Clinicopathological evaluation of microscopic colitis in patients referring to a hospital from 2006-2016

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Background & Objective: Microscopic colitis is a chronic inflammatory disease of the intestine, determined by bloody diarrhea and specific pathologic characteristics. The incidence of this disease reported 6.2 in every 100000 annually and is more common amongst women in comparison with men. Statistics show that the incidence of microscopic colitis has increased in the past decade. This disease is not well detectable through clinical investigation, and most people that are active in the health care field, have few knowledge of the etiology and pathophysiology of this disease. Due to sign and symptom similarities between microscopic colitis and inflammatory bowel disease, the diagnose of this disease is important.
Method: This is retrospective descriptive study conducted amongst patients with microscopic colitis where the subjects were chosen through sampling census from subjects with microscopic colitis diagnosed from 2006-2016 in Yazd hospitals. A check list was used in order to collect cognitivist, clinical and pathological data. The collected data were entered into SPSS version 19 software and were analyzed by statistical test.
Results: Out of 104 samples under investigation 71 were male and 33 cases were female. The most common clinical symptom included non-bloody diarrhea (88.5%). Also, the most affected patients were in the age group of 30-50 years old.
Conclusion: According to the result it seems the prevalence of microscopic colitis is greater amongst males than females, but the effects of gender on prevalence is still questionable.

E-PS-06-042

Anorectal melanoma: report of two cases

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Background & Objective: Melanomas are malignant tumours that develop from the pigment system. The anorectal localization is characterized by its rarity, it represents 1,5% of all melanomas and less than of 1 % of anorectal cancers, the lack of standards for the management and its poor prognosis. Our purpose was to describe cinical, pathological and immunohistichemical features of anorectal melanoma.
Method: We report two cases of malignant anorectal melanoma which were diagnosed in our pathology department of the university hospital of Monastir.
Results: Both patients were female aged 56 and 75 years old. Clinical symptoms were dominated by rectal bleeding and both of them underwent a rectoscopy which objectified the presence of a budding tumour. Biopsies were done in each rectoscopy and were sent to our department of pathology. The two biopsies showed in common the presence of a malignant tumour proliferation made of non-cohesive cells of variant size with eosinophilic cytoplasm. The nuclei had a fine chromatin and prominent nucleoli. Both tumours showed a brown pigment in the cytoplasm of tumour cells or macrophages. In the immunohistochemical study, HMB45, Melan A and PS100 were strongly positive. Extension staging showed an advanced metastasis in the liver in the two cases. The first patient refused the treatment and the second one was lost to follow up.
Conclusion: In this study, we focused on a rare localization of melanoma characterized by its poor prognosis and high metastatic potential showing the importance of an early diagnosis based on histology and confirmed by immunohistochemistry in order to start an adequate treatment which still uncodified.

E-PS-06-043

Adenosquamous carcinoma of the colon: a case report

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Background & Objective: Adenosquamous carcinoma is a rare colorectal tumour with both glandular and squamous histologic components. To the best of our knowledge only few cases have been reported in the literature. We report a new case of this rare histologic subtype.
Method: We report a case of adenosquamous carcinoma of the right colon diagnosed in our pathology department.
Results: A 46-year-old female was hospitalized for large bowel obstruction syndrome. Computed tomography (CT) showed irregular process tissue of the right colic angle, responsible for an occlusive syndrome with distension of the right colon, the appendix and the terminal ileum. The patient underwent in emergency right hemicolectomy with D2 lymphadenectomy. Histopathological examination revealed mixed adenocarcinoma and squamous cell carcinoma. Finally, the mass was diagnosed as an adenosquamous carcinoma with lymph node metastasis (T3 N2a M0). Adjuvant chemotherapy was prescribed. There has been no evidence of tumour recurrence during 18 months since the chemotherapy treatment completion.
Conclusion: Adenosquamous carcinoma has been reported to be rare (0.06 of all malignant colorectal tumours) and to possess a highly metastatic potential. It consists of both squamous cells and glandular cell components. The clinical presentation, gross findings and treatment of this tumour is similar to those of adenocarcinoma of the colon but has a more aggressive clinical course and a poorer prognosis.

E-PS-06-044
Our clinical and histopathological findings of gastrointestinal stromal tumours (GISTs): 10-year experience
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Background & Objective: The aim of this study is to report our case series of Gastrointestinal Stromal Tumours (GISTs) and revise the clinical and histological findings for ten years.
Method: A retrospective search was made to collect all cases diagnosed for GISTs for last 10 years,85 cases of GISTs identified. The clinial findings such as age, sex, tumour localization and size; histopathological findings such as pattern, presence of necrosis, mitotic index, C-kit(CD117) expression as well as expression CD34 and S100 ; Ki67 proliferation index, distant metastasis status were evaluated.
Results: The mean age at diagnosis was 58 (range34-90), while the male to female ratio was 0,93(41males/44 female). The tumour was located in the stomach in 51 patients (60 %), small intestine in 27 patients(31.7 %), colon in 3 patients(3.52 %), omentum in 1 patient(1.17%) , pelvis in 1 patient(1.17 %), intraabdominal in 1 patient(1.17%) and liver in 1 patient(1.17%). 4 of cases had multiple tumours (4.7 %) and 5 patient had distant metastasis (4.70%). The mean tumour size was 6.32cm(range 0,1 cm- 28 cm). Expression ratio of C-kit (CD117) 96%, CD34 83.52% and S-100 10.58% was observed. The mean mitotic index was 13/50BBA and Ki-67 proliferation index was %5.3.
Conclusion: Although rare, GISTs are the most common mesenchymal tumours of the gastrointestinal (GI) tract. The prognosis of these tumours is unpredictable. Prognostic parameters such as risk grup, cell type, cellularity, immunstain score (intensity and diffuseness) should be also included in the pathology reports.

E-PS-06-045
IL-6/STAT3+ immune cells in the tumour microenvironment predicted cancer progression
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Background & Objective: The IL-6/STAT3 signaling in innate immune cells is required for the immunosuppressive and tumour-promoting effects of tumour-associated macrophages and of some other inflammatory cells (ICs).
Method: Surgical biopsy samples from 95 patients with colorectal cancer (CRC) (n=48 males, n=47 females) at the age of 66.43±1.017 were investigated immunohistochemically for IL-6 and STAT3. MSI testing was done, where 62 patients had MSI and 33-MSS. The patients were followed up until March 2018.
Results: The number of IL-6+ ICs in tumour stroma was statistically significantly higher in MSS patients as compared to MSI patients (p=0.033). The number of STAT3+ ICs in the invasive margin (IM) was higher in I+II tumour stage as compared to patients in III+IV tumour stage (p=0.006). The number of IL-6+ ICs in IM and tumour stroma was higher in patients with I+II as compared to III+IV tumour stage. There is a tendency for the patients with III+IV tumour stage having higher STAT3+ ICs infiltration they had worse survival ($\chi 2=2.92$, p=0.087).
Conclusion: The presence of IL-6+ ICs in the tumour stroma and of STAT3+ ICs in IM was higher in MSS patients and therefore could explain the worse prognosis and tumour promoting activities of the immune cells. Higher number of STAT3+ ICs in advanced tumour stages correlated with shorter survival and thus support ed the thesis of immunosuppression in tumour microenvironment following activation of prooncogenic genes.

E-PS-06-046
Significance of the immunohistochemical marker Muc 5AC in diagnostics of sessile serrated adenoma of the colon with BRAF mutation
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Background & Objective: It is known that sessile adenoma (SSA) have increased production of mucins, one of which is Muc 5AC, while in other adenomas of the colon it is practically not expressed. In the presence of a mutation of the BRAF gene, the expression of Muc 5AC in SSA is enhanced. Thus, the aim of our study was to perform a comparative evaluation of the expression of Muc 5AC in the SSA group with and without mutation of the BRAF gene.
Method: Twenty-six patients from 31 to 80 years old (mean age 58 years) were examined. Histological sections were stained with haematoxylin and eosin, and PAS reaction with alcin blue. Immunohistochemical staining was carried out with the help of immunostimers Ventana Beuch Mark Ultra (USA). Determination of mutations in the BRAF gene (p. V600E) was carried out by real-time PCR.
Results: In the genetic study of SSA, mutation of the BRAF gene was detected in 53.8%, in 46.2% - mutation was not detected. In the SSA group with mutation, in all cases, pronounced cytoplasmic expression of antibodies to Muc 5AC along the entire length of the crypt was detected. In the group without mutation of the BRAF gene, a weak and focal expression was found in 69.2%. In 30,8% - expression of Muc 5AC was absent.
Conclusion: Thus, we believe that Muc 5AC can be used as a marker of SSA with the presence of mutations of the BRAF gene and the potential risk of malignant SSA.

E-PS-06-047
Comparison between the endoscopic and pathologic diagnoses in colon carcinoma
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Background & Objective: Colonoscopy coupled with biopsy is currently the ”gold standard” in diagnosis algorithm of colonic neoplasia. The study compared the pathological assessment of colorectal carcinomas (CC) by endoscopy coupled with biopsy and then on surgical resection sample (SRS).

Method: The study group included 104 CCs (78 with monophasic/monomorphic and 26 with biphasic histological aspect) with endoscopy and biopsy followed by surgery and pathologic assessment of SRSs. The assessed parameters were: Tumour site on colon segments (TS), tumour extension on the colon circumference (TCE), tumour dimensions (TD) and tumour gross aspect (TGA) then tumour histology (THP) and grading (TGd). Statistical correlations were assessed with $\chi 2$ test.
Results: Endoscopic assessment (EA) of TS and TGE had a high sensitivity (S) ("p"<0.0001). S was decreasing for EA of TGA and TD, with a discordant diagnosis of 25% and 29% respectively but with "p"<0.0005. The EA of THP and TG had high S in monomorphic tumours. THP was underrated on biopsies in biphasic tumours (deeper tumour areas being less differentiated) and TGd was correctly assessed on biopsies only in superficial tumours. However, in both situations, "p" was <0.0005.
Conclusion: The preoperative morphological assessment of colorectal tumours has correlated with postoperative examination, with an absolute concordance higher than 70% for all assessed parameters. However, the histopathological diagnosis on preoperative biopsies is only indicative, the final verdict being that on SRSs.

E-PS-06-049
Development of lymph node pathology dissection after laparoscopic gastrectomy

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Background & Objective: The lymphatic system of the stomach is a multidirectional and complex network composed of lymphatic nodes and vessels. Lymph node metastasis is the most important prognostic factor in curable gastric cancer and lymph node dissection is one of the main research in gastric cancer.
Method: A total of 70 patients who underwent standardized laparoscopic D2 lymph node dissection for advanced gastric cancer between January 2017 and March 2018 were included in the study. Characteristics of the patients: age (mean) 61 years; sex (M:F) 1:1,1. Numbers of detection LNs mean 30, min 9, max 67.
Results: According to the site of the tumour (upper, medium and low), lymph node metastases are more frequently observed in specific stations. ACs of the U/3 are associated to lymph node metastases in 20% of cases. ACs of the m/3 of the stomach in 11% and ACS of the l/3 – 14%. We have founded correlation between location (long axis) and pN1 (r=0,33 p=0,0008). In ACs U/3 - nodes of station 1, 2 and 4sa are more frequently involved in metastasis. In ACs M/3 - LN stations more frequently involved are 3, 4d and 4sb and 6. In ACs L/3 5, 4d and 4sb and 6. In most cases, regardless of the location of the tumour, another 7 and 9 groups of LN were affected.
Conclusion: For the gross dissection of lymph nodes, it is important to find the correct anatomical plane. The knowledge of the lymph node spread in gastric cancer is crucial to make a correct pathology gross dissection.

E-PS-06-051
PPI induced antral G-cell hyperplasia: a case report

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Background & Objective: Antral G-cell hyperplasia or pseudo-Zollinger Ellison Syndrome is a rare entity characterized by a marked hypergastrinaemia. It is associated with increase in the number of G cells, poor response to secretin stimulation test and absence of gastrinoma in the pancreas or duodenum.
Method: This is the case of a 62 years old woman, presented with intensive nausea, vomiting and weight loss, who was treated with proton pump inhibitors. Antral gastric mucosa biopsies were obtained.
Results: Histological evaluation of the tissue samples revealed focal linear and micronodular hyperplasia of endocrine cells in the gastric pyloric mucosa. Moderate chronic gastritis caused by *Helicobacter pylori* was also observed. Substantial mucosal atrophy or intestinal metaplasia were not observed. The endocrine cells were highlighted by immunostains for chromogranin and synaptophysin.
Conclusion: Any condition that lowers gastric acid concentrations may cause G-cell hyperplasia, including extensive multifocal atrophic gastritis, pernicious anaemia, vagotomy and prolonged treatment with proton pump inhibitors (PPIs). Occasionally, long standing G-cell hyperplasia progresses to multiple small micronodular clusters that have the potential to give rise to G-cell tumours (G-cell NETs). More commonly, it can lead to the development of ECL hyperplasia, which progresses further to the development of ECL micronests and eventually carcinoid tumours. Nevertheless, studies have demonstrated that G-cell hyperplasia and its subsequent hypergastrinaemia resulting from PPIs use is not associated with the development of gastric carcinoids in humans. This suggests that, although hypergastrinaemia is an essential prerequisite for the development of carcinoid tumours, it on its own is not sufficient for tumour formation.

E-PS-06-053
Precancerous lesions and carcinoma of the stomach in endoscopic submucosal dissection specimens

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Background & Objective: Endoscopic submucosal dissection (ESD) is effective method of diagnosis and treatment of patients with precancerous lesions and gastric tumours. The present study aimed to evaluate clinicopathological features and histological appearances of ESD stomach specimens.
Method: The study was performed on gastric samples of 22 patients after ESD in Kaliningrad with pathology of the stomach: 16 (72,7%) - with epithelial lesions, 6 (27,3%) – with nonepithelial pathology. 16 samples with epithelial lesions have been studied to evaluate clinicopathological features and morphological peculiarities using histological methods (H&E), immunohistochemistry also was applied in some cases (CD3, CD79a, Ki-67).
Results: 16 patients (7 men, 9 women)) with epithelial gastric lesions aged 51 years to 77 years. Pathology processes location: 1) cardia - 12,5%; 2) body – 43,8%; 3) antrum - 25,1%; 4) pylorus -18,6%. Epithelial gastric pathology (cases): 1) early gastric cancer (8); 2) other diseases and comorbidities - tubular adenoma (2), hyperplastic polyp (2), chronic gastritis without atrophy (2), chronic gastritis with atrophy (5); 3) background processes and precancerous lesions - intestinal metaplasia (3), dysplasiagrade II-III (7). Immunohistochemistry (CD3, CD79a, Ki-67) was useful for visualization of chronic inflammation and epithelial dysplasia.
Conclusion: Our findings confirms the high possibilities of ESD with morphology and immunohistochemistry examination for diagnosis of precancerous lesions and gastric tumours.

E-PS-06-054
Low grade and high grade neuroendocrine tumour with small and large cell features

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Background & Objective: Gastroenteropancreatic neuroendocrine (NE) neoplasms (GEP-NENs) have a broad range of morphology, from well differentiated NE tumours to poorly differentiated NE carcinomas (NECs). NEC of the stomach is rare and accounts for 1.5 % of all gastric cancers. Here, we report a NEC case, that has well differentiated NET areas.
Method: In a 58 years old male, PET scan displayed a 48x22 mm hipermetabolic lesion localized in cardia. Upper endoscopy revealed a large ulserovegetan mass with a biopsy diagnosis of NEC. Total gastrectomy and liver metastasectomy was performed. In gross examination,

there was a 7,5x5x3 cm mass in the proximal stomach. Morphologically, there were patternless solid areas composed of large and small cells as well as areas with trabecular/acinar pattern formed by monomorphic, regularly arranged cells with fine chromatin.
Results: Based on the 2010 WHO criteria, GEP-NENs were classified as NECs when the mitotic count is > 20/10 HPF and/or a Ki-67 index > 20%. Recent data suggested that NECs with well differentiated tumour morphology seems to have more favorable prognosis, leading to a new classification (2017). Accordingly, NE tumours with high Ki67 index showing organoid pattern is now classified as well differentiated NET, grade 3. There is currenty a debate as to whether these are two different entities, with different carcinogenetic pathways and cells of origin.
Conclusion: Current case describes an exceptional gastric NEC, with areas of well differentiated NET morphology, showing us that these entities may share same carcinogenetic pathways. Further molecular and clinical studies are needed to establish criteria to subtype NECs.

E-PS-06-055
A case report of clear cell sarcoma–like tumour of the gastrointestinal tract with liver and cutaneous metastases
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Background & Objective: Clear cell sarcoma-like tumour of the gastrointestinal tract (CCSLTGT) is a very rare and mesenchymal neoplasm arising within the wall of the small bowel, stomach, or large bowel, predominantly in young adults.
Method: A 44-year-old man with a history of CCSLTGT of jejunum on follow up presented with nodules in liver and subcutaneous tissue 4 years after jejenum resection.
Results: Histopathology of liver and subcutaneous nodules showed an epithelioid neoplasm which was diffusely infiltrating the stroma in sheets and nests. Usually the tumour consists of fascicles of small rounded cells which were separated by fibrous septa. The tumour cells had eosinophilic or clear cytoplasm and vesicular nuclei with prominent nucleoli. The immunohistochemical profile of the tumour was positive for S100, SOX10 and vimentin, focally positive for EMA and negative for PANCK, CD117, DOG1, HMB45, MART-1, chromogranin-A, synaptophysin. The microscopic appearance and immunohistochemical profile of the liver and cutaneous nodules were consistent with CCSLTGT metastases.
Conclusion: CCSLTGT is a rare malignant neoplasm. The diagnosis based on S100 and SOX10 protein positivity, the absence of melanocytic differentiation and it is associated with EWSR1-CREB1 gene fusion. CCSLTGT typically shows highly aggressive behavior. Lymph nodes and liver are the most common metastatic sites. Intraperitoneal spread, mediastinal lymph node and lung metastasis have been reported in a few cases. Our case is the first case metastasing to the subcutaneus tissue.

E-PS-06-056
An uncommon colonic tumour
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Background & Objective: adenosquamous carcinoma (ASC) account for less than 0.2% of colorectal malignancies. Histologically, it is an exceedingly rare colorectal neoplasm, characterized by both glandular and squamous differentiation. The symptomatic manifestations of ASC are much like those of colon adenocarcinomas. Coexistence of squamous carcinomatous components in carcinoma of the colon usually indicates a poorer prognosis than adenocarcinoma alone
Method: Here, we present the case of a 50-year-old female, who complained of abdominal pain and weight loss over a 3-month period of time. Biopsies from a colonoscopy ultimately revealed that this patient's colon cancer consisted with an adenocarcinoma. A left colectomy was performed.
Results: pathologic aexamination of sigmoid resection showed that subserosa were invaded by a tumour componed of sheets of squamous cells mixed to a glandular component. nerve or vascular invasion weren't observed. one regional lymph nodes was involved (T3N1a, IIIB, TNM staging AJCC/UICC for CRC). Proximal and distal resection margins were tumour free.
Conclusion: Adenosquamous carcinomas of the colon are uncommon tumours. The pathogenetic mechanisms of colonic adenosquamous carcinoma are not clearly understood, but several theories have been suggested. The clinical signs and symptoms of adenosquamous carcinoma of the colon and rectum are the same as those for an adenocarcinoma but colonic adenosquamous patients may experience a more aggressive clinical course and worse prognosis than colonic adenocarcinoma patients. The treatment of choice for adenosquamous carcinoma is surgical excision. The extent of operation depends on the location of the tumour. Adjuvant chemotherapy has been used in patients with stage C lesions of the colon; Early detection and radical operation with other available therapeutic modalities may improve clinical outcome.

E-PS-06-057
Undiagnosed primary lung carcinoma with initial manifestation of small intestinal rupture: A rare case report
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Background & Objective: Small intestinal metastasis as the first manifestation of a primary lung carcinoma is extremely rare. These patients may present with symptoms due to perforation or small bowel obstruction.
Method: We report the case of a 57-year-old man who was admitted to the hospital emergency unit with acute abdominal pain. Abdominal CT-scan showed that the cause of the acute abdomen was the presence of multiple tumour masses in the small intestinal wall, while thorax CT- scan revealed a peripheral tumour mass at the right lung, suggestive of a primary lung tumour, which was inaccessible by bronchoscopy. The patient underwent an emergency laparotomy. Intra-operative findings revealed a bulky tumour that caused perforation of the ileal wall. The patient was treated with Ileoileal resection-anastomosis.
Results: Histopathological examination showed a poorly differentiated malignant neoplasm, diffusely infiltrating the small bowel wall, with submucosal and intramural spread and multiple intravascular tumour deposits. Immunohistochemical examination showed diffuse positivity for CK AE1/AE3, CK7 and CK8/18, focal positivity for TTF1 and Napsin A, whereas CK20, p63, LCA, S100, and vimentin immunostains were negative. Overall the diagnosis was consisted with adenocarcinoma, probably metastatic from the lung. The molecular analysis of the tumour showed the L858R (c.2573T>G) mutation within exon 21 of EGFR gene. The patient died soon after the surgery.
Conclusion: Although small intestine metastasis of lung carcinoma is uncommon, should be kept in mind in patients with a history of lung primary tumour presenting with symptoms of acute abdomen, as early correct diagnosis is vital for appropriate treatment.

E-PS-06-058
Metachronous colorectal cancer: clinicomorphological and molecular characterisation of a series of 49 patients
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Background & Objective: "Multiple primary colorectal cancer" is still not well understood. This study aimed to investigate the clinicopathological

features and mismatch repair (MMR)-deficiency incidence in metachronous CRC (MCRC).
Method: A total of 49 consecutive patients (98 tumours) diagnosed with MCRC were selected from pathology files. MCRC was defined as a secondary tumour occurring outside the anastomosis area more than 6 months after surgery. For each tumour, clinicopathological characteristics were examined and were characterized for mismatch repair (MMR)-deficiency by microsatellite instability (MSI).
Results: Mean age at diagnosis was 68.6±2.3 and 71.7±2.3 years old for initial CRC and metachronous CRC, respectively. When we classified patients according to the first tumour anatomical location, 33 cases (67.4%) were located at distal colon (including 12 rectal cases (24.5 %)) and 16 patients (32.6%) were located at proximal colon (right or transverse). Most of them were well differentiated (82.9%). MCRC were mostly diagnosed at early stage of the disease and showed different location along the large intestine (63.3%) regarding initial CRC. MSI status of both initial and metachronous tumours were totally concordant being most of them MSS, only one case showed MSI for both paired-tumours (2.0%).
Conclusion: MCRC are not frequent in general population (2-12%). Although a higher incidence of Lynch syndrome between these patients could be expected, MSI incidence was similar to general population. Thus, we hypothesize that these patients should have other genetic or/and environmental factors predisposing to develop colorectal carcinoma, that still need further research.

E-PS-06-060
Features of the phenotype of severe dyslasia and early gastric cancer of the intestinal type
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Background & Objective: To identify the differences in severe dysplasia (SD) from early gastric cancer of the intestinal type (EGC) in immunohistochemical study (IHC) with antibodies (AB) to CK7, CK8/18, Muc1, Muc2, Muc5AC and p53.
Method: The material for the study was fragments of the gastric mucosa with SD and EGC from 21 patients. IHC with primary monoclonal AB of Leica Bond to CK7, CK8/18, Muc-1, Muc-2, Muc-5AC p53. Evaluation of the expression of AB was made by counting the number of expression cells per 100 cells of the tissue in 3 fields of vision (x40 increase) and giving the results as a percentage.
Results: Our study showed that for some AB were detected statistically significant differences in the number of expression cells ($p < 0.05$). Thus, EGC expresses CK7 more than 1.79 times that of SD (mean 31.76% versus 17.71%, respectively). A similar pattern in the study of the expression of Muc1: at SD - 6.86%, at EGC - 8.95% (1.3 times greater than the SD). But the amount of Muc2 expression cells at the EGC decreases by approximately twofold when compared with SD (mean 25.86% for SD, and 12.57% for EGC). Almost three times the number of p53 expression cells in the EGC is higher than in SD (mean SD 15.95% and EGC 46.9%).
Conclusion: The statistically significant differences between the SD and the EGC were revealed ($p < 0.05$) in IHC with AB to CK7, Muc1, Muc2 and p53; while statistically significant differences with AB to CK8/18 and Muc5AC were not detected.

E-PS-06-061
Hepatoid adenocarcinoma of colon with liver metastases: a case report
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Background & Objective: Hepatoid adenocarcinoma is a rare extrahepatic adenocarcinoma that morphologically and immunophenotypically mimics hepatocellular carcinoma. Most of the cases with colorectal hepatoid adenocarcinoma were reported in patients with inflammatory bowel disease.
Method: We present a case which was reported as hepatoid adenocarcinoma of sigmoid colon with synchronous liver metastases. Our case is 53 years old man, admitted to hospital because of rapidly weight loss. Colonoscopic examination revealed a mass in sigmoid colon which is away 25 cm from the anal verge. Hypoechoic masses in the hepatic parenchyma have been seen by abdominal ultrasonography.
Results: In the colonoscopic biopsy and resection specimen, the tumour was poorly differentiated and composed of sheets of polygonal-shaped cells with granular eosinophilic cytoplasm, centrally located nuclei and prominent nucleoli. The immunohistochemical profile showed expression of cytokeratin 20 , CD10, glypican 3 and cytokeratin 8/18. Neoplastic cells were negative for AFP and hepatocyte specific antigen. Eleven of 16 lymph nodes dissected were metastatic. The final diagnosis was hepatoid adenocarcinoma of colon with nodal involvement and metastasis of the liver.
Conclusion: In this report, we aim to highlight diagnostic difficulties in hepatoid adenocarcinoma of colon when patients have simultaneous masses in the liver.

E-PS-06-062
Hepatoid gastric adenocarcinoma: report of a case
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Background & Objective: Hepatoid Adenocarcinoma is a rare variant of gastric cancer with morphological similarities to Hepatocellular Carcinoma, characterized by elevated a-fetoprotein levels in the serum. The incidence of this subtype accounts for 0.38-0.78% of gastric carcinomas and has an extremely poor prognosis.
Method: We report a case of Hepatoid Gastric Adenocarcinoma. A 76-year old female presented to our hospital with epigastric pain and gastric perforation. A gastroduodenoscopy was carried out that revealed a large polypoid mass with a central ulceration. A distal gastrectomy with local lympnode dissection was preformed.
Results: An incision along the lesser gastric curvature revealed a bulky ulcerative tumour 5.8 cm in diameter that invaded both the muscularis propria and the serosa. Extensive sampling was carried out. Histological examination revealed a poorly differentiated neoplasm composed of polygonal eosinophilic cells arranged mainly in a trabecular fashion. Tumour cells presented abundant cytoplasm prominent nucleoli and high mitotic activity. Immunohistochemical control revealed that the neoplastic cells expressed diffusely AFP. On the basis of histological and immunohistochemical findings the diagnosis of a poorly differentiated gastric hepatoid adenocarcinoma was established. Metastatic disease has been detected in 15 from the 18 local lymphonodes excised.
Conclusion: Hepatoid carcinoma of the stomach is a very rare subtype that histologically mimics the appearance of hepatocellular carcinoma. The stomach is the most common location but is also observed in several other organs, such as ovaries, uterus, lung, colon etc. It is an aggressive malignant tumour that has dismal prognosis, even if it is diagnosed at an early stage.

E-PS-06-063
Histological findings of endoscopic mucosal dissection of early tumours of the gastrooesophageal tract. Over a 5 years view
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Background & Objective: Endoscopic mucosal dissection (EMD) is becoming the elective procedure of treatment early tumours of the

gastrooesophageal tract. Histological assesment of these specimens provides substantial information of diagnosis, prognosis and further treatment. This study reviews the clinico-pathological features and follow-up of cases included for EMD in our institution.
Method: Under strict endoscopic criteria during a 5-year period (2013-2018) 47 gastrooesophageal EMD have performed made in our institution. A number of histological findings have been systematically reported (localization, size, histological type, depth of infiltration, margin status) as well as gender, age and follow-up time.
Results: 74.4% of patients were males (35 vs 12 females). Average age at EMD was of 68.6 years (83-41). The most common lesion observed was low grade adenoma (19), followed by high grade adenoma/adenocarcinoma (15), hyperplastic polyp (8), GIST (1), squamous cell carcinoma (1), ectopic pancreas (1) and fibroinflamatory polyp (1). Size of resected mucosa was from 9 to 50 mm diameter (media 20.7 mm). Margins had no lesion in 78.3% of cases. The deepest neoplastic infiltration was of 4 mm (range 0.5-4mm). 4 patients had surgical resection. Average follow-up with endoscopic control was of 17.5 months (range 1-54). No death due lesion diagnosed on EMD was reported.
Conclusion: EMD is the selected treatment in early tumour of the gastrooesophageal tract in our institution. It is a less invasive procedure which provides substantial clinical information of obtained biopsies.

E-PS-06-064
Histopathological features and prognostic factors of gastric carcinoma
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Background & Objective: Gastric carcinoma (GC) is a heterogeneous disease with high mortality and variable histological features and genotypes. Our aims are to assess the clinicopathological features of a large series of GC and to identify features associated with patient outcomes
Method: Retrospective study of 206 cases of GC surgically resected in our institution between 2000-2017. Clinicopathological features of all cases were assessed and correlated with patient outcomes.
Results: 54.9% of patients were men and mean age was 71.19 years. 91.1% of tumours were symptomatic. Most tumours were located in gastric antrum or body. Microscopically, GC were mainly tubular (56.2%), discohesive (32.3%) and mixed (9.5%) carcinomas. Necrosis, tumour budding, desmoplasia, mucin pools and signet ring cells were observed in 26.2%, 25.4%, 51.5%, 19.4% and 41.8% of GC. Vascular and perineural infiltration were seen in 44.3% and 51.3% of cases. Advancing front was infiltrative in 63%. Most GC were diagnosed at pT3 and 69.1% showed lymph node metastases. 44.1% of patients showed recurrences and 25.6% of patients died due to the GC. Tumour recurrence was significantly associated with WHO/Laurén classifications, perineural infiltration, intratumoural inflammatory response, R1 resection and TNM stage. Patient death was significantly associated with WHO/Laurén classifications, tumour grade, presence of signet ring cells, advancing-front type, desmoplasia, TNM stage and recurrences.
Conclusion: Patient outcomes in GC are associated with known clinicopathological features such as TNM stage or WHO/Laurén classifications. However, the prognostic role of other histological features such as advancing-front type, desmoplasia and intratumoural inflammatory response should be further studied.

E-PS-06-066
Amphicrine-type mixed adenoneuroendocrine carcinoma, of gastrointestinal tract. Report of four cases
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Background & Objective: Mixed adenoneuroendocrine carcinoma (MANEC) is a rare tumour of the gastrointestinal tract presenting glandular and neuroendocrine components, each of them representing at least 30% of the tumour (WHO, 2010). In addition, it receives the name of amphicrine tumour with dual, endo and exocrine, differentiation within the same cell. Amphicrine-type mixed adenoneuroendocrine carcinomas are exceedingly rare lesions of the gastrointestinal tract. Here we report four cases of MANEC, three of them amphicrine carcinoma.
Method: Due to a recently diagnosed case, we reviewed the database of our hospital, obtaining a total of four cases with a diagnosis of MANEC, one in the small bowel and three in the large intestine-rectum, being three of them amphicrine-type mixed adenoneuroendocrine carcinoma.
Results: Morphologically, the tumour consists of areas of adenocarcinoma; in two cases, signet-ring cell carcinoma and in the other two cases, well and poorly differentiated adenocarcinoma, intermingled with areas of neuroendocrine carcinoma in three cases and neuroendocrine tumour, G1, in the fourth. Immunohistochemically, we distinguish the amphicrine carcinoma within MANEC, in which the neoplastic cells show bivalent differentiation, epithelial and neuroendocrine, with strong positivity for synaptophysin, CDX2, CEA and CK20. Furthermore, the same cells expressed neutral and acid mucin (Alcian-PAS stain).
Conclusion: Gastrointestinal MANECs are a heterogeneous group of tumours showing different morphological, clinical, and prognostic features. A correct diagnosis is important for carry out the correct treatment.

E-PS-06-067
Case report: aggressive malignant tumour from small blue cells - when electron microscopy helps
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Background & Objective: We report an interesting case of twenty-four years old man with extensive necrotic masses of stomach cardia. Due to a diagnosis of malignant adenoneuroendocrine carcinoma (MANEC) in a first examinated endoscopic biopsy a partial resection of oesophagus and partial gastrectomy were done.
Method: For the first examination several small endoscopic specimens were examined, finally samples from the resection were examined to. All of them were standardly embedded in paraffin and stained using haematoxylin – eosin method. Immunohistochemical examination of tumour tissue with ambiguous expression of CD56, Synaptofyzin, Chromogranin and negativity of CK, CK7, CK5/6, CK20 and others such as S100, AFP, CD117, CD99, EMA, CEA and CDX2 was also performed. An electron-microscopy was done to.
Results: The first, capture endoscopic biopsy was evaluated as MANEC in combination of poorely differenciated endocrine carcinoma (NEC G3) and well differenciated adenocarcinoma. A definitive biopsy conclusion from surgical resection was poorely differenciated endocrine carcinoma (NEC G3) without invasive adenocarcinoma, with only high grade dysplasia of glandular component. For the interobserver mismatch, cytogenetic examination (FISH) was also performed to exclude changes associated with PNET. In contrast, the presence of neurosecretory granules in electron microscopy confirmed the diagnosis of NEC.
Conclusion: The task of our case report is to alert reader to a diagnostically difficult case. In view of ambiguous immunohistochemistry and interobserver discrepancy an electron microscopy and cytogenetic analysis were diagnostic leaders in this case. Our patient died 14 moths from the first diagnosis.

E-PS-06-069

Primary polypoid malignant melanoma of the anus: a case report

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Background & Objective: Malignant Melanoma (MM) is generally considered as a malignancy of sun-exposed skin while detection in mucosal surfaces is rare, especially in the anus, just 0.05% of all colorectal malignancies. It is appearing usually in middle-aged to elderly patients with a slight female predominance and is thought to arise from malignant transformation of melanocytes that are normally present in the anal mucosa of transitional zone. We describe a case of polypoid MM of the anus in a 56 y.o. man, with no known previous history.
Method: We received as anal mass a grayish polypoid specimen of a maximum diameter 6.5cm with smooth surface. Multiple sectioning revealed a solid, grayish-yellowish lesion of elastic consistence.
Results: Histological examination showed an ulcerated neoplastic lesion, mainly composed from large epithelioid cells with marked cellular atypia and pleomorphism in a pseudoadenoid or compact pattern, intermingled with a significant number of spindle cells. Immunohistochemistry revealed strong MelanA, S-100, HMB45, SOX-10 positivity, while CK AE1/AE3, p40 and mutation BRAFV600E were negative, confirming the established diagnosis of polypoid anal MM.
Conclusion: Primary MM of the anus is a very aggressive neoplasm associated with poor prognosis. It is usually detected with delay in advanced stage because symptoms are non-specific and the lesion seems macroscopically like hemorrhoids or anal polyps. Current therapeutic treatments include systemic therapy based on molecular characteristics (BRAF, KIT) and wide local excision, if negative margins are achievable.

E-PS-06-070

Neuroendocrine tumours of the gastrointestinal tract: a retrospective evaluation and reclassification of 69 cases

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Background & Objective: Neuroendocrine neoplasia (NEN) of the gastrointestinal tract are heterogeneous neoplasms, with different morphological patterns and clinical behavior. Our aims were to analyze clinic-pathological features and to re-classify using the updated CAP guidelines.
Method: Patients diagnosed as NEN, NE tumour (NET), NE carcinoma (NEC), and/or mixed adeno-NE carcinoma (MANEC), NE- non-NE neoplasm (MINEN) on resection and/or biopsy specimens, between 2013 and 2017, were retrieved from the archives of our department
Results: We analyzed 47 biopsy and 22 resection specimens. There were 69 patients with a mean age of 57. Forty-two (61%) were male. Cases were diagnosed as NET grade 1(31.9%), NET grade 2(18.8%), NET grade 3(1.4%), large cell NEC (21.7%), small cell NEC (10.1%), and MINEN (15.9%). In 27% cases, other tumoural and non-tumoural pathologies including adenocarcinoma (n=8), NE dysplasia (n=4), adenomatous dysplasia (n=31), granulomatous inflammation (n=2) were observed. There was a statistical significance between the site and the NEN-subtype ($p<0.01$). NEN grade 1 cases were common in small intestine (12/22), whereas NET grade 2 cases were reported in the stomach (10/13) and 9/11 of MINEN cases were located in the stomach. The relationship between diagnosis and sex was statistically significant ($p<0.01$). Among female cases, 14/27 and 7/27 were NET grade 1 and 2, respectively. Ten of 11 MINEN cases were reported in male patients.
Conclusion: Statistical significant effect of the site of the tumour and sex of the patient in relation to the NEN-subtype may underline the difference in the carcinogenetic pathways and the cell of origin.

E-PS-06-072

Epithelial-mesenchymal transition features in gastric mixed adenoneuroendocrine carcinomas (MANEC)

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Background & Objective: To evaluate the epithelial-mesenchymal transition (EMT) aspects in gastric mixed adenoneuroendocrine carcinomas (MANEC).
Method: Six consecutive gastric MANECs were included in this study, diagnosed in our department over a period of four years. The diagnosis was based on the current WHO criteria. The two components, adenocarcinoma and neuroendocrine component, were identified on Haematoxylin and Eosin and were confirmed with IHC markers (synaptophysin, chromogranin, neuron specific enolase, cytokeratin AE1/AE3, 7 and 20). Tumour grade was appreciated with the use of Ki-67 index. The EMT was evaluated using the IHC markers E-cadherin, β-catenin, N-cadherin and vimentin. CD44 was used to explore the stemness features of the tumour cells.
Results: A male predominance was observed in our series of cases (5 males and one female), with ages ranging from 45 to 70 years, the most affected age group being 60-70 years. The tumour stages were pT 2, 3 and 4b. Four cases presented lymph node metastasis, while lymphatic vessel invasion was observed in all six cases. E-cadherin and β-catenin showed diffuse membrane expression in all the cases, with no nuclear positivity of β-catenin. N-cadherin and vimentin showed no positive reaction. CD44 was diffusely or focally expressed in the membrane of the tumour cells in both components of these cases.
Conclusion: The aggressivity of MANECs is not related to EMT process, but it might be induced by the adhesion molecule CD44.

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E-PS-06-073

The microsatellite instability and budding intensity in colorectal cancer

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Background & Objective: To evaluate the possible correlation between tumour budding and microsatellite status, in colorectal cancer.
Method: Microsatellite instability was prospectively quantified in 45 consecutive cases of patients diagnosed with colorectal carcinoma. They were divided into two groups: group 1 (n=23) with low budding- respectively group 2 (n=22) with high budding intensity. Microsatellite status was evaluated using the immunohistochemical (IHC) markers MSH-1, MLH-2 and PMS-2 and confirmed with PCR using the mononucleotides BAT25 and BAT26.
Results: Most of the microsatellite stable (MSS) cases (9 from 12; 40,90%) belonged to group 2 whereas the cases from group 1 were mostly diagnosed with high microsatellite instability (MSI-H): 13 from 17 cases (56.53%), with a p-value of 0.01. The other 16 cases showed low grade microsatellite (MSI-L) status (7 from group 1 and 9 from group 2). Higher pT ($p=0.047$) and pN ($p=0.036$) stages were observed in high budding tumours.
Conclusion: The high budding colorectal carcinoma is mostly an MSS tumour with high risk for lymphatic spread.

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E-PS-06-074

Triple trouble: synchronous mixed neuroendocrine-nonneuroendocrine neoplasm and gastrointestinal stromal tumour – a case report

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Background & Objective: Mixed neuroendocrine-nonneuroendocrine neoplasms (MiNENs) are rare tumoural entities of epithelial origin with two morphological components, a neuroendocrine and a nonneuroendocrine one in variable proportions. We report the occurrence of a high-grade gastric MiNEN with a synchronous gastrointestinal stromal tumour (GIST) in a 75-year-old female.
Method: Multiple endoscopic biopsy specimens and the gastric surgical resection specimen were routinely processed. HE staining and immunohistochemical tests were performed.
Results: The initial histologic examination of the endoscopic biopsies revealed a moderately differentiated, infiltrative adenocarcinoma of the stomach. Consequently, the patient underwent surgical resection. Gross evaluation of the gastric resection specimen identified a protruding, ulcerated lesion, located on the lesser curvature. Microscopically, the tumour mass presented two juxtaposed components: a moderately differentiated adenocarcinoma and, surprisingly, a solid component, with neuroendocrine features and high mitotic activity (>100 mitosis/10 HPF). Additionally, one of the sections submitted for analysis revealed a micronodule (1 mm) in the muscularis propria, consisting of spindle-shaped cells with uniform nuclei, delicate fibrillary cytoplasm and low mitotic activity. Immunohistochemistry confirmed the neuroendocrine component (CD56, Chromogranin and Synaptophysin positive), while the spindle-cell proliferation was CD117, DOG1 and CD34 positive, confirming the initial presumption of GIST.
Conclusion: This is, to our knowledge, the first reported case of a MiNEN coexisting with a GIST. While this incidental association may be of little impact to the patient's prognosis, it may suggest the existence of a complex pathogenesis and may provide a further step in deepening out otherwise limited knowledge and consensus regarding nomenclature, classification, and guideline of treatment for MiNEN.

E-PS-06-075
Gastrointestinal neuroendocrine tumours – pathological features with prognostic significance
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Background & Objective: Neuroendocrine tumours (NETs) originating in the gastrointestinal (GI) tract arise from the neuroendocrine cells which are responsible for producing and releasing a variety of hormones that regulate various functions of the digestive system. Our purpose is to study the relations between macroscopic, microscopic and immunohistochemical characteristics of this tumours and their impact on prognosis.
Method: We conducted a retrospective study on cases of GI-NETs diagnosed on surgical excisional specimens in Colentina University Hospital between 2010-2017 by evaluating demographic data, site and size, histological aspects and immunohistochemical markers as well as the staging and grading of the tumour.
Results: The study included 39 cases, 18 males with ages between 40-79 and 21 females with ages between 10-84 years old. Mean age at diagnosis was 59.3 years. The main localization was the colon 13 cases (33.33%), followed by the stomach 12 cases (30.78%), the small bowl 10 cases (25.64%) and the appendix 4 cases (10.25%). The average mitotic index was 17 mitosis/10HPF (ranging from 1 to 68 mitoses). The average Ki67 index was 21.15% (ranging from 1% to 90%). Both Ki67 index and mitotic index significantly correlate to tumour size. The location of the tumour correlates with the histological grading, most of the colonic tumours being poorly differentiated.
Conclusion: The number of mitoses and Ki67 index significantly correlate with the size of the tumour. The histological grade was found to be correlated with the location of the tumour. The behavior of GI-NETs can be predicted by anatomic site, tumour size, mitotic activity and Ki67 index.

E-PS-06-076
Colon signet ring cell adenocarcinoma. A rare condition with a poor prognosis. A report of three cases
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Background & Objective: Colon signet ring cell adenocarcinomas are uncommon, high-grade neoplasms, representing less than 1% of all tumours of the colon and rectum. This primary origin and at least 50% of the tumour showing a signet ring cell pattern spot the diagnosis. In this study we report three cases of primary signet ring cell adenocarcinoma of the colon and the particularities regarding immunohistochemical phenotype, microsatellite instability and prognostic factors.
Method: Three men aged 46, 62 and 81 presented with the following primarily complaints: abdominal pain, constipation, alterned bowel habits, but also haematochezia, weight loss, and anemia over a month duration. CT investigation identified a stenotic segment at colon with obvious shouldering. Surgery was performed and anatomopathological report set the final diagnosis of signet ring cell colonic carcinoma.
Results: Since clinical symptoms tend to occur late in the course of this adenocarcinoma subtype, most cases are usually detected at an advanced stage with a poor overall survival rate. Immunohistochemistry and microsatellite instability assesed the common points and differences in disease progresion.
Conclusion: The available literature suggests that the tumour staging is the best predictive factor for the prognosis of signet ring cell carcinoma of the colon where higher tumour staging means poorer prognosis. The bleak prognostic corresponded well with immunohistochemical phenotype and microsatellite instability.

E-PS-06-077
Mucinous adenocarcinoma of the stomach: a case report
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Background & Objective: Gastric cancer is one of the most common causes of cancer-related mortality. One million new cases are diagnosed annually, accounting for 700,000 mortalities worldwide. Mucinous adenocarcinoma (MGC) of the stomach is a rare histologic type of gastric adenocarcinoma accounting for ~2.6–6.6% of all gastric cancer. Literature on MGC is currently limited, mostly due to its rarity. Several studies have suggested that the prognosis is poor, whereas others reported no differences in characteristics and prognosis between MGC and non-MGC (NMGC).
Method: A 73-year-old man with a neoplasia of the antrum/pylorus/body was submitted to subtotal gastrectomy.
Results: Patient presented a ulcero-vegetant mass lesion with 9cm. Microscopically showed mucinous adenocarcinoma with tubules/cells in signet ring, which invades the entire wall reaching/serosa, with extensive mucin lakes. Response to the new standard neoadjuvant chemotherapy FLOT was Becker 1b (tumour regression <10% residual tumour). 35/52 metastatic lymph nodes.
Conclusion: MGC is rare and mainly detected at an advanced stage, with a poorer overall prognosis compared to NMGC. However, the prognosis of MGC (and according to our review of literature) disease stage was similar to that of NMGC. Therefore, the MGC histological subtype may not be an independent prognostic factor of gastric cancer. Further investigations on the origin and progression of MGC is required to help us clarify this entity.

E-PS-06-078
Number, size, therapeutic effect, and histological response of lymph nodes in locally advanced rectal cancers after neoadjuvant treatment
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Background & Objective: Neoadjuvant radiochemotherapy, followed by total meso-rectal resection, is the treatment in locally advanced rectal adenocarcinoma. The aims of this study are to: - identify the effect of neoadjuvant treatment on the size, number and therapeutic effect in Lymph nodes (LN) - investigate the incidence of extra-capsular invasion (ECI) in metastatic (LN) - determine the germinal center (GC) frequency in LN
Method: This is a retrospective and prospective study, approved by the Ethics Committee of school of Medicine and Pharmacy of FEZ, involving 129 patients with resected rectal adenocarcinoma after neoadjuvant therapy. Associations are made between lymph nodes characteristics and the histological response on surgical specimens
Results: The mean age of patients was 56 years, a sex ratio was 1.22, 67% (n=84) showed a good response, and a complete response was observed in 16% (n=20) of patients. 1421 lymph nodes was analyzed, the mean size was 3.33 mm, 41%(n=51) < 3,33 mm vs 59%(n=74)>= 3,33 mm. 48% of patients had a number of LN< 12 (n= 62) vs 67% (n=67), LN>=12, 63% of patients with an ypN + had a LN number < 12 vs 41% with an ypN0, p=0, 01 Therapeutic effect of LN have been observed in 40% (n=51) of patient. Extra-capsular LNI was identified in 32% (n=12) of patients with metastasis LN (n=38), only 4.5% of LN with ECI have a ypT <=2 vs 18%, ypT>=2, p=0.014, and germinal center was identified in 92%. 93% of LN with GC are good responders
Conclusion: The number and size of metastatic or non-metastatic lymph nodes are decreased after neoadjuvant treatment.

E-PS-07 | Digestive Diseases Pathology - Liver/Pancreas

E-PS-07-003
RNF43, Beta-catenin and E-cadherin expression in pancreatic adenocarcinomas

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Background & Objective: RNF43 (E3 ubiquitin-protein ligase RNF43 or RING type E3 ubiquitin transferase RNF43) functions as a tumour suppressor, which affects a predominant negative feedback mechanism in the Wnt/β-catenin signaling pathway. We aim to determine the expression by immunohistochemistry of RNF43, β-catenin and E-cadherin in pancreatic adenocarcinomas and correlate it with clinicopathological features.
Method: A Tissue microarray including 43 pancreatic adenocarcinomas, retrieved from the database of the Department of Pathology, University Health Network, University of Toronto, was stained with RNF43, β-catenin and E-cadherin antibodies. The immunostains were scored according to the percentage of positive cells stained as negative (0%-30%) and positive (>30% -100%). In addition, cell localization of the stain (nuclear, cytoplasmic and membrane) was recorded. Data analysis was performed using IBM SPSS Statistics (Version 21).
Results: Nineteen of 43 cases were negative for RNF43, 14 showed nuclear and cytoplasmic and 10 only cytoplasmic stain. Immunohistochemistry for β-catenin and E-cadherin was available for 32 cases. Negative stain for RNF43 was significantly associated with male patients (14/22) (p=0.03); it was also more frequently seen associate with larger tumours (>3cm) (12/24), perineural (17/35) and lymphovascular (13/27) invasion, extrapancreatic extension (18/39), pT3 stage (18/37), membrane β-catenin expression (11/16) and significantly with negative β-catenin cytoplasmic expression (p=0.012). Cytoplasmic RNF43 expression was more frequently associated with nuclear β-catenin and cytoplasmic and nuclear E-cadherin expression.
Conclusion: Our preliminary reports show that RNF43 immunoexpression in pancreatic adenocarcinomas is frequently lost and often associated with several unfavorable prognostic factors and with abnormality of β-catenin and E-cadherin expression.

E-PS-07-004
A rare case of advanced carcinoma arising in a choledochal cyst in a young adult

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Background & Objective: Choledochal cysts are relatively rare congenital or acquired cystic dilation of extrahepatic duct, intrahepatic duct, or both. Unresected choledochal cyst is clearly associated with increased risk of cholangiocarcinoma.
Method: This study reports a rare case of advanced cholangiocarcinoma arising in an unresected choledochal cyst in adulthood.
Results: A 26-year-old woman presented with the intermittent right upper abdominal pain of 3 weeks duration. Physical examination revealed an icteric woman with epigastric and right upper abdominal pain, tenderness in the right costovertebral angle and a positive Murphy's sign. Endoscopic retrograde cholangiopancreatography, computed tomography and magnetic resonance imaging demonstrated a Todani type IVa choledochal cyst. A 1.8 cm-sized solid tumour was detected in the distal common bile duct. Endoscopic retrograde cholangiopancreatography, computed tomography and magnetic resonance imaging demonstrated a Todani type IVa choledochal cyst. A 1.8 cm-sized solid tumour was detected in the distal common bile duct. On histological examination, moderately differentiated adenocarcinoma, arising in biliary intraepithelial neoplasia, grade 2 (BilIN 2) of choledochal cyst was confirmed. The tumour invades periductal soft tissue and pancreatic parenchyme and the infiltrative depth was 12.0 mm from the surface. She had 18 cycles of adjuvant chemotherapy (Gemzar/Cisplatin) and is presently on follow-up. No evidence of recurrence after 2 years of follow-up.
Conclusion: Associated biliary malignant tumour should always be considered in patients with choledochal cyst, especially in aged patients.

E-PS-07-005
Immunophenotype of ampulary and periampulary carcinomas in interrelation with hystogenesis of the pancreodododenal zone

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Background & Objective: Pancreatobiliary or intestinal immunophenotype AC could be explained by the localization of the primary tumour. The appearance of the intestinal phenotype in the PDAC is a controversial issue.
Method: To reveal differences of intestinal immunophenotype in patients with AC and PDAC after surgical treatment based on the morphogenesis of these tumours.
Results: On 6-7 gestational age (GA) the pancreas tissue gross was represented by a rounded formation of gray-pink color up to 1.0 cm. IHC - panCK, CK7, CK 20, CDX2 and MUC 1, 2, 5AC and 6 was negative. At 13-14 GA pancreas was well visualized gross in size from 1.5 to 2 cm. IHC the same at 6-7 GA. At 17-18 and 20-21 GA the pancreas was gross 3.5 cm in the form of a thin gray-pink strand. IHC was identical to reactions at 6-7. The cytoplasmic reaction with CK7 in the epithelium of the pancreatic ducts, and MUC1, appears for the first time at 20-21 GA, which indicates the beginning of the specialization and specification of the epithelium and probably in the necessity of digestion of the fetus.
Conclusion: The appearance of heterogeneity of the immunophenotype in AC and PDAC is explained by the peculiarities of embryogenesis of the pancreas. Morphological differences of the true intestinal immunophenotype in case of ampullary carcinoma and "incomplete intestinal metaplasia" in pancreatic ductal adenocarcinoma were revealed. Also, was revealed their interrelation with embryonic development of the pancreatoduodenal zone.

E-PS-07-006

Ex vivo liver volume evaluation by ultrasound volumetric formulas

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Background & Objective: It is clear that liver disease alters its texture and its size as well. The objective and important criteria of organ size is volume. This study objective is to ex vivo evaluate the possibilities of measuring the liver volume on the basis of linear dimensions of the organ by ultrasound volumetric formulas.
Method: During the forensic autopsy, the liver was removed from the abdominal cavity and measured by liquid displaced method in 70 cadavers. Liver size measurement was performed on sections of both lobes according to the principles of liver size determining with ultrasound. The percent of the liver volume deviation calculated by the most known formulas based on linear liver measurements in comparison with the actual volume of the organ, determined by the method of displacement of the liquid.
Results: The average volume of the liver, determined by the liquid displacement method, was 1325 ± 467 cm³. The average liver volume calculated by formulas ofM. Zoli et al. (1989), D. Glenn et al. (1994), D. Elstein et al. (1997), M. Patlas et al. (2001) and J.T. Childs et al. (2016), was 1720 ± 687, 1474 ± 639, 1513 ± 516,1620 ± 702 and 1238 ± 470 см³ respectively. The average percent of deviation of the calculated liver volume widely varies up to 29 % compared to the actual volume of the body. The minimal percent of the average deviation (4.6%) was in the J.T. Childs et al. formula.
Conclusion: The optimal formula for calculating liver volume is formula by J.T. Childs et al. (2016).

E-PS-07-007

Algorithm of diagnosis of pancreatic neuroendocrine tumours on fine needle aspiration specimens

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Background & Objective: Pancreatic neuroendocrine tumours (NET) benefit from surgical resection even in advanced cases and specific treatment with significant better prognosis that other pancreatic malignancies. Proper diagnosis on fine needle aspiration (FNA) specimens is very important for patients' management.
Method: We identified 7 cases of pancreatic NET diagnosed in our department in the last 3 tears (out of over 600 FNA) and then confirmed on surgical resection specimens. Usual and special stains, as well as immunohistochemical tests were used for diagnosis.
Results: Only in one case (female patients with pancreatic and hepatic mases and carcinoid type symptoms) the diagnosis was suspected before FNA. Most cases (5) were G2 NET, while 1 case was a G3 and one case a G1 NET. The most important histologic features was the presence of sheets and isolated cells with relatively monomorphous nuclei with granular chromatin and eosinophilic, granular cytoplasm, without acinar architecture. Immunostains for chromogranin, synaptophysin and neuron specific enolase confirmed diagnosis and Ki67 stain permitted grading in 5 out of 7 cases. Surgical specimens were obtained in all 7 cases, confirming FNA diagnosis.
Conclusion: Knowledge of cytologic characteristics of NET is useful in FNA diagnosis of pancreatic lesions. A correct diagnosis crucial for patients' treatment and outcome, since NET are less aggressive and more treatable tumours that other pancreatic malignancies.

E-PS-07-009

Soluble CD163 as a macrophage activation marker in chronic hepatitis C: relation to hepatic fibrosis and steatosis and insulin resistance

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Background & Objective: This work was designed to assess serum levels of sCD163 as a macrophage activation marker, in patients with chronic hepatitis C (CHC) in relation to hepatic fibrosis, steatosis and insulin resistance. In addition, hepatic expression of CD163 and alpha-smooth muscle actin (α-SMA), a marker for activated hepatic stellate cells, were evaluated.
Method: The study included 25 treatment-naïve patients with CHC and 15 healthy subjects. Serum sCD163 levels were measured using ELISA kit. Core liver biopsies obtained from patients were evaluated immunohistochemically for the expression of CD163 and α-SMA.
Results: Serum sCD163 levels were significantly higher in patients with CHC and patients with hepatitis C virus (HCV)-related cirrhosis compared with healthy subjects, and in patients with cirrhosis compared with patients with CHC. The total counts of CD163 positive cells (hepatic lobules and portal tracts); and α-SMA staining score were significantly higher in patients with HCV-related cirrhosis than in patients with CHC. Serum sCD163 levels and total counts of CD163 positive cells in the liver tissue on one hand showed positive correlation with homeostasis model of insulin resistance (HOMA-IR), METAVIR histological activity grade, fibrosis stage, and steatosis grade on the other hand. Serum sCD163 levels and total counts of CD163 positive cells in the liver tissue were positively correlated, and both showed positive correlations with α-SMA staining score.
Conclusion: Increased serum sCD163 levels and CD163 expression in the liver reflect macrophage activation in chronic HCV infection, which contributes to HCV-related liver injury and metabolic alterations including hepatic steatosis and insulin resistance.

E-PS-07-010

Primary hydatid cyst of the pancreas mimicking cystic pancreatic neoplasm: a case report

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Background & Objective: Hydatid Cyst (HC) disease is a zoonotic infection caused by larval stage of Echinococcus granulosus. Primary pancreatic HC is a rarely seen form even in endemic areas and accounts for about 0.19% to 2%. Establishing diagnosis may be difficult because clinical and imaging findings are similar to cystic neoplasms of pancreas. We present a case of HC in the head of pancreas which mimicked a cystic neoplasm on imaging.
Method: We report a case of HC of the pancreas presented with obstructive jaundice diagnosed in our pathology department.
Results: A 37-year-old male presented with upper abdominal pain and jaundice of 2 months duration. Physical examination revealed jaundiced skin color and scratch marks all through the body. Abdominal examination revealed a non-tender, globular swelling filling the right hypochondrium. Abdominal ultrasonography showed a cystic lesion of 52 x 30 mm in size located in the head of the pancreas adherent to the superior mesenteric vein, with a dilated common bile duct. Magnetic resonance cholangiopancreatography (MRCP) showed a cystic lesion in the head of the pancreas with a dilated proximal choledochal bile duct. Cystic neoplasm was strongly suspected peroperatively a cephalic pancreatectomy was performed. Histopathological examination was reported as HC of pancreas.
Conclusion: Presenting features of HC of the pancreas may masquerade as pseudocysts or cystic neoplasms. A definitive diagnosis can be made only at surgery and on histopathology. To avoid major pancreatic resections due to a mistaken diagnosis of pancreatic malignancy, pancreatic HC should be considered in the differential diagnosis of pancreatic cystic lesions.

E-PS-07-012

Primary hepatic clear cell myomelanocytic tumour (PEComa)

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Background & Objective: Report a case of primary hepatic clear cell myelomelanocytic tumour (PEComa) to define its histological features.
Method: A 42-year-old female presented with pain in right hypochondrium. Her liver function tests showed elevated SGOT, SGPT and GGT levels. On examination there was right hypocondriac lump. Contrast enhanced computed tomography (CT) of the abdomen showed 4x3 cm heterogeneously enhancing lobulated lesion in segment VII and a few lesions approximately 1 cm in length in segment 8, segment 5-6 junction and segment 4 of the liver. A segmental hepatectomy was done.
Results: On macroscopic examination, grayish yellow and crisp quality mass relatively demarcated from the surrounding liver parenchyma with a size of 4x3x3 cm was observed. Histopathologic examination revealed a tumour characterized by a population of large epithelioid cells with clear or eosinophilic granular cytoplasm, rich in glycogen. Immunohistochemically, the tumour cells were positive for HMB-45, Melan-A and SMA, but negative for epithelial markers, S-100 protein, and CD10.
Conclusion: Perivascular epithelioid cell tumours (PEComas) that show marked female predominance are mesenchymal neoplasms defined by the presence of histologically and immunohistochemically distinctive perivascular epithelioid cells. This tumour family includes angiomyolipoma, clear cell sugar tumour, lymphangioleiomyomatosis, and a group of rare, morphologically and immunophenotypically similar tumours arising at a variety of visceral and soft tissue sites. Hepatic PEComa is very rare neoplasm. The main differential diagnosis of hepatic PEComa includes clear cell variant of liver cell adenoma and hepatocellular carcinoma, metastases of various clear cell carcinomas and metastasis of malignant melanoma.

E-PS-07-013
E-cadherin in adenocarcinoma of pancreas
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Background & Objective: E-cadherin is important for cell-cell adhesion. Reduction and/or loss ofE-cadherin expression in adenocarcinoma of pancreas correlates positively with malignant transformation, invasion and metastasis of tumour. The aim of study was to examine immunohistochemically the expression of E-cadherin in adenocarcinomas of pancreas and their relationship with clinicopathologic parameters such as histological stage, grade, tumour size, sex and age of the patients.
Method: 15 women and 29 men with adenocarcinoma of pancreas treated surgically were examined retrospectively. The age of the patients ranged from 45 to 78 (mean age 65 years). The tumour specimens have been immunostained for E-cadherin.
Results: Absent or reduced expression of E-cadherin was observed in 10 of 12 (83%) stageII, 13 of 18 (72%) stageIII and 13 of 14 (92.8%) stageIVadenocarcinomas. The impaired expression of the E-cadherin was observed with a higher frequency in high-grade than in low-grade tumours 82% and 48% respectively, ($p<0.0001$). No relationship was fount between E-cadherin impaired expression and tumour size or sex of the patient. Absent or reduced expression was seen in advanced age of the patients.
Conclusion: Impaired E-cadherin expression was fount more frequently in high stage and grade tumours and in advanced age of the patients.

E-PS-07-014
Pancreatic tail solid pseudopapillary tumour in a young male
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Background & Objective: Solid pancreatic pseudopapillary tumours are rare neoplasms, about 1-3% of all pancreatic neoplasms and more commonly seen in women than in men. Most of the patients have nonspecific symptoms.
Method: We report our experience with a case report of SPT in a young man.
Results: A 26-year-old male person whom accidentally found a small tumour by transabdominal ultrasound investigation. Abdominal CT-scans a 2 cm size neoplasm arising from the body of the pancreas. He underwent a laparoscopic distal pancreatic resection with spleenectomy. Macroscopically, the pancreatic tumour was encapsulated measuring 1,0 x 0,7 cm. Histologically, the tumour was circumscribed by a thick fibrous capsule. The growth pattern of the tumour was soild, pseudopapillary structures. The solid areas were composed of poorly cohesive monomorphic cells that were admixed with hyalinized stromal bands containing thin-walled blood vessels surrounded by loosely cohesive tumour cells radiating around blood vessels reminiscent of pseudorosettes in ependymoma. IHC, tumour cells showed positive immunostaining with vimentin, β-catenin, progesterone receptor and synaptophysin focally. Resection margin was free of tumour.
Conclusion: Solid pseudopapillary tumour of the pancreas was first described by Frantz in 1959 and was included in the WHO classification in 1996. Solid pseudopapillary tumour of the pancreas are exceedingly rare in male patients. Due to their rarity, clinical data on SPTs in male patients are scarce in the literature. e majority of SPT are considered to be of low malignant potential with only 10-15% of cases being malignant, showing local infiltration, recurrence or distant metastasis.

E-PS-07-015
Unusual isotopic fractionation patterns of growing in vivo hepatocellular carcinomas of developmental age
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Background & Objective: Hepatoblastoma and hepatocellular carcinoma are both primary liver cancers in children with a relatively poor prognosis, however hepatocellular carcinomas are often chemoresistant with much worse cure rates. It has already been demonstrated that differences between hepatoblastoma and hepatocellular carcinoma exist on microscopic and molecular levels. We have evaluated an atomic level of hepatocellular carcinoma of developmental age with the use of Isotope Ratio Mass Spectrometry (IRMS), to search for potential differences in comparison with hepatoblastoma. The highest credibility of IRMS estimations which was proved by IRMS implementation into forensics demanded by legal constraints, gives the unique opportunity for an effective analysis based on a scarce number of samples, which seems especially desirable in the study of rare tumours.
Method: Isotopic composition of nitrogen and carbon in 6 frozen tissue samples from two growing in vivo hepatocellular carcinomas of developmental age were evaluated with the use of Continuous Flow Isotope Ratio Mass Spectrometer coupled with elemental analyzer.
Results: Isotopic signatures of both, nitrogen and carbon isotope ratios appeared different in hepatocellular carcinoma of developmental age comparing with hepatoblastoma.
Conclusion: Our findings highlight that differences between hepatoblastoma and hepatocellular carcinoma of developmental age reach as far down as the atomic structure of the examined entities and stay in compliance with observations that tumours characterized by the activation of transcriptional pathways typical for embryonic development, differ from other types of malignancies. It cannot be excluded that isotopic signatures revealed in our studies reflect the specific metabolic mechanisms responsible for different chemosensivity and disease outcome.

E-PS-07-017
Immunohistochemical evaluation of the expression of MAGE-C1 protein in hepatocellular carcinoma
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Background & Objective: Liver cancer is the 3rd most common cause of death related to cancer. Along with the diseases' constant increase worldwide, therapeutic and diagnostic approaches are making significant progress, including the appearance of new tumour biomarkers, such as MAGE-C1 protein. This protein belongs to the MAGE gene family but is also included in the Cancer- Testis genes group. MAGE-C1 is not expressed in normal cells with the exception of primary spermatocytes. On the other hand, its expression is related with a variety of malignancies such as melanoma. Taking all these facts into consideration, this project aimed to analyze the immunohistochemical expression of MAGE-C1 in hepatocellular carcinoma tissues and correlate it to clinicohistopathological parameters.
Method: During these experiments, 26 liver cancer tissues were used, in which in direct immunohistochemistry was conducted using anti-MAGE-C1 antibody. After that the expression of this factor was evaluated and then correlated to the parameters of interest.
Results: Our results showed a statically significant correlation between the expression of MAGE-C1 protein and a number of factors that included age, gender, HBV or HCV infection, Grade, Lymph node invasion, Nodules, AFP, Cirrhosis and status.
Conclusion: According to these results we came to the conclusion that MAGE-C1 can be an efficient prognostic marker for this malignancy and can be used as a drug target. However, future studies are needed to confirm these preliminary results, in order to be applied in clinical practice and therapeutic management.

E-PS-07-018
Transitional liver cell tumour: a case report
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Background & Objective: Hepatoblastoma (HB) is the most common malignant liver tumour in paediatric patients. The differential diagnosis between some types of HB and hepatocellular carcinoma (HCC) can be difficult, with similar morphological, immunohistochemical and molecular findings. A novel liver cell tumour that develops in older children and young adolescents that has hepatocyte-like phenotype which is distinct from HCC, has recently been classified as transitional liver cell tumour (TLCT). We are presenting a case of a 22-year-old female with metastatic TLCT.
Method: Patient with weight loss, vomiting and pain in upper abdominal quadrant. Elevation of serum α-fetoprotein (AFP = 12,800 ng/mL). The CT scan showed a lesion in the right lobe of the liver with 12.0 cm and paravertebral expansive lesion with infiltration in the vertebral body (L2).
Results: The pathological study of paravertebral biopsy demonstrated high grade primary hepatic neoplasia with overlapping morphological and immunohistochemical characteristics of HB and HCC, with positive immunoexpression for HepPar-1, beta-catenin, cytokeratins (AE1 / AE3) and AFP. The patient died five months after diagnosis and initiation of the treatment.
Conclusion: TLCT is a highly aggressive lesion that usually presents with large neoplasms and high serum AFP.

E-PS-07-019
Intraductal pancreatic acinar cell carcinoma: a case report
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Background & Objective: Acinar cell carcinomas (ACCs) are rare solid pancreatic neoplasms (1-2%) and rarely show intraductal proyections. We report a case of a purely intraductal acinar cell carcinoma without any invasive component.
Method: A 78-year-old man has choledocholithiasis by a solid intraductal mass that dilates the main pancreatic duct. The microscopic study shows the main pancreatic duct to be lined by tubulopapillary structures formed by atypic cells with scant eosinophilic cytoplasm, prominent nucleoli and plentiful mitotic and apoptotic figures. No mucin secretion or necrosis is detected. These cells express CK7, trypsin, chymotrypsin and BCL10. Focal CK19, Ca19.9 and chromogranin A. CK20, MUC5AC, CDX2 and synaptophysin are negative. Electron microscopy confirms cytoplasmic secretion granules. The diagnosis of an intraductal acinar cell carcinoma is made.
Results: ACCs show fairly aggressive behaviour and better prognosis than invasive ductal adenocarcinomas. Some ACCs exhibit intraductal growth, with patterns similar to intraductal neoplasias, forcing differential diagnosis with IPMNs and ITNs. However, our case is one of the first reports of a purely intraductal ACC. Also, 50% conventional ACCs have metastases at the time of diagnosis, with lower metastases rate in ACCs with intraductal growth (15%), implying better prognosis. So far, our patient remains free of recurrence or distant disease. A revision of any ACC during the last 10 years in our hospital showed no results.
Conclusion: Some ACCs exhibit purely intraductal complex growth patterns, mimicking intraductal neoplasias. Performance of BCL10, trypsin and chymotrypsin is necessary for differential diagnosis. This variant displays an indolent behaviour, implying a descent of the metastases rate at presentation.

E-PS-07-020
Pancreatic carcinoma: prognostic impact of galectin-3
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Background & Objective: Primitive pancreatic carcinoma is rare. Only 15% can be treated by surgery with curative intent at the time of diagnosis, which worsens its prognosis. To improve the prognosis, many immunohistochemical markers have been studied, like galectin-3. Our aim was to study the expression of galectin-3 in pancreatic cancer and determine its prognostic impact by studying its relationship with clinicopathological findings.
Method: We underwent a retrospective, analytic study in Pathology department of Habib Thameur Hospital over a period of 14 years (2003-2017). Primitive pancreatic carcinomas were collected. An immunohistochemical staining score was calculated for each sample by combining intensity and percentage of staining. A cytoplasmic and/or nuclear staining was considered as positive. The tumours were categorized into Gal3-low group (score ≤3) and Gal3-high group (score > 3).
Results: Thirty-five cases were analyzed. The patients' average age was 59 years. The sex ratio was 1.43. There were predominantly ductal adenocarcinoma (940/o), well-differentiated), classified into T3 (54%), N1 (67%). 87% of pancreatic ductal adenocarcinoma showed high levels of Gal-3 expression (Gal3-high). Gal-3 expression was significantly associated with tumour location (p=0.036) and histological type (p=0.002). No association was found with age, gender, tumour size, differentiation, vascular invasion, perineural invasion, pathological T status, or with pathological N status.
Conclusion: Our study showed that galectin-3 is overexpressed in ductal pancreatic carcinoma. Galectin-3 expression was significantly associated to the histological type and the tumour location, no correlation was shown with other parameters. These findings suggest that galectine-3 is not a useful prognostic marker in ductal adenocarcinoma of the pancreas.

E-PS-07-021
A case report of solid pseudopapillary neoplasia
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Background & Objective: Solid pseudopapillary neoplasia (NSP) is a rare pancreatic neoplasm, with low risk of distant metastasis and more

frequent in the third to fourth decades. The aim of this study is to determine the incidence of this tumour in Basurto University Hospital between 2000-2018.
Method: Only one case was found of a 35-year-old woman, with recurrent diarrhea, nausea and vomiting. CT and MRI were performed with suspicion of a pancreatic tail tumour measuring approximately 8.4 cm. A corpus-caudal pancreatectomy was performed with laparoscopic splenectomy.
Results: Macroscopically, the pancreas was replaced almost entirely by a 9 cm cystic formation. Histologically, it was a well-defined tumour composed of solid nests of discohesive and eosinophilic cytoplasm cells around small blood vessels, forming rosettes and giving a pseudopapillary appearance, with stromal hyalinization. Mitotic index was less than 5 mitosis / 10HPF, with positive staining for vimentin, alpha1-antitrypsin, CD10, RP, CD56, beta-catenin and chymotrypsin; and negative for CD117, synaptophysin, chromogranin, CKAE1-AE3, inhibin and PAS, with ki-67 of 10%.
Conclusion: The pancreas is an organ in which multiple cystic neoplasms settle. Most of them are included in more frequent lesions (pseudocyst, mucinous cystic neoplasm ...), but there are other less frequent entities that we must take into account in the differential diagnosis that, due to their rarity, are more complex to diagnose, as in our case. In the last eighteen years, there has only been this case reported in our hospital, with typical clinical and pathological features.

E-PS-07-022
Pancreatic metastasis on endoscopic ultrasound-guided fine needle aspiration: a study of 12 cases
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Background & Objective: Endoscopic Ultrasound-guided Fine Needle Aspiration Cytology (EUS-FNAC) is the most common procedure to obtain cytological specimen of pancreatic lesions. Pancreatic metastasis are uncommon and are found in a minority (3-12%) of patients. The objective of this study was to evaluate the role of EUS-FNAC in the diagnosis of pancreatic metastasis.
Method: A retrospective study was performed on the pancreatic metastasis diagnosed by EUS-FNAC between 2014 and 2017 in Department of Pathology, Hospital Universitario Marqués de Valdecilla. EUS-FNAC was performed with Rapid-On-Site-Evaluation in all the cases. Smears were stained with Diff-Quik and Papanicolaou stains. Immunocytochemical studies were performed in cell blocks with corresponding markers according to the diagnostic suspicion.
Results: Nine patients were men, and three patients were women. The mean age of patients was 62.83 years (range 49-84 years). We standarized the diagnoses according the Papanicolau Society of Cytopathology guidelines (Category I: 8%, II: 18%, III: 8%, IV: 8%, V: 8% y VI: 50%). Two patients underwent surgery and ten cases were surgery was not performed. The primary tumours of the pancreatic metastasis were adenocarcinoma of lung (4), CCR (3), duodenum (1), lymphoma (2), CRC (1) and squamous cell carcinoma of oesophagus (1). Sensitivity of EUS-FNA for the diagnosis of pancreatic metastasis was 85,7% (12 cases: 9 confirm pancreatic metastasis, 2 negative and 1 insufficient).
Conclusion: FNAC is a rapid, accurate, and minimally invasive procedure that is useful in the diagnosis of pancreatic metastasis and we show that the prevalence of primary tumours is fulfilled in our sample.

E-PS-07-023
The hidden cause of an acute severe liver injury in an adult female patient
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Background & Objective: An increasing number of people are using herbal supplements, unaware of their potential harmful effects. We report a rare case of severe liver injury due to use of herbal supplements containing Garcinia extract.
Method: A 50-year-old woman was admitted at the Fundeni Clinical Institute, Gastroenterology Department, in September 2017. The pacient complained of marked fatigability. Her laboratory profile revealed acute hepatitis, with an ALT of 700 mg/dl. Diagnostic evaluation was negative for autoimmune, biliary and viral hepatitis. 6 months later, in February 2018, her ALT level was 1170 mg/dl. After a careful anamnesis it was revealed that she was taking herbal supplements containing Garcinia extract since March 2017. She was ordered to stop taking the supplement. At her next visit in March 2018, after one month of not using the supplements, her ALT level was 474 mg/dl. A liver biopsy was performed. In April 2018, her ALT returned to normal levels.
Results: The liver biopsy showed marked lobular hepatitis, with frequent apoptotic bodies, focal and confluent necrosis and reduced portal inflammation, confirming the diagnosis of acute lobular hepatitis. Because her autoimmune antibodies and viral markers were negative and because her liver enzymes returned to normal after the ceasing the supplements, the diagnosis of drug induced liver injury caused by the Garcinia extract was made.
Conclusion: Our case emphasises the importance of performing a careful anamnesis of supplement use in cases that present with liver injury without any obvious etiology and the value of liver biopsy for a proper diagnosis.

E-PS-07-025
Factors influencing prognosis in pancreatobiliary neoplasms
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Background & Objective: The prognosis of some neoplasms is improving due to the development of targeted therapies. However, pancreatobiliary neoplasms remain one of the most aggressive tumours with a high mortality. The aim of this study is to analyze factors that influence prognosis in these tumours.
Method: Retrospective review of 190 patients operated with curative intent in a single large hospital. We have defined outcome both in terms of progression free survival (PFS) and overall survival (OS) and analyzed demographic and morphological data that influence prognosis.
Results: Most patients were women (92) and mean age was 69.69 (range: 38-86). 74.2% of the lesions originated in the pancreas, 12.6% in the biliary tract and 12.6% in the duodenal ampulla. The median PFS time was 12 months and the median OS 19 months. Progression was significantly associated to the presence of symptoms at the time of diagnosis, pancreatic location, biliopancreatic histology, mucin secretion, grade, vessel and perineural infiltration, T and N stage. Death was significantly associated to smoking, presence of symptoms at the time of diagnosis, pancreatic location, biliopancreatic histology, mucin secretion, grade and perineural infiltration. Other histopathologic factors like inflammatory reaction, desmoplasia and necrosis were not significantly associated to prognosis.
Conclusion: Our results confirm the poor prognosis of pancreatobiliary neoplasms, although ampullary location seems to be associated to a better prognosis. Long term survival is exceptionally rare in these neoplasms, despite adjuvant therapy after surgery. Histopathological factors, other than grade and vessel/perineural infiltration, do not seem to influence prognosis.

E-PS-07-026
Primary hepatic carcinosarcoma: a rare histopathological diagnosis in a female patient
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Background & Objective: Primary hepatic carcinosarcoma is a very rare and agressive biphasic malignant tumour, characterized by a combination of carcinomatous, either hepatocellular or cholangiocellular, and sarcomatous elements. The diagnostic classification and the molecular genetic mechanisms that are involved are still unclear.
Method: We report a case of a 77-year-old female patient who underwent surgical resection for a 65 mm heterogeneous mass in the left hepatic lobe discovered by contrast-enhanced CT during follow-up for chronic hepatitis C. The pathology report was elaborated after classical and immunohistochemical analysis of routinely formalin-fixed paraffin-embedded tissue sections obtained from the surgical specimen.
Results: The tumour was composed of an intimate mixture of epithelial and sarcomatoid neoplastic cells. Immunohistochemistry confirmed the biphasic nature of the lesion: the epithelial cells were positive for cytokeratins, HSA and GPC3, and negative for mesenchymal markers; the sarcomatoid neoplastic cells had an opposite immunostaining pattern, being diffusely positive for vimentin and SMA, and negative for epithelial markers. The hepatic tumour was diagnosed as carcinosarcoma according to the WHO 2010 classification. 4 months post-surgery, CT scan revealed supa- and infradiaphragmatic adenopathies and pulmonary metastases.
Conclusion: At present, hepatic carcinosarcoma is included in the group of malignancies of mixed or uncertain origin. The pre-operative diagnosis is difficult, as the imaging features are nonspecific. The prognosis is poor and the diagnosis is based on pathological examination, requiring a panel of immunohistochemical markers.

E-PS-07-027
Intraductal tubulo-papillary neoplasm of the pancreas: report of two cases

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Background & Objective: Intraductal tubulo-papillary neoplasm of the pancreas (ITPN) is a rare tumour that the WHO recognized in 2010 as a subtype of premalignant pancreatic neoplasm. Histologically, ITPNs are characterized by tubulopapillary growth, uniform high-grade cytologic atypia, necrotic foci, ductal differentiation, and without mucin. ITPNs also show particular immunohistochemical and molecular findings. These differences also highlight the fact that intraductal tubulopapillary pancreatic neoplasm is distinct from other similar neoplasms.
Method: We present two cases, diagnosed in 2016 and 2017 at the Universitary Hospital Miguel Servet, Zaragoza, Spain (case 1) and at the Hospital Center of Navarra, Pamplona, Spain (case 2).
Results: Case 1 78-year-old woman with personal history of colon adenocarcinoma and epigastric pain since a few months. A CT showed a neoplasm located in the body of the pancreas and resected with partial pancreatectomy. The neoplasm was diagnosed as ITPN based on histological and immunohistochemical findings. Case 2 63-year-old woman with personal history of colon adenocarcinoma and weight loss since two months. A CT showed a neoplasm located in the body of the pancreas, with invasion of duodenum. The patient were treated with neoadjuvant chemoterapy, with good response at three months and a hepatic lesion, consistent, based on histological and immunohistochemical findings, with metastasis of ITPN of the pancreas.
Conclusion: ITPN is a rare and distinct subtype of pancreatic intraductal neoplasm, and should be differentiated from other pancreatic tumours, including intraductal papillary and mucinous neoplasm and pancreatic ductal adenocarcinoma because ITPN has, usually, a favorable prognosis; nevertheless, characteristic immunohistochemical staining and molecular findings can be useful to distinguish them.

E-PS-07-028
Solid pseudopapillary tumour of the pancreas: clinical, histopathological and immunohistochemical features - a series of 13 cases

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Background & Objective: Solid pseudopapillary neoplasms (SPN) of the pancreas is a rare entity, representing 1-2% of all pancreatic tumours. The aim of this study is to present the clinicopathological and immunohistochemical characteristics of this rare neoplasm.
Method: We conducted a retrospective study of SPN diagnosed at Victor Babes National Institute of Pathology, Histopathology and Immunohistochemistochemistry Department between May 2010 and March 2018. We selected 13 cases. The criteria used to evaluate them were sex, age, morphopathology and presence of metastases. We performed a large panel of immunohistochemical markers, including vimentin, beta-catenin, CD10, chromogranin, synaptophysin, progesterone receptor and Ki67.
Results: Of all 13 cases, 12 were female. The mean age of the pacients was 31 years. Tumour size varied between 1.5 cm and 9 cm in diameter and the most common location was the head of the pancreas. Two cases had distant metastases, one in the liver and one in the transverse mezocolon. All cases presented positivity for vimentin, beta-catenin and progesterone receptor. All cases except one showed positivity for CD10. All cases were negative for chromogranin. Synaptophysin was done in 12 cases; it was focally positive in 9 tumours. Ki67 was performed in 5 patients and the mitotic index was under 5%.
Conclusion: SPN is a rare type of tumour. The immunohistochemistry panel should include at least vimentin, progesterone receptor, chromogranin, CD10 and beta-catenin. Its diagnosis is important because of its low malignant potential in comparison to other primary neoplasms of the pancreas.

E-PS-07-029
Recurrent giant liver cavernous hemangioma with Kasabach-Merritt syndrome – a case report with emphasis on the pathogenesis, imaging diagnosis, histopathology and immunohistochemistry

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Background & Objective: Hemangioma is a congenital benign tumour with mesenchymal origin, usually asymptomatic. The tumour is mostly discovered incidentally. We report a case of a recurrent giant hemangioma of the segment 4 of the liver.
Method: We present the case of a 43-year-old male patient, obese, admitted at Fundeni Clinical Institute for spontaneous ecchymoses of the lower limbs in January 2015. Abdominal ultrasonography revealed multiple tumour masses in the liver diagnosed as cavernous hemangiomas. The pacient underwent enucleation for liver hemangioma (segment 6 and 7) and left lateral sectionectomy. The hepatic tumour was associated with Kasabach-Merritt syndrome. At follow up, imagistic exams showed multiple liver hemangiomas treated with chemoembolization. In April 2017, MRI detected an 11-cm mass in the segment 4 of the liver. The recurrent hemangiomas were treated with chemoembolization and surgical enucleation.
Results: Gross description revealed in 2017 a hepatic tumour with the size of 12/9/8 cm. Microscopy evidentiated vascular spaces lined by flat epithelium, with variable sizes and fibrous stroma. In the adjacent liver were observed cavernous hemangioma-like vessels. Immunohistochemical stains for FVIII, CD31 and CD34 were positive, while β-cathenin was negative. The Ki-67 index was focally positive in the peritumoural hemangioma-like vessels, in small endothelial cell tufts, prominent in the vascular lumen. The patient is on the waiting list for liver transplant.

Conclusion: Given the pattern of Ki-67 stain, these peritumoural vessels could be involved in tumour progression and recurrence. Considering the unclear pathogenesis of giant hepatic hemangioma, the differential diagnosis of this entity represents a challenge for pathologists.

E-PS-07-030

Pancreas abnormalities associated with carcinoma of the ampullary and periampullary region

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Background & Objective: The abnormality of pancreas is a rare. Pancreas divisum is the most common variation of pancreatic duct formation and may be present in ~4-10 % of the general population.
Method: To reveal quantity of mostly common pancreatic abnormalities and estimate their relationship with carcinoma of the ampullary and periampullary region. We've examined 210 patients with different ampullary and periampullary carcinomas treated in Botkin Hospital between 2016-2018. PDAC was 148 (70,5%), AC - 61 (29,0%) and 1 case of minor papilla cancer (0,5%).
Results: Anomalies were represented by the pancreas divisum (PD) and annular pancreas. PD is a frequent anomaly and detected in 31/210. 27/61 resected cases of ampullary carcinoma associated with PD. Type 1 – 4/27, type 2 – 22/27 and type 3 – 1/27. PDAC associated in 3/148 and 1 case of minor papilla cancer we had founded PD (type 2). Statistical analysis an association between AC and pancreas divisum amounted to r=0,37, p<0,05. Annular pancreas was detected in only PDAC - 1/148
Conclusion: Pancreas divisum should be important to raise the suspicion of ampullary carcinoma in patients.

E-PS-07-031

Casual finding of pancreatic neoplasia in young patient

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Background & Objective: Solid pseudopapillary neoplasm (SPN) of the pancreas is a rare tumour which predominantly affects young women. It supposes a 0,13-2,7% of all exocrine pancreatic tumours. We present a new case and review of the literature.
Method: A 20-year-old woman with a personal history of nephritic colic who presented with a pancreatic head neoplasm like an incidental diagnosis in an abdominal ultrasound revision. An abdominal CT scan confirms the presence of a non-homogenous hypodense lesion, with thickened walls in the head of the pancreas. USE-FNA result was negative for malignant tumour cells. The treatment was a cephalic duodenpancreatectomy. The diagnosis was a solid pseudopapillary pancreatic neoplasm. She did not receive any neoadjuvant treatment. The patient remains stable at the present.
Results: Solid pseudopapillary tumour of the pancreas was first described by Frantz in 1959 and was included in the World Health Organization classification in 1996. It mainly affects young women. The initial presentation of SPT is nonspecific, being frequently an incidental finding. Main location is the tail and the head of the pancreas. Its radiological features (cysts) make preoperative diagnosis. Complete surgical removal is the treatment of choice. Microscopically, it was a well-defined tumour with an heterogeneous appearance. It shows necrotic haemorrhage, pseudocysts lined by cells with a pseudopapillary growth pattern and solid areas of poorly cohesive monomorphic cells.
Conclusion: It is important for the pathologist to be familiar with its salient clinical, cytopathologic, histopathologic and immunohistochemical features. Such knowledge is essential to differentiate it from other potentially more aggressive pancreatic neoplasms.

E-PS-07-032

Intraductal papillary neoplasm of the bile duct (IPNB): a case report of a challenging disease to diagnose

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Background & Objective: Intraductal papillary neoplasm of the bile duct (IPNB) is a rare bile duct neoplasm characterized by papillary growth within the bile duct lumen and is regarded as a biliary counterpart of intraductal papillary mucinous neoplasm (IPMN) of the pancreas. It is mainly found in far eastern nations, whereas in western countries it is very rare and the etiology is unknown. Here, we report a 78-year old woman, referred to our hospital because of repeating episodes of cholangitis.
Method: Imaging modalities revealed cystic lesions (with maximum size of 4,4 cm diameter) arising from the V segment of the liver. The patient underwent exploratory laparotomy, cholecystectomy, drain of a cystic mass under ultrasound guidance, and a tru-cut biopsy of the IVa segment of the liver.
Results: Macroscopically, the bile duct lumen did not exhibit alterations, whereas at the mucosal cystic duct surface a neoplasm was recognized. Histologically, the neoplasm in the cystic duct has a pancreatic-muscular morphological epithelial phenotype, while in the lymph nodes the metastasis is poorly differentiated with the presence of small tubular formations and a few cells with mucus, which are sometimes of a Signet ring type. With the Masson staining, the presence of intense fibrosis has been shown to give the impression that it surrounds the liver lobes.
Conclusion: Diagnosis of IPNB is still daring, especially in western countries due to its rare incidence. Precise clinical and pathologic features are in high demand for the exact diagnosis and treatment of IPNB as well.

E-PS-07-035

Mucinous cystic neoplasm of pancreas, an emergent diagnosis

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Background & Objective: Mucinous Cystic Neoplasm (MCN) of the pancreas comprises 10% of all pancreatic cystic lesions and 1% of pancreatic neoplasm. Most of them arise in the body and tail of the pancreas. They are more frequent in women (F/M 20:1). Microscopically, the neoplasms are lined by mucin-secreting columnar epithelial cells over and underlying ovarian-like stroma. Their correct diagnosis is increasing, largely due to better imaging studies and greater knowledge of this entity by the different medical specialists.
Method: Surgical specimens of pancreatectomy from our department files between 2000-17 were reviewed.
Results: 7 cases of women ages 40- 50, with MCN in the corpus and tail of the pancreas were identified, 6 of them in the last 3 years. Clinical histories were not relevant. Five cases had cytological studies obtained by EUS-FNA, showing benign cyst. A distal pancreatectomy was performed. Macroscopically, mostly unilocular cyst without ductal system comunication were observed. Histologically, all of them were lined by columnar epithelium with underlying ovarian-like stroma. One case had low-grade epithelial dysplasia. No adenocarcinoma was found.
Conclusion: We can suspect MCN in a young woman, with a pancreatic cyst lesion, located distal in the pancreas and a cytology of benign cyst by EUS-FNA preoperative. The definitive diagnosis is usually based on the examination of the surgical specimen. Histologically, ovarian-like stroma is a requirement for the diagnosis with CD10, ER and PR immunohistochemical positivity. An adequate sampling of the lesion is important to identify areas of epithelial dysplasia and rule out foci of infiltration.

E-PS-07-036

Refinement of preoperative diagnosis of solid pseudopapillary pancreatic neoplasms by endoscopic ultrasound-guided fine needle aspiration. Report of 2 cases with surgical specimens

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Background & Objective: Solid pseudopapillary neoplasms (SPNs) are very uncommon pancreatic tumours with a good prognosis, that occur mostly in young women. Cytology and cellular blocks obtained by Endoscopic Ultrasound-Guided Fine Needle Aspiration (EUS-FNA) add greater accuracy in preoperative diagnostic performance compared to imaging tests.
Method: We revised the cytology and cellular blocks of pancreatic tumours diagnosed by EUS-FNA in our institution between 2010-17.
Results: We identified 2 cases of SNP diagnosed in two women ages 39 and 65. The older one had a history of hepatitis B virus (HBV). In the computerized tomography (CT), both presented solid lesions in the body and tail of the pancreas measuring 2.5x2.3 cm and 10x7cm respectively. A cytology and cellular block by EUS-FNA was taken resulting in a preoperative SPN diagnosis. The diagnosis was confirmed in the surgical specimens.
Conclusion: SPN amounts to 1-2% of pancreatic neoplasms. It mainly affects women between the ages of 20-40. About 62% of the patients have a clinical history of HBV infections, as shown in one of our cases. A cytology and cellular block study obtained preoperatively by EUS-FNA, as a minimally invasive procedure, increases the diagnostic accuracy in SPN and allows their differentiation from intraductal papillary mucinous neoplasms (IPMN), neuroendocrine tumours, cystic mucinous neoplasms, etc. This can be extremely helpful in defining the surgical procedure.

E-PS-07-038

Signet ring cell carcinoma: an unusual diagnosis in the ampulla of Vater

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Background & Objective: Signet ring cell carcinoma (SRCC) of the ampulla of Vater is described by the WHO as a very rare variant of gastrointestinal adenocarcinoma, which is characterized by the presence of more than 50% signet ring cells. There have only been 32 cases described in this location.
Method: We report the case of a 72-years-old-woman, who presented with epigastralgia and constitutional syndrome. Imaging study showed an intra- and extra-hepatic obstruction originated in Oddy's sphincter suggestive of ampuloma. The patient was treated with a radical pancreatoduodenectomy surgery.
Results: Macroscopically, a firm, whitish tumour (2 cm) was located in the duodenal wall which histologically revealed a poorly differentiated adenocarcinoma, composed almost exclusively of signet-ring cells. It was limited to the duodenal wall, without affecting pancreatic or soft adjacent tissue. Immunohistochemical study suggested a pancreatobiliary origin. Local lymph nodes were negative and margins free of disease.
Conclusion: SRCC origin remains controversial. One theory suggest it originates from heterotopic gastric mucosa, while the other supports it comes from gastric metaplasia due to hyperacidity in duodenum. Surgery is considered to be the first line treatment. Owing to the rarity of cases reported in the literature, prognostic and clinical course remains uncertain. However, it seems to be defined by differentiation grade and tumoural stage. Compared to other gastrointestinal locations, the survival may be higher due to an early onset of symptoms and subsequent diagnosis, nevertheless further studies are needed to provide more information. Our patient is free of disease two years after surgery without adyuvant treatment.

E-PS-07-039

Amphicrine carcinoma of the ampullary region: a case report and review of the literature

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Background & Objective: Malignant amphicrine tumours are a group of tumours in which tumour cells show evidence of both epithelial as well as neuroendocrine differentiation. These tumours are extremely rare. To the best of our knowledge, this report describes the second case of amphicrine carcinoma in the ampullary region, who made us to report the case.
Method: We report the case of a 53-year old men admitted for jaundice. On examination of the computed tomography scan and endoscopicretrograde cholongio-pancreatography, a mass of about 1,4 cm in diameter was detected in ampullary region. A pancreatico-duodenectomy was performed, and the mass was found in ampullary region.
Results: On gross examination of the cut section of the tumour, the mass measured 1,4x1,2x1cm in size. Microscopically, the tumour was composed of cells have both exocrine and neuroendocrine differentiation, with mucus and neuroendocrine granules within the cytoplasm. Immunohistochemical these tumours are positive for both neuroendocrine as well as epithelial markers. A definitive histological exanimated was Amphicrine carcinoma of the ampullary region.
Conclusion: Amphicrine carcinomas are extremely rare, the optimal strategy of management is largely unknown, due to rarity of these neoplasms.

E-PS-08 | Endocrine Pathology

E-PS-08-001

Multiple endocrine neoplasia type 2A syndrome with atypical biological behavior – a case report and review of the literature

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Background & Objective: MEN2 is a syndrome with well studied genotype-phenotype correlation. There are two types (A and B) with specific characteristics, both of them strongly associated with pheochromocytoma and medullary thyroid carcinoma (MTC). 95% of the cases are type 2A. We aim to present a case of MEN2A syndrome with malignant pheochromocytoma and metastatic MTC, as well as a review of the literature.
Method: A 30-year-old male with a family history of MEN2A was referred to our institution for clinical investigation.
Results: Genetic testing revealed a germline RET codon 634 mutation, which is responsible for the vast majority of MEN2A cases and is included in the high risk category. Other codons can fit the highest or the moderate category, each of them with different recommended timings of surgical approach. Neck ultrasound showed bilateral involvement of the thyroid by two masses and multiple bilateral neck lymph nodes. Scintigraphy suggested the presence of bilateral pheochromocytoma. Adrenalectomy specimen unveiled a malign bilateral pheochromocytoma with PASS score > 4, both the CT scan and MRI suggested liver metastases, and total thyroidectomy specimen revealed a MTC stage pT4a N1b. This is unusual since, according to literature, MEN2A's pheochromocytomas are benign approximately 98% of the times, and MEN2A's MTCs are more indolent than MEN2B's.

Conclusion: This is a case of MEN2A syndrome diagnosed at a high stage, with surprisingly aggressive behavior and bad prognosis, which is a clinical course more associated with MEN2B.

E-PS-08-002

Modern methods for the structural characterisation of collagen in capsular invasion areas in papillary thyroid carcinoma

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Background & Objective: The purpose of this study was to identify changes in the collagen structure and organization in papillary thyroid carcinoma (PTC) nodule capsules which can be further used to compare non-invaded base capsule with areas of capsular invasion.
Method: Second Harmonic Generation (SHG) Microscopy based on a coherent second order nonlinear optical process known as second harmonic generation in which photons interacting with optically nonlinear materials, are effectively combined to form new photons with exactly half of the excitation wavelength was used for probing the molecular structure and structural organization in collagen-containing capsules. Images were acquired on 4-7 μm thick tissue sections mounted on glass slides without H&E staining. Collagen organization was evaluated from SHG images by intensity-based parameters (e.g. first and second order statistical moments, fractal and Helmholtz analysis) to quantify the capsular structure.
Results: In order to accomplish quantitative image analysis to identify invasion areas, we have used different texture analysis methods which provide parameters of the collagen distribution and organization from SHG images. An extended set of parameters were considered but only a few retuned statistically relevant results.
Conclusion: By combining SHG microscopy with quantification parameters for image texture analysis provided by the histogram analysis, gray level co-occurrence matrix, fractal analysis and Helmholtz analysis in the case of the collagen capsule surrounding PTC nodules, we have proven for the first time to our knowledge that the collagen distribution can be linked with a capsular invasion area in an objective manner. Our quantitative results can be further used to identify, in the future, pre-invasion area of Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFT-P) or Well-differentiated tumour of uncertain malignant potential (WDT-UMP), which may complete traditional histopathologic examination.

E-PS-08-003

Immunohistochemical study of gastroenteropancreatic neuroendocrine tumours

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Background & Objective: Study of all neuroendocrine tumours involving GI tract and pancreas, diagnosed in Alassad University Hospital/ Damascus University between the year 2006-2017.
Method: Our study involves 141 cases of NETs diagnosed by routine H&E stained sections of small incisional and endoscopic biopsies, and excisional cases, confirmed by short panel of basic neuroendocrine markers (synaptophysin, chromogranin, NSE) with evaluation of mitotic activity using Ki-67 immunostain. The evaluation of grade of tumours were based on the WHO classification, 2010.
Results: Cases of gastroenteropancreatic neuroendocrine tumours diagnosed in our facility are relatively rare, they form about 2% of all gastric tumours, and 0.2% of colonic tumours. Patients age ranged between 20-85 y/o, with median age of occurrence of 55 y/o, male to female ratio 78/63, most common primary site is in the stomach with a rate of 35.4% (50 cases) then the pancreas with a rate of 32.6% (46 cases), followed by small intestine with 16.3% (23 cases), appendix with 10.6% (15 cases) and finally the least in colon with 4.9% (7 cases). About 55% of cases were of grade1, 30% of cases were of grade 2, and grade 3 (NEC) formed 15% of studied cases. We also have one case of gastric mixed adenoneuroendocrine carcinoma.
Conclusion: NET of variable grades can occur in any part of the gastroenteropancreatic system, it should be thoroughly examined for accurate grading, WHO classification 2010 can be easily applied, and it gives a high rate of reproducibility.

E-PS-08-004

Clinicopathologic characterisation of a case series of ectopic adrenal tissue in adults

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Background & Objective: Ectopic adrenal tissue (EAT) can occur in several anatomical locations, which is best explained by disturbances of embryological development. EAT seems to be fairly prevalent at birth and regress with age. It is usually an incidental finding in surgical specimens. Clinical significance is minimal but rare reports of neoplasia developing in EAT exist. We aimed to characterize the clinicopathological features of EAT in adults.
Method: We retrospectively selected all EATs reported in two Portuguese tertiary centres (2008-2018) and reviewed their clinicopathological features.
Results: We identified 19 EATs in 16 patients (4 males, 12 females). One case was bilateral. One patient had three unilateral EATs. One patient had also splenic ectopic tissue. Mean age was 53 years (range:26-74 years). All cases were incidental findings. Fifteen were periadnexal (79%) and four located in testicular adnexa/spermatic cord (21%). Only two were macroscopically identified, consisting of bright yellow nodules. Mean microscopic size was 2.5mm (range:1-5mm), and 12 (63%) had a fibrous capsule. Representation of each cortical zone was variable, both in number (one zone:16%, two zones:63%, three zones:21%) and relative quantity (granulosa:9%; fasciculata:63%; reticularis:28%), with predominance of zona fasciculata. The only two cases with ample zona granulosa occurred in males. No medullary tissue was observed.
Conclusion: EATs are usually very small nodules, being rarely diagnosed in adults. They are found most often in surgical specimens that include structures along the path of gonadal descent. The overall architecture seems to mimic normal cortex however, the relative proportion of cortical zones is variable.

E-PS-08-005

The many faces of differentiated thyroid carcinoma

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Background & Objective: Diagnosis of thyroid tumours still remains an ardous and treacherous exercise. We describe a case of thyroid carcinoma with peculiar morphologic characteristics.
Method: A 35-year-old woman presented with a right thyroid nodule and normal levels of thyroid hormones. Fine needle aspiration revealed a follicular lesion of undetermined significance. Total thyroidectomy was performed. Grossly, the thyroid of 38grams presented a poorly defined nodule with white cut surface measuring 18x12x10mm in a background of multinodular goiter.
Results: Histologic examination revealed a tumour with follicular pattern and abundant fibrous stroma associated with focal lymphocytic thyroiditis. Nuclei were slightly irregular with even chromatin distribution. Nuclear clearing and pseudoinclusions were not observed. Within the tumour, small solid or rosetoid nests of cells (SNC) with similar nuclear characteristics were identified; some

cells were ciliated. Immunohistochemistry showed reactivity for thyroglobulin and TTF-1. A small group of cells in the periphery of lesion showed expression of calcitonin, chromogranin, synaptofisin and CD56. The SNC showed no expression of any of the abovementioned antibodies. A lymph node with unequivocal metastasis of papillary carcinoma (PC) was identified. Extrathyroidal extension and vascular invasion were not observed.
Conclusion: The diagnosis of PC was achieved because of lymph node metastasis. Although gross morphology suggested this diagnosis, the tumour had no cytological features typical of PC. Presence of a phenotypically different population poses the differential diagnosis between reactive C cell hyperplasia and mixed carcinoma, which further makes the case unusual. A small population of ultimobranchial derived cells remaining in the center of the tumour can not be excluded.

E-PS-08-006
Amphicrine signet-ring cell carcinomas of the stomach
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Background & Objective: To identify in the carcinomas of the stomach an amphicrine signet-ring cell component, the cells of which secrete mucus and neuroendocrine granules simultaneously.
Method: Histologically, immunohistochemically studied by 50 gastric carcinomas. Antibodies with chromogranin A, synaptophysin, NSE, Ki-67 were used.
Results: All examined tumours found to be heterogeneous in histological structure and degree of differentiation, combining glandular, neuroendocrine, signet-ring cell, mucinous and undifferentiated components. Neuroendocrine component was detected in 62%: in 4% occupying more than 70% of the area (neuroendocrine carcinoma), in 6% - from 30 to 69% (mixed adeno-neuroendocrine carcinomas), less than 30% of the area - in 52% of tumours. The amphicrine signet-ring cell component was detected in 26% of all carcinomas, most often (42.3%) in gastric cancers with a neuroendocrine component of less than 30%. The size of the foci of amphicrine signet-ring cell carcinoma varied from single cells and groups of them to foci of considerable size, occupying up to 25%. The background processes in all the observations were chronic atrophic gastritis with hyperplasia neuroendocrine cells.
Conclusion: The amphicrine signet-ring cell component is revealed in 26% of cases gastric carcinomas. Further studies are required to determine its clinical and prognostic significance.

E-PS-08-007
Expression of CD44, Cyclin D1 and p27 in thyroid follicular adenoma
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Background & Objective: The differential diagnostics of follicular thyroid nodules can be difficult even in surgical material (Yoon et al., 2014). Consequently, diagnostic problems urge to consider the value of tumour immunophenotype (Sobrinho Simões et al., 2011). In the current study, we assessed cell cycle regulation and stem cell differentiation in follicular adenomas.
Method: In a retrospective study, 20 patients with morphologically confirmed and surgically removed thyroid follicular adenoma were included. Tumours were diagnosed according to the classification and criteria issued by World Health Organisation (DeLellis et al., 2004). Expression of CD44, cyclin D1 and p27 was detected by immunohistochemistry and assessed as the fraction of positive cells (%). The measurements were performed by computer-assisted morphometry using NIS Elements (Nikon, Tokyo, Japan) software and optical system consisting of Eclipse Ci-L microscope/ DS-Fi2 camera (Nikon). Descriptive statistical analysis was applied, including estimates of mean±standard deviation and 95% confidence interval (Altman et al., 2000).
Results: The mean values of CD44: 58.5±32.6% [95% confidence interval: 44.2–72.8] and p27: 62.5±24.5% [51.5–72.9] in thyroid follicular adenoma showed no significant differences versus surrounding tissues: 43.3±27.7% [31.2–55.4] and 81.5±24.9% [70.6–24.9], respectively. The mean expression of cyclin D1 in thyroid follicular adenoma was significantly higher than in surrounding tissues: 63.3±19.3% [54.8–71.8] versus 18.5±11.3% [13.5–23.5].
Conclusion: Cyclin D1 is up-regulated in thyroid follicular adenoma and thus could have pathogenetical and/or diagnostic role.

E-PS-08-008
Expression of glypican-3 and HSP-70 in adrenocortical carcinoma: a challenging differential diagnosis in hepatic lesions.
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Background & Objective: A 52-year-old man presented with a mass involving the right adrenal gland and the right hepatic lobe, and highly suspicious for adrenocortical carcinoma (ACC) due to diffuse signs of Cushing syndrome. For the purpose of differential diagnosis and to exclude simultaneous hepatocellular carcinoma (HCC), immunohistochemistry against hepatic markers had been performed, revealing immunoreactivity for glypican-3 and HSP-70 in the neoplastic cells. This study aims to investigate expression of hepatic markers in ACC.
Method: Immunohistochemistry against glypican-3 and HSP-70 was carried out in seven cases of ACC taken from the archive of our Unit.
Results: All seven cases of ACC were negative for Glypican-3. With regards to HSP-70, four cases were negative for this marker, while three showed cytoplasmic and nuclear positivity staining.
Conclusion: Differential diagnosis between ACC and HCC can be challenging in asymptomatic patients with hepatic nodules. ACC, in particular its oncocytic variant, shows neoplastic cells arranged in trabeculae with nuclear atypia and eosinophilic and clear cytoplasm, similar to HCC. Synaptophysin, melan-A and inhibin-alpha are consistently positive in ACC whereas glypican-3 and HSP-70 are considered to be specific for HCC. However, our findings show that positive staining for glypican-3 and HSP-70 can be rarely observed in ACC. Acknowledgement of this finding is essential to avoid misdiagnosis of ACC liver metastases or involvement as hepatocellular carcinoma based on glypican-3 or HSP-70 positivity. Correct use and interpretation of immunohistochemistry, together with clinical information as well, are essential for differential diagnosis between those entities.

E-PS-08-009
Squamous cell differentiation in metastatic papillary thyroid carcinoma: Metaplastic reversion or progression?
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Background & Objective: Squamous cell differentiation (SCD) may occur in papillary thyroid carcinoma (PTC) only at metastatic sites.
Method: We have studied cytokeratin CK5/6 and P63 along with TTF1 and B-Raf immunohistochemical expression in neck lymph node metastases of thyroid PTC showing SCD (as well as in the primary thyroid tumour).
Results: The metastases were peculiar by the presence of cystic change and of SCD, features not seen in the primary thyroid PTC. The thyroid PTC expressed P63 focally and, TTF1 and B-Raf diffusely. CK5/6 was expressed only in the lymph node metastases, in the metastatic cyst lining and in SCD foci. Positive CK5/6 cubic/flat cells located basally/suprabasally (not luminally), in uni- or pluristratified epithelia, lined the

cystic zones of metastases. CK5/6 was also expressed in compact cell groups, by large, non-atypical, squamoid cells around the cysts as well as in small metastatic PTC-vesicles, by rare nondescript cells. P63 expression was strong in SCD, frequently absent in the luminal cells. TTF1 expression was mild and focal in SCD. TTF1-positive nuclei were seen in the luminal cells, above the CK5/6-positive and P63-positive cells in the SCD. Metastatic, both classical PTC- and SCD-epithelia expressed B-Raf.
Conclusion: The expression patterns of CK5/6, P63, TTF1 suggest a luminal/central-to-abluminal/peripheral direction for SCD development from PTC-epithelia in lymph node metastases. Whether this metaplasia type may reflect a regression to a less aggressive morphotype or a progression-switch to squamous cell carcinoma-type differentiation in a composite tumour remains matter of debate.

E-PS-08-010
Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) need not be confused with papillary thyroid carcinoma
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Background & Objective: NIFTP described by Nikiforov 2016 is now included in the 4th Edition of the WHO Classification. Despite the fact that potentially benign NIFTP shares most of the histologic features with encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC), consensus diagnostic criteria distinguished NIFTP from EFVPTC exist.
Method: Eleven females ranging in age from 36 to 51 underwent total thyroidectomy (N=7) and lobectomy (N=4) from May 2016 to March 2018. Four patients were suspected of having papillary thyroid carcinoma (PTC) (Diagnostic category Bethesda 5), two of follicular neoplasm (Bethesda 4 including one with suggestion NIFTP); Four patients were diagnosed with goiter (Bethesda 2) and one was diagnosed with PTC (Bethesda 6).
Results: Microscopic examination of the operative specimen revealed histological features of NIFTP in all 11 patients. Of 11 tumours ranging in size from 15 to 43 mm nine were encapsulated and two clear demarcated. In five patients NIFTP occurred in addition to goiter (N=4) and PTC (N=1). All 11 patients were alive with no evidence of disease in the 6-28 months follow-up (median 15).
Conclusion: Correct diagnosis of NIFTP according to established diagnostic criteria allows selecting a group of patients with a good prognosis who do not require adjuvant therapy such as radioactive iodine ablation.

E-PS-08-011
A giant adrenal myelolipoma: a case report
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Background & Objective: Adrenal myelolipoma (AML) is a rare, benign tumour of the adrenal gland composed of mature adipose and haematopoietic tissue. The latter component can be present in variable amounts. Most AMLs are small and asymptomatic and often found incidentally by imaging studies performed for other reasons or at autopsy. The aim of this study is to describe a case of a large-sized and symptomatic AML in a 56 year-old woman.
Method: In a case of adrenal myolipoma in a 56 year-old woman, the pathologic features of the tumour were studied and described.
Results: A 56-year-old female patient with history of high blood pressure, type 2 diabetes and hypothyroidism, presented with vague dull aching of the right hypochondrium evolving for about one year. MRI examination revealed an adrenal mass measuring 16 × 15 × 11 cm. It showed predominantly fat density. Gross examination of the removed tumour, 9 months later, showed a well circumscribed globular mass measuring 21 × 8 × 7 cm. On cutting, the tumour had yellowish regular greasy surface with reddish-brown areas underneath a thin capsule. Microscopic examination revealed a neoplasm composed predominantly of mature adipose tissue with intervening haematopoietic tissue. It was separated from the adrenal parenchyma by a continuous capsule. Diagnosis of AML was retained.
Conclusion: AML is a benign tumour that should simply be kept under routine follow up if small and asymptomatic. Giant and symptomatic forms are usually treated by adrenalectomy due to the risk of spontaneous rupture and intra-tumoural hemorrhage. Pathologists should be aware of this rare adrenal entity in order to make a correct diagnosis.

E-PS-08-012
Calcification (pseusopsammoma)-rich thyroid oncocytic adenoma with clear cell change
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Background & Objective: Abundant calcifications and clear cell change may occur in thyroid oncocytic adenoma (TOA). We aimed to report the features of a case of TOA peculiar by the presence of extensive calcifications and of a clear cell component.
Method: The TOA was detected on a right thyroidectomy specimen. The tumour was entirely analysed on microscopy.
Results: Clear cell change was observed in 15-20% of the cells. Numerous, focally confluent psammoma-type calcifications, resulting in macrocalcifications were detected. The nodule cells, uni- or multinucleated oncocytes, including those with clear cytoplasm, expressed heterogeneously TTF1, S100 protein, Bcl2, CD10 as well as CD138 and CD56. Lipid droplet markers adipophilin and TIP47 were also expressed.
Conclusion: In conclusion, we report a rare type of oncocytic thyroid adenoma, peculiar by the presence of macrocalcification and by the presence of clear cell change. Heterogeneity in membrane CD56 and/or CD138 expression as well as cytoplasmic heterogeneity of Bcl2 and lipid droplet marker TIP47 are possibly relevant for calcification and clear cell change, requiring further investigation.

E-PS-08-013
Morphological analysis of papillary thyroid carcinoma with psammoma bodies
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Background & Objective: During last decade, the proportion of thyroid cancer, among other types of cancer had a clear tendency to rise. Papillary thyroid carcinoma (PTC) is the most common cancer of this organ, constituting up to ca. 70% cases. For the majority of patients the general survival rate depends on the histological features of the tumour and on many other predictors, one of which is pathological biomineralization. The aim of the work is to carry out morphological analysis of the tissues papillary thyroid carcinoma with psammoma bodies.
Method: We have analysed the samples from 54 PTC patients and controls by using immunohistochemistry and spectroscopic techniques. The samples were divided into two groups: the PTC group included 24 cases of PTC with psammoma bodies and the control group was constituted of 30 PTC cases without psammoma bodies and other manifestations of pathological biomineralization.
Results: We have demonstrated the clear colocalization of osteopontin and calprotectin in the psammoma bodies and suggested the model for their laminated structure development. Immunostaining with of activated Caspase 3 antibodies revealed significantly higher number of apoptotic cells in the samples of PTC with PBs.

Conclusion: We have found intensive immunostaining with osteopontin antibodies in the tumour tissues and in the tumour surrounding, which indicates that osteopontin may counteract biomineralization. We have shown that the major component of PBs is hydroxyapatite.

E-PS-08-014

Retroperitoneal paragangliomas: a clinicopathological study of 3 cases

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Background & Objective: Paragangliomas are rare tumours occurs from extra-adrenal chromaffine tissues. Paragangliomas of the retroperitoneum arise from specialized neural cest cells distributed along the aorta in association with the sympathetic chain. This entity differs from others (head and neck paragangliomas) in its rarity and high malignancy potential. Our purpose was to analyze clinical and pathological features of three cases of retroperitoneal paragangliomas
Method: We reviewed the data of all patients managed for retroperitoneal paragangliomas from 2010 until 2018 from the archive of the department of pathology of "Fattouma Bourguiba" hospital in Monastir.
Results: There were 3 patients (all women) in the median age of 52 years (47-57 years). high blood pressure was the commonest clinical presentation. Radiology showed the retroperitoneal localization in three of them. All patients underwent surgical resection of the tumours which were the only treatment. The specimens were sent to the department of pathology. Macroscopically, all the tumours were encapsulated and the median size were 4 cm (2-5 cm). Under the microscope, tumour cells were oval or polygonal and arranged in nests or trabeculae, containing rich cytoplasm with eosinophilic fine granules. Large nuclei were strongly stained and exhibited round or oval nuclei.
Conclusion: Retroperitoneal paragangliomas are rare tumours. a definitive diagnosis can be reached only by histology which is often noncontributory to determining the benign or malignant nature of the tumour and in front of the potential of malignancy of these tumours; a follow up of patients is necessary.

E-PS-08-015

Prevalence of diabetic foot in 2009-2013 in a province

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Background & Objective: Diabetic foot is a complication which involves about 10-25% of diabetic people. Given that diabetes is growing, one of the most important complications about diabetic foot is ulcers and amputations. We aimed to evaluate this state in our patients.
Method: This retrospective descriptive cross-sectional study was done on diabetic patients referred to Shahid Sadoughi general Hospital in Yazd, during 2009¬-2013. Demographic data such as gender, age, type of treatment, history of smoking, blood sugar level, duration of infection, duration of diabetes, history of amputations, and hospitalization for ulcers, were extracted from Shahid Sadoughi hospital health information system (HIS). The collected data were entered into SPSS version 18 software and were analyzed by statistical tests.
Results: The results showed that the mean age of participants was 61.78 ± 13.36 years and the mean duration of diabetes in patients was 13.89 ± 8.7 years. Out of 165 patients, 54 (32.7%) women and 111 (67.3%) were male. The highest frequency of prevalence of diabetic foot was in 2013 and 47 patients (28.5%) were between 60-70 years old. Out of 165 patients under study, 59 (36%) were amputated. There was a significant relationship between the frequency of amputation as a type of treatment and the frequency of diabetes duration. (P-value <0.05)
Conclusion: Considering that diabetic foot ulcers are one of the most preventable complications of diabetes, it is possible to reduce the prevalence of diabetic foot ulcers and amputations by providing training programs for diabetic patients.

E-PS-08-016

A well differentiated neuroendocrine tumour with teratoma elements in sacrococcygeal region: rare case report

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Background & Objective: A well differentiated neuroendocrine tumour within teratoma is accounting for less than 1% of all testicular tumours, occurs in both children and adults. The majority of them have a favorable clinical outcome. We present a case of carcinoid tumour within teratoma arising in sacrococcygeal region in a 37-year-old man.
Method: According to the preoperative CT findings the diagnosis of teratoma was made and an incisional biopsy was performed. The specimen was formalin-fixed and processed for histopathological and immunohistochemical study.
Results: Histological examination showed well defined solid nests composed of small sized cells with granular eosinophilic to pale cytoplasm and round nuclei with salt and pepper chromatin in a prominent fibrous stroma associated with cysts that have stratified squamous epithelium containing yellowish keratinous material without skin appendages (epidermoid cyst). Neither necrosis nor mitoses (more than 2-10 per 10HPF) were found. No findings of germ cell neoplasia in situ (GCNIS) were observed. Immunohistochemically, the tumour cells were positive for CK8.18 (dot like) with coexpression of Chromogranin, Synaptophysin and CD56 whereas SALL-4, Glypican 3, TTF1, CDX2, SATB2, PAX-8, Isli-1, Serotonin were negative.
Conclusion: Carcinoid tumour within teratoma is usually diagnosed in postpubertal males, with the most common affected sites being the sacral region, mediastinum, retroperitoneum and other sites. Some of them are probably related to gain of isochromosome 12p. The pitfall of misdiagnosing an atypical carcinoid tumour should be avoided, as it can occasionally exhibit metastatic spread and requires a different or more aggressive therapeutic approach.

E-PS-08-017

Expression of beta-catenin in the papillary thyroid carcinoma

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Background & Objective: β-catenin protein acts in cell adhesion and gene transcription. Its aberrant expression is associated with carcinogenesis and metastasis. The aim of our study was to analyze the differences of β-catenin in histological variants of papillary thyroid carcinoma (PTC), in relationship with the main clinicopathological factors.
Method: The study group comprised 70 cases of PTC distributed in two groups, with low-risk (45 cases) and high-risk (25 cases), according to the histological variants. β-catenin was immunohistochemically assessed and its expression was quantified at membranar and cytoplasmic level by using two semiquantitative scores. Statistical analysis was performed to correlate β-catenin and clinicopathological prognostic factors.
Results: The membranar β-catenin presented low expression in 42 cases and high in 28 cases, whereas in cytoplasm its expression was low in 36 cases and high in 34 cases. These results were enhanced by the statistical analysis that revealed significant differences between membranar and cytoplasmic β-catenin expression. Our data also show statistically significant differences of membranar β-catenin expression (low versus high) between the two risk groups. Moreover, membranar β-catenin was correlated with tumour size (p=0.032) and tumour stage (p=0.029). No

statistical differences were obtained between cytoplasmic β-catenin and risk groups, and clinicopathological factors.
Conclusion: Compered cu low risk group, the high-risk group showed low membranar and high cytoplasmic β-catenin expression. The loss of membranar β-catenin and accumulation of cytoplasmic β-catenin could contribute to the more aggressive behavior of the histological variants considered with high risk.

E-PS-08-018
Ewing sarcoma of the adrenal gland
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Background & Objective: Ewing Sarcoma (ES) is a rare malignant tumour affecting mainly children and young adults. It is usually located in bones while adrenal gland localisation is extremely rare. We present the 28th case of ES of the adrenal gland in the English literature.
Method: A 30 year-old female patient was admitted to the department of surgery due to palpable mass of the right hypochondrium. CT scan revealed a 16cm tumour. CT guided FN biopsy was performed. The patient received neoadjuvant chemotherapy according to the VAC/IE protocol with good clinical response. Then she was subjected to right adrenalectomy. An enlarged adrenal gland with extensive hemorrhage appeared on gross sections. Microscopically, both FNB and surgical specimen showed sheets of small round / oval cells with scanty cytoplasm and few mitoses. Extensive necrosis was noticed. Immunohistochemical study was positive for Vimentin, CD-99, FLI-1, CK-8/18 and negative for AE-1/AE-3, S-100, Chromogranin, Synaptophysin, CD-57, CD-45 and Melan-A. Molecular study for EWS-FLI1 translocation was applied.
Results: The diagnosis of malignant mesenchymal neoplasm morphologically and immunohistochemically consistent with ES was made confirmed by molecular test. The patient received adjuvant chemotherapy according to the protocol. Pulmonary and bone metastases were detected 12 months after initial diagnosis
Conclusion: ES is an extremely aggressive tumour with bad prognosis and high mortality. Progress in molecular biology and genetics did not contribute in improving the overall survival.

E-PS-08-019
Non invasive follicular thyroid neoplasm with papillary-like nuclear features: report of an institutional experience
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Background & Objective: It was recently proposed that non invasive follicular variant of papillary thyroid carcinomas (PTCs) should be reclassified as "noninvasive follicular thyroid neoplasm with papillary-like nuclear features" (NIFTP) and treated conservatively. For a diagnosis of NIFTP, the criteria are strict. The entire capsule of the lesion must be embedded and examinedhistologically. The objective of thisstudywas to report ourexperiencewith NIFTP.
Method: We performed a retrospective study of 21 cases of NIFTP diagnosed at our departement, between 2016 and 2017.
Results: Our series included 2 male and 19 female patients. Mean age was 48 years old. Two patients presented with a single nodule and 19 patients presented with multinodular goiter. All patients underwent a surgical resection. A fine needle aspiration (FNA) cytology was performed in 23,8% of patients (n=5). The smears showed a benign lesion (n=2), vesicular neoplasm (n=2) and non conclusive (n=1). An intraoperative frozen section was performed (n=19), showed benign lesion (n=15) and was non contributive (n=4). On gross examination, mean size of the masses was 14,82 mm. It showed well circumscribed encapsulated solid mass. The final pathological examination confirmed NIFTP diagnosis by revealing follicular growth pattern withabundantcolloid. Nuclear features of papillary thyroid carcinoma were present. The lesion was well circumscribed with a fibrous capsule. A papillary microcarcinoma wasassociated (n=2).
Conclusion: The diagnosis of NIFTP should not be attempted on frozen sections as the nuclear features of NIFTP and the capsule of the lesion and invasion of the surrounding thyroid cannot be adequately assessed on frozen section.

E-PS-08-020
Thyroid tuberculosis mimicking a carcinoma
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Background & Objective: Thyroid tuberculosis is a rare form of extrapulmonary tuberculosis. The disease may present in different clinical forms, making diagnosis difficult. It raises a dilemma of differential diagnosis of a thyroid nodule before its surgical excision. The aim of our article is to present a form of thyroid tuberculosis associated with a lymph node localization of the disease raising suspicion of malignancy.
Method: We report the case of a 36-year-old woman with a suspected thyroid nodule and cervical lymphadenopathy.
Results: A woman presented with a left lateral cervical swelling. Cervical examination revealed a left painless submandibular swelling of 03 cm, firm, non-adherent to the deep and superficial planes and without any inflammatory signs. Nasal endoscopy showed a free cavum. A cervical ultrasound of the thyroid showed three contiguous left lobar nodules. These nodules measured 22, 11 and 7mm and were classified TIRADS 4B. Ultrasonography showed also homolateral lymphadenopathy with necrotic center of the left levels IIA and III. Fine needle aspiration was performed and concluded to the absence of tumoural cells. A left loboisthmectomy with cervicotomy were carried out. Frozen section was in favor of tuberculosis in both thyroid and lymph node. The final histological examination confirmed the diagnosis.
Conclusion: Thyroid tuberculosis is a rare affection. Its clinical presentation is variable. It can thoroughly simulate malignancy. Diagnosis is based on histological examination. This infection should be considered in endemic countries. The treatment is medical and the prognosis is usually favorable outside of other locations.

E-PS-08-021
Cavernous haemangioma of adrenal gland. Case report and literature review
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Background & Objective: Cavernous haemangiomas of adrenal gland (CHA) are extremely rare, benign, non-functioning vascular lesions. Great majority of them, are discovered as incidentallomas, either during imaging or at autopsies. Although, until recently, were erroneously considered to be neoplasms, in reality they are vascular malformations. So far, 64 documented cases of CHA have been described. We present a case of CHA and we review the relative literature.
Method: A 72-year-old man, with a history of arterial hypertension and diabetes mellitus was admitted to our hospital for hypertensive crisis, lasted for the past three months. Radiological investigation (ECHO, CT, MRI) detected an heterogeneous tumour mass of left adrenal gland, well delimited from the surrounding structures, with a maximum diameter of 7,5 cm. All laboratory findings, as well as endocrine secretion tests, were within normal limits. The patient, with a preoperative diagnosis suspicious for adrenal carcinoma, underwent transperitoneal left adrenalectomy.

Results: Gross examination showed an encapsulated sponge-like tumour, cystic at sectioning with areas of haemorrhage and necrosis, compressing and deforming the adrenal gland. On histology, an haemangiomatous lesion with dilated sinuses filled with blood and lined by a flat endothelium, was revealed. Remnants of stretched adrenal gland at the periphery of the tumour, were demonstrated. Immunohistochemical analysis with vascular markers (CD31, CD34) was positive. Postoperative course was eneventful and patient was discharged on the 5th postoperative day.
Conclusion: In view of the rarity of this tumour and the absence of any hormonal derangement or imaging characteristics, the diagnosis is based entirely on histological evaluation.

E-PS-08-022
The case of the four-time attempt of obliteration of the thyroid gland node with ethanol in the unspecified cystous form of the papillary carcinoma
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Background & Objective: The papillary thyroid cancer constitutes around 80% among all malignant tumours of this organ. A rare cystous form of the papillary carcinoma should be noted, featuring a cystous cavity with the tissue mass on the wall. Happening by this pathology are cases of incorrect interpretation of data obtained during the comprehensive ultrasound study resulting in erroneous treatment tactics and the use of minimally invasive methods, namely, the introduction of ethanol into the tumour cystous part.
Method: The patient was followed up at the community-basedpolyclinic for 6 years diagnosed with cyst in the TG isthmus, whilecomplaining of a formation on the neck anterior surface causing dysphagia. For 6 years, an ultrasound guided fine-needle aspiration puncture (FNAP) with aspiration of the cystous cavity content and introduction of 1.5 ml of 96% ethanol into the cavity was conducted four times with the 1.5-year interval. During the ultrasound examination in the specialized institution, the tissue component of 12 mm in diameter is detected. FNAP of the tissue component of cystous mass was performed; cytological – the papillary thyroid cancer.
Results: The patient was surgically treated. Found during the histological study in the isthmus of TG is a cystous node of 20 mm in diameter, with a dense area of 12 mm, representing the papillary thyroid cancer with the significant degenerative and dystrophic changes in the wall, calcifications.
Conclusion: This clinical observation demonstrates that the presence of the cystous cavity with the density area in the TG requires the additional morphologic verification before undergoing minimally invasive treatment methods.

E-PS-08-023
Synchronous multifocal medullary and papillary thyroid carcinoma in same thyroid gland
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Background & Objective: Coexistence of papillary thyroid carcinoma and medullary thyroid carcinoma in the thyroid gland is a rare condition. Only three cases of synchronous medullary and papillary carcinoma in the same thyroid gland have been described in the published literature.
Method: We report a fourth case of 49 years old woman who have multipl thyroid nodules. The result of fine needle aspiration for left lobe was undetermined significance of atypia. After known the high calcitonin level she operated to our surgical department with total thyroidectomy and central neck dissection.
Results: In pathological examination of the specimen showed synchronous multifocal papillary carcinoma and multifocal medullary carcinoma in both lobe of thyroid. One medullary carcinoma with 1.4 cm diameter and three focus of medullary microcarcinoma and three focus of papillary microcarcinoma are found in same gland. There were metastatic lymph nodes of medullary carcinoma in left and right central dissection 5/5 and 3/8 respectively.
Conclusion: While medullary thyroid carcinoma originates from parafollicular cells, papillary thyroid carcinoma originates from follicular cells. The presence of multiple foci of both types of malignancy in the same gland is very rare. Several theories for this coexistence have been proposed. Finally, the "collision theory" suggests that two independent tumours are located in the same lesion by simple coincidence.

E-PS-08-024
Mismatch repair gene MSH6 as a prognostic factor in pituitary neuroendocrine tumours
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Background & Objective: Knowledge of biological behaviour is crucial for clinical management of pituitary neuroendocrine tumours, but there has not yet been found any independent predictive marker of aggressive behaviour of pituitary adenomas (PAs). The immunopositivity of mismatch repair protein mutS homolog 6 (MSH6) has been positively correlated with temozolomide response in aggressive adenomas and pituitary carcinomas. The aim of this study was to assess the prognostic value of MSH6 immunoexpression for primary pituitary tumours, in a series of patients followed for at least nine years.
Method: This retrospective study included 51 patients diagnosed with a PA (33 non-functioning, 13 acromegaly, 4 Cushing´s disease and one prolactinoma) who did transsphenoidal surgery in a single center, between 2006 and 2008. MSH6 expression were immunohistochemically evaluated, correlating it with clinico-radiological and histopathological tumour parameters and post-operative progression/recurrence.
Results: Of 51 tumours, we observed MSH6 expression in 42 PAs (82.36%), which was higher in the clinically non-functioning cases immunohistochemically positive for FSH/LH (cellular mean: 35.78%) and lower in the patients with non-functioning tumours immunohistochemically positive for prolactin (cellular mean: 4%). There was no correlation with the number of mitosis, expression of Ki-67 and p53, and there were no significant association between the percentage of tumour cells according to age, sex, tumour size, invasiveness or post-operative tumour recurrence.
Conclusion: In the study group, the predictive factor of tumour aggressiveness for pituitary neuroendocrine tumours is not represented by the MSH6 status. We found no difference in MSH6 immunoexpression between recurrent cases and patients in remission.

E-PS-08-025
The impact of the new WHO classification of tumours of the thyroid gland on the frequency of particular thyroid tumours diagnoses - the single institution experience
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Background & Objective: Microscopic diagnostics of thyroid tumours is one of the most challenging fields of pathology. The implementation of fine needle aspiration caused an increase in frequency of minimally invasive follicular carcinoma diagnoses. In the considerable amount of cases the „invasion" of the capsule was an artefact caused by multiple punctures during biopsy. New WHO classification introduces a concept of tumours of uncertain malignant potential (UMP), which allows inclusion of the tumours that before would be classified as cancers to this group. The aim of the study was to evaluate the impact of the application of the new WHO classification of thyroid tumours on frequency of differentiated (particularly follicular) thyroid carcinoma diagnoses

Method: 509 cases of thyroid tumours consulted in the Department of Tumour Pathology in Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Gliwice Branch, Poland from 10th of September 2017 to 31st of March 2018 were analysed. Each case was evaluated by two pathologists. Cases of UMP were additionally assessed by the most experienced specialist
Results: Cancer or UMP was reported in 477 consultations. The most common diagnosis (81%, 389 cases) was papillary carcinoma and its variants. Follicular carcinoma was reported in 16 cases, which comprises only 3,35%. There were 38 UMPs diagnosed, which constitutes 8%: 26 Follicular Tumours of UMP and 12 Well-Differentiated Tumours of UMP
Conclusion: The introduction of the concept of UMP tumours in the new WHO classification of thyroid tumours resulted in significant decrease in percentage of follicular carcinoma diagnoses

E-PS-08-026
Hemangioma-like vascular proliferation of the thyroid: a potential diagnostic pitfall as a consequence of fine needle aspiration biopsy
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Background & Objective: Fine needle aspiration biopsy (FNAB) of the thyroid nodules can cause reactive histopathological changes, commonly including hemorrhage, granulation tissue, fibrosis and a wide variety of vascular proliferations which might represent a diagnostic challenge.
Method: We report the case of a 39-years-old female, with no particular clinical history, admitted to the hospital for a large, symptomatic thyroid goiter. Ultrasound evaluation revealed a large, 58 mm nodule in the left thyroid lobe, for which fine needle-aspiration cytology was performed, with a benign diagnosis (Bethesda 2). Total thyroidectomy was performed.
Results: At macroscopy, massive thyroid enlargement and multiple colloid nodules with a diameter ranging between 12 to 58 mm were noticed in both thyroid lobes. The microscopical features were consistent with a diagnosis of nodular goiter: multiple colloid nodules composed of follicles exhibiting variable size and shape, but no atypia. Secondary changes, including foci of hemorrhage, fibrosis and cystic degeneration were also observed. In the left thyroid lobe, some peculiar hemangioma-like vascular proliferations were also observed. Thick-walled, irregular vascular spaces lined by plump endothelial cells within a background of fibrinous or hemorrhagic material were noticed. However, some of the cells lining these vascular spaces revealed significant reactive atypia: appeared large, with irregular, pleomorphic, vesicular nuclei. A diagnosis of reactive hemangioma-like vascular proliferation in the setting of thyroid goiter was finally set.
Conclusion: The diagnosis of thyroid vascular lesions is not straightforward. The heterogenous disease spectrum consists of reactive lesions like benign endothelial proliferation, benign haemangiomas which must be differentiated from extremely rare malignant angiosarcomas.

E-PS-08-027
Large size oncocytic adenoma of the thyroid: a potential diagnostic pitfall
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Background & Objective: Large size oncocytic tumours of the thyroid require a correct macroscopical and microscopical evaluation of the specimen that is mandatory for the differential diagnosis between benign and malignant tumours, with impact on the patient's prognostic.
Method: We report the case of a 57-years-old female admitted to the hospital for a large, symptomatic goiter. Ultrasound evaluation revealed a 45 mm hypoechoic nodule in the left thyroid lobe, for which the fine needle-aspiration cytology yelled a benign diagnosis (Bethesda 2). Total thyroidectomy was performed.
Results: At macroscopy the nodule was well-circumscribed, compact, brown-yellow and with hemorrhagic areas. On light microscopy, the nodule was surrounded by a smooth capsula. The architectural pattern was solid, consisting predominately of nests and trabeculae and only few areas with a microfollicular pattern. The tumour was composed entirely of large, oncocytic type cells, with vesicular, centrally placed nuclei, with prominent nucleoli and mild atypia. No signs of capsular or vascular invasion and no features suggestive for endocrine necrosis or mitosis were observed, following exhaustive sampling of the tumour nodule and multiple sections evaluation. Immunohistochemistry revealed positive, intense staining for Thyroglobulin and CK AE1/AE2, while Calcitonin was negative. A diagnosis of oncocytic adenoma of the thyroid (OAT) was set based on the morphological and immunohistochemical aspects.
Conclusion: OATs are particularly prone to pose important diagnostic challenges in daily practice. These tumours should be distinguished from oncocytic variants of follicular (absence of capsular±vascular invasion), poorly differentiated (no signs of necrosis and absence of mitosis) and medullary (negative Calcitonin staining) thyroid carcinomas, respectively.

E-PS-08-028
Prognostic factors and classification systems in colorectal neuroendocrine neoplasms
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Background & Objective: The incidence of colorectal neuroendocrine tumours (CNT) is increasing due to the development of imaging techniques and screening protocols. CNT are rare and heterogeneous and they can be classified according to several grading and staging systems. Our aims are to identify clinicopathological prognostic features and to assess the role of different classification systems in these tumours.
Method: Retrospective study of all CNT diagnosed in our institution between 2000-2017. Clinicopathological features were collected and tumours were classified according to the AJCC (8th edition) and WHO (2010) guidelines.
Results: 49 cases were included in our study. Most patients were men (55.1%) with a mean age of 55 years. Tumours were mainly located in rectum and right colon (64.6% and 20.8%, respectively) and mean size was 22 mm. Distant metastases were identified in 24.5% of cases. CNT were mostly treated by endoscopical or surgical resection. Tumour grade (WHO) was G1, G2 and G3 in 56.8%, 4.5% and 38.5% of cases. 18.4% of patients showed recurrences and 8.2% died due to tumour. Level of invasion and classification according to WHO and AJCC cancer staging systems showed prognostic significance. AJCC staging systems for high grade CNT and well differentiated CNT were concordant. However, WHO and AJCC classifications showed some differences.
Conclusion: Level of invasion, tumour stage (AJCC) and grade (WHO) were significantly associated with patient outcomes. WHO and AJCC classification schemes were related but not equivalent, therefore a combined staging system may be developed to avoid confusion.

E-PS-08-029
CYP17A1 expression in prostate cancer
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Background & Objective: Hormonal therapy for prostate cancer aims to the inhibition of the androgen receptor (AR) signaling, by blocking

translocation of the AR to the nuclei, preventing its transcriptional activity. Among the mechanisms postulated to confer hormone resistance, is the up-regulation of genes encoding steroidogenic enzymes like CYP17A1.
Method: We immunohistochemically investigated the expression of CYP17A1 enzyme in parallel with AR nuclear expression, in a series of prostate cancer tissue form patients treated with prostatectomy.
Results: CYP17A1 was strongly expressed in the cytoplasm of prostate cancer cells, ranging from 0% to 100% of cells (median 50%). Thirty cases out of 53 (56.6%) expressed CYP17A1 in more than 50% of their tumour cells. The nuclear AR expression in cancer cells ranged from 0-90% among cases (median 30%). Out of 53 cases, 20 (37.7%) showed expression of the AR in more than 50% of cancer cells. A strong significant direct association between CYP17A and nuclear AR expression was noted ($p<0.0001$; $r=0.51$). This was confirmed in confocal immunofluorescent microscopy, where the nuclear expression of phosphorylated (active form) of AR was directly related to cytoplasmic expression of CYP17A1. Analysis of CYP17A1 expression according to histopathological variables, did not show any association with T-stage, Gleason score or PSA levels.
Conclusion: CYP17A1 steroidogenic enzyme is strongly expressed in half about of human prostate carcinomas, implying an intracellular androgen synthesis by cancer cells. CYP17A1 expression could have a value as a biomarker for the treatment of hormone refractory disease with specific CYP17A inhibitors.

E-PS-08-030
A rare case of cystic hemangioma of the adrenal gland
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Background & Objective: Cavernous hemangiomas of the adrenal gland are rare. Since the first cavernous hemangioma of the adrenal gland was surgically removed in 1955, only 64 cases have appeared in the medical literature. While there are certain features suggestive of the diagnosis, they fall short of being diagnostic. This lack of specificity in pre-operative studies often prevents a conclusive exclusion of malignancy from the differential diagnosis. We report the morphologic and immunohistochemical features of a case of cystic hemangioma that occurred in a woman.
Method: A 19-year-old female presented to our hospital with a short history of abdominal pain. CT showed a well-defined lesion in the middle of the right adrenal gland and MRI images are showed a multi-cystic mass on the right adrenal gland. The patient underwent open right adrenalectomy.
Results: Macroscopically the lesion consisted of a well-circumscribed mass measuring 8x6x4 cm. with small and large cysts filled with serous and hemorrhagic fluid. Microscopically the cysts filled with blood and lined by flat endothelial cells with no atypia and no mitosis. These cells were positive with CD34. Among these cysts there was tissue of normal adrenal gland and foci of fibrous tissue with calcifications. There was no evidence of malignancy. According to these histological features this mass was diagnosed as cystic hemangioma of the adrenal gland.
Conclusion: We conclude that preoperative recognition of cystic hemangioma which has an excellent outcome might help surgeons approach the patient conservatively.

E-PS-08-032
Gastrointestinal metastasis of primary thyroideal eptihelioid angiosarcoma with CYP2D6 c.506-1G>A polymorphism: molecular and immunophenotypical characterisation
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Background & Objective: Thyroid epithelioid angiosarcoma is a rare highly aggressive malignant vascular tumour, mainly seen in the Alpine region and few cases are described in non-Alpine patients. The t(1;3)(p36.3;q25) translocation is present some cases studied, leading to CAMTA1 expression by IHC. Further molecular characterization has yet to be done.
Method: A 62 years old non-Alpine white patient, with ulcerative colitis and underwent left hemi-thyroidectomy for a benign pathology (by clinical records). Subsequent two biopsies one year and fourth month after render a diagnosis of undifferentiated carcinoma in left laterocervical region. The patient consulted by gastrointestinal bleeding and endoscopic biopsies revealed metastasis of undifferentiated carcinoma. An intestinal resection was made. We review clinical, histological and molecular studies from OncoDEEP™.
Results: The histologic study showed arrangements of polygonal cells with prominent nucleoli and atypical mitosis in cleft-like spaces. Tumour cells were positive for endothelial markers such as CD31 and Factor VIII and expressed CAMTA1. The review of previous biopsies, including thyroidectomy specimen, showed similar features. The patient progressed with locoregional disease and bone metastasis and died after eighteen months from first surgery. The molecular study demonstrated a polymorphism CYP2D6*4 c.506-1G>A variant, which is found in pituitary and papillary thyroid tumours.
Conclusion: We present an atypical non-Alpine presentation of this rare neoplasm presenting with bleeding from intestinal metastasis leading to the diagnosis of a primary tumour located in the thyroid gland. The presence of a CYP2D6*4 is associated with cancer risk and may be related with the peculiar geographic distribution of this rare form of neoplasm.

E-PS-09 | Gynaecological Pathology

E-PS-09-001
Peculiar features of CEACAM1 and E-cadherin expression in the uterus
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Background & Objective: The aim of our study was to characterize the expression pattern of carcinoembryonic antigen related cell adhesion molecule 1 (CEACAM1) and E-cadherin in normal, hyperplastic and tumour tissues of the uterine, and to determine the potential correlation between these two adhesion molecules.
Method: 45 samples of the uterine tissue (normal, hyperplastic and tumour tissues) were selected for the study. The presence of CEACAM1 (C5-1X8–0.1μg/ml) and E-cadherin (EP700Y–0.5μg/ml) receptors was detected by the immunofluorescence analyses.
Results: E-cadherin is expressed on the basal surface and in the intercellular contacts by all cells of the normal endometrium and under the hyperplasia. The endometrial adenocarcinoma tissues showed a variable E-cadherin expression: basal-intercellular – under formation the glands by the neoplastic cells, entire membranous – under the solid growth of cancer cells and the decreasing expression – when the malignant progression is developing. Conversely, the CEACAM1 receptors are present on the apical surface of the normal and pre-tumour tissues of the uterus. They appear in the cytoplasm when the anaplasia level of the neoplastic cells is increased. It was determined that E-cadherin-positive cells are present when there is no CEACAM1 receptor expression.
Conclusion: The endometrial tissue shows a variable expression of CEACAM1 and E-cadherin receptors depending on the pathological changes in the uterus. Different patterns of these proteins indicate the absence of any functional correlation between them. However, the alterations of both protein location from cell membrane to their

disappearence or translocation into cytoplasm seems to represent novel markers for the appearance and development of the neoplastic process.

E-PS-09-002

The aggressive EpCAM+CD45+ phenotype in serous epithelial ovarian cancer

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Background & Objective: Epithelial ovarian cancer (EOC) is the leading cause of death for gynaecological malignancies, especially in western countries. Recently, Akther and colleagues identified a haemato (CD45) - epithelial (EpCAM) phenotype of serous EOC with aggressive features, both in ascitic fluid and primary tumours. This phenotype is drug-resistant (versus EpCAM+ neoplastic cells), highly invasive (mesenchymal gene expression) and consists of subpopulations of ovarian cancer stem cells (CD133+ and CD117+CD44+) with MCH I over-expression (ability to evasion of immune surveillance). These features suggest a possible role for EpCAM+CD45+ phenotype in development of peritoneal carcinomatosis and multi-drug resistance. Aim of the present study was to investigate EpCAM+CD45+ phenotype in EOC tissue samples of primary tumour, in ascitic fluid and, for the first time, extraovarian implants.
Method: EpCAM+CD45+ phenotype was assessed by immunohistochemistry (serial sections of FFPE samples were digitalized and then aligned to assess the co-localization) and confirmed by immunofluorescence in 5 cases of serous EOC. These results will be integrated and stratified using clinical and follow-up data (available for all 60 patients enrolled). Immunohistochemistry in the large series is in progress.
Results: EpCAM+CD45+ phenotype was found in extra-ovarian implants in all (5/5) investigated cases and in 60% (3/5) of primary tumours. Interestingly, the two discordant cases showed EpCAM+CD45+ phenotype only after chemotherapy (in all cases the positivity consisted of isolated small groups of cells).
Conclusion: Our preliminary findings showed that EpCAM+CD45+ phenotype was present in extra-ovarian implants of EOC, further supporting the role of this neoplastic phenotype in EOC carcinomatosis. The results will be confirmed on the complete cohort.

E-PS-09-003

Glandular carcinomas of the endocervix: a clinicopathological review – experience of a tertiary referral centre

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Background & Objective: We aimed to report the experience of endocervical adenocarcinoma diagnosis in a tertiary gynaecological referral centre.
Method: All endocervical adenocarcinomas diagnosed over a ten-year period (2008-2018) were reviewed. Histopathological features, association with Human Papilloma Virus (HPV) infection and clinical data were evaluated.
Results: Of the 23 cases retrieved, 10 were classified as adenocarcinoma NOS, 5 as endocervical adenocarcinoma, usual type, 3 as endometrioid carcinoma, 3 as villoglandular carcinomas, 1 as mucinous carcinoma, gastric type and 1 as adenocarcinoma in situ. The mean age at diagnosis was 48 years (30-80). HPV genotyping was performed in 4 cases, all positive for high-risk HPV genotypes (hrHPV). The majority of the cases (21, [91.3%]) represented invasive disease (stage I to III – most of them were stage I), whereas 1 (4.35%) was in situ and 1 (4.35%) had unknown stage. Only one patient died due to adenocarcinoma.
Conclusion: Our results do not parallel the classification reported in the literature, where endometrioid carcinomas are rare and account for no more than 5% of all endocervical adenocarcinomas. In our department, they account for nearly 13%. This difference might be associated with patient selection bias, population based susceptibility and a small sample size. In terms of HPV infection, all the adenocarcinomas tested for hrHPV had positive results. Most of our cases were detected in an early stage which was associated with a high survival rate.

E-PS-09-004

Uterine florid cystic endosalpingiosis

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Background & Objective: Endosalpingiosis is a rare benign entity, characterized by tubal epithelium outside the fallopian tube. It has been described since 1930 in multiple organs. Florid cystic endosalpingiosis (FCE) is a rare presentation in the uterus. We report a case of uterine FCE.
Method: Clinical history, radiological exams, macroscopic and histological features have been reviewed.
Results: 56-year-old woman with metrorrhagia and endometrial thickening, was submitted to three hysteroscopies and resections of endometrial polyps of over a period of 15 months. Abdominal CT scan showed a 33 mm endometrial polyp and a tubular, serpiginous structure of 60 x 28 mm adjacent exteding into the myometrium, suggestive of a haematosalpinx. She underwent a total hysterectomy: the uterus (101 g) was enlarged with a thin-walled collapsed cyst on the serosal surface of the fundus which communicated with a solid and cystic mass measuring 75 x 50 x 40 mm, traversing the full thickness of the myometrium to present as a polyp within the endometrial cavity. Ovaries contained benign serous cysts and fallopian tubes were normal. Microscopically there were cystic spaces of varying sizes lined by simple cuboidal and ciliated tube-type epithelium. No cytologic atypia was seen. The stroma between the glands and cysts was fibromuscular, with no evidence of endometrial stroma.
Conclusion: ECF of the uterus is a rare disease of unknown etiology, with indication for conservative treatment. The differential diagnosis includes benign entities (including mullerianosis, adenomyosis, florid mesonephric hyperplasia) and adenocarcinoma.

E-PS-09-005

Ovarian masses in children and adolescents: a case series

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Background & Objective: Ovarian masses in children and adolescents are unique due to their rarity and controversial management. Their incidence is estimated at 2.6 cases per 100,000 girls per year, and malignant ovarian tumours account for 0.9% of all childhood and adolescent malignancies. Although benign masses are more common than malignant ones, it is imperative to diagnose malignancy at an early stage by various multimodal diagnostic methods. The purpose of this study is to report a series of ovarian masses in children and adolescents and to describe clinicopathological aspects of these lesions.
Method: All ovarian masses in children and adolescents resected or biopsied in Habib Thameur Hospital from 2001 to 2018 were reviewed retrospectively. Patient's age, pathological data and outcome were obtained from medical records.
Results: Results 29 cases of ovarian masses were found: 7 mature teratomas, 4 serous cystadenomas, one mucinous cystadenoma, 5 serous cystadenofibromas, one endometriotic cyst, 7 follicular cysts, 2 cases of dysgerminoma, one case of gonadoblastoma, one case of juvenile granulosa cell tumour and one unclassified tumour. The age of patients was varying between 19 days and 16 years. The distribution of ovarian masses

varies with age with a predominance of benign cysts in adolescents. A predominance of benign tumours is verified in both children and adolescents.
Conclusion: In conclusion ovarian masses are rare in children and adolescents. Despite the predominance of benign ones, a high index of suspicion of malignancy should be kept in young patients.

E-PS-09-006
Coexistence of glandular carcinoma and squamous carcinoma in situ of the cervix in a pregnant woman: a case report and literature review
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Background & Objective: Adenocarcinoma comprises 10-25% of all cervical carcinomas in developed countries. The majority of cervical adenocarcinomas are associated with high-risk HPV. Usually, the detection of a high-grade squamous intraepithelial lesion (HSIL) occurs in older women with less frequent screening. We describe a case of adenocarcinoma associated with squamous carcinoma in situ within the cervix of a young pregnant woman.
Method: A 32-year-old pregnant woman with cervical cytology results of HSIL and adenocarcinoma in situ diagnosed during the first trimester underwent colposcopy. The biopsy revealed the presence of an adenocarcinoma with stromal invasion. The patient refused a pregnancy interruption, being treated by cervical conisation and caesarean section at 33 weeks. Three months after delivery, a hysterectomy, pelvic lymphadenectomy and bilateral salpingo-oophorectomy was performed.
Results: Pathological study revealed an endocervical adenocarcinoma, usual type, with foci of villoglandular differentiation. Immunohistochemically, the neoplastic cells were reactive for p16 and CEA, and negative for oestrogen receptors and vimentin. HPV genotyping had a positive result for HPV-16. A mesonephric duct hyperplasia was also observed.
Conclusion: The differential diagnosis of cervical adenocarcinoma includes several benign and malignant entities. Careful morphological examination and immunohistochemical evaluation are crucial for correct categorization and staging of these neoplasms. Screening has an essential role in the detection of cervical lesions in early stages, therefore avoiding aggressive treatments.

E-PS-09-007
Angiomyofibroblastoma of the uterine cervix occuring in a patient with breast cancer: a case report
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Background & Objective: Angiomyofibroblastoma (AMFB) is an uncommon, benign mesenchymal tumour which generally occurs in the vulvovaginal region. We report a case of cervical AMFB. To the best of our knowledge, this is the second reported AMFB of the uterine cervix in a patient with breast cancer in English literature.
Method: A 40-year-old female patient presented to the hospital with vaginal bleeding. In medical history she had a triple negative invasive ductal breast carcinoma which was treated with conservative breast surgery with axillary dissection and adjuvant chemo and radiotherapy in 2007. The gynaecologic examination revealed a polypoid mass located in both vagina and cervix. The patient was diagnosed with cervical leiomyoma and underwent total abdominal hysterectomy and bilateral salpingectomy.
Results: Macroscopically, a well-defined mass which was 6x5 cm in size was detected in the posterior cervix. The cut surface was solid and light yellow in appereance. Histologically, the tumour was characterized by hypercellular and hypocellular edematous areas mixed with small blood vessels. Randomly distributed blood vessels were thin walled and no extravasation of the red blood cells was noted. The tumour cells were uniform eosinophilic, spindle-shaped or epitheloid without mitotic figures or atypia. The immunohistochemistry showed strong positivity with desmin, vimentin, estrogen receptor (ER), progesterone receptor (PR), focal positivity with CD117 and caldesmon and negativity with CD34 and smooth muscle actin. According to these findings, the tumour was diagnosed as a "angiomyofibroblastoma".
Conclusion: A recognition of this entity is important to avoid misdagnosis of other angiomyxoid neoplasms such as aggressive angiomyxoma.

E-PS-09-008
Malignant mixed Mullerian tumours of the uterus: immunohistopathological analysis of a short series of cases
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Background & Objective: Malignant mixed mullerian tumours (MMMT) of the uterine corpus are rare and extremely aggressive biphasic tumours composed of intimately admixed epithelial and mesenchymal elements. They account for less than 1% of all neoplasms of the gynaecologic tract and occur almost exclusively in postmenopausal women.
Method: In this 3-year retrospective study, we analyze the clinical, histopathological and immunohistochemical features of 5 patients with uterine MMMT diagnosed and treated at the Emergency University Hospital in Bucharest Romania, between January 2015 and December 2017. Preoperative endometrial biopsy was diagnostic in only 2 cases.
Results: All patients presented with postmenopausal bleeding. Median age was 69 years. The patients were FIGO Stage IB and IIIA. In 4 cases, both the epithelial and mesenchymal components were high grade. One case presented with moderately differentiated endometrioid carcinoma. The other 4 cases featured a mixture of serous, clear cell and high grade endometrioid carcinoma. The sarcomatous components resembled leiomyosarcoma or high-grade endometrial stromal sarcoma. Three cases featured heterologous elements represented by rhabdomyosarcoma, osteosarcoma or neuroectodermal differentiation. Cytokeratins and Vimentin were diffusely positive in both components. ER and PR were more intense in carcinomatous areas, while CD10 was diffusely positive in sarcomatous areas. p16 and p53 revealed similar immunoreactivity in both components. Heterologous areas were focally positive for desmin, CD56 and synaptophysin.
Conclusion: The prognosis of MMMT is universally bad. Distinguishing it from pure sarcomas, adenosarcomas and undifferentiated carcinomas is extremely important because the malignant stroma may be inconspicuous and missed altogether, with the lesion being misdiagnosed as an ordinary carcinoma.

E-PS-09-009
Features of the inflammatory infiltrate in the tissue of the serous adenocarcinoma of the fallopian tube
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Background & Objective: The object of this research was to study the qualitative composition of the inflammatory tumour microenvironment in the serous adenocarcinoma of the fallopian tube and its influence on the immunophenotype of neoplasia.

Method: Immunohistochemical method was used to study the immune microenvironment (CD3, CD20, CD68 receptors). Tumour cells were examined for ER, PR, Ki-67 and p53 expression.
Results: The presence of the inflammatory infiltration and the increase in its intensity depended mainly on the degree of atypia of the cancerous cells and prevailed in the poorly differentiated neoplasias (66.7%). Its qualitative and quantitative composition depends on the reduction of the expression of the steroid hormones receptors in the tumour tissue and correlates with Ki-67 and p53 expression. Besides, the reduced T-cells infiltration and significant CD68+ -macrophages infiltration in the tissue of the serous adenocarcinoma of the fallopian tube is connected with the metastases in the regional lymph nodes.
Conclusion: Inflammatory cellular microenvironment in the malignant tumours of the fallopian tubes plays an essential role in the functioning of the cancerous cells and influences it greatly. The sensitivity of the cells to the steroid hormones falls and its proliferative and anti-apoptotic potential increases in response to the increase of the immune infiltration in the tissue.

E-PS-09-010
Correlation of histological grade of endometrial cancer with serum CA-125, CA 19-9, CEA and CA15.3
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Background & Objective: The histological grade of endometrial cancer patients is evaluated as a significant parameter that influences the risk of disease relapse. To date, there is little evidence in the literature suggesting that at least serum CA-125 and CA 19.9 levels correlate with the histological grade of endometrial cancer. The purpose of the present study was to investigate the correlation of grade with serum levels of CA-125, CA 19-9, CEA and CA15.3.
Method: We retrospectively retrieved patient records of postmenopausal patients with evidence of endometrial pathology (vaginal bleeding or endometrial thickness ≥ 5 mm determined by ultrasound examination). The study was based on a cohort of 178 patients that underwent dilatation and curettage between January 2013 and December 2016. The statistical analysis was performed with the IBM SPSS statistical package.
Results: Overall, 78 patients with endometrioid cancer grade 1 and 28 patients with grade 2 and 3 were detected. There was no difference in the mean patients` age among the two groups. Serum markers were comparable among the two groups and did not differ significantly. A difference was noted in the case of CA-125 which was very close but did not reach statistical significance.
Conclusion: Histological grade does not seem to influence the levels of cancer antigens in the sera of patients that have endometrial cancer. A potential association of CA-125 cannot be entirely ruled-out, however, given the lack of statistical significance in our study further studies are needed in this field to corroborate our findings.

E-PS-09-011
Uterine carcinosarcoma: a case report and literature review
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Background & Objective: Carcinosarcomas of the uterus (malignant mixed Müllerian tumours) are a rare occurrence, accounting for only 2–5% of all uterine malignancies. Affects women of older age and are, however, highly aggressive. Report a case of a 61-year-old patient with uterine carcinosarcoma.
Method: A biopsy was performed followed by hysterectomy at a tertiary hospital
Results: Female, 61 years old, with uterine tumour that has been externalized through the uterine canal. A biopsy was performed and the result was a malignant neoplasia. The biopsy was followed by a hysterectomy that diagnosed a carcinosarcoma.
Conclusion: Carcinosarcomas are characterized by an aggressive clinical course and an extremely poor prognosis. This type of tumour still has little information regarding it and it's limited to a few randomized experiments and case reports. It has been previously reported that 70-90% of tumour-related deaths occurred within 18 months after diagnosis and the other stufy in 39 months. It is important to consider this tumour as a differential diagnosis in older women with uterine tumour that has been externalized through the uterine canal.

E-PS-09-012
Giant cell endometrial carcinoma: a case report and review of literature
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Background & Objective: We report an unusual case of endometrial adenocarcinoma with a malignant giant cell component which is a rare type of poorly differentiated endometrial adenocarcinoma.
Method: A 75-year-old female presented with postmenopausal vaginal bleeding. After a positive for malignancy diagnostic curettage, she underwent a total hysterectomy with bilateral salpingo-oopharectomy and pelvic lymph node dissection.
Results: On pathology we recognized a dedifferentiated neoplasm with nearly 70% of atypical giant cells with extremely increased size. Some of these giant cells were multinucleated with high mitotic rate and a diffuse architectural pattern of growth. The rest 20% consisted of serous adenocarcinoma and 10% of high grade endometrioid carcinoma. The giant cells were positive in immunohistochemistry for ER, PR, p16, p53 and vimentin. Lymphovascular invasion was identified in the right parametrium even though the neoplasm was limited in the upper half of the myometrium. All lymph nodes were negative for metastasis.
Conclusion: Giant cell carcinoma is a rare and aggressive subtype although its morphological, immunohistochemical features as well as its biological behavior has not been clarified yet.

E-PS-09-013
Endometriosis and adenomyosis – still enigmatic entities
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Background & Objective: Endometriosis and adenomyosis represent two gynaecological entities, which have a common morphology, sometimes confused or associated, but distinct pathophysiology, which still arise controversies. We aimed to compare endometriosis and adenomyosis using morphoclinical criteria, in order to highlight their pathogenic theories, and to try to create a feasible diagnostic algorithm.
Method: This retrospective 5-year study included 290 cases of adenomyosis and 24 cases of endometriosis, diagnosed in women aged 30-73 years old who underwent hysterectomy with or without adnexectomy, simple excision or adnexectomy. The histopathologic diagnosis was made on standard histological sections, immunohistochemistry in selected cases, and corroborated with clinical data.
Results: Endometriosis was diagnosed by the presence of endometrial glands and stroma in the ovary, sometimes delimitating cystic spaces, or in cutaneous scars. Some cases presented incomplete histological criteria, the diagnostic being made by only one endometrial component, or by residual islands of siderophages. Adenomyosis represents endometrial glands and stroma in the myometrium, accompanied often by smooth muscle hyperplasia. Leiomyoma, benign ovarian cysts, endometrial simple

hyperplasia were significantly related to these two entities. Three adenomyosis cases were adenomatous polyps, six cases were associated with ovarian endometriosis, and two other cases were associated with endometrial adenocarcinoma. While endometriosis was firstly ultrasonographically diagnosed, adenomyosis was a histopathological finding.
Conclusion: Given that both entities have high risk of infertility and malignancy development, an early, accurate diagnosis is mandatory. A complex algorithm, based on a range of investigations, is necessary, mainly in asymptomatic cases, to increase the effectiveness of therapeutic options.

E-PS-09-014
ZC3H7B-BCOR high-grade endometrial stromal sarcoma with osseous metaplasia: a rare, newly described entity with many mimickers
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Background & Objective: Endometrial stromal sarcoma (ESS) is a malignant tumour of endometrial stromal origin that occurs in middle-aged women. High-grade ESS is a rare entity often associated with t(10;17) translocation resulting in the fusion of YWHAE and NUTM2 genes. Very recently, a new variant of high-grade ESS has been described, featuring unique histomorphological features. It is associated with t(X;22) translocation and ZC3H7B-BCOR fusion. This variant is less likely to be recognised as ESS and presents a diagnostic challenge, as its histological appearance mimics other malignant tumours of the uterus.
Method: We report a 52-year-old Chinese woman who presented with a one-week history of post-menopausal bleeding. Magnetic resonance imaging of the pelvis revealed a large lobulated mass within the uterus. Total hysterectomy with bilateral salpingo-oophorectomy and pelvic lymph node dissection were performed.
Results: Grossly, a solid, yellowish tumour nodule with infiltrative edges and variegated cut surface was seen in the posterior myometrium. Histological examination revealed fascicles of hypercellular, ovoid to spindled, mitotically active cells exhibiting nuclear enlargement, irregularity and coarse chromatin pattern, associated with extensive necrosis and focal osseous metaplasia. The malignant cells were immunoreactive to CD10 and cyclin D1. Nanostring® Sarcoma Panel revealed ZC3H7B-BCOR fusion.
Conclusion: ZC3H7B-BCOR high-grade ESS is a novel entity associated with poor outcome. The histomorphology mimics that of leiomyosarcoma, undifferentiated uterine sarcoma, carcinosarcoma and NTRK fusion-positive uterine sarcoma. It is associated with a unique immunohistochemical and molecular profile. Its awareness is important for an accurate diagnosis.

E-PS-09-015
Study of histopathology reports of loop electrosurgical excision procedure (LEEP) of cervical transformation zone and to see its correlation with preprocedure cervical biopsy or cytology, between 2011-2017, in our hospital
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Background & Objective: To study the contents of the histopathology reports of LEEP of cervical transformation zone, and their correlation with cervical biopsy or cytology, in our hospital between 2011-17.
Method: Our hospital records between 2011-17 yielded a total of 42 histopathology reports (41 patients) of loop electrosurgical excision procedure (LEEP). Their pre LEEP cervical biopsy, cytology reports were noted.
Results: The mean age was 48.3 years (median 47 years; age range 31-71). Out of 42 reports, four cases were submitted as outside blocks. Thirtynine (39) reports mentioned that all the tissue was submitted for histology. Deep cut examination was mentioned in 18 cases. The diagnoses included 19 CIN II/III, 3 micro invasive squamous carcinoma, 1 squamous carcinoma, 1 adenocarcinoma in situ (AIS), 1 adenocarcinoma, 4 CIN I and 13 cervicitis. In Seven out of 29 CIN II/III plus diagnoses (24.1%), margin positivity was seen. Margin was not commented upon in total 4 cases (CIN 1 or worst histology); one case being CIN II, and the other case was micro invasive squamous carcinoma (which subsequently had undergone radical hysterectomy). The concordance between LEEP and cervical biopsy or cytology was 66.7% (28/42 reports) for CIN II plus diagnoses. Discrepancy between CIN I and inflammation, between CIN I and CIN II as well as between ASC-H cytology and CIN 1 histology diagnosis were recorded as discordance.
Conclusion: The concordance rate between LEEP and cervical biopsy or cytology is 66.7% and has a scope for improvement.

E-PS-09-016
Case report of Wollfian tumour of the Fallopian tube
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Background & Objective: Wollfian tumour is a rare lesion first described in 1973. To date not more than 100 cases of the tumour are presented in the literature. The problem in diagnosis of the tumour is to differentiate it from endometrioid adenocarcinoma as well as Sertoli and Leydig cell tumours. The aim of the report is to present a case of Wollfian tumour and to give its morphologic and immunochistochemical characteristic.
Method: 43 y.o. female suffered from low abdominal pains. On US and CT a lesion located to the left from uterus and not connected with ovary was found. Lesion was heterogeneous, up to 50x45x40 mm in size, vascularized. A tubectomy and lesion resection was performed.
Results: On gross examination a round encapsulated lesion 50 mm in maximum dimension with yellow-to-gray cut surface was seen. On H&E stained slides the lesion was composed of monotonous cells with small round nuclei and pale cytoplasm, arranged in solid, cribriform and trabecular structures; stroma was myxoid. Tumour involved a Fallopian tube wall without an involvement of mucosa. On IHC tumour cells showed diffuse positivity for vimentin, pan-keratin, cytokeratin 7, calretinin and only focal positivity for estrogen receptor. Tumour cells were negative with cytokeratin 20, SALL4, EMA, S-100 and synaptophisin. Wild-type p53 expression was also noted. A diagnosis of Wollfian tumour of the Fallopian tube was made.
Conclusion: The case emphasizes an important role of clinical data together with histology and IHC in the diagnosis of this rare tumour.

E-PS-09-017
Intravenous leyomiomatosis a bening tumour with an agressive potential: a case report
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Background & Objective: Intravenous leyomiomatosis is a rare bening entity with a potential agressive behavior, characterized by intravascular smooth muscle masses of bening cells that grows in uterine and pelvic veins that often presents with a concommitant leiomyoma. When it extends to vena cava could cause congestive hearth failure and sudden death. Objetive: To report a case of a intravascular leiomyomatosis associated with a intrauterine leiomyoma
Method: A case of intravenous leiomyomatosis were retrieved from archives of the last 5 years at Viborg's Regions Hospital - Denmark. The clinical data, pathological findings and inmunhistochemical profile were reported
Results: A total histerectomy with bilateral salpinguectomy in a 45-year-old woman was performed with the clinical diagnose of intrauterine leiomyom. Histologicall findings revealed a 107 mm intramural

leiomyom that grew in whorled fascicles of uniform smooth muscle cells without cellular atypia, mitosis, or necrosis. In the intramural veins an intravascular growth of bening smooth muscle cells were found. Inmunhistochemical profile were reaktive for smooth muscle markers: Actin, desmin. Ki67 proliferation index were around 2% in the usual leiomyoma and in the intravascular tumour. A diagnose of a uterine leiomyom associated to an intravascular leiomyomatosis was reported. Surgical margins where uninvolved.
Conclusion: Intravascular leyomiomatosis is a rare tumour that is characterized by smooth muscle bening masses growing within the veins, that can reach the right heart through the uterine veins. It probably arises from the vein walls or spredning of a primary leiomyom into the adjacent venous structures. The main diferential diagnosis is a leiomyosarcoma with vascular invasion and a preoperative diagnosis can not be made. Complete resection are curative.

E-PS-09-019
CEACAM1 investigations in the vessels of the reproductive system organs
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Background & Objective: The aim was to investigate the presence of carcinoembryonic antigen related cell adhesion molecules 1 (CEACAM1) in the vessels of organs of the reproductive system and to define peculiar features of their expression depending on the type of tissues as well as vessels and the presence of vascular endothelial growth factor (VEGF).
Method: We studied the samples of normal and tumour tissues of the uterus, fallopian tubes, ovaries, breast, the prostate and testis. To determine the type of vessels, analyses of the samples on CEACAM1, CD31, Podoplanin and VEGF receptors were conducted.
Results: All the vessels in the investigated organs showed positive CD31 expression. Among them, a small amount of Podoplanin-positive vessels was detected. VEGF receptors were present in some vessels of the normal tissue but in most tumour vessels. The CEACAM1 expression was observed in endothelial cells of the thin-walled vessels (the arterial vessels were negative), which were both Podoplanin-positive and -negative. The VEGF-positive vessels showed also CEACAM1 expression in the endotheliocytes. A significantly larger amount of CEACAM1-positive vessels was detected in the prostate, fallopian tubes and ovaries rather than in the uterus, testis and breast.
Conclusion: The CEACAM1-positive vessels are present in all the organs of reproductive system. These protein receptors were observed in some amount of the lymphatic vessels and veins. Both normal and tumour tissues contain an irregular amount of CEACAM1-positive vessels. CEACAM1 expression was also detected in a part of VEGF-positive endotheliocytes. However, the CEACAM1 expression in vessels is not limited to neo-angiogenic endothelium as described by others.

E-PS-09-021
Bilateral luteinised ovarian thecoma with sclerosing peritonitis
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Background & Objective: We present the case of a 79 years old Caucasian woman who was admitted to the accident and emergency department with the signs and symptoms of intestinal obstruction. At laparotomy she was found to have bilateral ovarian masses with adherence to the omentum and bowel loops. She underwent a bilateral salpingo-oophorectomy, omentectomy and appendicectomy. Histology and immunohistochemistry confirmed bilateral luteinized thecoma and sclerosing peritonitis. We present the case for its rarity and consequent favourable outcome after more than 3 years of follow up.
Method: 38 blocks were sampled from the ovarian masses, uterus, tubes, peritoneum, omentum and appendix. These were routinely processed for histology and stained with antibodies for Vimentin, Actin, Desmin, CD56, Inhibin, MNF116, CAM5.2, EMA, Calretinin and Eostrogen receptors. A sample from the tumour was studied for FOXL2 mutation.
Results: Histology showed a spindle cell proliferation bearing 8-10 mitoses per 10 high power fields with an admixture of clustered cuboidal and eosinophilic cells. The spindle cells were positive for Vimentin only. The cuboidal cells were strongly positive for Calretinin, Inhibin, CD56, and oestrogen receptors in keeping with luteinized cells. Molecular analysis of the FOXL2 gene locus showed wild type sequence.
Conclusion: A case of bilateral ovarian luteinized thecoma with sclerosing peritonitis is presented with immunohistochemical findings and molecular analysis for FOXL2 mutation. The patient remains alive and disease free more than 3 years after discharge from hospital

E-PS-09-022
Extra-intestinal presentation of GIST: a report of two cases
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Background & Objective: Gastrointestinal stromal tumour (GIST) at extra-abdominal or retroperitoneal sites is rare, and diagnosis may be challenging.
Method: We report 2 cases presenting to gynaecological services.
Results: The first case is a 51years old with a posterior vaginal wall mass, which showed no connection to the rectum on MRI. Macroscopically, a 3.7cm fleshy white circumscribed mass was present, with overlying elevated intact vaginal mucosa. Histology showed a circumscribed spindle cell neoplasm, with variable cellularity and prominent nuclear palisading. Mitotic count was variable, with up to 7 mitoses per 10 hpfs. Necrosis was absent. Immunohistochemically, tumour was positive for c-KIT, DOG1 and CD34. An exon 9 KIT mutation was detected and diagnosis of extraintestinal GIST, high-risk, was made. The second case is of a 75-years old with pelvic discomfort. CT showed a large pelvic mass with intra-abdominal metastases present. Omental biopsy revealed a tumour composed of monomorphic small round cells with clear cytoplasm, in a myxoid stroma. Necrosis was absent. Immunohistochemically, the tumour was positive for DOG1 and Ckit. Ki67 proliferative index 10%. PDGFRA exon 18 mutation was detected. The morphology and immunophenotype were of an intra-abdominal epithelioid GIST. Subsequent resection confirmed a diagnosis of Epithelioid GIST, High-risk, likely arising from small bowel, with involvement of omentum, pelvis and transverse colon.
Conclusion: Extraintestinal GISTs are unusual. We present two cases with gynaecological presentation and highlight necessity of broad immunohistochemical panel, supported by molecular analysis, to make the diagnosis.

E-PS-09-023
Nitrogen fractionation processes in germ cell tumours in the light of the most modern method of direct cancer tissue investigation
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Background & Objective: Isotope Ratio Mass Spectrometry (IRMS) represents the advance technique which currently has been proved to be aplicable for cancer research. Although the most modern analythical methods are expected to play a leading role in biomedical research in future, it is important to realize what kind of practical value they present for cancer patients. IRMS offers the highest level of required expertise and it also met the highest requirements concerning measurement quality

and credibility even when based on non-numerous samples. We took this versatile approach to investigate isotopic profile of germ cell tumours of developmental age with and without the component of embryonal carcinoma or yolk sac tumour to reveal potential relation between isotopic fractionation processes and established biology of the examined entities.
Method: Nitrogen and carbon isotopic profiles of 18 frozen tissue samples from highly selected growing in vivo germ cell tumours of developmental age were evaluated with the use of Continuous Flow Isotope Ratio Mass Spectrometer coupled with elemental analyzer for simultaneous carbon-nitrogen-sulfur (NCS) analysis.
Results: Germ cell tumours with component of embryonal carcinoma and yolk sac tumour appeared significantly nitrogen depleted comparing with the examined tumours without these tissues.
Conclusion: Isotopic profile of nitrogen in germ cell tumours supports the thesis of relation of isotopic fractionation processes and cancer cell proliferation. The measurement of isotopic ratio of stable isotopes of nitrogen identifies entities characterized by worse prognosis, which need a more individual and complex approach.

E-PS-09-025
Stathmin-1 expression as a complement to p16 helps identify high-grade cervical intraepithelial neoplasia with increased specificity
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Background & Objective: The aim of this study was to investigate the addicional diagnostic value of STMN expression in SILs.
Method: A total of 26 samples were examined, LSILs (n=11), HSILs (n=9), invasive squamous (SCC) (n=5) and one case of invasive adenocarcinoma (ACA). Immunohistochemical analysis was used to evaluate Stathmin, p16 and Ki-67 expression. Positive STMN in SIL biopsies was defined as cytoplasmatic immunoreactivity in at least two thirds. For SCC and ACA, STMN was evaluated for the amount of and for intensity. P16 was considered positive when continuous stretches of nuclei with or without cytoplasmatic reactivity were positive in one third of the epithelial thickness.
Results: STMN was expressed in 8/9 of HSILs and was negative in all LSILs. P16 was expressed in all HSILs, and 3/11 LSILs. ACA case was STMN positive and p16 positive. SCCs were STMN positive in 2/5 cases, and negative in the rest of cases, p16 was positive in 4/5, and one case was negative. The sensitivity of STMN for differentiating between LSILs and HSILs was 88% compared with a sensitivity of 100% for p16. The specificity of STMN was 100% compared with a specificity of 72% for p16.
Conclusion: STMN is a highly specific biomarker for the diagnosis of HSIL lesions. In addition to the more commonly used immunohistochemical markers p16 and Ki-67, STMN would permit narrowing the proportion of p16-positive lesions that warrant consideration as HSIL. STMN can be useful diagnostic tool for identifying HSILs, especially in cases in which differentiating between LSIL and HSIL is difficult.

E-PS-09-027
Simultaneous ocurrence of clear cell carcinoma and colon adenocarcinoma metastasis in the same ovary: A case report
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Background & Objective: We report the simultaneous presentation of ovarian clear cell carcinoma and colon metastatic adenocarcinoma.
Method: A 82-year-old women with suspected neoplasm of left ovary. Bilateral ovarian tumours were observed, cystic right lesion of 49 mm and left solid-cystic tumour with central vascularization of 107 mm. During surgery, right colon neoplasia was detected.
Results: The left ovary histologically showed a large cellularity, with marked nuclear atypia, and abundant clear cytoplasm, arranged in cribriform glandular structures. Immunohistochemically the tumour cells were positive for CK7, PAX-8, CA-125, NapsinA and beta-catenina. Negative were CK20, CDX2, WT-1, estrogen and progesterone receptors, alpha-fetoprotein, OCT-4, PLAP and CD10. Near the surface, it was observed small area (8 mm), showed smaller cellularity with scanty eosinophilic cytoplasm, with marked nuclear atypia, arranged in glandular structures of different sizes, some with central dirty necrosis, these cells were positive for CDX-2 , beta-catenin and focally positive for CK7, and negative CK20, NapsinaA and PAX-8. Colon showed tumour histologically and immunoreactivity the same characteristics as the peripheral lesion exhibited.
Conclusion: The ovary is a common site of both primary and metastatic tumours. It may be the seat of simultaneous presence of more than one tumour. Some metastases may mimic a primary lesion. Colorectal adenocarcinoma is one of the most frequent metastatic tumours, and it is bilateral in <50% of cases. Most show positivity for CK20 and in a small proportion of cases they can show expression for CK7. The coexistence of a colon metastatic adenocarcinoma and primary ovarian clear cell carcinoma is very rare.

E-PS-09-028
Report of two cases of ovarian steroid cell tumours: morphological aspects and clinical-pathological correlation
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Background & Objective: The Steroid Cell Tumour is classified as a stromal tumour of the sexual cords, its incidence is low and it is composed of steroid hormone secreting cells. It frequently presents androgenic manifestations. Its behavior is unpredictable, although, there are morphological characteristics suspicious aggression (necrosis, nuclear atypia, >2 mitosis/10 HPF, size >7 cm). We present two cases diagnosed in different hospitals of Spain (HVL and HUMV) in the last two years.
Method: 68 and 62-year-old female patients, both derived from endocrinology for the study of hyperandrogenism, one of them without a known primary tumour and the other with a 3cm nodule in the right ovary with diagnostic suspicion of fibroma by NMR. Both patients underwent bilateral adnexectomy.
Results: Both pathological ovaries presented intact capsule and solid, yellow, well-defined tumours of 1.3 x 1 cm and 3.6 x 3 cm, microscopically composed of polygonal cells, with central nuclei, small nucleoli, eosinophilic-granular and spongy-vacuolated cytoplasm (rich in lipids), without necrosis, ≤2 mitosis/10 HPF and edematous surrounding stroma. No Reinke crystals were observed. Immunohistochemistry: positive alpha-inhibin, vimentin, melan-A and calretinin; negative CK AE1-AE3 and Ki67 <5%.
Conclusion: -Although melan-A and calretinin can stein Leydig cells, a Leydig Cell Tumour was not diagnosed due to the non-observance of Reinke crystals. -The anatomopathological study was important since the etiology of the hormonal disturbance was discovered. -One third of these tumours can malignify, although, our cases did not meet malignant criteria.

E-PS-09-029
Ovarian steroid cell tumour not otherwise specified in a postmenopausal woman: a case report
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Background & Objective: Ovarian steroid cell tumours are fewer than 0.1% of all ovarian tumours. The average age at diagnosis is the mid-20s, but patients can present at virtually any age.

Method: A 69-year-old postmenopausal female presented with abdominal pain and distention, she was diagnosed with hypertension and diabetes mellitus. Pelvic ultrasound-scan revealed massive ascites and a solid mass in the left ovary. Frozen section was observed benign sex-cord tumour. Macroscopic examination showed a well-circumscribed tumoural mass measured as 9 cm × 6 cm × 4 cm cut surface was grayish-yellow with areas of apparent hemorrhage.
Results: Histopathological examination of the tumour findings were consistent with ovarian steroid cell tumour NOS. There were 1 mitotic figures per each 10 high-power field (HPF) , grade 1-2 cellular atypia and haemorrhage. There was no necrosis. Ascitic fluid analysis for malignant cytology was negative. The patient was treated postoperatively with chemotherapy and is on regular follow-up.
Conclusion: The microscopic appearance of our case did not reveal any prominent finding in favour of malignancy. The most important factor to be determined in steroid cell tumours of the ovary is whether the tumour has malignant features or not. It is known that pathologically benign steroid cell tumours can behave in a clinically malignant fashion Therefore, careful followup is essential in such cases which do not have clinical or pathological evidence of malignancy.

E-PS-09-030
Uterine metastasis revealing a breast mixed carcinoma
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Background & Objective: solitary uterine metastases from extra-genital cancers are very rare. Breast cancer is the most common primary site for uterine corpus metastases, invasive lobular carcinoma being more likely to spread to gynaecological organs than invasive ductal carcinoma. Through this case we will discuss the clinico-pathological features of uterine metastases of breast carcinomas.
Method: a 62-year-old postmenopausal woman diagnosed with non-specific infiltrative carcinoma of the breast on a biopsy. in front of the locally advanced character, a neo-adjuvant chemotherapy was performed followed by a mastectomy.
Results: examination of the mastectomy specimen retains the diagnosis of infiltrating carcinoma of non-specific high-grade type. following her follow-up the patient presented one year after, a 5 cm uterine mass suggestive of a uterine leiomyoma on the radiology from which the decision of a hysterectomy with bilateral annexcetomy. macroscopically the uterine body had a 5 cm whitish fasciculated mural nodule. histopathological examination, including detailed immunohistochemistry, confirmed that the nodule corresponds to an invasive metastatic lobular carcinoma, infiltrating both the uterine myometrium and the leiomyoma.
Conclusion: Invasive lobular carcinoma metastasis particularly in the genital tract whose uterine location is the most common. It is confusing clinical diagnosis especially if it is a raising within leiomyoma. Rarely, uterine metastasis may be of a histological type different from primary mammary carcinoma, especially if it is mixed. In this case, the lobular component was certainly minimal, not interested in biopsy and mastectomy specimens, and was revealed as a metastatic uterine nodule. only histological examination and immunochemistery are able to retain the diagnosis.

E-PS-09-031
Use of p16 immunohistochemistry and hormone receptors to determine primary site of origin in endometrial and endocervical adenocarcinomas
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Background & Objective: A 44-year-old female presented with irregular vaginal bleeding. Her subsequent cervical smear raised the possibility of glandular neoplasia. Clinical investigations and imaging were inconclusive. An endometrial biopsy showed features consistent with atypical complex hyperplasia. The hysterectomy specimen contained an irregular endometrial and endocervical canal which was confirmed microscopically to be a well-differentiated adenocarcinoma with extensive endometrial involvement and involvement of the left ovary.
Method: The tumour showed weak patchy reactivity with oestrogen receptor (ER) and vimentin immunohistochemistry and focal strong reactivity with carcinoembryonic antigen (CEA). Strong diffuse reactivity was seen with p16 immunohistochemistry, in keeping with a well-differentiated HPV-related cervical adenocarcinoma.
Results: Recognition of endocervical adenocarcinoma can be challenging when tumour is present within both the cervix and endometrial cavity and even more so when the majority of the tumour is within the endometrium. Both tumours share similar morphological characteristics and cervical adenocarcinoma may simulate both complex atypical hyperplasia and endometrioid adenocarcinoma following invasion of the uterine corpus.
Conclusion: This distinction can be made using a panel of immunohistochemical markers including p16, ER and progesterone receptor (PR). Most adenocarcinomas of the cervix are related to high risk human papilloma virus (HR-HPV) and show diffuse, strong expression (block positivity) with p16 immunohistochemistry. Endometrial adenocarcinomas are not HPV-related but the majority retain hormone receptor expression. This panel is of particular use when macroscopic findings suggest involvement of both the uterine cervix and endometrium and also when ER/PR immunohistochemistry is not typical of endocervical or endometrial origin.

E-PS-09-032
Müllerian adenosarcoma of the female genital tract: report of 8 cases and review of the literature
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Background & Objective: Mullerian adenosarcoma is an uncommon mixed tumour containing a neoplastic but benign or mildly atypical epithelial element and a sarcomatous, usually low-grade, stromal component. The most common site is the uterine corpus but adenosarcoma also occurs in the cervix and ovary and more rarely in the vagina and fallopian tube
Method: Eight patients with Mullerian adenosarcoma of the female genital tract, who were diagnosed in the past 15 years, were analysed retrospectively focusing on clinicopathological features, treatment and prognosis
Results: Over a fifteen-year period, 8 adenosarcomas were diagnosed in our institution with age range of 19-86 years (mean: 55), in the endometrium (5), cervix (2) and ovary (1). Three cases displayed coexisting leiomyomas and one, endometrial adenocarcinoma. Histopathologically, the tumours were low grade without sarcomatous overgrowth. Immunohistochemically, the tumours focally expressed CD10 with low proliferation index. Six patients underwent surgery without any adjuvant treatment. None of them recurred.
Conclusion: Müllerian adenosarcoma is an uncommon low grade mixed tumour, usually unilateral, more commonly seen in endometrium and cervix. The treatment of choice is hysterectomy with bilateral salpingo-oophorectomy. Outcome is related to invasion of cervical/myometrial wall and sarcomatous overgrowth. The role of adjuvant radiotherapy and chemotherapy is not clear and has not been fully evaluated.

E-PS-09-033
Brenner tumour of the ovary and hepatic metastases: case report
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Background & Objective: Nowadays, Brenner tumours are classified as benign, borderline/atypical proliferative and malignant. Most benign Brenner tumours are small and are incidentally found in oophorectomy

specimens. In contrast, the borderline and malignant entities are rare and pose diagnostic challenges in routine practice.
Method: We present a case of a 69-year-old woman with 15x15 cm cystic pelvic mass with solid areas. There were multiple metastatic focci with central necrotic areas in the liver. The patient underwent total hysterectomy with adnexectomy. Excision biopsy of the largest liver metastatic lesion was also made. CT scans did not reveal any other possible primary site.
Results: Microscopic examination of haematoxylin-eosin stained slides manifested transitional epithelium with proliferative changes resembling low-grade urothelial carcinoma. Areas of malignant transitional cells with stromal and lymphovascular invasion were seen in the peritubar soft tissues. The liver biopsy examination revealed similar high-grade morphology. Simultaneous immunohistochemical examination of ovarian and liver tumours demonstrated positivity for cytokeratin 7, cytokeratin 5/6, p63. The tumour cells were negative for cytokeratin 20, WT 1, p16. The histopathological diagnosis was an ovarian malignant Brenner tumour with areas of borderline/atypical proliferative Brenner tumour and distant metastases to the liver.
Conclusion: Morphological diagnosis, immunohistochemical characteristics of borderline and malignant Brenner tumours and some debatable issues are discussed.

E-PS-09-034
Plexiform tumourlet as an incidental finding in a hysterectomy specimen
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Background & Objective: Leiomyomas are benign mesenchymal smooth muscle tumours found in 75% of hysterectomy specimens. There are several subtypes, among them plexiform leiomyoma. When they are microscopic findings are referred to as plexiform tumourlets. We report a case of plexiform tumourlet in a patient with history of invasive lobular carcinoma (ILC) and concomitant endometrioid carcinoma.
Method: A 64-year-old patient with history of ILC three years ago was admitted to the gynaecology department due to recurrent vaginal bleeding. An endometrial curretage was performed. Histological diagnosis was endometrioid carcinoma grade I arising in a polyp. A hysterectomy and bilateral saplingo-oophorectomy was performed. On microscopic examination residual endometrioid carcinoma was not present. Six uterine leiomyomas with a maximum diameter ranging from 1.2-4.3cm were found. A small tumour measuring 3 mm was found in the uterine wall. It consisted of small nests, islands, cords and tubules of epithelioid cells surrounded by loose stroma. Mitotic figures, pleomorphism or necrosis were absent. The differential diagnosis included plexiform tumourlet, uterine tumour resembling ovarian sex cord tumour and metastatic ILC. Immunohistochemical study was positive for SMA, Desmin, CD-56 and negative for AE-1/AE-3, EMA, Inhibin, WT-1 and CD-99.
Results: The diagnosis of leiomyomatous uterus consisting of six leiomyomas and a plexiform tumourlet was made. The patient is alive without any evidence of recurrence or metastasis fifteen months after surgery.
Conclusion: Plexiform tumourlet is a very rare variant of epithelioid leiomyoma discovered incidentally, showing benign clinical course.

E-PS-10 | Haematopathology

E-PS-10-001
Case report of a mediastinal histiocytic sarcoma in a 27-year-old
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Background & Objective: Histiocytic sarcoma is an extremely rare neoplasm of haematopoietic origin, that has a peak incidence in 4th-6th decade, arises in lymph nodes or soft tissue and has a poor prognosis. Although the histological examination is helpful, immunohistochemical tests showing histiocytic differentiation are crucial in the diagnostic process.
Method: We report a case of a 27-year-old male without any personal medical history, that presented to our clinic with retrosternal pain and dry cough of recent onset. CT examination revealed a large mass that projected to the anterior mediastinum and extended to the anterior wall through the left first intercostal space, without affecting the pectoral major muscle. A biopsy from the tumour was surgically removed and the specimen was sent to the Department of Pathology for investigation.
Results: The histological examination revealed a cellular proliferation composed of large cells, with granular cytoplasm and occasional vacuolization, irregular nuclei and evident nucleoli. Rare mitotic figure were also present. Immunohistochemistry showed diffuse reactivity for histiocytic markers (CD68, CD163, LCA), while dendritic cell markers (CD21, CD35), B cell marker (CD20), Langerhans cell markers (CD1a) and epithelial markers (CK AE1/AE3) were negative. CD117 and OCT3/4 negativity excluded a thymus carcinoma, respectively a germ cells tumour. Ki67 index was greater than 70% showing an increased proliferation rate.
Conclusion: We present a case of histiocytic sarcoma, a rare and aggressive tumour localized solely in the mediastinum, that rarely affects young adults. We emphasize the importance of the immunohistochemical examination showing histiocytic differentiation in the diagnosis of histiocytic sarcoma.

E-PS-10-002
Clinicopathological evaluation of bone marrow metastasis in 184 patients; experience of 10 years
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Background & Objective: Bone marrow (BM) involvement by metastatic tumour may cause symptoms mimicking involvement by leukemias and lymphomas. Imaging studies are often helpful, but BM examination is usually required to diagnose metastasis. The aim of this study was to evaluate the presenting features, morphological, clinicopathological and radiological features of BM metastasis in patients diagnosed in our institution, in view of the literature.
Method: The medical records of 184 patients diagnosed as BM metastasis between January 2008 and December 2017 were retrospectively reviewed; patients were reevaluated.
Results: Mean age was 51.7 (18 patients between 3 months to 18 years-old, 166 patients 19-86 years-old); 54.9% male and 45.1% female. Among these patients, 161 (87.5%) were diagnosed as malignant epithelial tumour, 18 (9.78%) neuroblastomas, three (1.63%) mesenchymal tumours, one (0.54%) malignant melanoma, one (0.54%) unclassified tumour. There were 111 patients diagnosed primarily as metastasis of the BM biopsies (Group-1). Seventy-three patients had been already diagnosed as a primary malignancy elsewhere, followed by the diagnosis of the BM infiltration, within a mean of 28 months of follow-up (range 0-128 months) (Group-2). The majority of the patients had thrombocytopenia, anemia, and elevated lactate dehydrogenase levels. Besides the BM, the most common sites of metastasis diagnosed on radiological studies were bone and lung metastasis, seen in the majority of patients in both groups. The mean overall survival was 11.6 months in Group-1 (range 1-116 months); 17.4 months for Group-2 (range 1-110 months), and on follow-up period up to 10 years, the total mortality rate was 84.2% (n: 155).
Conclusion: In conclusion, the most common primary tumours metastatic to the BM were breast, prostate, lung, gastrointestinal tract, and kidney in the adults; neuroblastoma, rhabdomyosarcoma, and Ewing's sarcoma in the childhood period in our series, with high mortality rates, and the diagnosis of BM metastasis is important for the decision of appropriate treatment regimen and estimating survival for these patients.

E-PS-10-003

Concomitant classic Hodgkin`s lymphoma and mycobacteriosis in a lymph node from a HIV infected patient

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Background & Objective: Human Immunodeficiency Virus (HIV) is associated with opportunistic infectious agents and intercurrent neoplasms. The incidence of Classic Hodgkin`s Lymphoma (CHL) among HIV-infected individuals is about 5-20 times the incidence in the general population. The purpose of this study is to report a case of a simultaneous CHL and Mycobacteria infection in a cervical lymph node from a patient with HIV.

Method: A 70-year-old man, with known HIV infection, presented with a 2-month clinical picture of fever without focus, accompanied by night sweats and weight loss. The computed tomography showed multiple lymphadenopathies and a cervical node was excised. Specimen was routinely processed and sections were stained with haematoxylin-eosin and Ziehl-Neelsen (ZN). Immunostains, as well CISH staining for EBV-encoded RNA (EBER) transcript, were performed.

Results: Histologically, the node presented an effacement of the normal architecture due to a diffuse proliferation of cells with a histiocytic phenotype, immunoreactive for CD68. Among these, scattered neoplastic cells with Reed-Sternberg (RS) morphology were identified, and immunoreactivity for CD30, CD15, CD20 and PAX5 was recorded. In the CISH-stained slide, EBV trace was observed in the nuclei of these RS cells. ZN-stain revealed the presence of acid-fast bacilli, sustaining lymph node mycobacteriosis.

Conclusion: This case illustrates the histological and immunohistochemical characteristics of a CHL with concomitant mycobacteriosis. The extensive infiltration by histiocytes, associated with the mycobacteriosis, may impair the diagnosis of lymphoma, making this a challenging case. Synchronous occurrence of these two entities is rare. Their coexistence should be taken into consideration to ensure appropriate patient management.

E-PS-10-004

The spectrum of HIV-associated lymphomas: a study of immunomorphological features, c-MYC expression and association with Epstein-Barr-Virus

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Background & Objective: HIV-associated lymphomas are an important public health concern; but due to the paucity of studies from the Indian subcontinent, the data available from India is underwhelming. Through this study we attempt to analyse: -Immunomorphological characteristics of different subtypes of HIV-associated lymphomas. Association of c-MYC in HIV-associated lymphomas. Expression of Epstein-Barr Virus (EBV) with HIV-associated lymphomas using IHC for EBV LMP1 and Rapid in situ Hybridization (RISH) for EBER on formalin fixed paraffin embedded (FFPE) tissue sections.

Method: The study was undertaken at Kidwai Cancer Institute, Bengaluru over a period of 7 years. 56 cases of HIV associated lymphomas for which FFPE tissue blocks were available were studied. Clinical characteristics such as age, gender, sites of presentation, serology findings and haematological parameters were obtained. The histological and immunohistochemical findings of all cases were analysed. A TMA was constructed on which IHC for c-MYC and ISH for EBER was performed. The cases we studied were diagnosed and subtyped according to the 2016 WHO classification of Tumours of Haematopoietic and Lymphoid tissues.

Results: The 56 cases analysed included 44 cases of non-Hodgkin lymphoma and 12 cases of Hodgkin lymphoma. EBER was positive in 47% cases and c-MYC expression was noted 70% cases of all HIV-associated lymphomas. 40% cases of HIV-associated lymphomas showed association with both EBV infection and were positive c-MYC expression.

Conclusion: Ours is the first study from India to examine the association of c- MYC with HIV-associated lymphomas and it showed a significant statistical association between the expression of EBER and c-MYC with different HIV-associated lymphomas.

E-PS-10-005

Pleomorphic and classical mantle cell lymphoma in the same lymph node – a rare case report

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Background & Objective: Mantle cell lymphoma (MCL) is a mature B-cell neoplasm which in more than 95% of cases carries a CCND1 translocation. MCL has several variant forms with distinct morphology that may pose diagnostic challenges.

Method: We report the case of a 75-year-old male patient that was referred to the Haematology Department with a three-month history of malaise, poor sleeping, weight loss, and night sweats; on physical examination he was cachectic, with multiple enlarged peripheral lymph nodes and a palpable spleen. Laboratory tests showed anemia and thrombocytopenia. On the CT scan, lightly enlarged nodes were observed in the head and neck, axilla, liver hilus, retroperitoneum, mesenterium and inguinal region. A femoral lymph node was removed and a bone marrow biopsy was performed.

Results: Pathological examination showed an enlarged lymph node with remnants of germinal centers that were infiltrated by a vaguely nodular proliferation of monotonous small lymphocytes alternating with fields of large blastic lymphocytes with irregular nuclei and small visible nucleoli, appearing as a transformation to diffuse large B-cell lymphoma. Both components were, however, positive for CD20, CD79a and Cyclin D1, SOX 11 and weak CD5. MIB-1 was higher in the pleomorphic than in the small cell component (35% and 5% respectively). Flow cytometry revealed an expansion of 75% B-cells: CD19, CD20, sIgM, sIgKappa, CD81, CD38, and CD305 positive –FISH analysis showed a CCND1 rearrangement in both the small cell and the pleomorphic component.

Conclusion: This is a unique case of MCL with a classical and pleomorphic variant in the same lymph node. MCL is not considered to transform from the classical form to the pleomorphic/blastic form, a opposed to other B-cell lymphoma's as follicular lymphoma or small lymphocytic lymphoma. The morphologic appearance of the pleomorphic variant of MCL can be similar to that of a diffuse large B-cell lymphoma and is a more aggressive form of the disease.

E-PS-10-006

Sporadic Burkitt lymphoma with atypical presentation in an old patient with consumptive diseases

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Background & Objective: Burkitt Lymphoma (BL) is a mature B-cell non-Hodgkin lymphoma, one of the most aggressive and rapidly growing malignancy, associated with chromosomal translocations that activate the c-MYC oncogene. The endemic BL is associated with malaria and EBV infections and affects the African children. The sporadic BL occurs worldwide and accounts for 1-2% of adult lymphoma, with a median age at diagnosis of 35. The immunodeficiency-associated BL mainly affects the people with HIV/AIDS.

Method: We present the case of a 68-years-old deceased man with a medical history of schizophrenia, pulmonary tuberculosis, chronic obstructive pulmonary disease and malnutrition. Specimen samples taken

from subcutaneous tissue, liver, lung and kidney were processed and examined with standard HE technique and Congo red stain. An indirect tristadial ABC-technique with NovoLink Polymer detection system was performed for CD20, CD10, CD68, S100, Ki67, UCHL1, AE1-AE3, HMB45, Vimentin and EMA.
Results: The forensic autopsy revealed a subcutaneous tumour located on the lower limb. Hepatic and pulmonary metastases were also observed. Microscopically, the subcutaneous tumour consisted of medium-sized neoplastic lymphocytes, with numerous mitosis and large apopototic debris laden-macrophages, producing a „ starry sky" pattern, suggestive to BL. Immunohistochemical markers were positive for CD20, CD10, CD68 and Ki67 (95%), which confirmed the diagnosis of BL.
Conclusion: The particularity of the case is the atypical presentation of sporadic BL at an advanced-age patient and the post-mortem diagnosis of disseminated disease, reflecting the high rate of proliferation and the unfavorable prognosis without treatment.

E-PS-10-007
Anatomic distribution and histological subtypes of primary gastrointestinal lymphomas – a preliminary study
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Background & Objective: Primary gastrointestinal lymphomas (PGIL) are rare tumours that can involve the whole GI tract. This study is aimed to examine the clinicopathologic features of PGIL.
Method: Histopathological records of PGILs diagnosed between 2006-2018 were analyzed retrospectively.
Results: The study consisted of 111 patients who were diagnosed with PGIL during a 12-year period. The pathological samples were obtained from endoscopic biopsies (n=90) and surgical resections (n=21). The mean age of the patients was 63.4 years (53.2% males, 46.8% females). Site of involvement was stomach in 75 (67.5%), small bowel in 20 (18%), large bowel/rectum in 14 (12.6%), and pancreas in 2 (1.8%) patients. Of 111 lymphomas, 106 (95.4%) were B-cell, and 5 (4.6%) were T-cell. Gastric lymphomas consisted of 65 (86.6%) diffuse large B-cell lymphomas (DLBCL), 6 (8%) MALT lymphomas, 1(1.3 %) mantle cell lymphoma (MCL), 1 (1.3%) Burkitt lymphoma, 1 (1.3%) plasmablastic lymphoma, and 1 (1.3%) T-cell lymphoma (unclassified). Amongst small bowel lymphomas, there were 13 (65%) DLBCLs, 3 (15%) enteropathy-associated T-cell lymphomas (EATCL), 2 (10%) MALT lymphomas, 1 (5%) anaplastic large-cell lymphoma, and 1 (5%) MCL. Large bowel/rectum lymphomas included 7 (50%) DLBCLs, 3 (21.4%) MCLs, 2 (14.2%) MALT lymphomas, 1 (7.1%) B-cell lymphoma (unclassifiable with intermediate features between DLBCL and Burkitt lymphoma), and 1 (7.1%) B-cell lymphoma (unclassified). Both of the pancreatic lymphomas were DLBCLs.
Conclusion: Accurate diagnosis of the type of lymphoma is important for correct treatment and determining prognosis. In our series, DLBCL was the most common pathological type of PGIL in all sites of the gastrointestinal tract followed by MALT lymphoma in stomach, EATCL in small bowel and MCL in large bowel/rectum.

E-PS-10-008
Bacille Calmette-Guérin (BCG) lymphadenitis in two cases
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Background & Objective: In our country, Bacille Calmette-Guérin (BCG) vaccine has been one of the routinely administered vaccines since 1952. Current application is one shot within the second month of life. Lymphadenitis is the most common complication of BCG vaccine.
Method: Two infant cases (7-months old and 12-months old) with BCG lymphadenitis are presented.
Results: Microscopic examination of both cases revealed sheets of large histiocytic cells which effaced the normal architecture of lymph nodes. These cells had round nuclei and large eosinophilic cytoplasm and showed minimal to mild nuclear atypia. Occasional bi/multinuclear forms were observed. In immunhistochemical examination they were positive for CD68, Fascin and CD163. CD3 and CD20 stains highlighted residual lymphoid tissue with disrupted T and B cell areas because of the histiocytic proliferation. Ziehl-Neelsen stains showed numerous pinkish-red acid resistant bacili inside the histiocytes. Gomori methenamine silver stain also highlighted these bacilliform microorganisms. Both cases were diagnosed as "Granulomatous lymphadenitis with acid-resistant bacilli".
Conclusion: Although BCG lymphadenitis is the most common complication of vaccination, it is rarely seen in healthy individuals. Both infants are under investigation for possible underlying causes such as immunosuppression.

E-PS-10-009
Renal intravascular NK/T cell lymphoma; a case report
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Background & Objective: We report a rare case of renal intravascular NK/T-cell lymphoma.
Method: A 79-year old Afro-Caribbean male, with hypertension and monoclonal gammopathy of undetermined significance, was admitted with acute nephrotic syndrome, anaemia and an elevated conjugated bilirubin level. There was no sign of haemolysis on blood film. Autoimmune screening was negative and a bone marrow trephine showed hypercellularity with no malignancy. Neither palpable lymphadenopathy nor hepatosplenomegaly was found. Imaging revealed diffusely echogenic kidneys suggestive of intrinsic renal disease. There were no signs of malignancy on unenhanced CT-scan.
Results: Renal biopsy showed small intravascular collections of large and highly atypical lymphoid cells. CD34 immunostaining confirmed clear delineation of the vascular lumina containing atypical cells. The atypical cells were positive for CD56, granzyme-B, CD3(focal), EBER, MUM1(weak), MYC(heterogeneous staining) and Ki67. Atypical cells were negative for CD19, CD20, PAX5, CD138, CD10, CD2, CD5, CD7, CD4, CD8, CD30, ALK, cyclin-D1, MNF116 and CAM5.2. Collapsing-type focal segmental glomerulosclerosis was present as well as tubuloreticular inclusions in endothelial cells on electron microscopy, most likely secondary to virally-driven lymphoid malignancy. The patient was diagnosed with EBV-positive intravascular NK/T-cell lymphoma. Peripheral blood and bone marrow aspirate flow cytometry did not show any abnormality. Supportive treatment was administered but the patient deceased within 3 weeks.
Conclusion: With only 18 cases of intravascular NK/T-cell lymphoma published, this is an extremely rare entity. The majority of cases involved skin and/or central nervous system. This case represents the first documented example of intravascular NK/T-cell lymphoma diagnosed on renal biopsy following presentation as acute nephrosis.

E-PS-10-010
Immunophenotype of the tumour cells depending on the immunoarchitectural patterns of nodular lymphocyte predominant Hodgkin lymphoma in the debut of the disease
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Background & Objective: Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) is a rare subtype of Hodgkin lymphoma (HL) with variable immunoarchitectural patterns of the tumour substrate. To compare of LP cells' immunophenotype with immunoarchitectural patterns NLPHL in debut of the disease.

Method: Diagnosis NLPHL in debut of the disease was revised and established in 60 pts (2010-2017, NRCH): m/f ratio is 3.6:1, median age – 37 (range 17-68). All patients was determined the immunoarchitectural pattern (WHO 2017) using IHC and clinical stages (Ann Arbor).
Results: All patients were divided into 3 groups depending on the immunoarchitectural pattern: I (only pattern A-18 pts, 30%; I-II stages 78%, III-IV stages -22%), II (mixed group-31 pts, 52 %; stages I-II - 42%, III- IV stages -58%), III (pattern E> 50% tumour growth-10 pts, 17%; II stage-10% - "tumour cell-rich" case, III-IV stages - 90%); 1 case with transformation in large B-cell lymphoma – LBCL (2%, IV stage). In all groups tumour cells have a standard immunophenotype (CD20+, OCT2+, PD.1-rosettes). We revealed differences in the immunophenotype of tumour cells in the expression of BCL2 and CD19. I group: CD19+ 1/6 (17%), except for "tumour cell-rich" case; BCL2+ 0/8, (0%). II group CD19+ 6/8 (75%), BCL2+ 6/17 (35%). III group CD19+ 4/4 (100%), BCL2+ 4/5 (80%), except for "tumour cell-rich" case. The case with transformation into LBCL CD19+, BCL2+.
Conclusion: Change of tumour cells' immunophenotype correlates with the immunoarchitectural patterns in continuum of THRLBCL-like transformation of NLPHL. "Tumour cell-rich" cases require detailed research.

E-PS-10-012

Diagnostic approach in Epstein-Barr-Virus-positive mucocutaneous ulcer: a case report and literature review

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Background & Objective: Epstein-Barr Virus-positive mucocutaneous ulcer (EBVMCU) is recently provisional entity described in 2016 WHO lymphoma classification with specific clinicopathological findings and treatment.
Method: A 68-year-old woman with a history of mycosis Fungoide IB stage and Diffuse Large B cell lymphoma, in remission after R-CHOP. About 4 years later it evolves with a ulcerated and circumscribed lesion in the posterior pharynx. A biopsy was performed showing mucosa with polymorphic inflammatory infiltrate with Reed-Sternberg-like cells, which were positive for CD20, PAX5, CD30, CD15 and EBER, besides being negative for CD3 and CD45. After 2 cycles of R-ESHAP the lesions disappeared.
Results: Mucocutaneous ulcers in immunocompromised and immunosenescent patients are common and may have several etiologies, such as infectious diseases, autoimmune conditions and lymphoproliferative disorders (LPD). With respect to the latter, we highlight EBVMCU, which is often characterized by a single and well circumscribed ulcer with indolent and benign clinical course. Histologically it is composed of necrosis and polymorphic inflammatory infiltrate and large cells resembling atypical immunoblasts or RS-like. In addition, it has EBV type II latency and activated immunophenotype B, being positive for PAX5, OCT2, CD30, MUM-1, EBER and LMP-1 and with variable expression of CD20, CD15, CD45 and CD79a.
Conclusion: EBVMCU is a rare clinical entity that should be considered in the differential diagnosis of mucocutaneous ulcers in patients in situations of attenuation of immunosurveillance.

E-PS-10-013

Mantle cell lymphoma with a mantle zone growth pattern: a case report

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Background & Objective: Mantle cell lymphoma with a mantle zone growth pattern (MCL-MZGP) is an uncommon subtype of B-cell lymphoma characterized by cyclin D1 positiv malignant lymphoid cells expanding the mantle zone and infiltrating the germinal centers they surround.
Method: A 70-year old male presented with an elevated PSA (>360) and enlargement of peripheral lymph nodes. The patient was investigated for prostatic malignancy, but MRI and core needle biopsy of prostate were normal. Inguinal and pelvic lymph nodes were excised for histopathological examination. H&E and immunohistochemical stains were performed on formalin-fixed and paraffin-embedded tissue sections. PCR analysis for clonality was performed according to the BIOMED-2 protocol. FISH analysis for t (11;14) translocation was performed using Vysis break-apart probes targeting the CCND1 locus.
Results: Microscopy of the inguinal lymph nodes revealed metastasis from prostatic adenocarcinoma. However, the pelvic lymph node architecture was partially effaced by crowded lymphoid follicles with expanded and confluent mantle zones, first suggesting lymphoid hyperplasia. However, immunohistochemical stainings demonstrated that these areas were infiltrated by malignant lymphoid cells positive for CD20, BCL2, cyclin D1 and SOX11. Molecular analyses showed monoclonal rearrangement of Ig heavy chain genes and t (11;14) translocation.
Conclusion: We described an incidental finding of MCL-MZGP by immunohistochemical and molecular analyses in patient who was examined for prostatic malignancy. Morphological evaluation of H&E stained sections was not immediately suspicious for lymphoma. Our case highlights the importance of immunohistochemical staining for cyclin D1 in the investigation of unexplained lymphoid hyperplasia in older patients.

E-PS-10-014

Fine needle aspiration biopsy with flow cytometry is a reliable method for defining diagnosis in primary thyroid lymphoma subtypes without the need for histopathological examination.

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Background & Objective: Diagnosis of primary thyroid lymphoma (PTL) is most commonly based on pathomorphological examination of surgical specimen from thyroidectomy or tru-cut biopsy, and occasionally on flow cytometry (FCM) of cell suspensions obtained by fine needle aspiration biopsy (FNAB). FNAB/FCM of PTL is a safe, rapid, and cost-effective procedure. The aim of our study is to show that FNAB/FCM is not only a sufficient method for PTL subtypes diagnosis, but also for defining PTL with possible MYC and BCL2 rearrangements, which is clinically important.
Method: We identified 34 cases of PTL in our database of over 10,000 lymphoma patients diagnosed by FNAB/FCM from 2000 – 2018. PTL cases were diagnosed by conventional cytological smears and FCM. Lymphoma cells were evaluated by 30 monoclonal antibodies. Lymphoma subtype was defined according to the WHO 2016 classification.
Results: Patients characteristics: female/male – 26/8, median age – 68 yr (range 31-89). The final diagnosis comprised: DLBCL, NOS (GCB) – 17/34 (50%), DLBCL, NOS (non-GCB) – 10/34 (29%), Burkitt Lymphoma – 2/34 (6%), and others – 5/34 (15%).
Conclusion: (1) Combined use of FNAB/FCM is a reliable and minimally invasive method for defining subtype of PTL with results obtained in 1.5 hour after FNAB. (2) We showed high diagnostic accuracy and effectiveness of FCM in PTL diagnosis. CD38 and BCL2 overexpression on PTL cells compared to normal T-lymphocytes correlates with MYC/BCL2 rearrangements, respectively. (3) Based on our results, we consider FNAB/FCM a method of choice for the diagnosis of PTL, which prevents thyroidectomy.

E-PS-10-015

Evaluation of CD10 protein expression in the diagnostics of follicular lymphoma: comparison of conventional immunohistochemistry on whole slides and tissue microarray with flow cytometry

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Background & Objective: Follicular lymphoma (FL) among all small B cell lymphomas is characterized by CD10 protein expression in most cases. The aim of the study was to compare results of CD10 expression by two methods: conventional immunohistochemistry performed on whole slides and tissue microarray (TMA) samples with flow cytometry.
Method: We collected cases of FL from 1999 to 2017 and from formalin fixed paraffin embedded material the TMA was constructed and IHC assessment of CD10 was repeated. All cases were revaluated according WHO 2016 FL grading system. Simultaneously, a group of patients had lymph nodes FCM. The results from both methods were compared statistically.
Results: Group of 115 FL was enrolled into study with male: female ratio 44:71 and median age 61 years (range: 28-93 years, SD=15.38). Majority of cases presented with low grade FL (89/77.39%; grade 1: 47/40.87%, grade 2: 39/33.91%); high grade was assessed in 22/19.13% cases (grade 3a: 19/16.52%, grade 3b: 2/1.74%). The CD10 expression was performed in 100 initial diagnostics, 93 TMA and 39 FCM cases, respectively with positive results as above: 73.00%, 73.12% and 74.36%. In 5 (12.82%) initial cases CD10 was negative while in repeated TMA and FCM were evaluated as strongly positive.
Conclusion: Flow cytometry is an efficient method to determine CD10 in FL at a comparable level as conventional immunohistochemistry. In some archival cases reducing sensitivity of CD10 staining was determined by lack of IHC standardization procedures.

E-PS-10-016

Epstein-Barr-Virus-positive diffuse large B-cell lymphoma, NOS: a case report and literature review

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Background & Objective: In 2008, the World Health Organization (WHO) listed EBV-positive diffuse large B-cell lymphoma (DLBCL) of the elderly as a provisional entity. However, many cases were described in young adults. As a result, the name was changed in the 2016 WHO lymphoma classification to "EBV positive DLBCL, not otherwise specified".
Method: Case Report: A 33-year-old man who complaineds of persistent cough for 3 months was found a right cervical lymphadenopathy. PET/CT scanning showed multicompartmental adenopathies. A lymph node biopsy showed numerous large cells, including Hodgkin and Reed-Sternberg (HRS) like cells in a background of small lymphocytes and histiocytes. The large cells were positive for CD20, CD79a, PAX5, OCT2, MUM1, PD-L1, CD30 and EBER; moreover, they were negative for CD45, CD3, CD23, CD15, BCL6, BOB-1 and ALK-1. After 6 cycles of R-EPOCH, the patient showed complete remission.
Results: Discussion: EBV(+) DLBCL, NOS has a broad range of morphological features that overlap with other EBV-related lymphoid proliferations, showing variable number of large cells and HRS-like cells, in a reactive background. The phenotype is B cell lineage, mostly of non-germinal center phenotype frequently CD30 positive, sometimes with CD15 co-expression. PD-L1 can be expressed. EBV latency type II is present in the majority of cases. Worst prognosis have been related to expression of CD30, PD-L1 and elderly patients.
Conclusion: EBV(+) DLBCL, NOS have worse prognosis compared with EBV-negative DLBCL, so, the search for EBV should be performed routinely in large B-cell lymphomas.

E-PS-10-018

Langerhans cell histyocitosis: a late debut of a rare disease diagnosed on a dental cyst

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Background & Objective: The Langerhans cell histyocitosis (LCH) is an uncommon haematologic disease characterized by a clonal proliferation of CD1a + myeloid dendritic cells with significant inflammatory component. LCH´s incidence ranges from 0.5-5.4 cases per million/year. Its prevalence is higher among whites, with a 2:1 male/female ratio affecting patients from the neonatal period to adulthood, although it is more common in children (0-15 years). Bone involvement either solitary or multiple is common, especially in the skull, such as lytic lesions with variable skin and/or multiple organ involvement.
Method: We present a 44-yo male with a 4 years clinical history of panhypopituitarism, diabetes insipidus and hyperprolactinemia due to an infundibular lesion that presented right facial pain and both, radiography and computed tomography showed a 1,8 cm cystic mass with cortical erosion of the bone on tooth 48. In contrast, MRI showed a solid mass highly suggestive of an odontogenic neoplasia (ameloblastoma).
Results: He underwent surgery and the histological finding was a polygonal cells proliferation with eosinophilic cytoplasm, oval nuclei with longitudinal grooves resembling coffee beans with abundant eosinophils and giant cells among with neutrophils, foam cells, lymphocytes, plasma cells, with frequent mitotic figures. The polygonal cell proliferation was S100 and CD1a positive.
Conclusion: LCH must be included as a differential diagnosis of persistent eczema, unexplained skin lesions or bone pain and diabetes insipidus among others as its initial presentation heterogeneity could mislead clinicians and delay diagnosis. It is a rare entity that requires a high index of suspicion and multidisciplinary management. Early diagnosis and treatment leads to a favorable prognosis.

E-PS-10-019

Bone marrow involvement in lymphoma: 8-year experience

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Background & Objective: The aim of this study is to report our case series of bone marrow (BM) involvement in lymphoma and revise the clinical and histological findings for eight years.
Method: A retrospective search was made to collect all cases diagnosed for BM involvement in lymphoma for last 8 years. 52 cases identified. The BM involvement frequencies and demographics in each type and subgroup of lymphoma were evaluated. Histopathological slides of the 52 patients diagnosed with BM involvement in lymhoma were reviewed.
Results: The mean age at diagnosis was 58.5 (range19-86), while the male to female ratio was 1.73 (33male/19female). The frequency of involved cases in different lymphoma types were 88.8% (46/52) in B cell Non-Hodgkin Lymphoma(B-NHL),9.61 % (5/52) in Hodgkin Lymphoma (HL), 1.92% (1/52) in Anaplastic Large Cell Lymphoma. B cell Non-Hodgkin Lymhoma involvement: 21% (10/46) Follicular Lymphoma (FL), 15.21 % (7/46) Lymphoplasmacytic Lymphoma (LpL), 10.8% (5/46) Mantle Cell Lymphoma (McL), 8.6% (4/46) Diffuse Large Cell Lymphoma (DLCL) and 8.6% (4/46) KLL/SLL. 4.7% (16/46) of B-NHL didn't demonstrated features of spesific subtype. For each group, the mean age diagnosis was 57.4 (McL), 62.8(KLL/SLL), 59(DLCL), 57.6(FL), 72.8(LpL) and 46.6(HL). The highest male to female ratio was 5/0 in HL.
Conclusion: In lymphoma staging, pathological detection with bone marrow trephine biopsy (BMT) remains the "gold standard". The BMT findings also have significant implications for clinical prognosis and therapy planning.

E-PS-10-020

Mast cell sarcoma, associated with acute myeloid leukemia - case report

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Background & Objective: According to the WHO 2017 the group of mast-cell neoplasms includes cutaneous mastocytosis, systemic mastocytosis, mastocytosis associated with clonal haematological non-mast cell lineage disease (SM-AHNMD) and mast cell sarcoma (MCS). MCS is an extremely rare entity characterized as a solitary neoplasm with a local infiltrative growth pattern, represented by mast cells with severe atypia. Aggressive invasive growth pattern is associated with metastasis, and in some cases it results in the development of myeloid/mast-cell leukemia in a short period of time.
Method: Male, aged 28, developed a persistent enlargement of the palatine tonsil, submandibular component of infiltrative tumour growth and intestinal involvement. Primary histological examination showed medium size tumour cells with severe atypia, moderate clear cytoplasm. Based on a CD45-positivity previously DLBCL was diagnosed. At further examination in NRCH using extended IHC, the tumour cells (CD33+, CD43+, CD45+CD56+, CD117+, tryptase+) with high index Ki-67 were observed. Primary histological examination of the bone marrow showed reactive changes. 4-month patient developed an AML (M5).
Results: Taking into account the literature data, the presence of c-KIT (D816V) mutation is not obligated for MCS. Acute monoblastic leukemia developed in the terminal stage tumour evolution as MCS-AHNMD.
Conclusion: Haematopathologists has low awareness of MCS due to its rarity. Unspecific morphological features and high probability of aberrant immunophenotype dictates the need for expanded IHC study for cases suspected of haematopoietic sarcoma, in particular MCS. The discussed case draws attention to the localizations of tumour lesion corresponding with physiological distribution of mast cells.

E-PS-10-021

Burkitt lymphoma associated with increased bone marrow blasts mimicking acute myeloid leukemia

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Background & Objective: Increased blasts in bone marrow in a percentage >20% of nucleated cells set the diagnosis of acute myeloid leukemia (AML). An exceptional case of Burkitt lymphoma associated with reactive blast elevation in bone marrow is presented.
Method: A 65-year-old male presented with diarrhoea, weight loss, anaemia and lymphocytopenia. CT revealed a left abdominal mass and wall thickening of the gastric body. During endoscopy, a flat ulceration of the lesser curvature was observed and biopsied. Bone marrow biopsy was also performed.
Results: Histologically, an ulcerated gastric tissue, diffusely infiltrated by neoplastic medium-sized cells with round or irregular nuclei and small nucleoli was observed. Many mitotic figures were found and Ki67 mitotic index was almost 100%. Immunostains for CD20, PAX5, CD10, BCL6, CD38, c-Myc were positive. FISH revealed translocation of MYC at band 8q24.21. Therefore, the final diagnosis was Burkitt lymphoma. Although bone marrow was not involved by the lymphoma, CD34 antibody revealed blasts in a percentage of 30%. All three lineages were quantitatively normal with maturation and without signs of dyspoiesis. Due to inadequate clinical and laboratory findings to support the diagnosis of AML, the blast elevation was considered to be a reactive process.
Conclusion: Increased blasts in bone marrow has been associated with several toxic, reactive or regenerative conditions, such as alcohol, drug abuse or liver cirrhosis. To the best of our knowledge, this is the first case of reactive blast elevation associated with Burkitt lymphoma and the need of clinicopathological correlation is emphasized, in order to avoid diagnostic pitfalls.

E-PS-10-022

CD56, Cyclin D1, p53 and p21 antigen expression in plasma cells as a prognostic factor of chronic kidney disease in 122 bone marrow biopsies cases of multiple myeloma

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Background & Objective: Aberrant antigen expression in malignant plasma cells play a role in the prognosis of multiple myeloma (MM) (Ngo, et al., 2009; Chang et al., 2007). One of the most common complications of MM is chronic kidney disease (CKD). The aim of the study is to investigate the relationship between the CD56, Cyclin D1, p53 and p21 antigen expression in myeloma cells and renal function of patients with MM.
Method: Bone marrow biopsies from 122 patients with primary diagnosed MM were examined with CyclinD1, p53, p21, CD56 antibodies. Kidney function was evaluated by MDRD formula and estimated glomerular filtration (eGFR) rate was calculated.
Results: p53 expression in myeloma cells correlated with elevated levels of creatinine level ($p=0.018$; $r=0.21$) and reduced eGFR ($p=0.021$; $r=-0.21$). Patients with p53 positive (+) myeloma cells had higher eGFR in comparison to patients with p53 negative (-) myeloma cells (Mean±SD, 66.7±44.5 vs 84.7±46.9 mL/min, $p=0.021$, Mann-Whitney U-test). CD56 expression in myeloma cells correlates with elevated eGFR ($p<0.0001$; $r=0.43$). Patients´ group with CD56 + myeloma cells had lower eGFR in comparison to patients with CD56 (-) myeloma cells (87.4±47.1 vs 45.8± 26.7 mL/min, $p<0.0001$, Mann-Whitney U-test). No significant association was found between CyclinD1, and p21 expression with eGFR.
Conclusion: MM patients with CD56 negative and p53 positive expression in myeloma cells had worst kidney function assessed by eGFR and as a result more advanced CKD stage and therefore it implied a graver prognosis of MM.

E-PS-10-023

Epidemiological, clinical and histopathological review of plasmablastic lymphomas in a University Hospital between 2010-2018

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Background & Objective: Plasmablastic lymphoma (PBL) was first described in 1997, as an aggressive lymphoid neoplasia that affected oral mucosae in HIV patients. Currently, it is considered a large B-cell lymphoma (LBCL) variant. Our aim is to establish the epidemiologic distribution, clinical features and pathological characteristics of PBL in Basurto University Hospital between 2010-2018.
Method: We have found four cases in this period of 8 years; three of them were HIV+ men, in their 40´s. The last patient was a 65-year-old woman with an orthotopic transplant. Two of them, present with digestives symptoms (abdominal pain and anemia). Another one resorted to hospital because of intense pleural effusion with dyspnea, and the last one presented a painful bilateral oropharyngeal mass.
Results: Histologically, all the cases presented as an atypical diffuse lymphoid proliferation of large cells with plasmocytoid features and high proliferation index (>90%). They were positive

with CD38, CD138, MUM1 and EMA, and lack of B and T lymphoid biomarkers (CD20 and CD3). All cases presented infection of VEB (EBER+). Only two of them had MYC translocation and one had IgH rearrangement.
Conclusion: In our series, all cases affected immunosuppressed patients with VEB infection, as shown in the literature. We have confirmed that localized cases present better prognosis. However, we have not confirmed that patients with MYC translocation have worse outcome.

E-PS-10-025
Ectopic mesothelial cell proliferation in axillary lymph node
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Background & Objective: Mesothelial cell inclusions are extremely rare in lymph nodes. These are generally located within a sinuses of mediastinal lymph node. It may mimic metastatic carcinoma and metastatic mesothelioma.
Method: A 68-years old woman presented to our hospital with breast mass. Core biopsy diagnosis was mammary carcinoma. The patient underwent breast-sparing surgery and sentinel lymph node biopsy.
Results: On microscopic examination, small clusters of cells with large, eosinophilic cytoplasm with small nuclei located within subcapsular sinuses of sentinel lymp node. Positive staining with panCK and Calretinin was observed in these cells. No atypical appearance was seen in these cells. These findings were compatible to ectopic mesothelial cell proliferation in sinuses of axillary lymph node.
Conclusion: Presence of mesothelial cells in axillary lymph node is very rare.

E-PS-10-027
The assessment of bone marrow megakaryocytes and microvessels co-localisation in patients with JAK2 or CALR-positive essential thrombocythemia
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Background & Objective: Essential thrombocythemia (ET) is characterized by presence of JAK2 or CALR mutation in more than 80% of cases. The aim of this study was to estimate megakaryocytes and microvessels co-localisation in bone marrow biopsies of patients with JAK2 or CALR mutated ET.
Method: We examined 30 bone marrow biopsies of patients with ET: JAK2-positive ET – 15, CALR-positive ET – 15. All samples were stained with CD34 monoclonal antibody (QBEnd/10) and digitalized. Coordinates of all microvessels and megakaryocytes were determined in the most informative 150 mm2 area of the digital slide. To assess the megakaryocytes and microvessels co-localisation we used the parametric Hernquist potential examination in MosaicIA (ImageJ plugin software). The hypothesis about the presence of co-localisation was accepted when the «interaction strength» (Str) between microvessels and megakaryocytes was greater than null. The random distribution of microvessels and megakaryocytes (null hypothesis) was disproven via the Monte Carlo method.
Results: In CALR-positive ET co-localisation of megakaryocytes and microvessels was present in all cases, mean Str ($\overline{Str}$) (standard deviation – SD) = 15.9 (10.8). In JAK2-positive ET the null hypothesis was approven in one case ($Str < 0$), in other cases $\overline{Str} = 11.3$ (5.6). No statistically significant differences between the groups were found ($p=0.164$).
Conclusion: We identified significant megakaryocytes to microvessels tropism in bone marrow biopsies of patients with ET regardless of mutational status.

E-PS-10-028
Tumour-infiltrating FOXP3-positive regulatory T-cells in follicular lymphoma
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Background & Objective: Follicular lymphomas (FL) are characterized by an often slow and heterogeneous evolution with risks of repeated relapses, chemotherapy resistance and a possible transformation into an aggressive lymphoma. Many studies underline the important role of tumour microenvironment of FL in its biological behavior. Here we evaluated the expression of FOXP3 in FL samples and searched for correlations with histoclinical and prognostic parameters.
Method: We retrospectively studied using immunohistochemistry (IHC) the expression of FOXP3 in 33 cases of FL, collected at the Salah Azaiez Institute. We evaluated the expression of FOXP3 in follicular lymphoma and searched for correlations between the proportions of FOXP3+ regulatory T cells (Treg) and the different histoclinical and prognostic parameters.
Results: We showed that the percentage of Treg FOXP3 + was significantly correlated with the histological grade of FL, independently of the FLIPI prognostic index (P= 4.6E-0.02). Transformation into Diffuse Large Cell Lymphoma (LBDGC) is associated with a marked reduction in the number of associated Tregs.
Conclusion: These results confirm the hypothesis that tumour infiltrating Tregs can modulate the tumour microenvironment and influence the biological behavior of FL. A better understanding of the biological role of Treg FOXP3 + in these lymphomas could help the development of therapeutic strategies based on immunomodulation of the tumour microenvironment.

E-PS-10-029
Multiple myeloma and other malignancies
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Background & Objective: In recent years, the risk of second malignancies in patients with plasma cell neoplasms appears to be increased, thought to be due to host-, disease-, and treatment -related factors. However, there are inconsistencies in the published data.
Method: We retrospectively evaluated the occurrence of histologically unrelated malignancies before and after the diagnosis of multiple myeloma (MM) in a cohort of 210 consecutive patients with MM diagnosed the last 15 years.
Results: We identified 22 patients (10.5 %) with one or more malignancies on top of MM. The median age of patients with myeloma and 1 or more neoplasms analyzed was 68 years (range 52–81). Six (27%) were females and 16 (73%) were males. Of these, twelve patients (55%) had a pre-existence malignancy at the time of myeloma diagnosis including 5 cases of prostate cancer, 3 of breast cancer, 2 of bladder cancer and 2 cases with myeloproliferative neoplasms. There were also two cases of concurrent diagnoses of MM with chronic lymphocytic leukemia and renal cancer, respectively. On the other hand, nine patients (41%) developed subsequent neoplasms after the diagnosis of myeloma including 2 cases of colon cancer, 2 cases of stomach cancer, 2 cases of melanoma and one case of marginal lymphoma, breast and skin cancer. Notably, there were a significant number of prostate cancers. Interestingly, recurrence of a previous malignancy was not observed.
Conclusion: In our study, the most common malignancies associated with MM were genitourinary, gastrointestinal, haematologic, breast and skin cancers. The biology behind such relationships remains unclear. Genetic predisposition, environmental exposures, or specific myeloma therapeutic options might account for this phenomenon.

E-PS-10-030

Primary testicular non-Hodgkin lymphoma: a single center experience and review of the literature

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Background & Objective: The purpose of this study is to evaluate the clinical characteristics, pathology and treatment outcomes of primary testicular lymphoma (PTL) patients treated at our hospital.
Method: We retrospectively enrolled patients diagnosed with PTL between June 2006 and September 2017 in our hospital.
Results: 10 patients with PTL out of 420 patients with non-Hodgkin lymphoma-NHL (2,3%) were enrolled. The mean age at diagnosis was of 66 years (range 50-81 years), mean follow-up duration 34,5 months (range 4-135 mo). Nine patients (90%) presented with a unilateral testicular mass or swelling, with a mean diameter of 6,2 cm (range 2,3-9,5 cm), whereas one of them (10%) presented with a bilateral tumour, measuring 2 cm in his left and 5 cm in his right testis. The most common pathology subtype was diffuse large B-cell lymphoma (90% of cases, 55% of them being of centroblastic variant/GCB). PTL demonstrates a continuous pattern of relapse and propensity for extra-nodal sites such as the central nervous system-CNS (1 patient). The majority of the patients underwent orchidectomy, followed by CNS prophylaxis and Rituximab- cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP) therapy, whereas some of them were treated with therapeutic and/or prophylactic radiotherapy.
Conclusion: Primary testicular non-Hodgkin lymphoma is an uncommon entity (2,3% of all NHLs) and with current combined modality treatment and central nervous system prophylaxis the outcome may be as good as nodal NHL. CNS relapse remains a significant issue and future research should focus on identifying the best strategy to reduce its occurrence.

E-PS-10-031

Pharyngeal extramedullary plasmacytoma with localised amyloidosis (amyloidoma)

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Background & Objective: Extramedullary plasmacytoma (EP) is an uncommon disease, characterized by a localized monoclonal plasma cell proliferation, in the absence of demonstrable systemic involvement. It comprises only 3% of all plasma cell neoplasms. The coexistence of EP and localized amyloidosis which are two uncommon diseases that are found mostly in adults with a predominance in males, it has been described in the literature. We have only found 4 cases in the literature. We report an additional case of these rare two entities in a 50 years old man.
Method: The specimen was fixed in formalin and embedded in paraffin. 4μm thin sections were cut and stained with haematoxylin and eosin (H&E). An immunohistochemical study was performed using commercially available antibodies against CD56, Ciclina D1, CD20, CD79a and kappa and lambda light chain. We also performed as well as special stain for Congo red (CR).
Results: Histological examination revealed a proliferation of mature plasma cells and deposition of hyaline amorphous extracellular materials. The CR-stain showed apple green birefringence of the homogeneous eosinophilic material under polarized microscopic examination, consistent with amyloid. Inmunohistochemical study showed in plasma cells positive expression for CD79a, CD20 and kappa immunoglobulin light chain. The amyloid deposits were positive also for kappa immunoglobulin light chain on immunohistochemistry.
Conclusion: The biochemical nature of the amyloid deposits was also shown to be of kappa immunoglobulin light chain, suggesting the pathogenetic relationship between the plasmacytoma and amyloid deposition in the pharynge of this patient. The fact that both the amyloid deposits and plasmacytoma share the same immunoglobulin light chain restriction (kappa-restricted) suggests that the former is secondary to the latter process.

E-PS-10-032

Diffuse large B-cell lymphoma with clear cell morphology

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Background & Objective: Diffuse large B-cell lymphomas (DLBCLs) with clear cell morphology are rare. The aim of this case report is to raise awareness regarding this unusual variant
Method: A 69-year-old woman has undergone a hysterectomy due to a previously diagnosed endometrial carcinoma. Intraoperatively, a mesenteric tumour with diffuse growth has been observed and biopsies have been obtained
Results: Microscopically, the tumour of the endometrium represented a serous endometrial carcinoma. The mesenteric tumour showed a dense infiltration of neoplastic lymphoid cells, arranged mainly in an alveolar growth pattern and surrounded by small, reactive, CD3 positive, T-cells. The neoplastic cells had large size with abundant clear cytoplasm and irregularly shaped nucleus. Nucleoli were observed in some of the nucleus. On immunohistochemical stains, the neoplastic cells showed the following immunophenotype: CD45+, CD20+, CD45RA+, CD79a+, PAX5+, BCL2+, CD38+, BCL6++/-, MUM1–/+, CD3-, CD45RO-, CD43-, CD5-, CD23-, CyclinD1-, TdT-, CD10-, CD30-, CD15-, ALK1-, κ-, λ-, EMA-, AE1/AE-, CK20-, CK7-, 34βE12-, S100-, MelanA-. Based on the histological and immunohistochemical findings, but also on the absence of mediastinal or generalized lymphadenopathy or splenomegaly, our final diagnosis was that of a DLBCL with clear cell morphology
Conclusion: DLBCLs with clear cell morphology are rare. This unusual variant should be differentially diagnosed from other lymphomas, such as primary mediastinal (thymic) large B-cell lymphomas and anaplastic large cell lymphomas, but also from other malignant neoplasms, such as carcinomas and melanomas. Pathologists must be aware of this rare histological finding in order to avoid misdiagnosis

E-PS-10-033

CD4-positive diffuse large B-cell lymphoma: a variant

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Background & Objective: Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma. It is rare to find aberrant expression of T cell antigens (exclusive of CD5) in DLBCL.
Method: We reported a 70-year-old female who presented with fever, abdominal pain and splenomegaly with pancytopenia. Because malignant lymphoma was suspected, diagnostic splenectomy was performed.
Results: The pathology was reported diffuse large B-cell lymphoma (DLBCL) primary involvement of the spleen and no distinct lymphadenopathy. Tumour cells showed marked pleomorfism, anaplasia and a high MIB1 proliferative fraction. Immunohistochemical study demonstrated that the neoplastic cells were CD20, MUM-1, BCL2, CD4, pax5 positive, CD3, CD5, CD7, CD8, ALK, BCL6, CD10, Granzyme, Perforin, LMP-1 negative. Bone marrow involvement was seen in bone marrow biopsy. morphologic and immunophenotypic findings, she was diagnosed as CD4+ DLBL, had stage IV disease with bone marrow involvement by lymphoma. The patient responded well to four cycle of R-CHOP regimen

both clinically and radiologically confirmed by PET-CT (complete remission). Additional 2 course of R-CHOP treatment is now planned to be completed of the treatment.
Conclusion: The finding of aberrant CD4 expression in DLBCL has rarely been reported in literature. Whether there are any clinical significance of expression of T cell associated antigens in DLBCL is still uncertain, It is important to be aware of such aberrant phenotypes to accurate diagnoses are made. Aberrant CD4 expression is DLBCL is a rare, but documented phenomenon that raises interesting biological and diagnostic considerations

E-PS-10-034
Lipofibroadenoma of the thymus: a case report
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Background & Objective: Lipofibroadenoma (LFA) is a recently described conventional type B1 thymoma variant, was classified into "rare thymomas" in the WHO classification.
Method: Here we report the case of a 21-year-old man who presented large left mediastinal mass, diagnosed incidentally on a routine follow-up chest radiograph. Chest computed tomography showed a large heterogenous, paracardiac mass, 23 cm diameter. Suspecting a liposarcoma from the PET and CT findings, the patient underwent surgical resection.
Results: The tumour was excised completely. Macroscopically, it was well circumscribed and cut surface showed gray-white solid fibrotic areas and tan-yellow colored areas of fatty tissue. Microscopic review revealed a tumour composed of thymic elements, mature adipose tissue and fibrosis. The histopathological diagnosis was a lipofibroadenoma of the thymus. The patient has been asymptomatic during 4-month follow-up.
Conclusion: Lipofibroadenoma is extremely rare type of thymoma, that histopathologically resembles fibroadenoma of the breast. LFA is slow-growing tumour commonly arises anterior mediastinum and might be associated with myasthenia gravis, hypogammaglobulinemia, pure red cell aplasia and any type of thymoma. The differential diagnosis of mediastinal masses contains thymolipoma, lipoma, liposarcoma. Lipofibroadenoma is considered a benign tumour and complete resection is curative.

E-PS-10-035
Histopathological investigation of non-secretory multiple myeloma
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Background & Objective: Multiple myeloma (MM) is the most serious of plasma cell dyscrasias, characterized by clonal proliferation of malignant plasma cells in bone marrow and subsequent overabundance of monoclonal immunoglobulin (M-protein). The predominant types of all MM are IgG, IgA and light chains, while the rest consist of IgD, IgM, IgE and non-secretory types. Specifically, IgE MM is very rare, with fewer than 50 cases reported so far. Moreover, IgE MM is characterized by the presence of t(11;14) (q13;q32). Here we present a rare case of non-secretory IgE MM.
Method: A 60-year-old woman presented with pathologic fractures in left femur and arm. The serum calcium, hemoglobin and creatinine values were normal. No M-protein spike was identified during serum electrophoresis, while serum concentration of IgG and IgM were decreased and that of IgE was normal. There was no Bence-Jones proteinuria.
Results: CT scan revealed a soft tissue tumour in left iliac infiltrating the surrounding bone. A guided biopsy from the mass showed a predominant population of plasma cells of varying degrees of differentiation positive for CD138, CD38, IgE and λ-light chain. The bone marrow aspiration showed the same microscopic features leading to the diagnosis of IgE MM. The patient underwent radiotherapy and now is under chemotherapy with bortezomib, thalidomide and dexamethazone. Over the last 10 months, no serious adverse events were observed.
Conclusion: Despite the absence of circulating M-protein, when there is high index of clinical suspicion for MM, bone lesion biopsy and extensive diagnostic work-up is necessary to rule-out non-secretory, rare cases of MM, including IgE type.

E-PS-10-036
Accurate detection of FLT3-ITDs and CEBPA variants in acute myeloid leukemia by anchored multiplex PCR and next generation sequencing
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Background & Objective: Acute Myeloid Leukemia (AML) is clinically and biologically heterogeneous, requiring the detection of mutations across multiple genes for characterization. FLT3-ITDs and CEBPA mutations represent important markers in AML, however they are difficult to detect by NGS due to the highly variable nature of ITDs, the high GC content of CEBPA, and the difficulty in mapping repeated sequences to a wild-type reference.
Method: We developed Archer® VariantPlex® myeloid assays based on Anchored Multiplex PCR (AMP™) to detect important mutations in myeloid malignancies, including FLT3-ITDs and CEBPA variants. AMP is a target enrichment strategy for NGS that uses molecular-barcoded adapters and single gene-specific primers for amplification, permitting open-ended capture of DNA fragments from a single end. This approach enables flexible and strand-specific primer design to provide better coverage of ITD-containing regions of FLT3 and GC-rich regions of CEBPA.
Results: In silico FLT3-ITD datasets enabled optimization of the Archer Analysis ITD detection algorithm. This algorithm used in combination with the VariantPlex Core Myeloid assay enabled detection of FLT3-ITDs down to <0.1% AF. Furthermore, we show 100% concordance of a VariantPlex Core AML assay with other methods commonly used to detect FLT3-ITDs from 25 blood and bone marrow samples. We detected concomitant non-ITD variants in FLT3 and NPM1 in some of these samples. Finally, we show >1000x unique molecule coverage across the entire coding region of CEBPA with 2M reads and 50ng input.
Conclusion: AMP provides NGS-based detection of complex mutation types that are relevant in AML, including FLT3-ITDs and CEBPA variants.

E-PS-10-037
An unusual case of nodular lymphocyte predominant Hodgkin lymphoma involving mediastinum and bone marrow
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Background & Objective: To present an unusual case of a 30-year-old male with nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) involving the mediastinum and the bone marrow at initial diagnosis.
Method: The patient presented with mediastinal lymphadenopathy. He reported the surgical excision of a cervical mass before two years, which was diagnosed as reactive lymphadenopathy. Without the presence of peripheral lymphadenopathy, mediastinal biopsy was performed. For staging purposes bone marrow biopsy followed.
Results: Sections from the mediastinal biopsy showed dense nodular lymphocytic infiltrate intermixed with scattered intra- and extranodular

large cells with multilobed nuclei, referred to as lymphocyte predominant cells (LP cells). These cells revealed positivity for CD45, CD20, PAX5, OCT2, BCL6 and MUM1. CD79a, CD30 and EMA were weakly positive. LP cells were usually surrounded by CD57 positive cells. There was a mixed immunoarchitectural pattern. Diffuse bone marrow involvement with many scattered LP cells was detected, raising the suspicion of large B cell lymphoma (LBCL). The presence of few B-cells and CD57+ cells favored the diagnosis of NLPHL with diffuse pattern (pattern E), despite the increase in the number of CD8+ cells.
Conclusion: NLPHL rarely involves mediastinum and bone marrow, let alone at initial diagnosis. The presented case illustrates that NLPHL should be included in the differential diagnosis when mediastinal lymphadenopathy occurs as an exclusive finding and when scattered multilobed cells are observed in bone marrow. Based on the microenvironment, there isn't always a clear distinction between NLPHL pattern E and LBCL.

E-PS-10-038
A rare case of synchronous chronic lymphocytic leukemia/small cell lymphocytic lymphoma and metastatic clear cell variant of cutaneous squamos cell carcinoma in cervical lymph nodes
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Background & Objective: Clear cell cutaneous squamous cell carcinoma(cSCC) is a very rare and aggressive entity. Patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) have susceptibility to develop simultaneous malignancies in 25% of the cases. Here we report a rare case of concomitant CLL/SLL and metastatic clear cell cSCC in the same cervical lymph nodes.
Method: A 69-year-old male presented with an exophytic, ulcerated cutaneous tumour arising in the genian region and multiple cervical adenopathies. Histopathological and immunohistochemical examinations of resected specimens were performed.
Results: Microscopically, the cutaneous tumour was composed of polyhedral clear cells with marked atypia, and limited areas of fusiform cells and squamous differentiation. The tumour was positive for CK5 and p63 and negative for PAS/S100/MelanA/CK7/TTF1. In the cervical lymph nodes, it was observed a partial effacement of the normal architecture by small neoplastic lymphocytes that were positive for CD5/CD20/CD23 and negative for CyclinD1. Two lymph nodes have also presented foci of epithelial proliferation with the same morphology and immunohistochemical profile as the genian tumour.
Conclusion: Simultanous metastatic clear cell cSCC and LLC/SLL is a rare event with poor prognosis. Recent reports suggested that 18F-FDG PET/CT may be useful in differentiation of sub-centimeter nodal metastasis of cSCC from the leukemic infiltrates of lymph nodes.

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E-PS-10-039
Immunohistochemical subtyping of patients with de novo diffuse large B-cell lymphoma treated with immunochemotherapy
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Background & Objective: Microarray analysis has shown that diffuse large B-cell lymphoma (DLBCL) expressing a gene expression profile (GEP) of germinal center B cells (GCB) has a better prognosis than that with a GEP of activated B cells (ABC). Because molecular analyses are impractical for routine applications, several immunohistochemical (IHC) algorithms have been developed to predict the cell of origin and/or survival. The aim of this study was to evaluate the IHC classification and prognosis of DLBCLs treated with immunochemotherapy.
Method: A total of 58 cases of DLBCL [33 nodal, 25 extranodal] were classified into GCB and non-GCB subtypes by Hans and Visco-Young (three-marker) IHC algorithms [immunostains: CD10, BCL6, MUM1, FOXP1, LMO2, BCL2]. Clinical data were available for 38 patients.
Results: The concordance between the two IHC algorithms was high [Hans: 19/58(32.8%) GCB, 39/58(67.2%) non-GCB; Visco-Young: 17/58(29.3%) GCB, 41/58(70.7%) non-GCB]. None of the algorithms showed significant differences in overall survival (OS) and disease-free survival (DFS). However, OS and DFS were significantly improved in the non-GCB group treated with RCHOP, compared to non-GCB group treated with RCOP (p=0.000 and p=0.046, respectively]. BCL6 overexpression was significantly associated with DFS (p=0.023). Low levels of BCL2 and high levels of LMO2 were significantly associated with GCB group, compared to non-GCB (p=0.000).
Conclusion: Our results suggest that the stratification based on IHC algorithms should be used with caution, especially in guiding treatment. The correlation of BCL6 with DFS indicates a possible predictive role.

E-PS-10-040
Unusual presentation of non-leukemic myeloid sarcoma in the breast
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Background & Objective: Myloid sarcoma is an extramedullary tumour of immature granulocytic series cells. These neoplasms are also referred to in the literature as granulocytic sarcoma, monocytic sarcoma, extramedullary myeloid cell, myeloblastoma and chloroma. It can often affected an organ such as skin, bone, head and neck. In the literature, infiltration of myeloid sarcoma of the breast has been observed in 67 cases. Eight of these cases are non-leukemic myeloid sarcoma.
Method: Case Report
Results: Our case is a 28-year-old female patient who applied to polyclinic because of the painless mass that is present in the outer breast of the left breast for 8 months. Ultrasonic evaluation revealed a hypoechoic solid lesion with a size of 5cm. Microscopic examination of the tru-cut biopsy revealed small round-cell malignant tumour infiltration with extensive necrosis. Immunohistochemical studies showed positive immunoreactivity with CD117, lysozyme, CD99, MPO, CD33 in tumour cells. No staining with LCA, vimentin, Pancytokeratin, CD3, CD20, desmin, CD34, synaptophysin, chromogranin A, Myo-D1, EMA was observed. A clinical investigation of myeloproliferative diseases has been proposed. Tumour infiltration was not seen in bone marrow biopsy. 5 months of chemotherapy and radiotherapy treatment were interrupted on the deterioration of the patient's condition.
Conclusion: Most myeloid sarcoma cases are associated with AML. It is rarely the first application reason for a patient who doesn't have any haematologic disease. Because of the width of the differential diagnosis spectrum of non-leukemic myeloid sarcoma of breast, this case is presented with its differential diagnosis.

E-PS-10-041
Gastrointestinal large B-cell lymphoma with IRF4 rearrangement - a case report
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Background & Objective: Large B-cell lymphoma with IRF4 rearrangement is a new entity in the WHO 2017 classification. This indolent entity

arises from germinal center B cells, in the cervical lymph nodes of children/young adults.
Method: Herein, we report a case of ileoceacal large B-cell lymphoma with IRF4 rearrangement.
Results: A 14-year-old female, with abdominal pain, underwent ileocaecal resection for invagination. Macroscopic examination revealed two ileal mass lesions, measuring 5 cm and 4 cm. Haematoxylin&Eosin stained sections revelaed nodular/follicular patterned lymphoid infiltration, composed of immunoblastic/centroblastic cells. Neoplastic cells were positive with CD20, and negative with CD3. MUM1, bcl-2 and bcl-6 were diffusely expressed. There were no reactivity for CD10, CD5, bcl-1, CD23. C-myc was positive in 50% of tumour cells. Ki-67 index was 70-80%. Neoplastic cells were also positive for CD38 and Kappa, and negative for Lambda, IgA, IgD, IgM, IgG, EBV-LMP, CD30, and PD-1. CD21 revealed an enlarged follicular dendritic cell network. The patient's age, clinical features, morphological findings, diffuse strong staining with MUM-1 and enlarged follicular dendritic architecture favored a diagnosis of large B-cell lymphoma with IRF4 rearrangement.
Conclusion: Albeit occasional immunoreactivity for bcl-2, "large B-cell lymphoma with IRF4 rearrangement" is a distinct entity, lacking t(14;18) chromosomal translocation and showing IG/IRF4 fusion and bcl-6 aberrations in some cases. This entity should be considered in the differential diagnosis of a lymphoid lesion with follicular/diffuse pattern and high-grade morphology in children and young adults. The diagnosis should be confirmed with immunohistochemical/cytogenetic analyses.

E-PS-10-042
Epstein-Barr-Virus positive mucocutaneous ulcer in a patient with Crohn's disease
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Background & Objective: Ebstein-Barr virus-positive mucocutaneous ulcer (EBVMCU) is a rarely diagnosed, Ebstein-Barr virus (EBV) and immunosuppression associated lymphoproliferative disorder, involving the oropharyngeal mucosa, the gastrointestinal tract, and the skin. Gastrointestinal EBVMCU in the background of inflammatory bowel disease is seldom reported.
Method: Here, we present a case of gastrointestinal EBVMCU in a patient with Chron's disease.
Results: A-57-year old male patient, under azathioprine treatment for Chron's disease, underwent ileal resection for intestinal perforation. On macroscopic examination, a mucosal ulceration of 2 cm, was observed, narrowing the ileal lumen. Histological sections revealed a superficial, expansile lesion, composed of scant, multinucleated, and multilobulated, Reed-Sternberg (RS)-like large cells, interspersed among fibrocytes and lymphohistiocytic infiltrate. The RS-like cells showed diffuse immunoreactivity with CD30, and fascin, focal immunoreactivity with CD15, and weak patchy staining with pax-5. Immunostains for CD3, CD20, CD4, CD5, CD7, CD8, ALK-1, perforin, granzym, CMV, and pancytokeratin were negative. EBV-LMP immunohistochemistry showed diffuse reactivity, which was confirmed by Ebstein-Barr encoding region (EBER) in situ hybridization. Considering the localization and the confined nature of the lesion, immunosuppression due to azathioprin treatment, and absence of history of haematolymphoid malignancy and lymphadenopathy, a diagnosis of EBVMCU was rendered.
Conclusion: EBVMCU is possibly an underdiagnosed entity, possessing similar histomorphological and immunohistochemical characteristics with Hodgkin Lymphoma. However, the localization of the lesion, history of immunosuppression and, the lack of clinical deterioration should alert the pathologist for the possibility of EBVMCU.

E-PS-10-043
Primary Burkitt-lymphoma of cerebellum with an unusual molecular pattern
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Background & Objective: Primary Lymphomas of Central Nervous System (CNS) represent less than 2 percent of primary CNS tumours. Primary Burkitt-Lymphoma (PBL) of CNS is extremely rare. We found only 21 cases since 1976 in literature. Only 2 of them were located in cerebellum.
Method: We demonstrate a case of a 29-year-old male patient, who suffered from dizziness, double vision, headache and nausea since one and a half week. A complete removal of a lesion 15 mm in maximum diameter at the left cerebellar peduncle was performed. The tumour was examined thoroughly with light microscopy, immunohistochemistry and molecular pathology. Literature was reviewed.
Results: We diagnosed a primary Burkitt-Lymphoma of cerebellum which showed not the typical MYC/IGH-translocation in FISH, but the typical MYC-break in break-apart-assay. This seems to be extremely uncommon. We found only one other case of PBL in CNS missing the typical MYC/IGH-translocation in literature.
Conclusion: PBL of CNS especially of cerebellum is extremely seldom. Most of them showed the typical MYC/IGH-translocation. But sometimes the MYC-gene found another partner for translocation. It is not clear if there is any prognostic or therapeutic relevance, but it should be further investigated.

E-PS-10-044
Case report of IgM multiple myeloma: diagnosing a rare haematologic entity
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Background & Objective: IgM multiple myeloma (IgM MM) is an exceedingly rare haematologic entity comprising only less than 0.5% of multiple myeloma cases. Given the rarity of this disorder, it makes it a challenge to differentiate from other more prevalent haematologic disorders. We report a new case of IgM MM with a brief review of literature.
Method: A 50-year old women presented with a low-back pain of approximately 2-months duration. Protein electrophoresis revealed an elevated b-globulin. Immunotyping results showed monoclonal gammopathy with IgM Kappa. Lumbo-sacral X-rays and magnetic resonance imaging (MRI) showed evidence of more sites of osteolytic bone destruction and D10 compression. The patient underwent a laminectomy and bone marrow biopsy.
Results: On gross examination, bone defects are filled with a soft, gelatinous and hemorrhagic tissue. Microscopic examination revealed a malignant cell proliferation characterized by round plasma cells with an eccentric nucleus, prominent nucleolus and clock face organization of chromatin. Immunohistochemistry stain showed that the tumour cells were positive for CD138 and negative for CD20 and CD 3. Based on these histologic and IHC findings, the final diagnosis of IgM MM was established.
Conclusion: Establishing a diagnosis of IgM MM is a challenging task, given rarity of the disease and the small number of reported cases in the literature.

E-PS-10-045
Littoral cell angioma of the spleen: a case report
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Background & Objective: Littoral cell angioma (LCA) is a relatively rececently described, rare splenic vascular tumour with no counterpart in soft tissues. It is considered as a benign neoplasm arising from the littoral cells lining the sinuses of the red pulp in normal splenic tissue.
Method: A 48-year-old asymptomatic man presented to our Hospital with multiple nodules at the inferior pole of the spleen apparent incidentally by radiological evaluation. A splenectomy was performed.
Results: Grossly, the spleen, measuring 13X7X4 cm, appeared multiple spongy, cystic, blood-filled nodules. Histological examination revealed anastomosing and congested vascular channels with focal projecting papillary fronds lined by cuboidal or plump endothelial cells. There were focal aggregates of intracytoplasmic eosinophilic globules. Occasionally, desquamated cells, macrophages and hemosiderin into vascular lumens were present. The lining cells were immunoreactive for endothelial and histiocytic markers, such as CD31 and CD68, rarely for the complement receptor CD21 and negative for CD34 and CD8 (markers that are typical of normal red pulp sinusoidal endothelium). The histological and immunohistochemical features were consistent with the diagnosis of LCA.
Conclusion: LCA is usually asymptomatic and incidentally discovered in the majority of cases. Although it is apparently benign itself and splenectomy is curative, a strong association has been shown between this neoplasm and other malignancies including lymphomas and carcinomas. LCA should be considered in the differential diagnosis of multiple or solitary splenic lesions, especially in asymptomatic patients.

E-PS-10-046
Morphological features as possible prognostic factor of early relapse Hodgkin lymphoma, nodular sclerosis
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Background & Objective: Hodgkin lymphoma (HL) is a potentially curable disease using modern therapeutic approach. According to the data of NRCH, Moscow, early relapses HL consists of 4% using risk-adapted therapy BEACOPP. Purpose of this study is morphological investigation lymph node biopsy material in debut and relapses HL and comparison with control group
Method: We assayed lymph node biopsy material in 14 pts(group 1) with early relapses HL for 2013-2017, median age 29 (19-48), f:m 6:1, all of them - IY clinical stage, B-symptoms – 78,6%, LDH above N -57%, "bulky"-28,6%. In 7/14 pts was achieved CR, and others – PR; time before relapses was 2-15 months (median 6). Control group (group 2, 11 pts) was formed with similar clinical and laboratory data (NS).
Results: 13/14(93%) pts had morphological variant NS. In 11/13 pts morphological substrate in debut and relapse of disease was similar and was characterized as NSII, 2/13- NSI; 7/13 -with marked eosinophilia. Detailed morphological analysis NSII among clasical tumour cells revealed significant population of small neoplastic cells (small Hodgkin-like) with undifferentiated morphology in the debut and the increase of this population in relapse in 9/11 (81,8%). Morphological data of group 2 with NS: NS II - 8/11, with lacunar variant in 50%, in 1/11 population of cells undifferentiated type was identified.
Conclusion: The presence of tumour population of undifferentiated type in debut of HL NSII may be additional prognostic factor of early relapse.

E-PS-10-047
Thrombophillia's impact on pregnancy
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Background & Objective: Thrombophilia is a prothrombotic state caused by the overactivity of coagulation factors, like factor V Leiden and prothrombin G20210A, or by the deficiency of natural anticoagulants, like antithrombin III deficiency, protein C deficiency and protein S deficiency. The aim of this study is to demonstrate that the encountered placental changes establish a causal link between thrombophilia and severe obstetrical complications.
Method: 24 patients with thrombophilia and pregnant in the third trimester were evaluated during the years 2016-2017.
Results: Paraclinical investigations -most of the patients presented with secondary anemia (median haematocrit level was 29%)due to significant hemorrhage (8 cases-33.3 %), chronic, consuming etiopathogenic mechanism, or due to the formation of significant retroplacental haematomas. Also, a large percentage presented the diagnostics of "nuchal cord" and "inflammatory syndrome" (7 patients in each case-29.7%), the latter being supported by complementary microbiological examinations (Klebsiella-2 cases, HPV-1 case and Escherichia coli-4 cases). Also serum leukocyte level was above the upper limit (median level = 12770/mm3). Fetal weight was not significantly affected, ranging between 2500-3000 grams. The fetal impact was investigated especially by fetal heart rate. Due to the proximity gestational age, cardiac frequency was maintained around 150 bpm, with a greater variation in 36-38 weeks.
Conclusion: Although thrombophilia has the potential to endanger the life of the fetus and the mother, under careful supervision, none of the patients from this study were severely affected.

E-PS-11 | Head and Neck Pathology

E-PS-11-001
Salivary gland clear cell carcinoma with delayed lung metastases after 13 years: a case report
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Background & Objective: Clear cell carcinoma (CCC) is a rare low-grade salivary gland malignancy. Over the years, issues with its classification were raised, as demonstrated by the existence of different nomenclatures. The consistent finding of a EWSR1-ATF1 fusion in most CCC supported its recognition as a distinct entity rather than a diagnosis of exclusion. However, similar rearrangements were recently reported in other head and neck clear cell mimics, highlighting the need to combine radiological, morphological and immunohistochemical features in differential diagnosis.
Method: We present a case of CCC with delayed bilateral lung metastases.
Results: A 51-year old female presented a slow growing 1,8cm palatal mass in 2004. The patient underwent wide resection with positive margins. Due to postsurgical complications, she didn't undergo further treatments. Between 2014 and 2016, she had multiple local recurrences treated with surgery and radiotherapy. In 2017, bilateral lung metastases were found. The patient is currently undertaking chemotherapy. Microscopical examination revealed a tumour composed of an admixture of clear and eosinophilic cells within a hyalinized fibrocellular stroma, with minimal atypia and rare mitotic figures. Immunoprofile: Cytokeratin+, p63+, myoepithelial markers-. FISH examination for the EWSR1 rearrangement was positive.
Conclusion: CCC has an overall good prognosis, with occasional recurrences and/or metastases to lymph nodes and there are very rare examples of distant metastasis described. No specific grading system is found, but some authors suggest that necrosis, high mitotic index and severe pleomorphism should be considered high grade for the purposes of a diagnostic report. The risk for metastases with delayed presentation may require long-term surveillance.

E-PS-11-003

An unusual case of epistaxis due to angiofibroma of the nasal cavity

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Background & Objective: Angiofibromas in the head/neck region are uncommon and usually occur in the nasopharynx, being reported almost exclusively in adolescent men. Extranasopharyngeal angiofibromas (ENA) are rare tumours that may occur in the mucosa of the upper respiratory tract. Aim: to describe a case of nasal ENA in a young woman.
Method: A 28-year-old woman was referred to our hospital due to a two-week history of progressive right-sided nasal obstruction and epistaxis, without previous known bleeding disorders. Routine clinical and laboratory work-up did not disclose relevant alterations. CT-scan and rhinoscopy disclosed a large polypoid lesion attached to the anterior nasal septum, obstructing the right nasal cavity, submitted to trans-nasal resection.
Results: The histological evaluation revealed a proliferation of bland spindle-shaped and stellate cells with plump nuclei and low mitotic index, admixed with vascular spaces of variable size. The squamous/respiratory-type superficial epithelium showed extensive erosion/ ulceration. The immunohistochemical study disclosed expression of androgen receptor in the spindle/stellate cells and of CD31, CD34 and WT1 in the endothelial cells. Diagnosis: nasal angiofibroma. The patient is well and without evidence of recurrence four months after surgery.
Conclusion: Despite rare, clinicians should consider ENA in the differential diagnosis of a nasal cavity tumour. Pathologists should be aware that ENA shares pathological features with juvenile nasopharyngeal angiofibroma, but may occur, as in the present case, in women and usually with shorter symptomatic time course. Adequate trans-nasal resection is considered a safe treatment option for nasal angiofibroma.

E-PS-11-004

Necrotising external otitis in an immunocompetent patient

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Background & Objective: Necrotizing ("malignant") external otitis is a severe infection affecting elderly, diabetics and patients with immunosuppression. It usually begins with interruption of the integrity of the skin lining of the external auditory canal. The causative agent is most frequently Pseudomonas aeruginosa that, in the context of immune impairment of the host produces extensive necrosis with tissue destruction. If it's not properly treated, it can progress to osteomyelitis of the skull base, a life-threatening condition.
Method: We report the case of a 45 years old female, with no relevant clinical history, presenting to the otorhinolaryngologist's office with a tumour occupying the left external auditory canal, accompanied by pain, otorrhea and hypoacusia, that had developed in the last three weeks after a minor trauma of the region.
Results: Otoscopic examination revealed an ulcerated, painful, haemorrhagic proliferative lesion with a soft consistency, and with a gray-greenish colour. The CT scan showed a soft tissue shadow obliterating the external auditory canal without bone involvement. Biological tests showed only moderate increasing of inflammatory markers. The tumour mass was surgically excised in multiple pieces, being highly friable and adherent on the auditory canal structures. The excised tissue fragments were sent to the pathology department to be analized. Histopathological exam revealed ulcerated auricular mucosa with abundant granulation tissue, necrosis and reactive hyperplasia and hyperkeratosis of the surrounding mucosa.
Conclusion: The final diagnosis was necrotizing external otitis, a neoplastic process being excluded. The pacient almost fully recovered under antibiotic and anti-inflammatory treatment, with only a minor tympanic membrane defect.

E-PS-11-005

Respiratory epithelial adenomatoid hamartoma – report of six cases with focus on mast cell recruitment

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Background & Objective: Respiratory epithelial adenomatoid hamartoma (REAH) is an uncommon lesion with a physiological mechanism not clearly established and its nature as a benign tumour, hamartoma or reactive inflammatory process still under debate.
Method: We retrieved six cases of diagnosed REAHs over a period of 10 years from our institution. Our purpose was to evaluate clinical, endoscopic and pathological aspects of REAHs and study differences in mast cell recruitment using Giemsa staining.
Results: Our findings revealed that, clinically, REAHs develop more frequently in men than women (2:1), with a majority of the patients being between 26 to 50 years old (66,66%), followed by the 51-80 years group. One third of the patients were smokers and another third associated nasal polyposis. The rate of mast cells was evaluated by counting in 10 high-power fields in the most inflammatory area, using Giemsa staining and focusing on their number in adjacent mucosa, glandular component and stroma. Mast cell density was found highest in stroma, followed by the glandular component. In addition, we observed a low mast cell density in the smoker patients compared to the non-smoker ones. A similar finding was noticed in patients who associated nasal polyposis in comparison with those who had no relevant clinical history.
Conclusion: REAHs are an unique entity with distinctive morphologic features. Mast cells have been extensively studied for their involvement in allergic reactions, autoimmunity and tumour genesis. A high density present in this lesion could point to an inflammatory cause, but a proper definition remains open for discussion.

E-PS-11-006

Connexin 32 expression in adenocarcinoma of nasal cavity and paranasal sinuses

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Background & Objective: Connexins are family of transmembrane proteins that build cell-to-cell channels in gap junctions. This study investigates the immunohistochemical expression of connexin (Cxn)32 in patients with adenocarcinoma of nasal cavity and paranasal sinuses. Adenocarcinoma of nasal cavity and paranasal sinuses is relatively rare subtype of the head and neck malignancy, that has variable biologic behavior, often with poor prognosis.
Method: This was a retrospecitve study which included patients with adenocarcinoma of nose and paranasal sinuses operated at Department of Otorhinolaryngology Sestre milosrdnice University Hospital in 5 years period (from 2012-2017). Immunohistochemical analysis was performed on a single representative block from 16 cases. We used primary antibody for connexin 32 (Abcam). Material was routinely processed and analyzed under the light microscope. The reaction was assessed semiquantitatively.
Results: All cases showed positive reaction for Cxn32. Precentage of positive tumour cells ranged from 10% to 100%. A total of 4 tumours (25%) showed 90% Cxn32 expression, 2 tumours (12.5%) showed 80%, 3 tumours (18.75%) showed 40%. The expression of the remainig seven cases was 10%, 20%, 30%, 50%, 60%, 70% and 100% in each case.
Conclusion: The preliminary data of our study showed positive reaction for Cxn32 in all cases of adenocarcinoma of nasal cavity and paranasal sinuses. Further studies are needed to explore immunochistochemical expression of Cxn32 in larger series of patients and its possible connection with other prognostic parameters.

E-PS-11-007

Tumefactive fibroinflammatory lesion: report of two cases

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Background & Objective: Tumefactive fibroinflammatory lesion (TFL) is an idiopathic, fibrosclerosing lesion with benign histological features, which clinically simulates a malignant neoplasm. To our best knowledge, less than 50 cases are reported in the literature, in various head and neck locations. TFL is composed of mature fibrous tissue with prominent collagenization intermixed with lymphocytes, neutrophils, and rarely plasma cells. Despite being infiltrative in nature, lack of atypia, increased cellularity, interlacing bundles or mitotic activity excludes a diagnosis of sarcoma. Treatment is still controversial and long follow-up is required since recurrence is common. We aim to analyze the clinicopathologic characteristics of TFL cases diagnosed in our institution.
Method: Two cases diagnosed in our institution between January 2016 and March 2018 were identified. Clinical features were retrieved from the archives and histological characteristics were reviewed.
Results: Case 1: Male, 41 years, presenting with a large expansive mass centered in the right jugular foramen, and VIII, IX, X, XI, XII cranial nerve compression symptoms. Case 2: Male, 68 years, presenting with a right frontal/orbital lesion, inducing maxilla erosion, palpebral edema, exophthalmia and right visual deficit. In both cases, biopsy was performed. Morphologically typical fibrosclerosing lesions were observed, with invasion of nearby anatomic structures and prominent inflammatory infiltrate, rich in lymphocytes, neutrophils and plasma cells. Atypia, increased cellularity or mitosis were not found.
Conclusion: TFL is a rare, idiopathic, benign lesion, for which an association with IgG4 has been suggested. As an aggressive malignant tumour mimicker, full knowledge and understanding of TLF is fundamental for a correct diagnosis and treatment.

E-PS-11-008

Pallatine tonsil metastasis of caecal mixed neuroendocrine-non-neuroendocrine neoplasm: a unique case in literature

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Background & Objective: Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) is a rare mixed tumour, each component constituting at least 30% of the tumour. We herewith report a case of a tonsillar metastasis of a right colonic MiNEN, the first ever reported to our best knowledge.
Method: A 68-year-old male patient presented with odynophagia and left tonsillar swelling. Medical history was significant for a right hemicolectomy 6 months earlier, due to a caecal MiNEN. During physical examination an ulcerated area on the upper pole of the enlarged left palatine tonsil was observed, highly indicative of malignancy and a radical left tonsillectomy was performed.
Results: Histological and immunohistochemical examination demonstrated many tumour cells positive for CKAE1/AE3 (some in a "dot-like" pattern, suggestive of neuroendocrine differentiation) and synaptophysin, with a few being immunostained for CK20 as well. The final diagnosis was a metastasis from the previously diagnosed caecal MINEN, amphicrine type.
Conclusion: This is the first ever-reported palatine tonsillar metastasis of a colonic MiNEN. Only thirteen cases of tonsillar metastases from colorectal primaries have so far been reported, among which five concerned poorly differentiated (signet-ring cell) and the rest of them well and moderately differentiated adenocarcinoma. Although rare, the eventuality of tonsillar metastases should always be included in the differential diagnosis panel.

E-PS-11-009

Plunging ranula presenting as a subcutaneous neck mass: a diagnostic dilemma

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Background & Objective: Ranulas are rare mucoceles associated with sublingual gland. They develop slowly and present as a translucent swelling in the floor of mouth, resembling "belly of a frog". A plunging ranula arises when a simple ranula extends into neck. It may present as a mass without visible intraoral involvement. Such cases can cause diagnostic dilemma with other mass lesions of neck and diagnosis mostly relies on histopathological examination.
Method: Twenty-year-old male patient referred to our hospital with a neck mass, which was present since birth. Physical examination revealed a suprasternal, subcutaneous, 3 cm, mobile, soft mass. Patient was referred to ultrasonography with preliminary diagnosis of lipoma. Ultrasonographically, mass was described as 33x15 mm cyst with dense content. The lesion was excised and submitted to pathology with clinical diagnosis of sebaceous cyst.
Results: Macroscopically, sample consisted of 20 cc pale yellow-white gelatinous material. Abundant mucus, muciphages and rare inflammatory cells were seen microscopically. No epithelial lining was detected. The case was interpreted as ranula.
Conclusion: Ranulas are retention cysts developing from mucous extravasation. Aetiology is unknown, but association with congenital anomalies, trauma, and sublingual gland diseases were described. Almost all ranulas are pseudocysts, epithelial lining is uncommon. A plunging ranula without intraoral component is very rare. When ranula presents only as a neck mass, like this case, clinical differential diagnosis is difficult, including thyroglossal duct cyst, branchial cyst, epidermoid cyst, lipoma, vascular malformations. Plunging ranulas can clinically and radiologically mimic other lesions and histopathological evaluation may be the only method for correct diagnosis.

E-PS-11-011

Primary or metastatic neuroendocrine carcinoma of the pyriform sinus?

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Background & Objective: Metastasis to the pyriform sinus are excessively rare. They are hardly considered when evaluating a pyriform sinus mass.
Method: We hereby present the case of a 78-year-old man who presented to the ENT clinic with a one-month history of intermittent odyno-dysphagia. Physical exam revealed a left palpable 1.5cm level IIA lymphadenopathy, and a 6cm dome-shaped right posterior thigh mass. A flexible laryngoscopy showed a polypoid mass of the left pyriform sinus, measuring 1.5 x 0.8 cm on the CT scan. Both pyriform sinus and thigh lesions were surgically removed.
Results: On one hand, microscopic examination of the pyriform sinus mass showed round small ghost cells, embedded in a largely necrotic tissue. Those cells only maintained immunohistochemical expression of cytokeratin AE1/AE3. CD45, CK20, Synaptophysin, ChromograninA and Cytokeratin 5/6 staining weren't significant. A small cell neuroendocrine carcinoma was suspected. On the other hand, the thigh mass consisted of sheets of round blue cells, exhibiting a finely granular and dusty chromatin. Frequent mitoses, karyorrhexis and areas of necrosis were also found. The cells were positive for ChromograninA, Synaptophysin, Cytokeratin AE1/AE3 and CK20, the last two being further characterized by a dot-like pattern. The diagnosis of a Merkel cell carcinoma (MCC) was made. Assessing both lesions simultaneously, we concluded that the pyriform mass was a metastatsis of the MCC.

Conclusion: Metastases in the pyriform sinus are scarce in the literarture. Our case is the first of MCC. If not for the full clinical examination and the thigh mass resection, the diagnosis would have been missed.

E-PS-11-012

Chondroblastic osteosarcoma in the jaw of a young adult

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Background & Objective: A 25-year-old male with a history of chemotherapy-treated acute lymphoblastic leukemia at the age of 13, presented with a left mandibular mass. Segmental mandibulectomy was performed following diagnosis by incisional biopsy and neoadjuvant chemotherapy.
Method: Histopathologic diagnosis was reached by means of light microscopy and immunohistochemistry.
Results: The incisional biopsy revealed an atypical spindle cell proliferation with osteoid production and large areas of atypical cartilage. Mitotic count was >10/10 HPF. Spindle cells' immunophenotype was SATB2 (+), CD99 (+), S100 focally (+), MDM2 (-), fVIII (-). In the surgical resection specimen, tumour's maximum diameter was 4,5 cm. The tumour showed extensive intramedullary growth and transcortical infiltration of the bone with extension into the lamina propria of the oral mucosa. No significant necrosis was noted.
Conclusion: The diagnosis of chondroblastic osteosarcoma was established. Chondroblastic variant of osteosarcoma poses a diagnostic challenge in needle biopsy specimens, where sites of osteoid formation - if sparse - may be inconspicuous or even not sampled at all. Since chondrosarcoma in the jaw is far more uncommon than chondroblastic osteosarcoma, osteoid production must be sought exhaustively. The percentage of tumour necrosis after neoadjuvant therapy should be reported, as it holds prognostic value.

E-PS-11-013

Secretory carcinoma of salivary gland in a 4 years old girl with 25 years follow up

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Background & Objective: Secretory carcinoma of salivary glands (synonym: mammary analogue secretory carcinoma) is a recently recognized tumour and shares similarities with secretory carcinoma of breast. Most cases are reported in adults and diagnosis is confirmed by characteristic morphology, immunohistochemistry and is associated with ETV6-NTRK3 gen fusion.
Method: We present a case of 29 years woman with metastasis to cervical lymph node whose material was send to our hospital for histopatological consultation in 2017. Medical history analysis revealed that in 1992 at age 4 the patient had surgically removed salivary gland tumour and the diagnosis of pleomorphic adenoma was established. In 1993 second operation was performed due to the tumour recurrence and mucoepidermoid carcinoma (MEC) was diagnosed. In 2002 lymph node metastasis occurred and was resected with diagnosis of metastatic MEC. In 2017 after 25 years from the malignancy onset the patient had the second cervical lymph node metastasis.
Results: We collected paraffin blocks from 1992, 2002 and 2017, compared morphological features of tumours from three operations together with immunohistochemistry assessment (S100 and GATA3 positive, DOG1 negative). The diagnosis of secretory carcinoma was established and ETV6-NTRK3 gen fusion was confirmed in next generation sequencing.
Conclusion: Probably this is a case of the youngest patient with parotid secretory carcinoma in Poland which is a low-grade carcinoma mimicking both benign and malignant salivary gland tumours. Long term follow-up is recommended due to late onset possibility of cervical lymph node metastasis.

E-PS-11-014

Malignant tumours of the nasal cavity and paranasal sinuses: a case series of 28 patients

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Background & Objective: Malignant tumours of the nasal cavity and paranasal sinuses are rare. They represent less than 1% of all cancers and 3 to 5% of all head and neck malignancies. Their overall prognosis is poor due to the complex anatomy of the sinonasal region, the insidious clinical progression and the multitude of histological subtypes of tumours in this area. The aim of this study is to report a case series of malignant tumours of the nasal cavity and paranasal sinuses and to discuss their epidemiological, clinical and pathological features.
Method: We retrospectively collected the data of 28 cases of malignant tumours of the nasal cavity and paranasal sinuses, diagnosed at the Department of Pathology of Habib Thameur Hospital in Tunis over a period of 18 years.
Results: The mean age of patients at the time of diagnosis was 57.3 years, with a sex ratio of 2.1. The nasal cavity represents the site of predilection for these tumours (60% of cases). The different histological subtypes encountered were: squamous cell carcinoma (keratinizing type in 4 cases and non-keratinizing type in 3 cases), melanoma (6 cases); nonintestinal-type adenocarcinoma (3 cases), adenoid cystic carcinoma (2 cases), nasal NK/ T lymphoma (4 cases), large B-cell lymphoma (2 cases), olfactory neuroblastoma (2 cases), embryonal rhabdomyosarcoma (one case), sinonasal undifferentiated carcinoma (one case). The diagnosis was aided by immunohistochemistry in all cases.
Conclusion: The prognosis of these cancers depends on several parameters such as age, sex, anatomic location, histological type, grade and stage. Unlike the literature, we found a high prevalence of melanoma in this region with a poor prognosis.

E-PS-11-015

Clinic pathological evaluation of laryngeal lesions and the survival rate of patients with laryngeal cancer from 2007-2012 in a hospital and radiotherapy center

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Background & Objective: Larynx function is so compound. Respiratory function and sound effects are the laryngeal duty. The sound difference is the most symptom in laryngeal lesions. Squamous cell carcinoma is the main type of laryngeal cancer. Patient`s prognosis is dependent on location and tumour staging.
Method: This descriptive, cross-sectional study was undertaken among patients with larynx lesions who came to Shahid Sadouqi hospital and Shahid Ramazan Zade radiotherapy center during the period of 2007-2012 was evaluated, finally, the histopathological results and their survival were analyzed. Their smoking state and their treatment from patient`s hospital folders have been reviewed.
Results: Histopathological reports showed 37.8% of them were malignant masses, 62.2% of them were benign masses. Most of malignant masses were in more than 60 years old patients. 75% of patients were women and 25% were men. Total laryngectomy was done in 48.6%, partial laryngectomy was done in 12.9% and 38.5% laryngectomy was not done. 87.2% of patients were smoker and 12.8% of patients did not

smoke. Patient`s survival whom total laryngectomy was done is 61.756 months, patient`s survival whom partial laryngectomy was done is 76.714 month and whom laryngectomy was not done is 40.558 month. Patient`s survival who are men is 56.747 month and patient`s survival who are female is 44.7 month.
Conclusion: Our study indicated that the risk of laryngeal cancer in patients varies markedly according to the sex, age, and smoking. Survival in patients who were treated with both laryngectomy and radiotherapy was better than other treatments.

E-PS-11-016
NUT carcinoma: a case report of two head and neck cases in adults
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Background & Objective: NUT carcinoma (or NUT midline carcinoma) is an aggressive tumour with a poor prognosis, defined by the presence of NUclear protein of the Testis (NUT) gene (NUTM1) rearrangement and t(15;19) translation. It's a rare entity arising primarily in the midline of teenagers and young adults. The objective of this study was to describe the clinical, radiologic and biological features of NUT carcinoma in adults.
Method: We present two adults Head and Neck NUT carcinoma (48 and 32 years-old) with histology, immunohistochemistry and molecular confirmation. The first case was located in the maxillary sinus and the second in the larynx. This case presented with regional lymph node involvement.
Results: In both cases, it presents as a poorly differentiated carcinoma composed small blues cells with, in the maxillary case, some abrupt keratin pearls. Mitoses were numerous. Necrosis and apoptosis were observed. In both cases, NUT antibody was positive by immunohistochemistry and the translocation was found by Fluorescent In Situ Hybridisation (FISH). The patients were first treated by conventional chemotherapy, but a rapid progression leads to surgery after one cure. The clinical evolution was aggressive with rapid fatal clinical outcome in both cases.
Conclusion: NUT carcinoma is an aggressive disease, refractory to conventional therapy. It's an underdiagnosed entity, which should be taken into consideration when poorly differentiated carcinoma is diagnosed, even in adults. Early identification of the specific rearrangement of NUT gene is useful to propose the optimal therapeutic strategy, including anti-NUT target therapy.

E-PS-11-017
Low-grade papillary Schneiderian carcinoma: report of a case of a newly described entity with molecular characterisation
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Background & Objective: Schneiderian epithelium is a peculiar transitional ciliated epithelium of ectodermal origin lining the sinonasal tract. Benign schneiderian inverted papilloma is the most common neoplasm in this area. Squamous cell carcinoma (SCC) arising from Schneiderian papilloma is the main, albeit uncommon, schneiderian malignancy reported, associated with mutually exclusive EGFR somatic mutation or HPV infection. Recently, a new entity, cytologically resembling inverted papilloma, but characterized by increased mitotic activity, stromal invasion, bone destruction, and malignant behaviour with locally recurrent/metastatic disease over 10 year follow-up has recently been reported in sinonasal tract. The entity has been defined low-grade papillary schneiderian carcinoma (LGPSC).
Method: We describe the histlogical, molecular and clinical characters of a tumour showing features consistent with LGPSC.
Results: The tumour presented as an obstructive nasal pseudopolypoid mass in a 68yo male, showing, on endoscopic biopsy, basaloid epithelial proliferation, mild citologic atypia, abundant eosinophilic citoplasm, mild or no keratinization, a complex architecture with papillary exophitic and pushing invasive growth pattern, granulocytic infiltrate, increased mitotic activity and variable Mib1/Ki-67 index (5-30%). Tumour cells were positive for p63 and p40 and showed increased p53 and p16 expression. EGFR and k-RAS activating mutations and HPV infection were excluded. The patient underwent endoscopic surgery with complete mass resection. The tumour did not recur over a 8 month follow-up.
Conclusion: The recognition of LGPSC and their distinction from inverted papillomas and conventional papillary carcinomas is important to correctly orient patient care, contribute to data collection on its natural history, and provide material for the investigation of involved oncogenic pathways.

E-PS-11-018
It is neither a mistake nor an accessory tragus; it is an oropharyngeal hairy polyp
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Background & Objective: The objective of this study is to be aware of the entity "hairy polyp" and to emphasize on its histologic and clinical presentation.
Method: A white polyp with a « cutaneous surface » and spiked vellus hairs was referred to our department with the mention « dermoid cyst ». Because of previous mistakes and confusion between patients' specimens, we were sure that there was an error. Thus, we were waiting for histology examination. This revealed a cartilaginous core with some striated muscle. The pedunculated polypoid mass was lined by keratinizing squamous epithelium. A rim of pilo-sebaceous adnexal structures was present in the periphery. This was consistent with an accessory tragus of the ear although it was huge with a 3.5cm in great dimension. Reviewing the chart of the patient was mandatory.
Results: The patient was a 7 month-year-old female. She had had many obstructive and respiratory distress episodes. The mass seemed to be attached to the palate-pharyngeal muscle and was actually in the oral cavity and not periauricular. The diagnosis of oropharyngeal hairy polyp was so made.
Conclusion: In the francophone literature we are used to, the adjective « hairy » is missing and the lesion is called « hamartomatous polyp » or choristoma. This explains the delay to do the right diagnosis. When we are general pathologists, we have to be aware of rare entities and we must discuss with physicians to disclose more easily some challenging diagnoses.

E-PS-11-019
Lymphadenoma with very focal sebaceous differentation: a diagnostic challenge
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Background & Objective: Lymphadenomas are benign tumours of the salivary glands that lack sebaceous differentiation and because of their low frequency and lack of knowledge among pathologists, it poses difficulties with lymph node metastasis of carcinoma. We present a case to consider its morphological features and facilitate its diagnosis.
Method: Clnical case of a 71-year-old male with a tumour of 36 mm diameter in the right submaxillary gland who only refer increase of the submaxillary gland size, without any other sign or symptom.
Results: Microscopic findings: Solid and small cystic epitelial islands composed of cells without atipia and duct like structures, all mixed with a dense lymphoid stroma that contains reactive lymphoid follicles. Many of the cyst lumen has secretions and it is also seen small amount o

sumbaxilary gland tissue at the peripherie. Isolated and sprinkled cells with sebaceous differentiation can be seen. Ki 67: 2%.
Conclusion: Lymphadenoma is an infrequent variant of sebaceous lymphadenoma that poses problems in terms of differential diagnosis with a lymph node metastized carcinoma. In this case, the presence of duct structures and lymphoid stroma that extends both in the tumour and submaxillary gland tissue, suggests a salivary gland tumour, specifically a lymphadenoma. The presence of sebaceous cells isolated, helps to conclude in the diagnosis of the variant: Lymphadenoma with very focal sebaceous differentation.

E-PS-11-020
Sebaceous adenocarcinoma; an approach to a diagnosis of exclusion
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Background & Objective: Sebaceous adenocarcinoma (SC) is a rare primary tumour of salivary glands. There are 33 cases reported in the literature of SC of the parotid gland and 6 cases of the minor salivary glands. The diagnosis of SC is one of exclusion but the identification of clear cells within a malignant epithelial tumour of the salivary glands should raise the possibility of SC. The differential diagnosis of tumours with clear cell morphology is wide and includes SC, clear cell carcinoma NOS, epithelial-myoepithelial carcinoma, myoepithelial carcinoma, mucoepidermoid carcinoma, acinic cell carcinoma, squamous cell carcinoma with clear cells and oncocytoma. In addition, the possibility of metastases with clear cell morphology were also considered.
Method: This report focuses on a case of a female patient who presented with a lump in the buccal mucosa. We describe the case and expand on our approach using morphological assessment, tinctorial stains and immunohistochemical profiling to narrow the wide differential diagnosis.
Results: The histology from the buccal mucosa revealed a malignant subepithelial tumour composed of polygonal cells with distinct cell membranes and pale eosinophilic to reticulated cytoplasm. Tinctorial stains were negative for glycogen and mucin in the tumour cells. Immunohistochemical staining supported the diagnosis of sebaceous adenocarcinoma including Androgen receptor in greater than 70% of tumour cells.
Conclusion: The clinicopathological and morphological characteristics of this very rare tumour are discussed and our approach to narrowing the broad differential diagnosis is detailed with use of tinctorial stains and immunohistochemical profiling.

E-PS-11-021
A case of rhinosporidiosis in a 53-year-old man clinically mistaken for nasal polyp
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Background & Objective: Rhinosporidiosis is a rare chronic granulomatous disease endemic in some areas of Asia, such as South India and Sri Lanka but cases have been reported in Europe, America and Africa, because of migration. Rhinosporidium seeberi is an aquatic protistan parasite, classified under Mesomycetozoea. It involves the mucus membranes through transepithelial infection due to contact with contaminated water, and the lesions present clinically as polypoid, soft masses (sometimes pedunculated) of the nose (more often), throat, ear, and even the genitalia in both sexes.
Method: A 53-year-old Pakistani man presented with aggravating epistaxis, rhinorrhea and unilateral nasal obstruction. Clinical assessment revealed a unilateral mass in the right nasal vestibule, arising from the lower lateral nasal septum. After excision, we received a tan polypoid lesion measuring 2,2X1,3X1 cm with a narrow excision base of 0,2X0,2 cm.
Results: Microscopically, there are numerous prominent globular cysts measuring 120-350 nm in diameter in the submucosa. The cysts represent thick walled sporangia including large numbers of endospores. The background is heavily inflamed comprising of lymphocytes, eosinophils and neutrophils.
Conclusion: Rhinosporidiosis, although rare in Europe, should be included in the differential diagnoses of polypoid nasal lesions, especially in people with Asian ancestry. It should be distinguished from Coccidioides immitis and other fungal infections and also from the oncocytic type of sinonasal papilloma.

E-PS-11-022
Extensive oncocytic metaplasia in a pleomorphic adenoma
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Background & Objective: Pleomorphic adenoma is the most common salivary gland tumour. It is characterised by plethora of morphological appearances including myxoid, hyalinized, chondroid, osseous, squamous etc. However, predominantly oncocytic cells in pleomorphic adenoma are extremely rare with only 19 cases reported.
Method: A 36-year-old female presented with a submandibular gland mass which had been present for 1 year. Fine needle aspiration had shown blood only. On excision, a partly cystic haemorrhagic lesion and partly homogenous mass was seen.
Results: Microscopic examination showed a monomorphic eosinophilic cellular mass composed of plasmacytoid myoepithelial cells with vesicular nuclei. These oncocytic cells were S100 and androgen receptor positive. Blending into the homogenous sheets of oncocytes were epithelial components composed of tubules, myxoid areas and foci of cystic changes. Pseudo-infiltration of capsule with satellites nodules were noted. These features were of a pleomorphic adenoma with extensive oncocytic metaplasia.
Conclusion: Oncocytic metaplasia of ductal and acinar cells is commonly encountered in normal salivary glands however primary oncocytic neoplasms and tumour-like lesions are comparatively rare. All the oncocytic salivary gland lesions are usually biologically indolent. Hence, oncocytic change in a pleomorphic adenoma is likely to have good prognosis and indeed no recurrent cases have been reported till date. However, the appearances can be a common cause of misdiagnosis of malignancy.

E-PS-11-023
Papillary neoplasms of the middle/inner ear: report of 2 sporadic cases and lights on the 4th edition of the W.H.O. classification of tumour of the ear
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Background & Objective: Papillary malignant tumours of the middle/inner ear are rare entities, grouped together by the 4th edition of the W.H.O. Classification of Tumours of the ear. We report an aggressive papillary tumour of middle ear and an endolymphatic sac tumour with similar features, purposing a further simplification by classifying these two neoplasms in a unique entity.
Method: We report two cases of papillary middle and inner ear neoplasms, with similar clinical presentation, histologic features and treatment.
Results: Clinically, both patients had symptoms ascribable to middle ear disfunction. Both audiograms revealed a transmission hearing

loss and tympanograms were flat on the side of the lesion. Both cases were treated with complete surgical excision, which was curative. On histologic examination, both neoplasms had a single or pseudostratified epithelium of columnar or cuboidal cells, arranged in papillary structures, with bland atypia and a low proliferation index. Moreover, the endolymphatic sac tumour had a very particular expression of both acid and neutral mucins, which made this case a unique one. The first case was localized in the tympanic cavity and was diagnosed as aggressive papillary tumour of middle ear and the second one was localized in the mastoid process, with a first localisation in the inner ear and was classified as an endolymphatic sac tumour. In none of the cases was found association with von Hippel-Lindau disease.
Conclusion: For the similar general features of these two neoplasms, treatment and outcome, we propose, in the near future, to consider the possibility to include them in a single pathological category

E-PS-11-025
Salivary gland anlage tumour of the nasopharynx: a case report and review of literature for spectrum of histopathological characteristics
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Background & Objective: Congenital salivary gland anlage tumour (congenital pleomorphic adenoma) of the nasopharynx is a neoplastic lesion which usually presents with nasal and upper respiratory tract obstruction in the neonatal period. The adenoid like nasopharyngeal mass may be life threatening with respiratory distress and feeding difficulties. Timely diagnosis is essential to prevent the occurence of respiratory complications in later childhood.
Method: We present a 8-year-old boy who had some difficulty in breathing and breastfeeding in the neonatal period due to an adenoid like nasopharyngeal mass.
Results: An excisional biopsy was performed with a clinical diagnosis of adenoid hypertrophy. At operation, a firm nasopharyngeal mass covered by intact mucosa was resected. The well circumscribed solid mass was 2.3 cm in its greatest diameter. Histological examination revealed solid and cystic squamous nests and numerous duct-like structures within collagenised stroma. Both epithelial and myoepithelial differentiation was noted in the tubular component.
Conclusion: A comparative review of the clinical and histopathologic features of the published cases was made. We would like to stress that the possibility of salivary gland anlage tumour should be considered in the differential diagnosis of neonatal respiratory distress cases.

E-PS-11-026
Hamartoma of hard palate: a case report
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Background & Objective: Hamartoma is a benign malformation made up of disorganized mixture of cells and tissues. Clinical and histopathological findings are sometimes confused with benign or malignant tumours. Hamartomas can ocur almost anywhere in the body but commonly observed in lung, pancreas, spleen, liver and kidney. They are rare in the head and neck region. We present a patient with hamartoma occured on the hard palate.
Method: Firstly, the surgical specimens were evaluated with frozen section. Then they were formalin-fixed and parafin embedded. The sections were stained with routinary H&E.
Results: A 15-year-old female presented with a oral cavity mass that had been growing for the last one year. Clinical examination revealed a slightly exophytic lesion approximately 2×2 cm in size with red surface on the hard palate. Surgeons requested intraoperative consultation because of the lesion mimicking malignant tumours. Histopathological results were benign. Routine microscopic examination demonstrated disorganized tissues under the stratified squamous epithelium, such as local salivary gland lobules, proliferative vascular structures, adipose tissue, peripheral nevre tissue and mixed inflammatory cells in the connective tissue. The findings were compatible with hamartoma.
Conclusion: Palatal hamartomas are extremely rare. Only 4 hamartomas of hard palate have been reported in the English literature. The treatment is surgical and the prognosis is good without recurrence. But it is important because it can confuse with malignant tumours. Therefore the case is worth to be represented.

E-PS-11-027
A rare case of curious a palatine tonsillar metastasis
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Background & Objective: Metastasis to palatine tonsils are rare, accounting from only 0.8% of all tonsillar tumours. Only 10 cases of tonsillar metastases from neuroendocrine lung carcinoma have been reported with only one case of large cells neuroendocrine lung carcinoma.
Method: We present a rare case of a man who showed apical alveolar condensation and mediastinal adenomegaly, diagnosed with large cells neuroendocrine carcinoma. Four months later he developped a left tonsillar metastasis.
Results: A 40-year-old man who presented a chest pain and a bronchial syndrome. Chest CT showed apical alveolar condensation and mediastinal adenomegaly. A lymph node biopsy concluded to a seminoma on the presence of proliferating tumour of large tumour cells with a clear cytoplasm, oval nuclei, heterogeneous chromatin, prominent nucleous and numerous mitoses. The patient received an appropriate chemotherapy but without any response. A review of this same biopsy concluded to a non-small cell lung carcinoma due to positivity to Cytokeratine and TTF1. Then a new chemotherapy is started. One month later, the patient showed difficulties in swolling. Medical imaging has shown an infiltrating process at the left tonsil for with the patient had a tonsillectomy. The histological examination concluded that the tumour was neuroendocrine on the presence of chromogranin and synaptophysin immunoreactivity. A rereading of the mediastinal lesion as well as the tonsillar lesion allowed considering the diagnosis of tonsillar metastasis of a lung neuroendocrine tumour thanks to the immunoreactivity to the neuroendocrine markers and to TTF1 in both tumours.
Conclusion: Pathways and prognostic implications of these metastasis still not fully understood because of their rarety.

E-PS-11-029
Co-occurence of calcifying odontogenic cyst and odontogenic fibroma: case report
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Background & Objective: The calcifying odontogenic cysts (COCs) are developmental odontogenic cysts and they are frequently associated with odontogenic tumours. The odontogenic fibroma (OF) is a rare, benign, expansively slowly growing, noninfiltrating odontogenic tumour. Co-occurence of COC and OF are not reported in English literature.
Method: The surgical spesimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E.

Results: 15 years old male patient had a mass on mandibula. Computed tomography (CT) showed that there was a mandibular radiolucent lesion. Microscopically; luminal epithelium of cystic lesion is non-keratinized stratified squamous type. Epithelium shows luminal proliferations which have well defined layer of palisading basal cells and loosely arranged suprabasal epithelial cells. The epithelium also shows numerous ghost cells and calcification. There is a broad fibrous connective tissue layer under the epithelium which shows myxoid changes. There are some collagen fibers and odontogenic epithelial islands in fibrous connective tissue. Immunohistochemical findings revealed that odontogenic epithelial islands were positive for pancytokeratin.
Conclusion: OF is classified as a neoplasm of odontogenic ectomesenchyme containing varying amounts of inactive odontogenic epithelium. COCs present as well-circumscribed cystic proliferations with a fibrous connective tissue wall lined by odontogenic epithelium. Also there are some ghost cell keratinization in odontogenic epithelium. This is the first case of COC with central odontogenic fibroma. The most important clinical effect of this case presentation is the awareness of such combined lesions. Thus, it is possible to be aware of appropriate surgical treatment to avoid recurrence or more destruction by residual lesions.

E-PS-11-031
Papillary carcinoma as an incidental finding in laryngeal squamous cell carcinoma resection specimen: a case report and review of the literature

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Background & Objective: The occurrence of two synchronous, primary cancers is a rare event. Thyroid carcinoma is incidentally found in the resection specimen after surgery for head and neck cancer in 0.3–1.9% of the patients. Synchronous appearance of the laryngeal squamous cell carcinoma (LSCC) and thyroidal papillary carcinoma (TPC) is an unusual histological finding.
Method: We present a case of a 55yrs old male with LSCC stage III, who underwent radical neck dissection, where incidentally, in the thyroid tissue of the lateral dissection, was found intra-cystic TPC. During a period of time from 2014- 2017 in our Pathology Institute, 155 patients were diagnosed with LSCC in laryngectomy specimens. In only one of them was simultaneously found TPC (0.64%).
Results: Histologically the LSCC was graded as moderately differentiated. In lateral dissection, in thyroidal tissue, was found intra-cystic TPC, which was formed from complex, branching papillae with fibrovascular core, lined with cuboidal cells with overlapping nuclei and optically clear chromatin.
Conclusion: The synchronous appearance of LSCC and TPC is a rare finding. We recommend that the preoperative ultrasonography investigation of thyroidal gland in patients with laryngeal carcinoma, should be included in the routine preoperative examination procedure, and that diagnosed patients must be evaluated individually with regard to tumour extension. Thyroid neoplasms are often less aggressive than other carcinomas of the head and neck, therefore, early diagnosis and radical surgery is the recommended treatment for these patients.

E-PS-11-032
An analysis of salivary gland tumours: 5-year, single-institution experience

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Background & Objective: Salivary gland tumours accounted for 5-10% of head and neck cancers. The resection of these tumours is one of the treatment methods. In this study we aimed to evaluate frequency and demographic features of salivary gland tumour types in our department.
Method: Retrospective analysis was performed for biopsies of salivary gland tumours at Marmara University Hospital between 2014-2018. There were revealed 124 cases of tumour resection.
Results: Median age of cases was 49 (48,5 for benign tumours, 52 for malignant tumours). In malignant tumours, 20 cases (53%) were male. The number of male patients who have benign tumour was 49 (57%). 86 cases were benign salivary gland tumours as follows: 61 pleomorphic adenoma, 17 Whartin tumour, 2 basal cell adenoma, 1 ductal adenoma, 1 canalicular adenoma, 1 cystadenoma, 1 myoepithelioma and 2 unclassifiable cases. 38 cases were malignant salivary gland tumours as follows: 13 adenoid cystic carcinoma, 8 mucoepidermoid carcinoma, 4 acinic cell carcinoma, 3 salivary duct carcinoma, 3 myoepithelial carcinoma, 3 adenocarcinoma, NOS, 2 squamous cell carcinoma, 1 secretory carcinoma, 1 large cell carcinoma.
Conclusion: In this study, the most common benign tumour of salivary gland is pleomorphic adenoma and the most common malignant tumour is adenoid cystic carcinoma.

E-PS-11-034
Tissue remodeling in experimental temporomandibular joint disorder

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Background & Objective: Clinical experience suggests that variety of exogenous and endogenous factors cause and perpetuates the symptoms of temporomandibular disorders (TMD). Chronic pain as one of the major symptom of TMD affects the quality of patient's life. To assess the significance of trauma-induced osteoarthritic and soft tissue changes in pathogenesis of the experimental TMD was the aim of present study.
Method: Ten mature 9-month male rats were material for present study. Experimental arthritis caused by occlusion disorders modeled in 5 cases of temporomandibular pathology (main group). Other five rats were on standard diet with normal parameters of temporomandibular joint (controls). After experiment, joints structures with surrounding soft tissues were studied morphologically and with morphometry evaluation.
Results: Experimental impaired occlusion in teeth of upper and lower jaws resulted in structural remodeling both in joints tissues and soft tissues next to them. Multiple injuries were found in articular disc of the main group animals. Trauma induced compensatory hypertrophy of the masseter muscle, stroma lesions with perifocal inflammation were detected in cases of experimental TMD. Morphometric evaluation revealed higher area, width, length and perimeter of the rat's muscles fibers on the side of TMD compared with control group.
Conclusion: Our data present the morphological evidence that chronic inflammatory response due to cartilage and articular surface injury as well as adaptive remodeling of soft tissues surrounding joint may cause the TMD symptoms, seen in patients with the similar pathology.

E-PS-11-035
Immunohistochemical expression of cancer stem cell markers in the salivary glands of Sjögren's Syndrome patients

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Background & Objective: Sjögren's syndrome (SS) is a complex autoimmune disease characterized by local exocrine glandular involvement. The regeneration of the salivary gland after inflammation has been attributed to putative stem cells. Cancer stem cells (CSCs) are a rare population of undifferentiated tumourigenic cells and exhibit biological properties similar to those of normal tissue stem cells.

Method: The salivary gland tissue of 10 SS and 4 normal patients were used for this study. Immunohistochemistry was performed for ALDH1, CD44, and CD133.
Results: ALDH1 expression was reveled at the acinar in the normal patients but not in the SS patients. The expression intensity of ALDH1 was markedly lower in the SS patients than the normal patients. The ductal cells of the normal salivary gland tissue showed moderate to weak cytoplasmic CD44 staining in the base of cells. In the SS patients, CD44 staining intensity and area of acinar cells was lower than in the normal patients. CD133 showed negative or focal weak expression in the acinar and duct cells of the normal salivary glands. However, nuclear CD133 staining was frequently observed in the acinar, ductal, and myoepithelial cells in the SS patients.
Conclusion: The expression features of ALDH1, CD44, and CD133 are different in the salivary glands of SS patients. All the acinar, ductal, and myoepithelial cells can presumably act as stem cells in the damaged salivary glands of SS patients. There is a need for more research to search for the meaning of these differences and to correlate the clinicopathologic factors.

E-PS-11-036
Salivary gland pleomorphic adenoma with extensive necrosis simulating a malignant neoplasia: report a case and literature review
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Background & Objective: Ischemic or haemorragic infarction has been described as an uncommon but possible complication of fine-needle cytology sampling in numerous tumours, more frequently the thyroid and salivary glands. We report a case of spontaneous infarction occurring in a submaxillary gland pleomorphic adenoma (PA) simulating malignancy. In our knowledge less than a dozen similar cases have been reported in the literature
Method: 19-year-old male with submaxillary gland mass suspicious Rx of solid cystic neoplasia. BAG was performed showing abundant necrosis and scarce epithelial cells with marked atypia, not diagnosed but suspicious of malignancy. The gland was removed for filiation
Results: In the histopathological study of the specimen, the salivary gland surrounding the lesion showed a PA with massive ischemic infarction, with squamous metaplasia and ghost cells. This features were similar to the findings of the previous BAG. The patient had not undergone any type of invasive study before.
Conclusion: Spontaneous infarction of PA appears to be rare but should be considered in the differential diagnosis of malignant neoplasms because necrosis may mimic carcinoma. It should be included in the differential diagnosis of squamous cell-containing lesions of salivary glands and must be considered in the list of possible pitfalls in salivary gland cytopathology or BAG.

E-PS-11-040
Ewing's sarcoma of maxilla. A rare case report
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Background & Objective: Ewing's sarcoma is a rare malignant tumour. Literature shows that less than 3% of the tumour originates in the maxillofacial region, with 1% occurring in jaws. Primary maxilla involvement is rare, and only 30 cases have been reported so far.
Method: Here, we are reporting a case of Ewing's sarcoma primarily affecting the maxilla in a 23-year-old man. The patient's complaints at time of presentation are due to the mass effect of the tumour (gr.dim: 3,5 cm), its rapid growth, the swelling of the affected area and the pain sensation. In the present case, a complete surgical excision of the lesion was done.
Results: The histological findings showed a small round blue cell proliferation. The cells were arranged in sheets and scant cytoplasm. Given the differential of a small round blue cell tumour including neuroendocrine carcinoma, rhabdomyosarcoma, lymphoma etc, a panel of immunohistochemical stains was performed. The neoplastic showed strong staining with CD99 and Vimentin, additional stains for epithelial differentiation (Cytokeratin), haematologic and lymphoblastic markers (CD45 and TdT), rhabdoid differentiation (Desmin) and neuroendocrine differentiation (NSE, chromogranin and Synaptophysin) were all negative. These findings are consistent with those of Ewing's sarcoma/PNET.
Conclusion: Ewing's sarcoma is an aggressive malignancy which rarely affects the maxilla. Initial treatment should be aggressive resection with wide margins. This gives good local control. It carries better prognosis than Ewing's sarcoma of the long bones. And, postoperative adjuvant treatment, regular follow-up and documentation is mandatory.

E-PS-11-041
Morphological changes of structure of the tympanic membrane during its transformation to retraction pocket in children - risk of cholesteatoma
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Background & Objective: The retraction pocket (RP) is an invagination of the tympanic membrane (TM) into the tympanic cavity and it is caused by recurrent or chronic negative pressure in the middle ear. An alternative hypothesis for the pathogenesis is related to the persistence of an inflammatory reaction. Retraction of the TM is one of the theories of genesis of the cholesteatoma.
Method: We examined TM taken during standard operations at Paediatric ENT Department with diagnosis of RP of pars tensa in stages II or III by Charachon classification. We prepared paraffin sections stained with haematoxylin and eosin (HE), Van Gieson , Verhoeff, Alcian and PAS. We conducted evaluations of the continuity of the basement membrane, cellular proliferation and collagen stroma of the middle layer of the tympanic membrane.
Results: We have described following findings as frequent in pars tensa RP: hyperkeratosis, parakeratosis, papillomatosis, spongiosis and intraepithelial infiltration. Regressive changes in collagen stroma, atypical hypervascularisation, presence of fragmentation of elastic fibers and presence of inflammatory infiltrate were found too. We demonstrated the dependence of the density of capillaries on hyperkeratosis (p=0,00837) and on the thickness (p=0,00802), than the interaction of hyperkeratosis and thickness (p=0,00726) and the dependence of the subepithelial inflammation on the thickness (p=0,0188) and papillomatosis (p=0,0463).
Conclusion: The morphological and functional changes of the RP show that there is an active process in the tympanic membrane, potentially leading to the development of cholesteatoma. A continuum of progressive histological features akin to cholesteatoma is noted with increasing grades of retraction by Charachon classification (II-III).

E-PS-11-042
Primary carcino sarcoma of the larynx
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Background & Objective: Carcinosarcoma (CS) is a malignant tumour with a dual sarcomatous and carcinomatous component. This tumour entity has been described in many epithelial organ, but it still rare in head and neck. Most of the reported cases occurred in the main salivary glands. The localization of a CS at the level of the larynx has already been

described but remains exceptional and poses particular diagnostic and therapeutic difficulties. Through this case of CS of the larynx in a patient of 79 years we will discuss the anatomo-clinical and immunohistochemical features of this rare entity.
Method: This is a 79-year-old patient with no history who presented with a dysphonia of increasing severity evolving since 6 months. Direct laryngoscopy reveals the presence of a nodule that takes the entire left vocal cord, hence the decision to excise the lesion.
Results: Macroscopically it was a well-defined nodule, firm with a smooth surface sized 2 cm. The nodule was lineed by a squamous carcinoma in situ. The rest of the nodule was made of of fusiform cells arranged in a storiform or fasciculated pattern. some cells were mononucleated with marked nuclear atypiasand inconspicious nucleoli, sometimes with a lipidized cytoplasm. epithelial component was CK + and EMA + while the sarcomatous component was Cd68 +, aml + vim + CK-EMA-.
Conclusion: laryngeal CSs pose a significant diagnostic challenge for the pathologist with morphological and immunohistochemical aspects overlapping with other benign and malignant fusiform cell tumours. Pathogenically, the current conception favors the epithelial-mesenchymal transition theory. Pronosis in stead is very poor.

E-PS-11-043
Nasopharyngeal tuberculosis: a report of 25 cases
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Background & Objective: Tuberculosis is uncommon in the nasopharynx even in areas where tuberculosis is endemic like Tunisia. Majority of patients of nasopharyngeal tuberculosis present with neck mass, nasal obstruction, rhinorrhoea, epistaxis, otalgia and hearing loss. The diagnosis of nasopharyngeal tuberculosis is often difficult because nasal endoscopic and radio-imaging evaluation can only offer a differential diagnosis. It is only confirmed by combined histological and bacteriological studies. The aim of the study was to present a case series of nasopharyngeal tuberculosis over a period of 10 years and to describe different pathological patterns associated to the diagnosis.
Method: In a case series of 25 patients diagnosed with nasopharyngeal tuberculosis, clinical and pathological parameters were analyzed and discussed.
Results: Age of patients ranged from 9 to 76 (average age is 42.7) with a sex ratio of 0.4. The most common clinical presentation was nasal obstruction associated to cervical mass. The endoscopic findings are regular mucosal thickening (9 cases), polypoid mass (6 cases) and mild inflammatory or normal apparent aspects in the remaining cases. Pathologic examination of nasopharyngeal biopsy samples reveals, invariably, granulomatous inflammation showing epithelioid and giant cells. Caseous necrosis was seen in 13 cases. In one case, a simultaneous biopsy of a labial budding mass revealed a well differentiated squamous cell carcinoma.
Conclusion: Although nasopharyngeal tuberculosis is a rare entity, it should be considered in the differential diagnosis of nasopharyngeal inflammation or masses, especially in a patient with a history of tuberculosis.

E-PS-11-044
Rhinocerebral mucormycosis: a report of 8 cases
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Background & Objective: Mucormycosis is an acute fungal infection with poor prognosis. Rhinocerebral presentation is the more frequent form. This infection occurs predominantly in immunocompromised patients. Historically, poorly controlled diabetes mellitus has been the most common underlying risk factor. Due to its rapidly life-threatening course, the infection requires immediate surgical and medical intervention. The aim of the study is to present a case series of eight patients with sinonasal mucormycosis.
Method: It is a retrospective study of 8 cases of rhinocerebral mucormycosis collected at our department of pathology. Clinicopathological parameters, diagnostic criteria and evolution were obtained from medical records.
Results: A male predominance was noted with a sex ratio of 6/2. The mean age was 55 years. Uncontrolled diabetes was noted in all cases. Presentation was exophthalmos, rhinorrhea, ophtalmoplegia, loss of visual acuity in the majority of cases. Peripheral facial palsy was observed in two cases. Diagnosis was made on surgical biopsies in all cases. Mucoral hyphae were identified on HE stain and Grocott (empty, thin-walled, non-septate, branch at right angles hyphae). Variable associated inflammatory reaction was noted: pyogranulomatous in four cases, granulomatous in one case and non-specific inflammation in three cases. Medical antifungal systemic therapy was instituted in all cases. Four patients died few days after diagnosis.
Conclusion: Given the non-specific initial clinical signs of rhinocerebral mucormycosis, a clinically suspicious lesion should be histologically examined in order to establish an early diagnosis.

E-PS-12 | History of Pathology

E-PS-12-001
The questionnaire portraits of three Russian pathologists
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Background & Objective: This work has the aim to collect and systematize the biographical information on Russian pathologists Vasily Ivanovich Kedrovsky, Leon Manusovich Shabad and Leonid Vasilievich Sobolev.
Method: According to the questionnaires prepared by me.
Results: None.
Conclusion:
Famous Russian bacteriologist, pathologist and leprologist Professor Vasily Ivanovich Kedrovsky
Born on December 30, 1865 in the village of Ovchuhi, Vladimirsky district of Vladimir province, in family of priest. Studied at Vladimir Theological Seminary, expelled for participation in so-called "Seminary Revolt" (1884); graduated from Shuya male gymnasium (1886) and immediately entered the Law Faculty of Moscow University, but in the 1st semester he moved to the Faculty of Medicine, which graduated with a degree of Doctor with Honors (1891); after graduation is left at the Pathology Department; defense of thesis on topic "Conditions of oxygen life of anaerobic bacteria" (1896); Doctor of Medicine (1896). Supernumerary laboratory assistant and assistant prosector, Pathology Department, Moscow University; Director, Bacteriological Institute of University; Head, Pathological Bacteriological Laboratory, Psychoneurological Institute; Head, Leprosy Department, Central Tropical Institute, etc; found that under certain conditions, the causative agents of leprosy and tuberculosis can change the nature of growth in nutrient media, acid-resistant and other properties and go into acid-resistant forms, and for the first time the causative agent of leprosy is cultured outside the body, the possibility of vaccinating leprosy to animals has been proved, and its epidemiology has been substantiated; Honored Scientist. Research interests: Issues of microbiology, epidemiology and pathological anatomy of leprosy and tuberculosis. Author of scientific works devoted mainly to the experimental study of epidemiology and

pathological anatomy of leprosy and tuberculosis. Member of the International Association of Leprologists (1926). Died on December 4, 1937 in Moscow on the 72nd year of life. Buried (ashes stored in the columbarium) at the Novodevichy cemetery of Moscow.

Famous Russian experimental pathologist and oncologist Academician Leon Manusovich Shabad (19.01.1902-29.08.1982)

Born in Minsk in merchant family. Graduated from the 1st Leningrad Medical Institute (1924) and Postgraduate Course at Pathology Department. Prosector and consultant in hospitals of Leningrad and Moscow, etc. Head, Laboratory of Chemical Carcinogenesis, Research Institute of Experimental and Clinical Oncology, Moscow. One of the founders and creators of national experimental and preventive oncology; pioneer in study of carcinogenic substances; the founder of the theory of precancer and school of experimental oncologists. Author of about 400 scientific works, including 8 monographs. Member of the CPSU, board of the All-Union Society of Oncologists and Pathologists, etc; put forward the concept of circulation of carcinogens in human environment and developed a morphological classification of forms of precancerous changes in animals and humans; described the development of tumours in the offspring of animals when exposed to oncogenic substances; awarded the International prize by the United Nations "For outstanding research work on studying the causes of cancer and fight against it" (1962). Motto: It is necessary to demand from yourself and your loved ones as much as you cannot do. Only then will you do everything that you are capable of. Distinctive feature: Born mentor, was rosary, stubborn, highly tactful and at the same time very persistent, fluent in French, German and English languages. Hobbies: Liked to keep his diaries, which were a model of punctuality and clarity, engaged in versification and wrote prose. Died in Moscow on the 81st year of life from a stroke. Buried at Kuntsevo cemetery of Moscow.

Sobolev Leonid Vasilievich - outstanding Russian scientist-pathologist (27.02.1876 - 16.03.1921)

Born in Trubchevsk, Orel province, in the family of titular counselor. Graduated from the St. Petersburg Imperial Military Medical Academy (1898) and for his scientific work "To the question of the retention mucous cysts of the colon" was awarded the prize named after Prof. T. Illinsky (1897); defense of the thesis on the topic "To the morphology of the pancreas, with its duct ligation, diabetes and some other conditions" (1901). Prosector, Privat-Docent, Pathology Department, Military Medical Academy (1904-12); retired for health reasons (1912). First showed that the islets of Langerhans are organs of internal secretion, and their function is the regulation of carbohydrate metabolism, the violation of which leads to sugar diabetes; as a result of microscopic studies of pancreatic preparations of a number of animals, came to the idea of the existence of a substance regulating sugar metabolism; pointed to the possibility of obtaining an active antidiabetic drug from the pancreas. Scientific interests: Researches are connected with development of questions of pancreatic pathomorphology, etc. Author of 25 scientific works, including a number of training manuals for doctors and students. Distinctive feature: Modesty, isolation, diligence, good command of the German language. Died in Petrograd at the age of 45 years from multiple sclerosis. Buried at the Smolensk Orthodox cemetery in St. Petersburg. The following inscription is carved on the headstone monument: Privat-Docent of the Military Medical Academy: SOBOLEV Leonid Vasilievich, dead 16/III1921.

E-PS-13 | Infectious Diseases Pathology

E-PS-13-001

Pulmonary actinomycosis: a case report

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Background & Objective: Actinomycosis is a rare chronic disease caused by Actinomyces spp., anaerobic Gram-positive bacteria that normally colonize the human mouth and digestive and genital tracts. We present the case of a 76-year-old male, heavy smoker, who presented with dyspnea. Chest CT revealed a right lower pulmonary lobe consolidation with a large ipsilateral pleural effusion, and PET-CT showed a right lower lobe lesion measuring 5.9 cm in greatest diameter with high metabolic activity. Lung cancer was highly suspected and right lower lobectomy was performed. The patient remained afebrile during his hospital stay.

Method: We received a lobectomy specimen measuring 14x10x4cm. There was a peripherally located compact and firm, grayish-whitish and partially brownish-tan lesion measuring 5.9 cm in greatest diameter.

Results: Histological examination revealed an abscess with centrally located aggregates of gram-positive bacteria in the form of "sulfur grains". The abscess was surrounded by dense fibrous tissue and abundant foamy histiocytes. The inflammatory cells extend to the chest wall as in pleural empyema in organised phase.

Conclusion: The above findings are consistent with gram-positive bacterial infection of the lung of the thoracic actinomycosis type. Actinomycosis is a chronic, slowly progressive bacterial infection which uncommonly (in the 15% of actinomycosis cases) afflicts the lung or other intra-thoracic organs. Thoracic actinomycosis can be clinically misdiagnosed as lung cancer or tuberculosis. Thus, lung biopsy is usually performed to exclude malignancy. Early diagnosis allows for appropriate therapy with excellent prognosis.

E-PS-13-002

Mucor appendicitis resolution following surgical excision without anti-fungal therapy

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Background & Objective: Mucormycosis is an invasive fungal disease, whose risk is associated with immunosuppression. Mucor appendicitis is a very rare entity. The main therapy usually includes a combination of surgical debridement and antifungal drugs

Method: A case report.

Results: A 19-year old male was admitted due to neutropenic fever and abdominal pain, eleven days after completing chemotherapy for Extra-skeletal Ewing sarcoma. A diagnosis of acute Appendicitis was made and an appendectomy was performed. The patient recovered un-eventfully and he was discharged. On histopathology - the submucosa of the appendix was infiltrated by fungal hyphae consistent with invasive Mucor infection. PAS and silver stains for fungal hyphae were positive. A PCR test on the paraffin was positive for Rhizopus microsporus. The results were available after discharge, and since the patient was doing well it was decided to continue follow up with no further antifungal treatment. Ten months after surgery, the patient is doing well.

Conclusion: A combination of Anti-fungal drugs with surgical debridement has been shown to increase survival in patients with Mucormycosis. None of the previously reported cases of Mucor appendicitis resolved following surgical treatment alone. Despite the lack of anti-fungal therapy, our patient had favorable clinical course, possibly related to his host characteristics (young age, lack of comorbidities, transient neutropenia and a localized disease). This case highlights the importance of considering uncommon pathogens as causes of common diseases such as appendicitis. Further studies should look into the relative clinical significance of surgery and anti-fungal therapy in the management of this disease.

E-PS-13-003

Ileal cystoisosporiasis: an uncommon etiology for chronic diarrhea

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Background & Objective: Cystoisosporiasis is caused by infection of the small intestine enterocytes with the coccidian parasite Cystoisospora

belli. The most common symptom is watery diarrhea. The aim of this report is to raise awareness of this uncommon, but treatable, cause of chronic diarrhea mostly in immunosuppressed patients.
Method: Review of clinical data and histological sections obtained from ileal and colonic biopsies from a 33-year old HIV-positive woman with longstanding chronic watery diarrhea of unknown etiology. Periodic acid-Schiff (PAS) and Giemsa stains were performed.
Results: Relatively large and eosinophilic subnuclear and perinuclear encysted zoites were found in ileal enterocytes. They were PAS positive and associated with discrete inflammatory reaction with eosinophils and slight villous atrophy. Colonic biopsies and stool examination were unremarkable.
Conclusion: Cystoisospora belli organisms can easily go unnoticed on histological sections. One must know and carefully search for this parasite in order to diagnose it in the appropriate clinical setting. Correct etiological diagnosis is important for directed treatment.

E-PS-13-004
Primary hydatid disease of scapulae: a case report
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Background & Objective: Hydatid disease (HD) is a serious public health issue in endemic areas. It usually manifests in liver and lung but, although rarely, it can develop in almost any part of the body. Hydatid disease in unusual locations may be a challenging diagnosis.
Method: We present a case of a 17-year old woman who was admitted to our hospital with pain over her right shoulder. In physical examination a scapular mass with fistula to skin was detected. On CT lytic lesion with cortical destruction was seen inside the bone. On MRI, this lesion was reported as it may be caused by osteomyelitis. Surgical resection was made. On histological examination we found germinative membranes and protoscolex formations intermixed with bone sequestrums.
Results: Hydatid cyst diagnosis was made. Whole body scans were made but all organs were negative. She was treated with albendazol. After 5 months her indirect hemaglutination test came negative. After 1 year of follow-up there are no recurrences.
Conclusion: Primary bone involvement is a very rare entity in the english literature. And should be considered in differantial diagnosis in cystic bone lesions.

E-PS-13-005
Leukocyte ratios in the early diagnosis of Dengue Fever
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Background & Objective: Dengue is an acute febrile illness endemic in the Indian subcontinent and a potentially fatal viral infection that can terminate in dengue hemorrhagic fever and shock syndrome. Along with detection of dengue specific IgM antibodies/ non-structural protein 1, NS1, platelet count has been the only accessory laboratory test used to support the diagnosis of dengue infection. The aim of our study was to evaluate the utility of leukocyte counts and their ratios in the early diagnosis of dengue fever.
Method: This retrospective study was conducted in the department of Pathology, Fr Muller Medical College, Mangalore, from May to June 2017. Peripheral blood leukocyte counts of patients clinically presenting with dengue like illness and for whom anti-dengue antibody test was requested were included in the study. Patients who had negative results for NS1 protein/ IgM antibody were taken as negative control.
Results: A total of 197 blood samples were examined. Dengue IgM/ NS1 was positive in 104 cases. Male to female ratio was 1.4:1. Most patients (25%) were in the third decade. A significant difference in the total leukocyte count, percent differential leukocyte count and platelet count was seen between the positive and negative groups (p value <0.0001- 0.487). In the analysis of receiver operating characteristic curves for dengue infection, areas under the curves were 0.675, 0.529, 0.662 respectively for neutrophil: lymphocyte, neutrophil:monocyte, monocyte:lymphocyte ratios respectively.
Conclusion: Leukocyte counts and their ratios are promising, easily doable inflammatory biomarkers which can play a crucial role in early diagnosis of dengue and initiation of appropriate therapy.

E-PS-13-006
Measles infection in a 17-year-old female patient: an avoidable autopsy report?
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Background & Objective: Measles virus is an extremely contagious virus, spread by aerosols and droplets from respiratory secretions of acute cases, with immune suppression as an invisible hallmark. Vaccination against measles is effective and is included in the Portuguese National Immunisation Programme since 1974, where this virus was declared eliminated in 2015 (WHO-Regional Office for Europe). In 2017 Measles infection cases have increased in Europe, mostly in non-vaccinated communities, and 35 people died of the disease. Portugal was considered a high-risk country by the Directorate-General of Health. We present a case report of the only death in Portugal attributed to Measles.
Method: Female, 17 years, non-vaccinated against Measles virus, with personal history of psoriasis and with a recent EBV infection, was hospitalized in our Institution with measles and pneumonia. After three days in the PICU, the patient died and a clinical autopsy was performed.
Results: Gross examination showed heavy and condensed lungs with congestion, hepatosplenomegaly, and slight congestion of encephalic vessels. Histopathologic features include generalized interstitial pneumonitis and diffuse alveolar damage. There were no signs of encephalitis.
Conclusion: Despite only 1/1000 patients dies due to Measles infection, the world must maintain a commitment to measles vaccine programs. In this epidemiological context histopathologic examination should not only look for measles virus alterations but also for secondary infections.

E-PS-13-007
Crimean-Congo hemorrhagic fever (CCHF): analysis of two cases from the endemic region
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Background & Objective: There are several endemic areas in the Republic of Kazakhstan, including areas where Crimean Congo hemorrhagic fever (CCHF) occurs on an annual basis. According to the 2001-2011 data from the Ministry of Public Health, there were 75 cases of CCHF. In 2009, a CCHF outbreak was recorded in the region, when eight people died, and in 2016 – 2017, four people died from the CCHF infection in the South Kazakhstan region.
Method: We undertook a retrospective analysis of two lethal cases of the CCHF. Both cases were confirmed by the results of molecular and serological analyses.
Results: A 12-year-old boy was hospitalized in a severe condition with a cough, nose bleeding, and fever. Ecchymosis has affected arms, legs, and his back. The patient's condition progressively worsened over the course of next two days, with the development of pulmonary hemorrhage. On the third day, the patient died. A 40-year-old woman was admitted to the hospital with nausea and vomiting blood. The condition of the patient worsened with the development of hematemesis. CCHF was suspected, and despite intensive treatment, there were signs of pulmonary hemorrhage, uterine bleeding, and generalized seizures. On the third day after her admission, the patient has died.

Conclusion: In both cases, despite different clinical manifestations during the prehemorrage phase, an autopsy revealed almost identical signs, including massive alveolar hemorrhage and hemorrhages in the gastrointestinal tract. Moreover, morphological findings in the first case included isolated invasive Aspergillus tracheobronchitis (Type I), which, apparently, contributed to the malignant course of the infection.

E-PS-14 | IT in Pathology

E-PS-14-001

Implement American Joint Commission on Cancer (AJCC) checklists via the College of American Pathologist checklists (CAP-eCC) for structured data transmission to health records and analytic repositories in support of precision medicine

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Background & Objective: To support precision medicine initiatives at Henry Ford Health System the latest AJCC checklists (8th Edition) were implemented, complying with regulatory standards and leveraging a new taxonomy. Distribution of this information in structured format to downstream systems was a key objective. Integration of structured cancer information into such databases will allow for predictive modelling of clinical and financial outcomes as well as improved research directed communication.
Method: AJCC 8th Edition Cancer checklists were deployed using the CAP-eCC's deployed using the mTuitive xPert Client for Pathology (mTuitive, Centerville, MA) as integrated into the CoPathPlus anatomic pathology laboratory information system (AP-LIS) (Sunquest Information Systems, Tucson, AZ) to report structured pathology cancer data. This allows for highly efficient, accurate data entry for structured pathology cancer reporting.
Results: Approximately 75 AJCC, CAP-eCC's, were implemented following technology deployment, testing, and training. There were extensive changes in the number of checklists, data elements, and using interface enhancements. Technical enhancements such as unique keying of the data elements (c-keying) allowing for interoperability and the ability to extract to structured XML(JSON) files. Communication servers, allow files to distribute to downstream systems such as: HER; tissue biorepositories; cancer management systems; and enterprise data warehouse. All systems leverage this single source of information.
Conclusion: Pathology information is critical to cancer care in precision medicine initiatives. Integration into downstream systems has been a key challenge for pathology. Using a coordinated approach, we have been able to integrate such data into multiple systems from a single source of truth.

E-PS-14-002

Implementation of whole slide imaging instrument interfaces are critical to support safe, efficient high throughput digital pathology

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Background & Objective: To support high throughput whole slide imaging workflow, integration of imaging devices with patient registration and reporting systems is critical to efficient, safe operation. To accomplish this, HL7 interfaces were implemented between our laboratory information system and our whole slide imaging systems. Clinical laboratory instrumentation has typically been tightly integrated into this type of communication however only recently have such requirements become necessary in anatomic pathology.
Method: HL7 Interfaces were specified, designed, tested, and implemented between CoPathPlus Anatomic Pathology Laboratory Information System (AP-LIS) (Sunquest Information Systems, Tucson, AZ) and whole slide imaging (WSI) platforms, consisting of the Roche iScan Coreo and the iScan HT as well as Ultra cISH instruments using the Ventana Connect middleware (Roche, Basel, Switzerland).
Results: Implementation of a functional HL7 interface, allowed data from the AP-LIS to pass directly to the WSI devices and the cISH instruments eliminating dual order entry and slide relabeling. Manual processing time dropped from 2-15 minutes per case to zero as slides were labeled at the time of histology and orders passed to downstream systems with no user intervention. This allowed AP-LIS labels to be used directly on cISH instruments and eliminated manual annotation/labeling of cases on WSI devices. A study of 5000 slides showed no patient identity mismatches, interface transmission errors or bar code read failures by either WSI or cISH instrumentation.
Conclusion: Implementation of HL7 interfaces between AP-LIS and WSI platforms are possible to implement and are critical to workflow allowing efficient and safe implementation of this technology.

E-PS-14-005

Modern digital tools to build a remote intraoperative diagnosis equipment

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Background & Objective: Digital pathology has already a long period in its implantation. However, new developments and tools appear continuously favoring the incorporation into routine diagnosis. Besides nowadays no high cost investment are need with advancements in telecommunications. We planned to incorporate a new equipment for remote intraoperative diagnosis
Method: Our microscopes have conventional digital photography cameras (Panasonic GF6, GF7 and GX800) with WIFI connectivity capacities (802.11b/g/n). We normally connect them with smart phones and tablets. As most wireless devices have a single WIFI adaptor, occupied with the camera connection, and thus preventing simultaneous connection to networks, we connect the tablet/phone through a USB cable with a desktop computer with the software "scrcpy". It allows a real time presentation of the mobile device screen within the computer monitor, showing all the camera captures from the microscope. For remote access we use a VPN connection to the desktop computer or either a "Teamviewer" connection.
Results: The pathologist has full real time direct access to the frozen sections our technicians prepare and review in the microscope and conduct them within the slide selecting magnification and display areas. For difficult or doubtful areas the technicians take with the camera high resolution (16 Mpx) still photographs that are transmitted to the computer for immediate review.
Conclusion: The development of this remote intraoperative system have no additional cost. The image quality is high combining real time video with high resolution still images. The key feature is the experience of our technicians both in handling gross specimens and in the use of microscope.

E-PS-15 | Molecular Pathology

E-PS-15-001

Toward the automated scoring of fluorescence in situ hybridisation using a confocal whole slide image scanner

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Background & Objective: The standard, manual scoring for FISH is labor-intensive and time-consuming. Confocal imaging has the ability to perform serial optical sections with thick specimen imaging, which is critical for three-dimensional tissue reconstruction for volumetric spatial analysis. The purpose of this study was to establish the protocol of

scanning and image analysis toward automated FISH scoring system development.
Method: 20 archival break-apart FISH slides (4um thick) were used and the regions of interest were selected for confocal scanning. Several parameters (interval and number of layer) with 0.16um/pixel resolution were performed. The images were viewed and an adequate number of ROIs to define at least 200 nuclei with interpretable signals were obtained by the subsequent analysis. For the nuclear segmentation, nly the sphericity parameter was manually decided to exclude overlapping nuclei, while the other parameters were decided automatically. Spot detection was done by fully automated algorithms. The accuracy of nuclear segmentation and spot detection were assessed.
Results: Confocal scanning provided sharp images with spatial information of spot signals. By our semi-automated algorithms in Imaris, nuclear segmentation and spot detection were successfully performed. The number of each signal patterns were correlated with the clinical result. Our decided scanning protocol is 7 layers with 0.6um interval.
Conclusion: We established the semi-automated method of FISH scoring with confocal WSI scanner. This method was helpful to obtain accurate information more efficiently than conventional methods. According to the protocol and the data of this study, we are currently developing an in-house software for the fully automated FISH scoring system also considering deep learning.

E-PS-15-002
Comparison of DNA- and RNA-based parallel sequencing approaches for the detection of MET Exon 14 skipping mutations

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Background & Objective: Activating MET exon 14 splice site mutations are increasingly described in non-small cell lung cancer (NSCLC). These mutations lead to an alternate splicing and result in MET exon 14 skipping. This study compares three parallel sequencing approaches, a DNA- and RNA-based multiplex PCR approach and a DNA-based hybrid capture approach.
Method: Twenty-four NSCLCs with MET exon 14 skipping mutations were evaluated. DNA and total nucleic acid (tNA) were extracted from formalin-fixed, paraffin-embedded material. DNA was analysed with a custom GeneRead V2 panel (Qiagen) and a custom SureSelect XT HS panel (Agilent). tNA was analysed with the FusionPlex Lung panel (Archer). Sequencing was performed on the MiSeq or NextSeq (Illumina). An in-house software pipeline, the Archer Analysis software or the SureCall software (Agilent) were used for analysis.
Results: 23/24 MET exon 14 skipping mutations were detected by all parallel sequencing approaches. One mutation was not detected with the RNA-based panel. Additionally, the three approaches were investigated in terms of workload, time, cost and material. For the hybrid capture as well as the RNA-based multiplex PCR approach up to 200 ng DNA / tNA are needed and they are more expensive than the DNA-based multiplex PCR approach, which requires 40 ng DNA.
Conclusion: This study showed that RNA-based parallel sequencing approaches can be used to detect mutations that lead to alternate splicing. In DNA-based approaches, the splicing effect can only be verified by literature data. However, a DNA-based approach can be used to identify and name the exact mutation, which is not possible on RNA-level.

E-PS-15-003
An extremely rare case of PDGFRA D842Y mutation in stomach gastrointestinal stromal tumour

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Background & Objective: Most gastrointestinal stromal tumours (GISTs) are associated with molecular changes in two genes: KIT and platelet-derived growth factor receptor-α (PDGFRA). However, only 3% to 5% GISTs harbor PDGFRA mutation. The majority of PDGFRA-mutant GISTs have an epithelioid morphology and originate in the stomach. Most tumours carry substitution affecting codon D842 in exon 18 which entails imatinib resistance. The exception is an extremely rare (only 7 reported cases) mutation involving D842Y codon.
Method: Gastric and hepatic lesions were studied histologically, immunohistochemically and genetically.
Results: This report presents a case of GIST in a 70-year-old male patient. Computed tomography showed gastric mass infiltrating III liver segment. The patient had undergone gastric and partial hepatic resection. Pathological examination revealed 5.1cm sized tumour arising from the gastric submucosa consisted of epithelioid cells with mild to moderate nuclear atypia. Mitotic activity was 46 mitotic figure per 50 high-power fields. Immunohistochemically the tumour cells were: DOG1(+), CD117(-/+), SMA(-/+), CKAE1/AE3(-), HMB-45(-), S100(-), MelanA(-), MITF(-), CD34(-), Desmin(-). Immunoprofile of metastatic lesions in the liver corresponded to GIST metastasis. Risk of progression according to Miettinen&Lasota classification was defined as high (55%). Mutational analysis revealed PDGFRA exon 18 mutation (p.D842Y). No mutation in KIT gene was identified.
Conclusion: Type of harbored mutation may affect not only the diagnosis of GIST but also the treatment strategies. Currently risk classifications for GISTs incorporate mitotic rate, tumour size and localization, without taking into account mutational status of the tumour. Mutational analysis has a predictive value for sensitivity to molecular-targeted therapy, especially in KIT negative or only weakly positive GISTs.

E-PS-15-006
Implementation of novel methods, markers or sample types in molecular pathology – quality assurance aspects

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Background & Objective: Biomarker analysis is crucial for detection and management of colorectal and non-small cell lung cancer. Over time, new methodologies, biomarkers and sample types have been introduced in routine practice, and laboratories were challenged to implement these rapidly and accurately. This study aimed to reveal existing validation practices in molecular pathology and the experienced difficulties.
Method: Participants to external quality assessment (EQA) schemes of the European Society in Pathology in 2016 and 2017 were invited to complete a survey. Inclusion criteria consisted of laboratories who (partly) changed their analysis method, tested PD-L1 as a new biomarker, or analyzed circulating tumour DNA from plasma as a new sample type.
Results: Fortyfive laboratories from 21 European countries responded within 1 month. 78% of participants had a written procedure for validation or verification, and 51% adhered to a specific guideline. 84% of laboratories performs revalidations, in 29% even for small protocol changes. Samples were mainly selected by literature review (69%) or manufacturers' recommendations (62%) and originated mostly from the laboratories' own biobank (87%). Hurdles were reported in the pre-analytical (44%), analytical (47%) and post-analytical (36%) phases. Participants reported problems with controlling pre-analytical variables (41%) and finding cases for rare mutations/antigens (30%). On analytical level, selection of appropriate methods and control cases (both 27%), and validation of varying degrees of positivity (24%) were reported. Post-analytical problems consisted mainly of bio-informatics analysis (23%) and correlation with clinical context (20%).

Conclusion: Differences in practices and problems were apparent and will be linked to the laboratories' EQA performance and background.

E-PS-15-007

Longitudinal analysis of error causes and follow-up in external quality assessment schemes

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Background & Objective: External quality assessment (EQA) schemes of the European Society of Pathology for non-small cell lung cancer and metastatic colorectal cancer have revealed erroneous results in biomarker analysis which can significantly compromise patient safety. This additional study aimed to evaluate the error causes and corrective actions undertaken, and to link them to longitudinal EQA performance and laboratory characteristics.
Method: Participants with at least one analysis error in non-educational cases of the Lung EQA schemes between 2015 and 2017, or one analysis error or technical failure in the Colon EQA schemes between 2016 and 2017 were contacted with a survey. In total, 131 unique laboratories from 31 countries responded, yielding 174 surveys including 278 errors for further analysis.
Results: The majority of problems occurred in the post-analytical phase for fluorescent in-situ hybridization (FISH) (56%, n=52) and immunohistochemistry (IHC) (40%, n=87), compared to analytical problems for variant analysis (40%, n=123). For FISH and IHC, the most reported causes were interpretation errors (37% and 25%, respectively) versus methodological problems for variant analysis (24%), the majority of them reported for commercial kits (70%). The most performed actions were staff training (22%) and protocol revision (17%). Errors followed up by the pathologist and molecular biologist were less likely to result in a genotyping error and technical failure in the next scheme, respectively.
Conclusion: These results highlight a difference in error causes and management for specific techniques, and stresses the need for error management in the complete test process.

E-PS-15-008

A comparative study of the Herticad test kit (BIOCAD) and the antibody HER-2 / neu Pathwey 4B5 (Roche-Ventana) approved by Food and Drug Administration in breast cancer

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Background & Objective: A comparative study of the concordance of the detection HER2 expression by the Herticad test kit (BIOCAD, FCC (Federal Service for Surveillance in Healthcare) Approved in Russia) and HER-2 / neu Pathwey 4B5 antibody (Roche-Ventana, FDA (Food and Drug Administration) Approved/FSS Approved in Russia) in breast cancer.
Method: The study was complete on TMA matrices created with 3D Histech TMA master. The blocks included samples of breast cancer with known HER2 status: 0; 1+; 2+ with and without amplification; 3+. Total number of samples - 180. The slides were stained in 9 independent laboratories using the Herticad test's kit protocol. The reference slides were stained with HER-2 / neu Pathwey 4B5 (Roche-Ventana) antibody. Similar slides were stained twice on the same instrument, for seven inconsistent days.
Results: The concordance of staining samples with values of 0; 1+; 3+ was 100%. Discrepancies with a tendency to underestimate were found in 6 samples with tumour status (3.33% of the total number). The main difficulties occurred in samples with the number of membrane-stained cells was approaching 10%.
Conclusion: The concordance of the Herticad test kit (BIOCAD, Russia) and HER-2 / neu Pathwey 4B5 (Roche-Ventana) kit was 96.67%. So, the Herticad test kit (BIOCAD, Russia) can be considered validated according to statistical criteria. Herticad test kit (BIOCAD, Russia) can be used to determine HER2 status in breast cancer.

E-PS-15-009

Clinical validation of a sensitive real-time PCR assay for detecting EGFR mutations in plasma ctDNA from patients with non-small cell lung cancer

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Background & Objective: Plasma based EGFR mutation testing is emerging for patients with advanced non-small cell lung cancer (NSCLC) when tumour tissue is unavailable. A fast and sensitive real-time PCR method (AmoyDx Super-ARMS) has been developed for detection of EGFR mutations in plasma circulating tumour DNA (ctDNA). Clinical validation was conducted in present study.
Method: The status of EGFR mutation of exon 19 deletions, L858R and T790M in ctDNA were analyzed using AmoyDx Super-ARMS EGFR Mutation Detection Kit (Super-ARMS EGFR) and droplet digital PCR (ddPCR) in a cohort of NSCLC patients. The degree of concordance between Super-ARMS EGFR and ddPCR was calculated. Further, the concordance between EGFR mutation status in ctDNA detected by AmoyDx Super-ARMS and that in matched tumour tissue DNA was assessed.
Results: In the cohort of NSCLC samples, the sensitivity, specificity and concordance rates for Super-ARMS EGFR test compared with ddPCR were 100%, 88% and 91% for exon 19 deletions (N=113), 96%, 92% and 93% for L858R (N=113), 92%, 100% and 97.8% for T790M (N=86). The sensitivity, specificity and concordance of the Super-ARMS EGFR assay for plasma EGFR mutation detection compared to tumour tissue EGFR mutation status were 82.0% (50/61), 100% (48/48), and 89.9% (98/109), respectively.
Conclusion: Super-ARMS EGFR assay is a sensitive and reliable method for the detection of EGFR mutation in lung cancer plasma ctDNA samples.

E-PS-15-012

Lung adenocarcinoma with concurrent anaplastic lymphoma kinase and c-ros oncogene 1 rearrangement: a case report and review of the literature

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Background & Objective: Anaplastic lymphoma kinase (ALK) and c-ros oncogene (ROS)1 are prognostic and predictive tumour markers in non-than other oncogenes such as EGFR, KRAS, or C-MET. Their positivity is 2.6% and 1.3%, respectively, and patients who have mutations in both genes are extremely rare.
Method: we report a 61-year-old male diagnosed with acinar adenocarcinoma who was shown to have both ALK and ROS1 rearrangements but was EGFR and C-MET mutation-negative.
Results: we report a 61-year-old male diagnosed with acinar adenocarcinoma who was shown to have both ALK and ROS1 rearrangements but was EGFR and C-MET mutation-negative. He was treated surgically and received targeted therapy. Our review of the literature revealed that few such cases of concurrent ALK and ROS1 rearrangements have been reported.
Conclusion: This information furthers our understanding of the molecular biology underlying NSCLC which will aid the selection of optimal treatment for patients with more than one driver mutation.

E-PS-15-013

Screening of recurrence related MiRNA in DCIS and functional study of MiRNA-654-5p

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Background & Objective: Ductal carcinoma in situ (DCIS) contribute to 20%-30% of new diagnosed breast cancer. Although breast cancer–specific mortality of DCIS is extremely low, a small portion still relapse which leads to poor prognosis. For the limited poor prognostic patients follow-up data, little is known about the molecular mechanism for DCIS recurrence.
Method: By miRCURY LNA™ microRNA Array and qPCR on DCIS samples with or without microinvasion in different prognostic patients, potential DCIS recurrence related miRNAs were screened out and further validated. The expressions of relevant genes are verified by qPCR. Functional study of miRNA-654-5p in DCIS progression was conducted.
Results: We got 68 candidate miRNAs after miRNA array screening on paired samples between good and poor prognosis DCIS with or without micro invasive lesion samples. By qPCR, distinct miRNA expression profiles can be detected in 4 recurrent and 12 non-recurrent DCIS patients. While in 5 recurrent and 17 non-recurrent DCIS-Mi patients, miRNA expression profile was totally different. A panel of miRNAs was examined in DCIS samples with different prognosis. MiRNA-654-5p is consistently up regulated in bad prognosis samples. In vitro experiment, miRNA-654-5p was verified being able to promote metastasis in MDA-MB-231 cell line.
Conclusion: The panel of high-risk miRNA we screened in DCIS and DCIS-Mi was totally different. MiRNA-654-5p is consistently up regulated in poor prognostic DCIS patients and plays a essential role in DCIS progression.

E-PS-15-014

Activating PDGFRA mutations in the inflammatory fibroid polyps - an important pitfall in differential diagnosis

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Background & Objective: Inflammatory Fibroid Polyp (Vanek's tumour, IFP) is rare and benign tumour of the gastrointestinal tract with an incidence from 0,1% to 2% of gastric polyps. Histologically, IFP is mesenchymal tumour of unknown lineage localized in the submucosa and characterized by vascular and fibroblastic proliferation with an inflammatory infiltration rich in eosinophils. Genetic studies revealed that IFP is driven by activating mutations in exons 12, 14 and 18 of platelet derived growth factor receptor alpha (PDGFRA) gene with frequency among case series ranged from 22% to 70%.
Method: Archival cases of IFP diagnosed in 2017 were investigated pathologically and immunohistochemically. Molecular analysis, whenever tissue material was available, was established to determine the status of PDGFRA exons 12, 14 and 18 mutations, including p.D842V.
Results: Genetic testing was carried out in 4 of 6 cases of IFP. The patient age ranged from 42 to 71 years with a 1:2 male to female ratio. IFP were localized in small intestine (3) and stomach (3). Tumour size varied from 4mm to 35mm. PDGFRA mutation was found in 2 of 4 analyzed cases-one in small intestine and one in gastric tumour. Mutations in exon 12 (p.Val561Asp) and 18 (p.D842V) were identified respectively. None of the cases was positive for CD117 or DOG1 immunohistochemically.
Conclusion: Differential diagnosis should take into account not only the clinical and endoscopic image and the result of genetic analysis but principally the microscopic assessment with immunohistochemistry which play an important role in establishing the final diagnosis. Obtained results correspond with the literature data about genetic background of IFP and relationship between tumour location and mutated exon.

E-PS-15-015

Expression of TNF-related apoptosis inducing ligand receptors in different types of human cancer

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Background & Objective: TNF-related apoptosis-inducing ligand (TRAIL) is type 2 membrane protein belonging to the TNF superfamily and has an ability to bind to 2 agonistic (TRAIL-R1/DR4 and TRAIL-R2/DR5/KILLER) and 3 antagonistic decoy (TRAIL-R3/DcR1/TRID, TRAIL-R4/DcR2/TRUNDD and OPG) receptors respectively. Lately, TRAIL has garnered significant attention due to its ability to kill cancer cells and as a potential targeted therapeutic in cancer.
Method: From donor paraffin blocks including surgical samples the tissue microarray multiblocks containing 2 cancer samples diameter 1mm from each patient were constructed. Immunohistochemistry was performed using antibodies: Anti-TNFRSF10A (LS-B604), Anti-TNFRSF10B (LS-B2074), Anti-TRAIL-R3/DCR1 (LS-C373895). A semi-quantitative method for evaluation of immunostainings was applied including scoring system based on intensity (0-no staining; 1-weak, 2-intermediate and 3-strong staining) and an appropriate cellular localization of reactions (Anti-TNFRSF10A and Anti-TNFRSF10B: cytoplasmic/granular, Anti-TRAIL-R3/DCR1: cytoplasmic).
Results: A group of 161 patients with: colorectal adenocarcinoma (32 patients/19.9%), pancreatic adenocarcinoma (40 patients/24.8%), gastric adenocarcinoma (32 patients/19.9%) and urothelial carcinoma (57 patients/35.4%) were enrolled in this study. The percentage of total positive cases were: 87.53% - TNFRSF10A (excluding urothelial cancer which was completely negative), 100% - TNFRSF10B and 93.16% - TRAIL-R3/DCR1 respectively.
Conclusion: Major TRAIL receptors were highly expressed in different types of human cancers. Further studies are needed to understand the TRAIL receptors role in molecular pathogenesis of cancer. In the future it may lead to the use of targeted therapies focused on TNF-related apoptosis pathway.

E-PS-15-016

Molecular profiling of lung and colorectal cancer: added value of next generation sequencing

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Background & Objective: The results of DNA and RNA molecular profiles obtained from non-small cell lung cancer (NSCLC) and colorectal patients (CRC) since the implementation of a Next Generation Sequencing (NGS) panel in a diagnostic laboratory setting were analyzed. A review of the detected mutations in its clinicopathological context was performed and the hypothetical increased number of patients suitable for a targeted therapy was tested.
Method: The series included 364 patients, 211 with NSCLC and 153 with CRC. DNA was extracted and libraries were prepared with a 22 gene panel. Only NSCLC were tested with a RNA NGS panel for rearrangements in 4 genes.
Results: In NSCLC, 235 mutations were detected. Mutations in EGFR (19%), KRAS (22,8%), TP53 (49,7%) and, ranging from 0,5% to 6%, in ALK, ERBB4, FGFR2, FGFR3, MET, DDR2, PIK3CA, BRAF, PTEN, NRAS, MAP2K, STK11, CTNNB1, SAMD4 and FBXW7 were detected. At a RNA level the 3,5%, 1,4% and 2,1% of NSCLC showed an ALK, ROS1 and RET rearrangement respectively. No NTRK1 alteration was detected. In CRC, 272 mutations were detected. Mutations in KRAS, NRAS, BRAF, TP53, PIK3CA, SMAD4 and FBXW7 were

detected in 52%, 3,4%, 14,2%, 57,4%, 18,9%, 10,1% and 8,1% of patients, respectively. Moreover, mutations in ERBB2, ERBB4, FGFR1, FGFR2, FGFR3, MET, DDR2, AKT, PTEN, MAP2K1, STK11, NOTCH1 and CTNNB1, ranging from 0,7% to 5%, were detected.
Conclusion: Molecular profiling by NGS increases over 50% the NSCLC and CRC patients suitable for a targeted therapy and also provides significant prognostic information.

E-PS-15-017
The future of cancer classification: evidence-informed pathology
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Background & Objective: The definitive diagnosis and classification of individual cancers underpins the care of individual cancer patients, as well as research into cancer causation, prevention, diagnosis and treatment. The WHO Classification of Tumours (the 'WHO Blue Books'), run by IARC, acts as the main conduit for data to reach diagnosis and provides the standards against which pathologists assess tumours.
Method: The focus of cancer research organisations is often on genetics and whole genome sequencing, but in addition, vast amounts of data are now being generated on individual patients by hospitals from digital histopathology, radiology, and endoscopy as well as molecular pathology and genetics.
Results: The data are held in a plethora of in-house and commercial databases, many of which are excellent. However, translating the information through to transformation of clinical care and cancer prevention is proving a slow process with many barriers.
Conclusion: IARC has proposed a new collaboration framework termed the "International Collaboration for Cancer Classification and Research (IC3R)" to answer this need. It will seek to harmonize cancer-related data generation by IC3R members, provide standard-setting for analytical procedures, and identification of critical gaps (e.g. non-uniform annotations, classifications, bioinformatics).

E-PS-15-018
Association between clinicopathological characteristics and rasmutation in colorectal cancer: experience of a university hospital
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Background & Objective: KRAS and NRAS mutations are useful markers for predicting responses to anti epidermal growth factor receptor (EGFR) monoclonal antibodies, especially in metastatic colorectal cancers (CRC). The correlation between clinicopathologicals features and complete RAS status has never been established in Moroccan patients. The aim of this study was to identify new distinct subsets of colorectal cancers based on clinicopathological features and complete RAS genotype of 60 colorectal cancer patients.
Method: A total of 60 patients with colorectal cancer were included in this study. We reviewed clinical characteristics from the patient's medical records and pathology reports. Tumoural DNA was extracted from formalin-fixed, paraffin-embedded (FFPE) tumours. RAS molecular testing was investigated by polymerase chain reaction (PCR)- sequencing and pyrosequencing technology Q24 PyroMark system (Qiagen, Hilden, Germany).
Results: Age range of the patients was 18 to 92, with mean age of 52.37 ± 13.7 years. Histologically, the majority of the tumours were adenocarcinoma (56%) and tumours with mucinous differentiation accounted for 40.2%. There was 41.6% (n= 25/60) of KRAS mutations exon 2, distributed between 15 KRAS codon 12 mutants (60%) and 10 KRAS codon 13 mutants (40%). NRAS mutations were found in 3.7% of our sample. RAS-mutated colorectal cancers compared with RAS wild-type colorectal cancers, were significantly associated with female gender (P=0.04), classical adenocarcinoma subtype (P=0.07), and microsatellite stable phenotype (P=0.003).
Conclusion: RAS mutations were found in 41.6% of all patients. RAS mutational status, in particular KRAS exon 2 has distinct clinical, pathological, and molecular characteristics (female gender, microsatellite stable phenotype and adenocarcinoma subtype).

E-PS-15-020
Identification of HNF1B mRNA splicing variants in different tissues – preliminary results
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Background & Objective: Hepatocyte nuclear factor 1 homeobox B (HNF1B) is a transcription factor that regulates the expression of multiple genes involved in the cell cycle modulation, apoptosis susceptibility and glucose metabolism. Several studies described that downregulation of HNF1B may contribute to drug resistance in ovarian cancer, and overexpression of HNF1B may cause aberrant retention of the G2 checkpoint which leads to chemoresistance. Little is known about HNF1B mRNA splicing variants and their clinical impact. Our aim is to comprehensively study HNF1B mRNA by identification of tissue-specific splicing variants and their expression in different tumour and non-tumour samples from uterine corpus, pancreas, large intestine and prostate tissues.
Method: Characterized RNA (RIN), isolated from RNA later stored tissues, was subjected to cDNA synthesis by SSIII transcriptase and random hexamers. The HNF1B mRNA transcription variants were identified by high-sensitive NGS deep sequencing (MiSeq, Illumina) of all presented exon-exon junctions obtained by in-house multiplex PCR approach.
Results: Several major (Δ5, Δ6-8, Δ7, Δ8) and 9 minor novel splicing variants were detected, and two thirds of the variants showed tissue-specific expression.
Conclusion: High sensitivity variant detection revealed a series of novel HNF1B splicing variants. Quantification of these in a wide range of different tissues by qPCR analyses using splice-site specific primers is ongoing.

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E-PS-15-021
Frequency of subtypes of EGFR mutation in our cohort: is Exon 19Del mutation the most frequent?
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Background & Objective: Screening tumour samples for a range of EGFR mutations improve our ability to identify the patients most likely to benefit from anti-EGFR therapy. Our aim here is to demonstrate our cohort's frequencies of EGFR mutations.
Method: The cases of this study were tested at our center from 2015 to 2017.
Results: In our study we had 1014 cases which had been searched for EGFR mutations and, 138 (13,6%) of 1014 had EGFR mutation. The mean age whole EGFR mutated cohort was 62. Among EGFR mutated group, there was mutation in 11,5% of cases (N=16)on Exon 18,50,7%(N=70) on Exon 19del,6,5% on Exon 20,33,3%(N=46) on Exon 21 and, two of cases had mutations on both Exon 21 and Exon 20 T790M, one had mutations on

both Exon 19 and Exon 20 T790M and, one had mutations on both Exon 18andExon 21. The number of female and male populations were 224 and 790;72 (32,1%) of 224 and 66 (8,3%) of 790 were positive for EGFR mutation, respectively.
Conclusion: Most common mutations of EGFR were 19del and Exon 21, respectively, and the most of the EGFR mutated patients were female, correlated with literature. From the view of therapy, 19del mutations are well known mutations to have good response to the anti-EGFR therapies and the response rates to targeted therapy of these mutations are higher than the others with many new drugs. Acknowledgement: Special thanks to Tuna Cemal Gedik who did data searching and helped to analysis of dataset.

E-PS-15-022
Association of SDHx mutations with their mRNA and protein expression levels in carotid body tumour
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Background & Objective: Carotid body tumours (CBTs) are rare neoplasms arising at the bifurcation of carotid arteries. The majority of CBTs are associated with genetic mutations in SDHx (SDHA, SDHB, SDHC, and SDHD) genes encoding the four subunits of succinate dehydrogenase (SDH; mitochondrial complex II). This complex participates in both the citric acid cycle and the electron transport chain, playing an essential role in energy metabolism. Evaluation of SDHx mutational status using immunohistochemistry (IHC) is a common practice in laboratory. However, in this case the real frequency of mutations could be misestimated; the inactivation of SDHx can be mediated by another mechanism, such as DNA methylation, microRNA regulation, etc.
Method: Exome sequencing of 15 CTBs, including of samples with mutated and wild-type SDHx genes, was performed on NextSeq 500 System (Illumina) at the EIMB RAS "Genome" Center. Using IHC and quantitative PCR (qPCR) methods, the associations between mutational status of SDHx and their mRNA and protein expression levels were analyzed.
Results: In 40% of samples, mutations in distinct SHDx genes were undetected by IHC. Samples with no mutations were positively stained by SDHx in 53% of cases. According to qPCR data, mRNA levels of SDHx genes correlated negatively with not all potentially driver mutations.
Conclusion: Thus, we have found that not all mutations in SDHx are associated with the expression changes at mRNA or protein levels. Whole gene sequencing should be used to evaluate mutation status of SDHx genes properly.

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E-PS-15-023
Distinct functional consequences of HER2 gene amplification in colorectal and lung adenocarcinomas
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Background & Objective: HER2 oncogene amplification, being accompanied by its overexpression, is an established driver event in breast and gastric carcinomas. The functional role of HER2 in the pathogenesis of other tumour types is less defined.
Method: 2401 archival samples of lung carcinomas (LC) and 1969 samples of colorectal carcinomas (CRC) were subjected to HER2 copy number analysis. Selected tumours with amplification of this oncogene were further subjected to HER2 immunohistochemistry and mRNA quantitation. In addition, the expression levels of some neighboring genes located in 17q12-21 amplicon were analyzed.
Results: The frequency of HER2 amplification was similar in both groups, being 100/2401 (4.2%) in LC and 84/1969 (4.3%) in CRC, respectively. 10 (82%) out of 12 analyzed HER2-amplified CRCs demonstrated clear evidence for HER2 protein and mRNA overexpression, while this estimate approached only 3 (27%) out of 11 for LCs. Expression analysis of GRB7, STARD3, and LASP1 revealed a statistically significant correlation between HER2 and STARD3 levels [r=0.571, Spearman test]. High STARD3 expression was observed in HER2-amplified CRCs but not LCs [p = 0.03].
Conclusion: HER2 amplification is frequently accompanied by gene overexpression in colorectal but not lung adenocarcinomas. STARD3 gene belonging to 17q12-21 amplicon demonstrates evidence for activation in HER2-amplified colorectal neoplasms and therefore deserves further analysis.

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E-PS-15-025
Differential expression of microRNAs in gastrointestinal neuroendocrine tumours
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Background & Objective: Determine the profile of differential expression of microRNAs in GEP-NETs, in tumour tissue and adjacent normal tissue and correlate their profile with the expression of the biomarker possible regulated by them.
Method: We selected 19 cases corresponding to patients with GEP-NETs from small intestine or colon Total RNA was isolated from paraffin embedded tissues; previous microdissection of tumour and normal tissue, the quantification of the miRNAs expression level was performed using TaqMan MicroRNA Assays and the differential expression was evaluated by applying the comparative method ΔCt and Ct.
Results: We found overexpression of miR-96 (0.0058), miR-145 (0.0025) and miR-182 (0.0038) with a fold change of 4.55, 3.07 and 8.13 respectively, a downregulation of miR-19a (0.0268) in tumour tissue compare to the normal one. Higher difference was found in the relative expression of miR-200a in G1 tumours vs G2 tumours. Observed a strong correlation in 84% (16/19) and 63% (12/19) of the cases between ATRX with miR-19 and MTOR with miR-96 respectively
Conclusion: We characterized 5 miRNAs, 3 microRNAs significantly upregulated (miR-96, miR-145 and miR-182) and one downregulated (miR-19a) in tumour compare with normal tissue. The high expression of ATRX was correlated with the loss of miR-19a expression and the downregulation of MTOR with the upregulation of miR-96. Identify and demonstrate neuroendocrine specificity and to validate candidate miRNA biomarkers, can be usefull if they could assist in evaluating the biological behavior of these neoplasms.

E-PS-15-026
DNA extraction from formalin-fixed paraffin embedded tissues: the influence of the storage period of the tumour blocks on DNA quantity and purity
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Background & Objective: Archived formalin-fixed paraffin embedded (FFPE) tissue is an invaluable resource for retrospective molecular genetic studies. However, the proper selection of the tumour sample is critical to generate accurate results. The aim of our study was to investigate if the storage period of the FFPE blocks had a significant effect on the isolated DNA.

Method: We examined the quantity and purity of the isolated DNA from 212 FFPE tissue blocks that had been stored in our department for up to 10 years. The cases corresponded to 163 papillary thyroid carcinomas, 43 papillary thyroid microcarcinomas and 6 follicular thyroid carcinomas, respectively. The DNA extraction protocol was based on a precipitation method (MasterPureTM DNA purification kit, Epicentre), in accordance to the manufacturer instructions, optimized in our laboratory. A spectophotometer was used to determine the yield (A260) and purity (A260/A280 ratio) of the isolated DNA.
Results: We successfully isolated good DNA quantity and purity from all our study cases (mean concentration: 489.3±372.6ng/μl; mean A260/A280 ratio: 1.67±0.19). Moreover, no statistically significant differences were observed between tumour blocks stored for 1-3 years, 4-6 years and 7-10 years, respectively, both in terms of DNA quantity (p=0.374) and purity (p=0.124).
Conclusion: Our DNA extraction technique provided a good range of DNA concentrations and purity. Moreover, we demonstrated that the storage period of the FFPE blocks does not have a significant influence on the DNA quantity and purity.

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E-PS-15-027
Combination of second generation TKI resistance mechanisms - a case report
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Background & Objective: Secondary TKI treatment resistance is usually associated with mutations in the EGFR gene. T970M mutation has been reported to occur in patients undergoing TKI therapy and has been related to acquired resistance. While the T970M mutation contributes to a major part in acquired resistance, a number of other mutations or phenotypic alteration including small cell change can also be accountable. The following case highlights the importance of phenotypic change along with resistance mutation.
Method: -
Results: A middle aged woman presented with a poorly differentiated adenocarcinoma of the lung harbouring c.2573T>G (L858R) activating mutation of exon 21 of the EGFR gene in November 2015. Second generation TKI treatment started immediately after the diagnosis with excellent clinical response. 13 months later worsening clinical signs and cerebral metastases appeared. cfDNA testing revealed T790M mutation of the EGFR gene along with previously known c.2573T>G (L858R) mutation. A third generation TKI treatment started. Despite of the third generation TKI treatment two months later systemic dissemination was diagnosed clinically. The lady deceased four months later and postmortem examination was carried out, which revealed small cell phenotypic change of the tumour.
Conclusion: In this case T970M mutation occurred with small cell phenotypic change, but the therapy targeted T970M mutation only. The small cell component led to disease progression, and systemic dissemination. Our case highlights the importance of combined acquired second generation TKI resistance mechanisms.

E-PS-15-028
Colorectal adenocarcinomas and miRNA expression profiles
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Background & Objective: Colorectal cancer (CRC) is one of the most commonly diagnosed cancers and a major cause of cancer death. MicroRNAs (miRNAs) regulate gene expression by post-transcriptionally suppressing mRNA translation or by causing mRNA degradation. This study is concerned to identify the expression profile of miRNAs in CCR and evaluate their clinical applicability.
Method: We used CRC tissue samples and normal colorectal epithelial tissue datasets. Prior to the initial miRNAs testing, samples were evaluated for tumour content by basic histopathological examination using haematoxylin-eosin stained slides and immunohistochemical diagnostic. We conducted an expression analysis of miRNAs by using quantitative Reverse Transcription-Polymerase Chain Reaction (RT-PCR), in CRC, as compared to normal mucosa (NOR), in order to identify candidate miRNAs involved in CRC progression.
Results: RT-qPCR analyses, showed 13 significantly deregulated miRNAs in colorectal lesions. Among these miRNAs, some miRNAs were up-regulated (like miR-21, miR-143, miR-145), whereas others miRNAs were down-regulated (miR-141). We also found that the expression levels of miR-31, miR-141, miR-224-3p were significantly different in patients with colon cancer compared with that in healthy controls.
Conclusion: Our results confirmed that several miRNAs were abnormally expressed in colorectal lesions and showed that several miRNAs could mark the transition from NOR to CRA, thereby marking progression from the early steps of cancer. The research was made possible following completion of the project POS CCE 2.21., ID 1844, SMIS 48750, CEDMOG.

E-PS-15-029
MicroRNAs expression in colorectal cancer - preliminary data
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Background & Objective: MicroRNAs (miRNAs) are small non-coding RNA molecules that post-transcriptionally regulate gene expression by base-pairing to mRNAs. Since microRNAs are involved in the regulation of tumour suppressor and oncogene pathways, their altered expression is associated with the development and the progression of various human cancers. In this study we aimed to identify the miRNA signature of the colon tissue from patients with colorectal cancer.
Method: Using Human Cancer Pathway Finder miRNA PCR Array, Qiagen, USA, we measured the expression of 84 mature miRNAs in 18 colorectal cancers affected tissues and their paired normal tissues. Analysis of the results was performed using Free miRNA PCR Array Data Analysis, Qiagen, USA.
Results: We identified 2 overexpressed miRNAs and 13 downregulated in terms of Fold Regulation (2<FR<-2). Among these, miR-132-3p, miR-215, miR-378a and miR-17a showed statistical significance ($p<0.05$).
Conclusion: We identified four miRNAs as potential markers for CRC. Additional studies on larger cohorts of CRC patients are necessary for validating these miRNAs as promising candidate markers in colorectal cancer.

E-PS-15-030
Assessment of plasma levels of circulating DNA in metastatic castration-resistant prostate cancer patients
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Background & Objective: Prostate cancer is one of the most common cancers worldwide. The effectiveness of primary therapies for castration-resistant prostate cancer (CRPC) may vary depending on individual characteristics; however, clear criteria for the selection of the optimal therapy are not determined. Extracellular circulating nucleic acids such as DNA, RNA, and microRNA in plasma can be considered predictive biomarkers for various types of tumours. Apoptotic and non-apoptotic cell death are major

contributors to circulating DNA (cfDNA). Furthermore, the ratio of the plasma levels of cfDNA fragments from apoptotic (90-115 bp) and non-apoptotic (200–250 bp) cells can be associated with the effectiveness of the therapy.
Method: Using 30 plasma samples obtained monthly from six CRPC patients, we measured plasma levels of cfDNA fragments via quantitative polymerase chain reaction (qPCR) analysis. This work was performed using the equipment of the EIMB RAS "Genome" Center (http://www.eimb.ru/rus/ckp/ccu_genome_c.php).
Results: Levels of all cfDNA fragments in all samples were significantly elevated at the initiation of therapy. Furthermore, levels of cfDNA fragments of non-apoptotic origin (200-300 bp) decreased gradually in samples obtained from five patients, thereby potentially indicating the effectiveness of the therapy.
Conclusion: qPCR-based determination of plasma cfDNA fragment levels can be used subsequently to evaluate the effectiveness of therapy in CRPC patients; however, further studies with larger patient populations are warranted to determine correlations with clinical characteristics.

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E-PS-15-031
FKBP5 gene expression in rheumatoid arthritis provocation
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Background & Objective: Psychological stress has been shown to impact risk for medical conditions, such as cardiovascular disease, cancer, and immune disorders. An important modulator of stress responses is the FK506-binding protein 51 (FKBP5/FKBP51) that acts as a co-chaperone and modulates glucocorticoid receptor activity in response to stressors. To determine the impact of FKBP5 gene activity in rheumatoid arthritis (RA) development.
Method: Droplet digital PCR and qPCR were used for gene expression analysis in 60 RNA samples adjusted by age (28 RA patients, 12 relatives and 20 healthy volunteers without complex disorders) extracted from venous blood. Statistical analysis was performed by R Studio packet program.
Results: Our study indicates that lowest mRNA level of FKBP5 gene was detected in group of RA relatives (19.1±2.68 copies/μl) with increasing its activity in healthy volunteers (49.3±10.5 copies/μl) and in RA patients (159.5±26.7 copies/μl). Such elevated level of FKBP5 in RA patients can be caused by therapeutics (such as glucocorticoid receptor antagonists) and in healthy donors elevated level of FKBP4 may be caused by casual chronical stress and increased level of cortisol.
Conclusion: There are only limited studies conducted to FKBP5 gene activity in complex disorders. The role of FKBP5 gene in provoking and development of complex diseases still unclear that need further investigation.

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E-PS-15-032
Evaluation of gastric atrophy in BRCA1 germ-line mutation carriers and non-carriers
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Background & Objective: Standards for surveillance of BRCA1 mutation carriers are currently limited to early detection of breast and ovarian cancers. However, BRCA1 germ-line defects are also associated with elevated risk of gastric cancer (GC) accounting for approximately 3% of the incidence of this disease. This study utilized endoscopic and morphological examination of the gastric mucosa to compare the frequency of preneoplastic and neoplastic lesions in asymptomatic BRCA1 mutation carriers and control individuals.
Method: 106 carriers of deleterious BRCA1 alleles (median age: 47; range: 19-74) and 74 control subjects (median age: 57; range: 28-82) were enrolled in the study. During endoscopic examination, five gastric biopsy specimens from each patient were collected and assessed according to OLGA (Operative Link for Gastritis Assessment) system.
Results: No instances of intraepithelial or invasive gastric carcinoma were revealed. Severe atrophy (OLGA stages III-IV) was observed in 5/106 (4.7%) BRCA1 mutation carriers vs. 5/74 non-carriers ($p = 0.74$). In the group of mutation carriers, there was a weak correlation between the degree of atrophy and the age of patients (Spearman's $r = 0.33$, $p = 0.001$). Loss-of-heterozygosity (LOH) was performed for 11 tissue specimens obtained from atrophic glands; none of these samples demonstrated somatic deletion of the wild-type BRCA1 allele.
Conclusion: BRCA1 germ-line mutations are not associated with an elevated prevalence of precancerous lesions in gastric mucosa.

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E-PS-15-033
Study of ex vivo sentinel node of colon in a clinical hospital by OSNA method
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Background & Objective: Colorectal cancer is the third party in frequency among men (after those of lung and prostate) and the second one in women (after that of breast) in developed countries. The classical histopathological study evaluates 1% of the lymph node as a whole and in consequence patients could have been underdiagnosed and might have benefited by adjuvant treatments. In recent years several studies have been published (GACELA, CLOSER, ARSENAL) monitored in different autonomous communities (Andalusia, Salamanca, Barcelona…). Because of the results obtained, Clinical Hospital decides to incorporate this technique in Aragon to improve the quality of the diagnosis in patients.
Method: In 2017, this technique was commenced by ex vivo analysis of colon node, in which after removing the piece, methylene blue is injected to detect the Sentinel node and it will be processed if it meets the established criteria. OSNA method uses the same principles (Lynorhag and Lynoamp) and equipment as in the breast study. It consists of crushing of the marked node and mARN is obtained after a series of centrifugation to count the number of copies of tumour CK-19 containing and compare the values obtained with the set parameters.
Results: This method provides the number of CK-19 copies in the piece and its equivalence with the clinical nomenclature of macrometastasis (++), micrometastasis (+) or without metastasis (-).
Conclusion: Establish a reliable, reproducible and economically viable model for the molecular staging of colon Sentinel nodes. Rescue for chemotherapy patients with false NO diagnosed with conventional techniques.

E-PS-15-034
EGFR mutation in metastatic pulmonary squamous cell carcinoma - a rare case
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Background & Objective: Epidermal growth factor receptor (EGFR) gene mutations have been reported to be clinically significant in non-

small cell lung cancer (NSCLC). However, because most previous studies focused only on adenocarcinomas we focused on squamous cell carsinoma.
Method: We herein present the case of a 83-year-old male smoker, diagnosed with stage IV squamous cell lung carcinoma, with femoral bone metastasis.
Results: Histopathological examination of the femoral head resection surgical material revealed that it was compatible with low differential carcinoma metastasis. Immunohistochemical p63, p40, CK5 / 6, CK7 and pancytokeratin studies showed diffuse positive staining in tumour cells. It was considered to be compatible with pulmonary squamous cell carcinoma metastasis. In the tumour block, ALK and ROS gene rearrangements were assessed by FISH and negative results were obtained. The C.2573T> G point mutation was detected in the EGFR gene exon 21 by PCR. Treatment of tyrosine kinase inhibitor was initiated because of EGFR mutation. The patient is alive.
Conclusion: The incidence of EGFR mutations was positively associated with nonsmall cell carcinoma especially adenocarsinoma. In the study of Shin et al, a high incidence of EGFR mutations was observed in patients with adenosquamous cell histology (45.5%), which is in agreement with previous studies in Asian population that have reported a high frequency of EGFR mutations in tumours with this histology (28.6% to 38.2%). In the same study, the rate of EGFR mutation was about 4% in squamous cell carcinomas.

E-PS-15-036
Optimisation of enrichment protocols for colorectal circulating cancer cells detection

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Background & Objective: Circulating tumour cells (CTCs) identified in the1800s and presumed responsible for the metastatic process shed from the tumours in the peripheral blood where they can be enriched, detected and analysed. Their detection is promising for efficient anticancer therapies, but due to their very low concentrations , CTCs detection and identification still remain challenging requiring high analytical methods, in a combination of enrichment and detection. CTCs detection is based on their physical or biological properties. Epithelial and tumour cells express CD326 antigen (EpCAM) and cytokeratins, extensively used in enrichment strategies. The aim of our study was the development and optimization of an enrichment protocol for colon cancer tumour cells.
Method: We used for CTCs enrichment a positive selection kit based on the EpCam antigen expression (MACS CD326 (EpCAM) Tumour Cell Enrichment and Detection kit - Milteny). This is selecting blood EpCAM expressing cells based on their magnetic separation. The mononuclear cells were isolated by gradient density centrifugation, labeled with EpCAM magnetic beads and then separated on magnetic column. To validate our experiment, we spiked into a normal blood sample various concentrations of HT-29 adenocarcinoma cells and recovered them after performing the enrichment protocol.
Results: Our results show the ability to recover the HT-29 adenocarcinoma cells at low concentrations proving the high efficiency of the enrichment method. Moreover, we were able to detect the separated cells by flow cytometry after their fluorescent staining with cytokeratins.
Conclusion: Our enrichment method was validated by flow cytometry analysis of the separated cells populations.

E-PS-15-037
Mucosal gene expression profile in Ulcerative Colitis: ISG15 as putative marker of remission state

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Background & Objective: A number of gene expression studies performed in inflammatory bowel diseases (IBD) have provided significant information towards systemic and local inflammatory response. The aim of this study was to identify the differences at gene expression level in mucosa from patients with active ulcerative colitis (UCA) and patients in remission (UCR) compared with normal controls.
Method: Eight adult patients with a diagnosis of UC, (four with active lesions and four in remission) and three controls (without IBD) were enrolled in the study. All the individuals underwent mucosal biopsy during colonoscopy. Gene expression profile was evaluated by PCR array using the Human Crohn's Disease RT2 Profiler PCR Array (PAHS 169Z, Qiagen).
Results: Among the 84 genes investigated, 60 genes were differentially expressed in terms of fold regulation (2<FR<-2) in UCA (57 up-regulated and three down-regulated) and 37 in UCR (36 up-regulated and one down-regulated) compared to controls. Genes with statistical significance ($p<0.05$) in UCR patients compared to controls, were CASP1, LYZ and ISG15. However, since a significant up-regulation of both CASP1 and LYZ was observed also in the UCA group, only ISG15 levels remained associated to the remission state.
Conclusion: These preliminary data represent a starting point for defining the gene profile of UC in different stages in Romanian population. Identification of genes implicated in UC pathogenesis could be useful to select new therapeutic targets.
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E-PS-16 | Nephropathology

E-PS-16-001
IgG4 related disease with unusual morphology

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Background & Objective: Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated condition with unclear etiology, that has characteristic pathologic, serologic, and clinical features.
Method: A 43-year-old woman complained of an abdominal pain. Abdominal ultrasonography showed a mass at the lower pole of left kidney extending to renal sinus. She also had enlarged paraaortic lymph nodes, a peripancreatic cyst-like lesion and multiple small nodules in the lungs. Patient underwent radical nephrectomy.
Results: Renal tumour was 3.5x3.5x3 cm in dimensions with indistict margins. Its microscopy revealed a fibroinflammatory process strongly suggestive of IgG4-RD. It was consisted of lymphoplasmacytic infiltrate, frequent lymphoid follicules and eosinophils, storiform fibrosis, and obliterative phlebitis. IgG4 expressing plasma cells were diffuse and abundant. Interestingly, there were numerous Touton-like multinucleated histiocytes in the lesion widely distributed among other elements. Serology supported diagnosis of IgG4-RD.
Conclusion: The diagnosis of IgG4-RD is complex that requires a combination of clinical examination, imaging, histological, and serological analyses. The three major histologic findings according to international consensus statement are: 1) a dense lyphoplasmacytic infiltrate; 2) storiform fibrosis; and 3) obliterative phlebitis. Our case shows that multinucleated histiocytes may occur in IgG4-RD and should not exclude its diagnosis. Awareness of this issue is required as we have learned that a biopsy from one of the enlarged cervical lymph nodes of our patient was signed out as tuberculous lymphadenitis 5 years ago despite negative cultures.

E-PS-16-002
Rapidly progressive C1q nephropathy in a child
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Background & Objective: C1q nephropathy is one of the rare form of glomerulopathy, characterized by dominant C1q deposition. It occurs rather in children and young adults with proteinuria or nephrotic syndrome. Clinical and hitological presentations predict patient's prognosis. We experienced a case of rapidly progressive C1q nephropathy in a 4-year-old girl.
Method: She caught a cold and edema appeared two years ago. She was diagnosed as nephrotic syndrome without hematuria or renal dysfunction and treated with predonisolone 2 mg/kg/day. Two months later, a renal biopsy was done. Methylpredonisolone pulse therapy, administration of cycloinsporine and MMF were not effective. Her GFR lowered and she began to be treat with peritoneal hemodyalisis in five months later. The patient had no evidence of SLE or HIV.
Results: The renal biopsy contained 66 glomeruli. Almost all the glomeruli showed segmental to global lesion. The mesangial area increases with matrix and pale eosinophilic deposits, resulting in nodular lesion. There were crescent formation with adhesion. Tubular degeneration was prominent. Immune fluorescent examination showed positive staining of C1q and IgG in the mesangial area and along the capillary wall. Electron microscopically, dense deposits were seen in the mesangial area, subendothelium and subepithelium. Podocytes showed marked foot process effacement with villous transformation.
Conclusion: In C1q nephropathy, outcome is known to be poor, however, its progression to ESRD is known to be commonly slow. Srivastava et al has reported rapidly progressive C1q nephropathy similar to our case. We discuss on the correlation between its hitology and clinical presentation.

E-PS-16-003
Alport syndrome: a very unusual entity
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Background & Objective: Alport Syndrome, first described in 1927 is a rare genetic disorder characterized by progressive kidney disease and abnormalities of the ears and eyes caused by defects in the gene that encodes the several chains that form the type IV collagen, the major structural component of glomerular basement membranes. Its prevalence is estimated at 1/50 000.
Method: A 22-yo male with a clinical history of rhinitis, slightly high THS levels, cognitive delay, attention deficit, hyperactivity, sensorineural hearing loss and microscopic hematuria with progressive kidney disease. His brother, mother and grandfather also had microscopic hematuria, A kidney biopsy was performed and the gross examination under the stereoscopic microscope revealed a white granular deposit on its surface. A fragment was blindly removed and frozen for immunofluorescence stains, another one was placed in glutaraldehyde for electronic microscope and the remaining tissue was fixed in formalin and processed for light microscope.
Results: Light microscopic examination demonstrated segmental lesions of the tuft, with a focal and segmental glomerulosclerosis like pattern, interstitial expansion due to chronic tubulointersticial nephritis and tubular athropy and the white granular deposits previously described were interstitial lipid filled foam cells. The ultrastructural study demonstrated thickening of the GBM and several strands forming a basket-weave pattern. Electro dense granules were also found.
Conclusion: Clinical treatment and dialysis are used to treat patients with end-stage renal failure and kidney transplantation is usually successful, but about 10% of transplanted patients develop nephritis in the graft. This typical case with all its characteristic features is presented as it is important to recognize Alport syndrome early in the course of the disease to improve longevity and prognosis.

E-PS-16-004
A rare case report: IgG4 related disease in nephrectomy specimen
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Background & Objective: IgG4 related disease (IgG4-RD) is a recently recognized multi-systemic fibro-inflammatory disorder. Here we report a case of a male patient who presented with a large solitary solid renal mass without a previously known history of IgG4-RD.
Method: A 52-year-old male patient with renal colic symptoms was consulted. Contrast enhanced computer tomography scan showed an ill-defined solid solitary hypo-vascular mass lesion in the left renal pelvis, which was considered suspicious for renal cell carcinoma. The patient underwent laparoscopic left nephroureterectomy.
Results: Gross examination revealed a white firm fibrotic homogenous mass-like lesion measuring 9cm at the pelvis and inferior pole. Dense mononuclear tubulointerstitial nephritis and storiform fibrosis were the most remarkable histopathological findings. The mononuclear inflammatory cells were predominantly consisted of plasmacytes. Occasional eosinophils and focal mononuclear tubulitis were noted. Obliterative phlebitis was frequently identified. IgG4+ plasma cells were counted more than 100/HPF in the maximum expression area.
Conclusion: Diagnosis of IgG4-RD is based on morphological and immunohistochemical findings: dense lymphoplasmacytic infiltrate rich in IgG4 (+) plasma cells, storiform fibrosis, and obliterative phlebitis. IgG4-RKD is mostly diagnosed in the patients with previously known history of IgG4-RD on needle biopsies. We report a case of IgG4-RKD in a male patient who presented with a large solitary renal mass without either a previously known history or extra-renal organ involvement. Clinicians, radiologists and pathologists should be aware of the possibility of IgG4-RKD even in such an unexpected scenario.

E-PS-16-005
Acute renal failure and hypercalcemia as the first manifestation of sarcoidosis - case report
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Background & Objective: Hypercalcemia can lead to significant impairment in renal function. Hypercalcemic nephropathy can arise by increased absorption or ingestion of calcium or by depletion of calcium from skeleton. We report a case of sarcoidosis in young male where the initial presentation was elevated serum calcium level and acute renal failure.
Method: Laboratory evaluation revealed acute kidney injury with the serum creatinine of 6.24 mg/dL, and e-GFR 13.4 mL/min. Proteinuria was 2g/24h. His CT Chest revealed mediastinal adenopathy. The patient denied the consumption of calcium-containing medications, and vitamin D. An ultrasound -guided percutaneous kidney biopsy was performed.
Results: The kidney biopsy did not reveal noncaseating granulomatous inflammation. Glomeruli appeared normal in size and cellularity. Tubular degenerative changes were accompanied by intraluminal and interstitial basophilic calcifications, consistent with calcium phosphate. The calcium phosphate composition of the renal calcification was confirmed with the von Kossa stain. The interstitiun showed inflammation composed of lymphocytes, as well as focal tubular atrophy and interstitial fibrosis. Immunofluorescence staining for IgG, IgA, IgM, C3, C1q, kappa- and lambda- light chains was negative. Based on the renal biopsy findings a diagnosis of tubulointerstitial nephropathy with calcium phosphate

deposits, consistent with naphrocalcinosis was made. Following of the renal biopsy results the patient was worked up for etiologies of nephrocalcinosis. Based on clinical findings and lymph node biopsy, the diagnosis of sarcoidosis was established.
Conclusion: In summary, this case indicates that sarcoidosis must be taken into consideration in patients with nephrocalcinosis and acute renal injury.

E-PS-16-006
Fibrinogen A alfa-chain amyloidosis – case report
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Background & Objective: Amyloidosis is a disorder characterized by the deposition of aggregates of insoluble fibrils originating from proteins that exhibit anomalous folding. It is classified according to the nature of their causative precursor protein. We report a case of hereditary fibrinogen A alfa-chain amyloidosis (AFib) diagnosed by immunofluorescence.
Method: A 48-year-old woman from Northern Portugal presented with proteinuria of 1,69 g/day, hypertension and hypercholesterolemia without history of underlying inflammatory disease or family renal disease. A renal biopsy was done.
Results: On histological examination the renal biopsy displayed abundant glomerular amyloid deposition without vascular or interstitial involvement. Direct immunofluorescence (DIF) showed strong reactivity for fibrinogen in the absence of serum amyloid A, transthyretin and immunoglobulin light chains (kappa and lambda). The genetic study performed in peripheral blood revealed a point mutation in fibrinogen A alfa-chain gene - p.Glu545Val.
Conclusion: Variants of AFib cause the most common type of hereditary renal amyloidosis in Europe. In Northern Portugal there have been reported families with this type of amyloidosis. The predominantly glomerular involvement by amyloid associated with the demonstration of fibrinogen in the DIF should lead to the suspicion of this type of amyloidosis in the appropriate clinical and epidemiological context. Identification of amyloidogenic protein is of utmost importance for therapeutic management and ensures family screening.

E-PS-17 | Neuropathology

E-PS-17-001
An unusual case of central nervous system anaplastic haemangiopericytoma with epithelioid component
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Background & Objective: Solitary fibrous tumours (SFT) and haemangiopericytomas (HPC) of the central nervous system are mesenchymal spindle cell neoplasms of a common diagnostic spectrum, both characterized by NAB2-STAT6 gene fusion. Isolated case reports have documented the uncommon finding of an epithelioid component within these tumours. We report one such case, resected from the left cerebellar-pontine angle of a 41-year-old woman and confirmed by molecular analysis.
Method: In addition to the usual H&E-stained section, a panel of immunohistochemical stains, fluorescent in-situ hybridization (FISH) for SYT gene rearrangement and targeted sequencing using Archer®Fusionplex® Sarcoma Analysis kit with confirmatory RT-PCR of the gene fusion of interest were performed.
Results: The tumour comprised densely packed spindle cells with numerous thin-walled vessels. A focal epithelioid component, featuring pleomorphic cells arranged in nests and pseudoglandular structures was also present. Mitotic activity was brisk, up to 29/10 high-power fields. Only the spindle cells showed CD34 positivity, whereas the epithelioid component was highlighted by CAM5.2. Both spindle and epithelioid components were positive for BCL-2, CD99 and focally for STAT6. FISH for SYT gene rearrangement was negative. NAB2(exon:4)-STAT6(exon:2) gene fusion was detected by the aforementioned sequencing assay and RT-PCR, confirming the diagnosis of an anaplastic HPC.
Conclusion: Practising pathologists should include HPC as a differential diagnosis when encountering tumours with biphasic morphologic patterns in the central nervous system. The finding of a NAB2-STAT6 gene fusion will help to confirm the diagnosis. Nevertheless, in view of its rarity, the implication of an epithelioid component within a SFT/HPC on prognosis and treatment remains unclear.

E-PS-17-002
Gerstmann-Sträussler-Scheinker disease: a case report
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Background & Objective: Gerstmann-Sträussler-Scheinker disease is a genetically determined fatal neurodegenerative disorder, part of the familial prion diseases. It is a progressive cerebellar syndrome, with pyramidal signs and progressive cognitive decline.
Method: We report the case of a 61-year-old woman who had two brothers and a sister with cognitive decline started in the fifth decade of life, suspected of Alzheimer's disease. When her sister died, her brain was studied and the sister was diagnosed with Gerstmann-Sträussler-Scheinker. After that, a molecular study of the PNRP gene was performed in our patient, finding a heterozygous mutation in codon 218. When our patient died, eight years after the initial symptoms, the central nervous system was studied and she was also diagnosed with Gerstmann-Sträussler-Scheinker disease.
Results: The histological study showed multiple multicentric PrP-amyloid plaques in the cerebral and cerebellar cortex, along with spongiform change and associated with widespread neurofibrillary tangles in the cerebral cortex.
Conclusion: The actual case shows the histological, immunohistochemical and genetic characteristics of Gerstmann-Sträussler-Scheinker, a genetically determined form of human prion disease. A disease that produces a progressive cognitive decline with a fatal ending. With the histologic study of the brains of the two sisters and the molecular study of our patient, it had been possible to establish the diagnosis of GSS and rule out familial Alzheimer's disease.

E-PS-17-003
A primitive neuroectodermal tumour in an adult: Case report
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Background & Objective: The histopathologic features of a primitive neuroectodermal tumour (PNET), appearing as an intracranial mass in an adult for a solid tumour.
Method: A 32-year-old woman with new-onset symptoms of visual disturbances not attributable to structural changes of the eye was intermitted in our hospital for further investigation. An MRI scan performed in the dome showed an extraparenchial sphincter coagulation process located beside the right frontal bone, measured at 2, 7 x2, 93 x3, 4 cm, with broad contact with the meninges. The formalin fixed tissue was studied with haematoxylin/eosin.
Results: Microscopic examination showed a malignant small round neoplasm in a diffuse pattern displaying a brisk mitotic rate as well as

necrosis and was set for differential diagnosis between glioblastoma and PNET. This case was sent for consultation and immunohistochemical examination. The Immunohistochemical profile showed intense diffuse immunoreactivity for synaptophysin and NKX2.2. No immunoreactivity for FOX2B, CD99, Pankeratin, EMA, ER, PR, GFAP, NF and chromogranin-A. The cell proliferation marker ki-67 was 40%.
Conclusion: This occurrence is extremely rare, because PNET typically appears in patients aged 5 - 25 and it is an aggressive neoplasm. Due to this low incidence, universally accepted guidelines are still unavailable.

E-PS-17-004
Brain and pulmonary metastasis from type A thymoma: case report of an extremely unusual malignancy
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Background & Objective: Type A thymoma, a relatively uncommon subtype of thymoma, is a low-grade thymic epitelial neoplasm composed of bland spindle or oval cells with few or absent lympocytes admixed. Extrathoracic metastasis are rarely reported, but long-term follow up is recomended to stablish an adequate treatment.
Method: We describe a patient presenting an unusual clinical course, characterized by pulmonary and brain metastasis during follow-up.
Results: Our patient presented an anterior mediastinal mass in 2007 and a complete thymectomy was surgically performed through median sternotomy. Tumour infiltrated the fibrous capsule microscopically, invading the surrounding adipose tissue of the mediastinum. Histological analysis revealed a neoplasm characterized by bland-looking spindle-shaped epithelial cells with scattered lymphocytes, consistent with type A thymoma. Surgical margins were free of tumour, and adjuvant radiotherapy was administered. A chest CT in 2014 revealed a small nodule in lower left lung lobe and resected with wedge resection. In 2018, during a visual disorder episode, a CT showed an intraparenquimatous round lesion on the right parieto-occipital brain lobe and resected with right occipital craniotomy. The histologic examination of two lesions showed a well defined, round-shaped nodule, consistent with metastasis of type A thymoma.
Conclusion: Extrathoracic metastasis from thymomas, often associated with type B thymomas or thymic carcinomas, are rarely reported; despite of type A thymoma is considered a low-grade malignancy, without any significant risk of local recurrence or metastasis, many reports have suggested that thymomas may relapse or spread many years after resection of the primary tumour. The current case shows that long-term follow up is compulsory to detect recurrences and to stablish the best treatment.

E-PS-17-005
Pathogenetic mechanism of limb girdle muscle diseases: an integrated approach
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Background & Objective: Neuromuscular diseases are a heterogeneous group of disorders due to a different eziopathogenetic mechanism, age of onset, follow-up and clinical characteristics, therapy and prognosis. Muscle biopsy is indicated in patients with a suspected myopathy from the clinical point (presence of muscle weakness, muscle cramps or discomfort and muscle fatigue with activity) associated with any special investigation such as serum enzymes, muscle imaging and electromyography. The diagnostic work-up need data from different methods which also play a key role in pathogenetic mechanism definition which is still largely unknown for many limb girdle muscle diseases.
Method: All histological, histochemical and immunohistochemical and morphometric analysis are performed on frozen tissue. Electron microscopy must be carried out on thin sections of epoxy embedded material.
Results: The immunohistohemical analysis is performed to identify specific protein loss suggesting a final molecular approach to obtain a definite diagnosis. The main aspect is related to the relationship between type I and type II fibers evaluated by morphometric approach using dedicated software. The ultrastructural analysis is a useful tool to clarify the pathogenetic mechanisms and to make a differential diagnosis based on the presence of submicroscopic markers. The ultrastructural analysis allows to show nuclei, myofibrillar sarcoplasma, extramyofibrillar and mitochondria alterations or to reveal some new sarcoplasmic or nuclear structures (filaments, fibrillar structures, lysosomal inclusions).
Conclusion: In conclusion, the diagnosis of neuromuscular diseases needs a multidisciplinary approach with a complex diagnostic work-up. The muscle biopsy plays a key role to address the genetic study allowing to a future tailored gene therapy.

E-PS-17-007
Desmoplastic infantile astrocytoma: a rare case
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Background & Objective: Desmoplastic infantile astrocytoma and ganglioglioma (DIA/DIG) is a rare benign (World Health Organization as grade I) glioneuronal tumour. The tumour typically occurs in infants, most often as a large and cystic lesion. DIA/DIG are slow-growing tumours, with good prognosis after complete surgical removal, and rarely require chemotherapy or radiotherapy. However, there have been few cases of DIA that demonstrated malignant features and/or spontaneous recurrence or metastases.
Method: We report a case of a 6-month-old girl who presented with progressive restless and crying. Computerized tomography (CT) of the head revealed a large predominantly cystic tumour on right parietooccipital lobe. The patient underwent subtotal resection and re-operated twice because of haematomas.
Results: Histopathological examination revealed mainly spindle astrocytic proliferation and poorly differentiated component of the tumour was diagnosed as DIA/DIG. Neoplastic astrocytes were positive for GFAP and the poorly differentiated cells were positive for Neu-N.
Conclusion: We wanted to present this case because infantile astrocytoma and desmoplastic infantile ganglioglioma (DIA/DIG) is very rare.

E-PS-17-009
Angiolipoma of the spine: a case report and review of the literature
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Background & Objective: Angiolipomas are benign tumours that rarelyy occur in the spine, accounting for <1.5% of all spinal neoplasms. Angiolipomas are rarely considered in the differential of a spinal space-occupying lesion and may be mistaken for a malignant tumour on pre-operative imaging.
Method: We report a case of thoracic spinal angiolipoma and review the literature using the Pubmed/Medline databases of spinal angiolipoma cases reported between 2000-2017.
Results: A 48-year-old female presented with a 7-year history of bilateral lower limb numbness and weakness. Magnetic resonance imaging showed an extradural mass in the posterior epidural space extending from T6-T9 that was isointense on T1-weighted scan and mildly hyperintense on T2-weighted scan. The clinicoradiological differentials included epidural meningioma, lymphoma, neurogenic tumour, epidural hemangioma, and an epidural metastasis. The patient underwent a laminectomy and surgical excision, which resulted in resolution of symptoms.

Histopathological examination of the mass showed a lesion composed of mature adipocytes and vascular elements consistent with an angiolipoma. Our literature review showed 97 spinal angiolipoma cases reported between 2000-2017. Majority of the cases were in females, occurred in the thorax, manifested as chronic paraparesis, numbness, and lower back pain, and were hyperintense on T2-weighted imaging on magnetic resonance imaging. All cases were treated with laminectomy and/or surgical resection with majority having favourable outcomes.
Conclusion: Spinal angiolipomas are rare, benign neoplasms that manifest with progressive neurological symptoms. It is important to consider this entity in the differential diagnosis for a spinal epidural lesion because of their favourable prognosis with surgical resection.

E-PS-17-010
Intrasellar meningioma: a case report
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Background & Objective: To present a case of an intrasellar meningioma in a 33yo male patient.
Method: The patient presented with a history of 1.5-year fatigue, anemia and erectile dysfunction. Hormonal tests demonstrated low levels of ACTH, Cortisol, FSH, LH and Testosterone. Formal visual field testing showed normal findings. An MRI scan revealed an intrasellar heterogeneous mass measuring 24x24x17mm, with suprasellar extension causing displacement of the optic nerves, the optic chiasm and a pressure imprint to the 3th ventricle. The mass was incompletely resected through transsphenoidal approach (total dimensions 18x15x3mm) and sent to our laboratory where it was examined using haematoxylin and eosin slides, as well as immunohistochemical techniques.
Results: Microscopically the tumour was composed of epithelioid tumour cells with nuclear pseudoinclusions, forming lobules, as well as fascicles of spindled cells, in a collagen matrix, with the presence of whorls and psammoma bodies. The tumour cells were positive for Vimentin, EMA and p63, focally positive for S-100, Ker AE1/AE3 and Ker 8-18, while CD34 was negative. Ki-67 was estimated at less than 5%. These findings were compatible with the diagnosis of Grade I transitional meningioma.
Conclusion: Meningiomas are a group of mostly benign slow growing neoplasms, with the majority arising in intracranial, intraspinal or orbital locations. They are more common in females, with a median age of patients being 65years. The most common lesion of the sellar region is the pituitary adenoma, while meningiomas account for 1% of all lesions of the sellar region and 5% of all sellar neoplasms.

E-PS-17-011
A case report of papillary tumour of pineal region
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Background & Objective: To present a case of a tumour located in the region of the pineal gland. Our patient presented with a history of headache and disturbance of vision. An MRI was performed indicating a tumour probably a pineocytoma. The tumour was surgically resected.
Method: Our specimen composed of brown tissue fragments totally measuring 1,5X1,5X0,3 cm. The H&E stain showed a tumour with papillary architecture or solid morphology which consisted of small cells with eosinophilic to clear cytoplasm and round to oval nuclei without considerable pleomorphism. 0-1 mitosis was observed/10HPF. Tumour necrosis or vascular proliferation were not present. Immunohistochemical study showed positivity for CKAE1/AE3, vimentin, S100 protein, while synaptophysin was only focally positive. EMA, GFAP, chromogranin Aand PgR were negative. Ki67(MIB1) was estimated to be positive in 8% of the tumour cells.
Results: A diagnosis of a papillary tumour of the pineal region was considered morphologically and immunohistochemically confirmed.
Conclusion: Papillary tumour of the pineal region although rare, should always be considered in the differential diagnosis of tumours located in the area of the pineal gland.

E-PS-17-012
Pleomorphic xanthoastrocytoma with anaplastic features: a case report
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Background & Objective: Pleomorphic xanthoastrocytoma (PXA), one of the rarest CNS malignant neoplasias of astrocytic origin was first described in 1979 and it is classified as a WHO grade II malignancy, with a rather good prognosis. On the other hand, pleomorphic xanthoastrocytoma with anaplastic features (PXA-AF) tends to behave as a WHO grade III anaplastic tumour.
Method: A 54-year-old male came into the ER with a history of worsening migraines. The radiology studies revealed a left temporal, partially cystic tumour with a mural nodule and marked perilesional oedema. Patient underwent a left-sided pterional craniotomy and multiple white-tan, fragmented tumour-tissue specimens were sent to our Pathology Laboratory.
Results: Microscopically, there were compact and hypocellular areas composed of pleomorphic cells with abundant eosinophilic cytoplasm or xanthomatous/foamy appearance {GFAP (+), S100 (+), CD34(+ focally), EMA (-), CAM5.2 (-), HMB45 (-), Vimentin (-)}. Mitoses were >5/10HPF and there was prominent necrosis. Reticulin stain showed increased density and fragmentation of reticular fibers. Based on the histology and the immunohistochemistry findings, the tumour was signed out as a PXA-AF.
Conclusion: PXA-AF is a rare bird as there have been less than 20 case reports in the last 30 years. The WHO 2016 classification of tumours of the CNS categorizes both PXA and PXA-AF (now known as anaplastic pleomorphic xanthoastrocytoma) under "Other astrocytic tumours". Tumour grading according to histological findings and immunophenotype is strongly encouraged. CD34 patchy staining is a major finding which can be helpful when making a differential diagnosis from giant cell glioblastoma multiforme.

E-PS-17-013
Role of pathologist in driver of treatment of CNS tumours
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Background & Objective: The incidence of Central Nervous System (CNS) tumours is gradually increasing. Furthermore, metastatic neoplasms are frequently seen in neuropathology practice as a major cause of mortality and morbidity. This poster will focus on answering these questions and share the value of a multidisciplinary approach in the management of brain tumours in neurosciences, which is gradually increasing in importance, and how pathologists execute this art.
Method: For this purpose all scientific datas searched base on pubmed, also include last edition books. Briefly explained; number of metastases, macroscopic and microscopic features, primary CNS neoplasms in the differential diagnosis of metastases, approach to neoplasm of unknown primary in CNS, site specific or restricted markers, ancillary testing.
Results: Pathologists try to reach a more accurate diagnosis by mentally filtering a synthesis, comprising age, radiological characteristics and microscopic findings in the sample sent, starting already from the intraoperative diagnosis process.

Conclusion: In conclusion, pathologists are aware of their responsibility in neurosciences which is increasing in importance, know the value of a multidisciplinary approach in the management of brain tumours together with oncologists, surgeons and radiologists and play an important role in the administration of individualized molecular treatment in metastatic cancers such as lung, breast and melanoma cancer by using skillfully immunohistochemical arguments not only in the accurate diagnosis of primary tumours but even in tumours where the primary source cannot be identified radiologically.

E-PS-17-014

Primary central nervous system lymphoma associated to Dandy-Walker malformation, a very difficult diagnosis

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Background & Objective: Primary central nervious system lymphoma is a rare disease in immunocompetent patients, with an incidence of 5/1,000,000 person-years.

Method: We describe a case and review the literature.

Results: 47 years-old woman, with Dandy walker malformation and hydrocephaly, developes headache, somnolence and vomits. MRI shows addicionaly an ependymal/subependymal linear and nodular lesion highlighted by the contrast with perilesional edema was observed aroud temporal, occipital and frontal horns of lateral ventricles. Multiple cytologies were taken, reporting cells with moderate atypia of medium size and scarce cytoplasm suspected of malignancy. CSF biochemistry detected hypoglycorrha-chia, high protein levels, and high ADA. After presenting progressive cognitive deterioration, derivation and cultures were performed without finding germs, empirical treatment was given for mycobacteria and parasites without improvement. When corticosteroids were added, an undulating course was observed, however, it showed multiple convulsive episodes and hyperthermia, finally dying 1,5 months after without a definitive diagnosis. An autopsy was made and the study of CNS shows a cellular proliferation formed by round, medium-large cells, with scarce basophilic cytoplasm and atypical nuclei infiltrating sheets and intense necrosis, the brain tissue adjacent to the lateral ventricles, nuclei from the base, geniculate body and internal capsule. It also compromised meninges, bulge and spinal bulb. The tumour cells were positive for CD20, BCL2, BCL6, MUM1 and EBV and were negative for CD3 and CD10. The rest of the organs were studied, including lymph nodes and bone marrow, without being compromised by lymphoma.

Conclusion: We present because it is an infrequent pathology and its association to malformations make more complicated to reach a timely diagnosis.

E-PS-17-015

Central nervous system hemangioblastomas: three case reports

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Background & Objective: Central nervous system hemangioblastomas (HGB) are rare benign vascular tumours. Cerebellum is the most common location (83%). They can occur either sporadically (67 %) or associated with Von Hippel–Lindau disease (VHL; 33 %).

Method: A retrospective study of cases of HGB diagnosed in our department between 2006 and 2017. The histopathological as well as clinical characteristics of this rare disease are discussed.

Results: Three cases were reported. All the patients were men, aged 13, 52 and 58-year-old. One patient presented with intracranial hypertension's symptoms, the second with a static and kinetic cerebellar syndrome and the third with a headache. One patient had a familial history of VHL disease. In all cases, imaging revealed a vascularized cerebellar tumour. In two cases, the lesion was resected. In the other case patient underwent a biopsy. In all cases, microscopic study showed a tumour formed by large numbers of thin-walled, fairly closely packed blood vessels and intervening polygonal stromal cells with clear cytoplasm and hyperchromatic nuclei. Immunohistochemical studies revealed no staining for keratin and Pax 8 in stromal cells.

Conclusion: The main histopathologic differential diagnosis of HGB is metastatic renal cell carcinoma. Although hemangioblastomas are benign tumours and generally are not invasive in nature, its pathogenic action derives from its mass effect and from peritumoural edema. Advences in microsurgery techniques allow total resection with a low mortality rate.

E-PS-17-016

Primer pleomorphic xanthoastrocytoma with anaplastic features: a case report and review of the literature

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Background & Objective: Pleomorphic xanthoastrocytoma(PXA) is a rare astrocytic tumour that is seen less than %1 of all astrocytic glial tumours. It is classified as a low-gradetumour (Grade II)according to WHO classification of tumours of the central nervous system. It usually occurs in young adultsand children. PXAs are typically located on the supratentorial region, especially on the temporal lobe, which is considered as superficial involvement, as a well-circumscribedmass. It is known to have favorable prognosis. Only %9-20 of PXAhas anaplastic features.

Method: 25-year-old woman who visitedthe ER of our hospital due to having seizures. It was not accompanied by any neurological symptoms and physical defects. Brain MRI with contrast, showeda well-defined lesion in the right parietal region, which has aheterogeneoussolid-cystic component, and a 2x2 cm mass. In histopathological examination of the lesion, it was composed of plump, spindle-shaped cells, which haveelongated nuclei with pale-pink cytoplasms and also mono-multinuclear astrocytes with bizarre nuclei with large, pink granular cytoplasms. There were lipid droplets present in some these cells, which are referred to as 'xanthomatous cell'. There was necrosis and mitoses were less than 5 /HPF. In the immunochemical panel of the said lesion;GFAP and CD34 staining showed expression in tumour cells, and Ki-67 proliferation index indicated was %2. Silver staining showed reticulin fibers surrounded by individual cells.

Results: PXA is rare astrocytic neoplasm. After being surgically removed they have the tendency to recur. %9-20 of recurrent tumours progress to anaplastic transformation.

Conclusion: Primer PXA with anaplastic featuresis extremely rare. We presented this case that review of the literature.

E-PS-17-017

Metastatic meningioma to the thoracic pleura

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Background & Objective: Meningioma is a neoplastic growth originating from the leptomeninges. Meningiomas comprise approximately 15% of the primary brain tumours. The majority are benign; less than 1% metastasize. They are most likely to be found in adults older than 60; the incidence appears to increase with age. Rarely are meningiomas found in children. They occur about twice as often in women as in men.

Method: This report describes a case of metastatic anaplastic meningioma involving the thoracic pleura in a 47-year-old woman.
Results: The patient was treated surgically 1,5 years earlier for an anaplastic meningioma of the right parietal vault. One year later, the patient presented thoracic neuralgia and the CT reveal an intrathoracic mass. Percutaneous CT-guided core biopsy is performed for the evaluation of the indeterminate thoracic mass. Histological findings were compatible with anaplastic meningioma (grade III WHO).
Conclusion: Meningiomas arise from arachnoidal cells, most of which are near the vicinity of the venous sinuses, and this is the site of greatest prevalence for meningioma formation. Usually grow slowly, and may reach a large size before interfering with the normal functions of the brain. The resulting symptoms depend on the location of the tumour within the brain. Headache and weakness in an arm or leg are the most common symptoms. However, seizures, personality changes, and/or visual problems may also occur. Extracranial metastases from brain meningiomas is a rare, but well-documented entity. Metastases occur mostly in the lungs, pleura and liver, but may also affect lymph nodes and bones.

E-PS-17-018
Histopathological lesions in a skeletal muscle regeneration model of adipose tissue implantation
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Background & Objective: Skeletal muscle has the ability to regenerate and restore its histology after injury if several reintegrative factors are present (revascularization, reinnervation and longitudinal tension). We have a model of adipose tissue to reconstruct volumetric loss in skeletal muscle where some of these factors are lacking. Our objective is to study histological changes at medium and long term in this model.
Method: Wistar rats previously anaesthetised were removed a piece of muscle in the tibialis anterior muscle using a cylindrical punch. The defect was filled with a same size piece of adipose tissue taken from the same animal inguinal space. Rats were sacrificed at 21, 28 and 90 days post-implantation, muscles were removed and fast frozen. Cryosections were stained using histological, histochemical and immunohistochemical techniques.
Results: Regenerating muscle fibers showed several cytoarchitectural changes that included: fibers with myonuclei clumps, ring fibers, snake-coiled, central spot, split and fragmented muscle fibers.
Conclusion: These lesions can be explained on the basis of the lack of reintegrative factors. The use of animal models were etiopathogenesis can be controlled can be very useful to understand changes appearing in human biopsies.

E-PS-17-019
Prognostic value of immunohistochemical expression of bcl-2 and p53 in glioblastomas
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Background & Objective: Glioblastomas are the most prevalent primary brain malignancy and the prognosis is poor. Age, cognitive status, extent of surgical resection and adjuvant treatment are among the main prognostic factors. Some immunohistochemical markers seem to have a prognostic interest but the results are not unanimous and are sometimes contradictory. The aim of our study was to evaluate the prognostic value of p53 and bcl-2 antibodies in glioblastomas and to find a statistically significant relationship between the expression of these antibodies and the recurrence.
Method: Fifty-two cases of glioblastoma were identified in the Department of pathology of the Military Hospital of Tunis between 2005 and 2016. An immunohistochemical study was performed followed by a statistical analysis analysing the correlation with the recurrence and the overall survival.
Results: The average age of patients was 56 years old. The 1-year survival and 2-year survival were 33% and 4% respectively. The median progression-free survival was 26 weeks. The median survival was 35 weeks. There was Tumour recurrence in 37% of cases. Bcl-2 was expressed in 35% of cases. P53 was present in 13% of cases. Bcl-2 and p53 had no statistically significant relationship with survival and with progression-free survival.
Conclusion: Our study concluded that there's no Prognostic value of bcl-2 and p53's immunohistochemical expression in glioblastomas.

E-PS-17-020
Craniopharyngioma - a case report
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Background & Objective: Craniopharyngioma is one rare slowly developing, usually benign tumour. In majority of cases, such tumours grow above the anterior upper lip of pituitary glandand are located mainly on Sella Turcica. Strike 0,12-2/100.000 people a year and they constitute the 2-5% of all brain tumours. Consequently, the rareness of its development constitutes a significant motivation for its notification and its analysis to scientific community.
Method: A Male patient was diagnosed with craniopharyngioma after MRI with maximum size 2 cm due to often and intense headaches. Subsequently, he was treated with laser for 3 years because of his not surgically removable area. The irradiation of the area caused metacentric angiopathy and in combination that the incident is one hypertensive patient, came up the automatical rupture of the vessels and the formation of subarachnoid bleeding and haematoma. Regarding the symptomatology, he had visual disorders and breathlessness, for around 3-4 days before his death. Finally, the cause of death was cardiopulmonary failure due to pressure on the basic brain structures.
Results: Such tumours are connected with a lot of symptoms from the central nervous system, endocrine systemand eyes. Its sizeis 2-4cm. The diagnosis it depends on clinical and radiological finds and it is confirmed by histological examination.
Conclusion: The most usual and efficient technique for treatment is total surgical removal accompanied by radiotherapy. Nonetheless, after every therapy, there is the danger of many complications like pituitary insufficiency and the development diabetes insipidus.

E-PS-17-021
Analysis of survival and prognostic factors of patients with brain glioma
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Background & Objective: To estimate survival and prognostic factors of brain glioma patients diagnosed in the National Center for Pathology, Mongolia.
Method: We retrospectively analyzed data of 107 glioma patients, who were diagnosed from January 2006 to May 2017. There were 52 (48.5%) male-patients and 55 (51.5%) female-patients, as totally. The mean age was 38.04 years old (ranged from 3 to 77). Clinico-pathologic analysis was performed by using archival slides and formalin-fixed, paraffin-embedded tissue. The Kaplan-Meier method was used for survival analysis, and we used univariate and multivariate analysis for prognostic factors.

Results: All among the cases, glioblastomas were most frequent 35 (32.7%), followed by diffuse astrocytomas 18 (16.8%). Regarding to anatomic location, involvement of multiple lobes was predominated 33 (30.8%), followed by the frontal lobe 22 (20.6%). Overall survival time of gliomas was 19.2 months, for low grade gliomas 28.5 months and 11.7 months for high grade, respectively. According to overall survival, tumour grading ($p<0.001$) and surgery type ($p<0.005$) were independent prognostic factors.
Conclusion: Histological tumour grading and surgery type were independent prognostic factors of glioma patients in Mongolia.

E-PS-17-022
A case of Lafora disease diagnosed by axillar skin biopsy
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Background & Objective: Lafora disease is a rare, progressively deteriorating, neuromethabolic disease. The clinical picture is characterized by large variety of seizure types, myoclonus and subsequent cognitive decline.
Method: A 26 years old woman which presented to emergency unit with three days of increased frequency in myoclonus and seizures. The histopathological assesment performed upon clinical suspicion showed PAS positive cytoplasmic inclusion bodies in the basal region of the eccrine and apocrine gland duct of the axilla.
Results: Axillar skin biopsy was performed and the material was histopathologically reported as "Compatible with Lafora Disease".
Conclusion: We would like to make an emphasis on that it is very important for the pathologist to consider Lafora Disease through differential diagnosis when they come across with a biopsy material of a patient whose history containing of resistant series of seizures, myoclonus and cognitive decline.

E-PS-17-023
Gliosarcoma transforming from giant cell glioblastoma: a case report and review of the literature
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Background & Objective: Gliosarcoma and giant cell glioblastoma (GCG) are a variant of IDH wild- type glioblastoma. while gliosarcoma is accounted for 2% of all glioblastomas, giant cell glioblastoma is accounted for <1%. Gliosarcoma is a biphasic neoplasm that is composed of glial and mesenchymal differantiation. GCG is characterized by bizarre, multinucleated giant cells and occasionally by abundant reticulin network.
Method: A 48-year-old woman visited our hospital with headache and weakness of leg and arm. Brain MRI showed irregularly demarcated, 31x27, 19x14 and 13x11 mm sized masses in the parietal lobe. Microscopic examination revealed necrotic background with mostly multinucleated giant cells, arranged like pseudorosette and perivascular accumulation. These cells showed expression by GFAP. We diagnosed this case as "Giant Cell Glioblastoma". After five months; the patient wasback with similar symptoms. Radiological examination showed 5x3 cm sized mass in the right frontal lobe. Microscopically; in neuropil matrix, pleomorphic glial cells like conventional glioblastoma and spindle cells with ovoid nuclei, pink cytoplasm arranged both of fascicles and whorl pattern. Glial component showed expessionof GFAP and S-100, mesenchymal component showed expression of vimentin. We reported it as "gliosarcoma". After another four months, the patient presented with confusion and radiologically multipl focus on cerebral, cerebellar region was identified. Histomorphologically tumour was compatible with gliosarcoma
Results: Gliosarcoma is a rare and aggressive tumour. Giant cell glioblastoma has better prognosis, although both of them are grade IV tumours.
Conclusion: We presented this case and review of literature.

E-PS-17-024
Intracranial lipoma: rare case
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Background & Objective: Intracranial lipomas are rare developmental lesions, predominantly occurring in the interhemispheric location. They are usually well-encapsulated masses. The masses are often benign, and they most often develop between the age of 40 and 60. Lipomas are characterized by high signal intensity on T1- and T2-weighted images on magnetic resonance imaging (MRI).
Method: 64-years-old man who has diabetes mellitus, was admitted to our hospital with headache. The MRI revealed an intracranial mass in the posterior fossa. Neurosurgeons excised the mass.
Results: Grossly, the tumour measured 6x4.5x3.5 cm in diameters and it was as yellow fat and fragmented. Histopathological examination revealed features consistent with a lipoma with some benign glands and there was no evidence of any malignant transformation.
Conclusion: Dermoid cyst should always be considered as the main differential diagnosis of a such lesion. The lack of presence of all three germ line exclude this entity and we diagnosed this mass as "intracranial lipoma with teratomatous elements".

E-PS-17-025
Intracranial epidermoid cyst; a rare case
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Background & Objective: Epidermoid cysts are rare benign slow growing tumours. They account for approximately 1% of all intracranial tumours.
Method: A 22-year-old woman presented with 3-month history of headache and diplopic vision. She had no relevant past medical history. Magnetic resonance imaging revealed an 4 cm diameter a cyst-like lesion in the right cerebellopontine angle. The lesion removed with surgical excision.
Results: On microscopic examination; wall of cyst lined by keratinized epithelium with distinct granular layer. The cyst contains lamellated keratin. The diagnosis of epidermoid cyst was made.
Conclusion: We present the clinical, imaging, and pathological findings in a patients with epidermoid cyst. They differ from dermoid cysts and mature teratomas were very important. Very rarely, squamous cell carcinoma arising in a cerebellopontine epidermoid cyst. They respond well to surgical excision, although it is recognized that complete excision of the tumour capsule is often not possible due to the high risk of damaging adherent neural or vascular structures. They may recur after incomplete resection but do so over many years. We reported this case because of the rarity of these tumours in this localization and to point to differential diagnosis.

E-PS-18 | Ophthalmic Pathology

E-PS-18-001
Conjuctival melanoma arising from a conjunctival nevus: Histopathological considerations of an uncommonly rare malignancy
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Background & Objective: Conjunctival melanoma is a rare tumour which accounts for 2% of all ocular malignancies. It can arise de novo, from a preexisting nevus or from primary aquired melanosis. This potentially lethal tumour may metastasize via the ipsilateral lymph nodes and in rare cases through the lacrimal duct into the nasal cavities. The best treatment of conjunctival melanoma is its prevention through excision of its precursor lesion.
Method: We report a case of an 81-year-old woman presenting with a pigmented conjunctival lesion on the right eye. Upon local examination, a darkly pigmented, elevated mass on the bulbar conjunctiva was described at the internal angle of the right eye. The mass was excised under peribulbar local anesthesia and sent for histopathological examination.
Results: The final diagnosis was primary conjunctival melanoma developed from a preexisting nevus. Additional immunohistochemical tests have been performed to confirm the diagnosis.
Conclusion: In all pigmented lesions of the conjunctiva, exclusion of a melanoma is mandatory. Incidence of conjunctival melanoma appears to be on the rise. Any patient suffering from a conjunctival melanoma should be referred to an ophthalmo-oncological center for proper treatment. An indefinite follow-up is required for developing novel methods of treatment since the rate of recurrence is very high. Immunohistochemical stainings were vital to distinguish between a nevus and a melanoma and were crucial in establishing the correct diagnosis.

E-PS-18-002
Epibulbar osteoma: a case report of a rare entity
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Background & Objective: Choristomas, form of heterotopia, are benign congenital proliferation of histologically mature elements not normally present at the site of occurrence. These congenital tumours belong to the group of dysembryoplasias and their frequency is 1 to3 per10.000 births. Epibulbar choristomas has several pathological type and osseous choristoma represent the rarest form known as 'epibulbar osteoma'. Our aim was to study the clinical and histological features of this rare entity.
Method: An 11-year-old girl presented a painless calcified tumour in the superotemporal bulbar conjunctiva of the left eye, that was noticed by the parents 7 years previously as a swelling and thought it was increasing in size. The tumour was treated by a surgical excision.
Results: The formalin fixed specimen was processed for histopathological examination. Macroscopically, it corresponded to a nodule measuring 7mm*7mm with hard consistency. Section of the specimen stained with haematoxylin and eosin showed the presence of cortical lamellar bone surrender by thin layer of connective tissue.
Conclusion: Epibulbar osteoma is a rare benign congenital tumour. The diagnosis is essentially histological. The management include two options: observation or surgical excision. And the prognosis is excellent.

E-PS-18-003
Intraocular involvement by mycosis fungoides with large cell transformation
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Background & Objective: Intraocular involvement by mycosis fungoides is a rarely reported event. We present a case of mycosis fungoides with CD30-negative large cell transformation presenting with a worsening vision. The ocular involvement was the first sign of systemic involvement and was a harbinger of CNS involvement.
Method: Literature on intraocular presentations of mycosis fungoides is reviewed and presented.
Results: A woman in her 7th decade of life presented with decreasing vision in her left eye. Examination showed hazy vitreous with 3+ cells. Given a history of mycosis fungoides, vitreous biopsy and a wash were performed. Cytology showed showed large atypical dyscohesive lymphoid cells with abundant cytoplasm, irregular nuclei, dense chromatin, and frequent mitoses. Immunohistochemistry showed the tumour cells were positive for CD45, CD3, CD4 (focal), TIA1, CD56, and granzyme B (focal), and were negative for CD20, CD8, CD5, and CD30. The Ki67 labeling index was > 80%. Diagnosis of intraocular involvement by mycosis fungoides with large cell transformation was made. Shortly after the diagnosis, the patient was discovered to have a frontal lobe brain mass.
Conclusion: The intraocular involvement by MF is quite rare. It can take a form of isolated vitreitis, panuveitis with vitritis, chorioretinal plaques and tumours, and isolated optic nerve involvement. The presenting symptoms of intraocular involvement include blurred vision, blindness, ocular pain, diplopia, and papillary edema. Intraocular involvement is a poor prognostic factor as it is staged IVB (visceral involvement) and it can also portend CNS involvement as in this case.

E-PS-18-004
Adenocarcinoma of the lacrimal gland: a case report
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Background & Objective: Primary ductal adenocarcinomas of the lacrimal gland are very rare and usually show histological and immunohistochemical similarities with salivary duct carcinoma. They constitute less than 5% of all biopsied orbital lesions. The most common epithelial malignancy in this location is primary adenoid cystic carcinoma. Adenocarcinoma is rare and is considered a lacrimal counterpart of salivary duct carcinoma, of which the majority are known to express androgen receptor (AR).
Method: We present the case of a 67-year-old male who reported a mass in the right upper eyelid and exophthalmos of two months of evolution. In the CT scan, a mass measuring 3 x 2 cm in the right lacrimal gland infiltrates soft tissues.
Results: Ocular exenteration was performed identifying a tumour mass in the right lacrimal gland that infiltrated periorbital fat and adjacent periosteum. Histologically, it was a moderately differentiated ductal type adenocarcinoma. In the immunohistochemical study, CK7, CEA, EMA and Androgen receptors (AR) were positive.
Conclusion: Lacrimal gland ductal type adenocarcinoma are rare but highly aggressive tumours. Complete excision with adjuvant radiotherapy is recommended. The clinical behavior, prognosis, and treatment of these tumours are still poorly defined. Early recognition of this highly aggressive tumour ultimately may help to delineate its management. In this way, IHC for AR is an important diagnostic step in this kind of tumours.

E-PS-18-005
Melanocytoma of the conjunctiva - about a case
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Background & Objective: Melanocytoma is a very rare entity, this hyperpigmented tumour is usually observed in the uvea and optic nerves but it can be found at the level of the conjunctiva.
Method: we report the case of a woman A.M aged 64 years old, consult for a pigmented conjunctival neoformation on acquired melanosis, this neoformation is situated at the level of the inferotemporal region of the right eye and has been evolving for nine months. A biopsy excision was realized.
Results: we received a piece of excision from a pigmented conjunctival neoformation after inclusion in full and numerous recounts we find a

regular conjunctival mucosa hyperplastic in places the underlying chorion is dissociated by numerous melanophages between these melanophages we find regular melanocytes with round small central nuclei an Immunohistochemistry study was made objectif : HMB45 :positif CD68 :positif Melanocytoma is a very rare pigmented tumour of unknown prevalence while melanocytoma would be more common in African patients. long considered a malignant tumour, patients with this lesion were enucleated, on 1962 Zimmerman et Gasson have shown the benin character of melanocytoma, the histological aspect is represented by a melanin-filled plump cells, the nuclei are small and round whereas in melanoma the cells are fusiform or epitheloid with a large nucleus nucleus
Conclusion: melanocytoma is a rare benign tumour must be differentiated from melanoma which is poor prognosis

E-PS-18-006
Histiocytoid/signet ring carcinoma of the eyelid. A case report of the "Monocle Tumour"
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Background & Objective: Histiocytoid, Signet Ring carcinomas are a group of poorly differentiated adnexal carcinomas which mainly occur within the eyelids of elder men (median age 65 years). These tumours are considered a subtype of eccrine carcinomas and due to their characteristic clinical presentation which involves both eyelids have been named "monocle tumour". Up until now about 29 cases have been reported in English literature.
Method: We report a case of a 65-year old man with a long standing, gradually growing mass which at first was situated on his upper right eyelid and then began to invade the other eyelid and the orbit. Exenteration was performed and sent the full specimen to our laboratory.
Results: Gross pathology revealed an ill-defined mass involving both eyelids and the periorbital fat. Histology revealed a neoplasm composed of small cells that resembled histiocytes with small round hypercromatic nuclei and abundant lightly eosinophilic cytoplasm. Tumour cells were infiltrating diffusely, forming indian-file like cords with targetoid-like patterns around adnexa and vessels. Immunohistochemical control indicated that neoplasmatic cells expressed ER, GCDFP15, E-Cadherin, CK7, GATA3 but not CK20, FLI1, Chromogranin, S100. The diagnosis was Signet Ring Cell/ Histiocytoid Carcinoma.
Conclusion: Due to the rarity of these tumours one should make this diagnosis only if a metastasis from lobular carcinoma can be ruled out since they present overlapping morphological and immunohistochemical features. The treatment of these tumours is excision with wide margins. Antiestrogen therapy has been used to have some success in advanced cases.

E-PS-18-007
Orbital primary extranodal marginal zone lymphoma spreading to adjacent soft tissue
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Background & Objective: Ocular lymphoma is a rare disease, constituting 1% to 2% of non-Hodgkin lymphomas and 8% of all extranodal lymphomas. In our pathology department is verified only one case of Orbital primary extranodal marginal zone Lymphoma during last 5 years
Method: In July 2017, a 54-year-old male presented with 2-year progressive vision loss in his right eye. He had been generally healthy and denied any significant past medical history. Intraocular pressure of both eyes was within normal limits. Examination revealed mass, anterior and posterior size 5,5 cm and vertical size was 3.2 cm, spreading to around of the optic nerve, inferior and superior rectus were infiltrated and causes left side ptosis. A suspicious clinical diagnosis melanoma or choroidal hemangioma was made. We received tissue specimens from eye in our Lab.
Results: By histological examination there were following changes: Cells were small to medium sized, irregular neclei and inconspicuous necleoli. There were neither blood vessels nor pigmented cells. Also, was done immunohistochemistry and result showed us: CD20 and CD79a were diffusively positive, BCL2 was positive, CD5 negative, CD23 was positive in remaining germinal centres and ki67 was diffusively positive, other lymphoid markers were negative.
Conclusion: This case is presented for its unconventional presentation, rarity of occurrence, and difficulty in diagnosis. With tumour markers such as CD20 and CD79a, BCL2, CD23 and etc. and suitable results confirmed the presence of orbital primary extranodal marginal zone Lymphoma spreading to adjacent soft tissue.

E-PS-19 | Other Topics

E-PS-19-001
Desmoplastic small round cell tumour: a case report in association with mature teratoma
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Background & Objective: Desmoplastic small round cell tumour (DSRCT) is a rare and aggressive neoplasm that occurs mainly in young male patients. Although the histogenesis of DSRCT remains unknown, it is suppossed that this tumour originates from a progenitor cell with potential for multiphenotypic differentiation. The aim of this report is to present a case of DSRCT in a young female patient previously diagnosed with mature teratoma of the ovary.
Method: We report here a case of DSRCT in a 23-year old woman complaining of diffuse abdominal pain and distension for 2 months. Taking into consideration her pathological history (a mature teratoma of the left ovary 6 years ago), it was believed that these symptoms were related to the previous surgical intervention. Radiological investigations and intraoperatory findings showed numerous nodular masses (between 0,5 cm and 10 cm diameter), widespread within abdomen and pelvis.
Results: Morphology was consistent with DSRCT. Immunohistochemical profile showed the coexpression of epithelial, mesenchymal and neural phenotypes. The cytogenetic studies were positive for the EWS-WT1 translocation.
Conclusion: To make a correct diagnosis, a combination of immunohistochemical staining and cytogenetic analysis is useful and very important.

E-PS-19-004
Systemic inflammation under shock of various geneses: variants of development
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Background & Objective: Hemorrhagic shock under the acute pathological blood loss (APBL) in obstetrics, and septic shock under sepsis are one of the main reasons of lethality in ICU. The pathogenesis of APBL had not earlier been considered, but the pathogenesis of sepsis (by Sepsis-3) is not already considered from the point of view, by which systemic inflammation (SI) is a common pathological process. We have previously assigned SI-scale to define probability of development of SI and its phases. There are three the most critical phases: phases of the primary and the secondary flogogenic impact and depressive phase. Goal. To characterize the development of systemic inflammation under shock of different genesis.
Method: The following groups were entered into the retrospective study: septic shock (SS) n=31, including acute process (AP) n=14, age – 54.9 ±16.4 years, lethality – 71.43%; tertiary peritonitis, long and sub-acute

process (SAP), n=17, age – 50.2±5.6 yrs., lethality – 94.12%; hemorrhagic shock under pregnancy and delivery - n=22, age 30.3±1.3, lethality – 26.9%. The SI-scale was used (own design). Phases of SI were registered by intensity of systemic inflammatory response.
Results: We identified SI development in patients with SS (AP and SAP) and with hemorrhagic shock in 100% of cases. The phase of flogogenic impact was revealed in patients with hemorrhagic shock in 40.90%, with SS: under AP in 78.57% and under SAP in 5.88% of cases. The depressive phase dominated in patients with SS (SAP) – 94.12% of cases.
Conclusion: Different phases of systemic inflammation dominated under shock of variant genesis.

E-PS-19-005
Follicular lymphoma with plasmacytoid differentiation: a case report and review of the literature
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Background & Objective: Follicular lymphoma (FL) is one of the second most frequent type of non-Hodgkin lymphoma (NHL), more common in the United States and Western Europe, accounting for about 20% of all lymphomas worldwide, which in China is lower than Western countries. The median age of diagnosis is at 65 years (2). Though classification considered that tumour cells can differentiate into plasmacytoid cells. But with plasma cell differentiation of follicular lymphoma tissue morphology is special, rarely reported at China and abroad.
Method: We reported one case of follicular lymphoma (FL) with plasmacytoid differentiation, and combined with literature to analyze its pathology, immunophenotype, cytogenetic and prognostic characteristics.
Results: The FL mainly consists of centrocytes and centroblast, which was composed of plasma cell-like cells. Immunohistochemical staining results, such as CD20, CD10, Bcl-2, and Bcl-6 was diffuse positive in tumour cells; CD21 and CD23 staining showed that the FDC network was present; CD138, CD38, MUM1 were positive in plasma-like cells; and lambda was positive, but kappa was negative, showing monoclonal results. Gene detection also supported diagnosis of FL, Grade I. The patient was treated with chemotherapy and radiotherapy, which had achieved complete remission (CR), and thirty-six months after diagnosis, she was alive without relapse.
Conclusion: We have reported one case of our encounter, combined with the literature, pathological features, immunophenotype, cytogenetic characteristics, differential diagnosis, as well as treatment and prognosis for further analysis.

E-PS-20 | Paediatric and Perinatal Pathology

E-PS-20-001
Contribution of foetopathological examination in neonatal deaths
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Background & Objective: Fetopathological examination is an important tool used for the identification of the case of death. We proposed to highlight the contribution of fetopathological examination in the establishment of the cause of death to improve the management of future pregnancies.
Method: We conducted a retrospective study in the neonatology and fetopathology departments of the Maternity and Neonatology Center of Tunis. Our Study carried out over a period from January 2011 to December 2016. We included all newborns admitted to the Neonatal Resuscitation Unit who died there before the 28th day of life and in whom a fetopathological examination was performed.
Results: We collected 53 cases, of which only 34 corresponded to our inclusion criteria. Sex ratio was 1.8. 50% of mothers were aged between 20 and 29 years old. Regarding the causes of neonatal deaths, we observed the dominance of respiratory pathologies (31%) then palliative cares with 18%. Next come neurological causes and heart disease with 9% respectively. Other causes include inherited diseases of metabolism (6%) and sudden deaths (6%). A total conformity between fetopathological and neonatological examinations was noted in 27% of the cases, a partial agreement in 40%, a total unconformity in 27% and in only 6% of the cases the fetopathological examination didn't show any abnormalities.
Conclusion: To conclude, we emphasize of the importance of fetopathological examination in the determination of the cause of neonatal deaths by providing an exhaustive diagnosis essential to the management of future pregnancies and to provide a psychological comfort to the family and to the medical profession.

E-PS-20-002
Monochorionic twin pregnancy with one anencephalic twin showing additional malformations
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Background & Objective: Background: Congenital malformations are frequent in twin pregnancies, anencephaly being one of them. We describe a case of monoamniotic monochorionic pregnancy, with one anencephalic twin, whose autopsy also revealed aplasia of the left lung and agenesis of the left kidney.
Results: Case report: A 32-year old pregnant patient was transferred from Psychiatry (because of a suicide attempt) at 29 gestational weeks. The only ultrasound at 21 gestational weeks revealed a twin pregnancy with one anencephalic twin. Her medical history contained only psychiatric problems. At admittance to Gynaecology, the ultrasound diagnosis was confirmed. At 33 weeks an urgent Cesarean section was performed. Both twins were hypotrophic, the anencephalic twin died after 2 hours and was sent for autopsy together with the placenta. Placenta was monoamniotic monochorionic, one umbilical cord contained single umbilical artery. The length of the left foot of the newborn was appropriate for gestational age and he showed typical features of anencephaly. At autopsy, the right lung contained two lobes, the left main bronchus ended blindly with a 0.5 cm node of reddish tissue (histologically proven to be a node of undeveloped lung tissue) at its end. The pulmonary artery showed one opening that could be probed only towards the right lung. Left kidney and ureter were absent. Other organs were grossly and histologically unremarkable.
Conclusion: Conclusion: The prevalence of anencephaly is higher in monochorionic twins and is usually discordant. In singleton pregnancies anencephaly was described in association with other developmental abnormalities but none of them was pulmonary aplasia.

E-PS-20-003
Dissection particularities and histopathological aspects of an acephalus acardius amorphus twin
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Background & Objective: Acephalus Acardia is extremely rare complication of multiple pregnancies and very uncommon congenital malformation. It is among the most severe malformations described in fetuses frequently occurring in monochorionic twin pregnancies due to twin-to-twin transfusion syndrome. The severity of the syndrome depends upon the type of the anastomoses arising between the vascular networks of the two fetuses.

Method: We report a case of monochorionic twins, one being an acephalus acardius amorphus fetus, showing features of extreme sistemic immaturity with no structured organs. Gross examinations have been performed on the dismorphic twin and placenta, along with the histological examination of tissue samples
Results: We observed gross dysmorphic features in the malformed twin and extensive vascular anastomoses in the fused placenta, suggesting that the low pressure and hypoxigenated blood which nourished it could explain the extremely severe dismorphic sequence. Also, the placenta showed the vascular anomalies leading to the twin-to-twin transfusion syndrome. The histopathological examination showed a plethora of findings from immature tissue with distorted architecture to peculiar histological structures such as blood vessels lined by melanocytic like cells.
Conclusion: Monochorionic twins present high risk of complications, ranging from premature delivery to fetal death. The causative event of the acardia acephalus is controversial as divergent hypotheses have been pointed out, such as primary cardiac dysmorphogenesis versus hemodynamical mechanism, based on the abnormal vascular communication between embryos resulting secondary atrophy of the heart and dependent organs

E-PS-20-004
Vascularisation of the placental villi at gestational hypertension and preeclampsia
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Background & Objective: Comparative morphometric study of the placental villi vascularization degree in preeclampsia (PE) and gestational hypertension (GH).
Method: Complex morphological study of 21 PE-placentas (15 moderate and 6 severe), 7 GH-placentas and 10 placentas from uncomplicated pregnancies(control) was performed. Morphometric indices of terminal villi vascularization was determined on CD31 immunohistochemical preparations.
Results: At morphometric analysis of control group, the average number of villi capillaries was 6.2±0.4, the average values of the cross-sectional area and perimeter were 186.2±14.8mkm² and 51.2±3.2mkm, respectively. In GH-placentas, area and perimeter average values were 2.6% and 3.7% higher than the control ($p>0.05$). The number of capillaries corresponded to the control, but the average values of sectional area and perimeter exceeded the control indices by 33.4% and 19.6%, respectively ($p<0.05$). The PE parameters of villi and their capillaries less than at the control group: average values of the villus capillaries area and perimeter at moderate preeclampsia by 21.5% and 15.2% respectively, and at severe - 30.1% and 22.5%, respectively ($p<0.05$). The average number of capillaries reduced by 6.5% and 4.8% at moderate and severe forms. The vascularization degree indexes of villi were lower than control by 15.2% at moderate and 16.8% at severe preeclampsia.
Conclusion: In GH-placentas, the increase of the villi size and capillaries, characterizing the development of compensatory processes. On the contrary, the PE-development characterized by decrease in their size and a decrease in the indicators of vascularization, which reflects the placental hypoxia development.

E-PS-20-005
Morphological and immunohistochemical features of foetal membranes in the pathogenesis of preterm labor
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Background & Objective: Preterm labor (PL) is a pathologic condition caused by multiple etiologies. Every third preterm infant is born to mothers with an intra-amniotic infection, but the main mechanism in other cases remains unknown. The aim was to evaluate morphological features and NOD-1 receptor (nucleotide-binding oligomerization domain-containing protein-1) expression in fetal membranes in cases of PL.
Method: We performed histological (H&E) and immunohistochemical studies on the paraffin-embedded slices of fetal membranes using NOD-1 primary polyclonal antibodies (1:100;Thermo Fisher Scientific, Ventana, Roche). We analyzed 6 cases with term uncomplicated pregnancy (NTP), 12 – with PL (9–vaginal labour (PLV), 3–cesarean section (PLC). We excluded all samples with chorionamnionitis.
Results: The intensity of immunohistochemical reaction was estimated by means of program NIS-Elements. In PLV fetal membranes were characterized by specific alterations facilitating their rupture: thinning, vacuolization of cytotrophoblast, necrosis and micro ruptures of fibroblastic layer. In NTP group NOD-1 expression was intensive in all layers of membranes. NOD-1 expression was lower in PLC in comparison with PLV and NTP groups ($p<0.05$). We did not find significant difference between NTP and PLV groups ($p>0.05$).
Conclusion: Peculiar morphological features and activating pro-inflammatory signal cascades in structures of fetal membranes may be triggers of the specific physiological mechanism that facilitates their rupture.

E-PS-20-006
Postmortem MRI allows to determine the pulmonary hypoplasia as the cause of newborns death with congenital diaphragmatic hernia
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Background & Objective: To study the possibilities of postmortem MRI to pulmonary hypoplasia evaluation in deceased newborns with congenital diaphragmatic hernia.
Method: The results of postmortem MRI examination and autopsy of 23 newborns are compared. C-group (control) - 6 dead newborns without diaphragmatic hernia and lung pathology. DH-group - 10 newborns that died from congenital diaphragmatic hernia. SDH-group - 7 newborns who died after surgery for congenital diaphragmatic hernia. Before the autopsy was performed 3T MRI. On T2-WI in axial projection determined the cross-sectional area of the right (SLR) and left (SLL) lungs and internal perimeter of the thorax (PT). Calculated pulmonary-thoracic ratio (PTR): (SLR+SLL)/PT. At autopsy, pulmonary hypoplasia was assessed by calculating the ratio of lung weight to body weight (LBR) and counting radial alveoli on histological preparations.
Results: On the MR-tomograms, the cross-sectional area of both lungs was minimal at DH-group (666.4mm²) and maximal in C-group (2447 mm²). PTR was also minimal in DH-group (2.75) and maximal in C-group (9.35). In SDH-group, it exceeded the DH-group values by 2.3($p<0.05$) times but was less than C-group by 31.8%($p<0.05$). LBR in DH-group was less by 73.3% of the value of C-group($p<0.05$). The mean values of radial alveolar count in lung tissue in C and DH groups were 5.2 and 2.2, respectively.
Conclusion: Postmortem MRI can be used as an objective method of neonatal hypoplasia diagnosing. The PTR-value less than 5 is indicate of pulmonary hypoplasia as the direct cause of newborn death.

E-PS-20-007
Incomplete pentalogy of Cantrell with associated skeletal malformation
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Background & Objective: Pentalogy of Cantrell (POC) is a rare congenital syndrome characterized by the presence of 5 major malformations: abdominal wall defect, sternal cleft with or without ectopia cordis, anterior

diaphragmatic defect, diaphragmatic pericardial defect and various intracardiac anomalies. Case report: 28-year-old healthy primigravida with a gestational age of 18 weeks was reffered for a routine gynaecological check-up. The antenatal ultrasound showed a fetus with large thoraco-abdominal wall defect incompatible with postnatal life. The patient underwent induced abortion in 18+1 weeks of gestation.
Method: Routine autopsy and postmortem radiologic examination of the aborted male fetus were performed.
Results: On examination there was a large anterior thoraco-abdominal defect with protrusion of small and large bowel, stomach, spleen, pancreas, liver, right kidney, right adrenal and a part of right lower lung lobe. A defect of the anterior part of diaphragm as well as pericardial defect were noted. No intracardiac defects were found. Left upper limb was severely malformed. CT examination revealed rudiments of scapula and humerus; clavicle and ulna were completely absent, oligosyndactyly of the left hand was present. The spine showed severe scoliosis. Genetic examination revealed normal male karyotype (46, XY).
Conclusion: POC is a rare complex syndrome with varying degrees of incomplete expression and associated anomalies. We refer a new case of incomlete POC with associated malformation of skeleton of left upper limb. This case also demonstrates the usefulness of combination of routine autopsy and modern postmortem imaging methods, that enhance diagnostic quality and completeness of the autopsy report.

E-PS-20-008
NOD-1 expression in placental villi in pregnancy-related complications
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Background & Objective: NOD-1 receptors (nucleotide-binding oligomerization domain-containing protein-1) are expressed by trophoblast throughout gestation. It was established that NOD-1 activation leads to signaling cascade that generates an inflammatory response, characterized by the cytokines production. The aim was to determine whether NOD-1 expression varies in different complications of pregnancy.
Method: We performed histological (H&E) and immunohistochemical analysis (Ventana Medical Systems, Roche) on the paraffin-embedded slices of placental tissue using NOD-1 primary polyclonal antibodies (1:100; Thermo Fisher Scientific) from 5 women with uncomplicated pregnancy and 15 with different complications (4 cases – early-onset preeclampsia (EOP), 3 patients – late-onset preeclampsia (LOP), 4 cases – with intrauterine growth restriction (IUGR) without PE and congenital fetus malformations, 4 women – with preterm labor (PL). The intensity of immunohistochemical reaction was estimated by means of program NIS-Elements.
Results: Histological examination revealed no placental impairment and syncytiotrophoblast shedding in IUGR, versus PE. NOD-1 expression was higher in IUGR (0.362±0.064; p=0.028) compared to EOP and LOP (0.328±0.036 and 0.238±0.048, respectively), PL (0.314±0.028) and NP (0.250±0.050).
Conclusion: Thus, it is likely both IUGR associated and not associated to preeclampsia may be due to the pro-inflammatory response. Higher NOD-1 expression probably reflects peculiar involvement signaling cascades.

E-PS-20-009
Multicystic cavernous lymphangioma of omentum – a unique case with unusual clinical presentation
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Background & Objective: Cavernous lymphangiomas are relatively rare, found mainly in newborns and are considered more a hamartogenic lesion than a true neoplasm. Although they may arise in different locations, their occurrence in omentum is very rare. Here we present a paediatric case of huge omental cystic lymphangioma presenting clinically as massive hydrocele.
Method: We report a case of otherwise healthy 1,5-year old boy who presented with a voluminous hydrocele in the left side of scrotum. Intraoperatively, the surgeon identified spongiform mass in the inguinal canal prolapsing into the left scrotum, which turned out to represent a multicystically transformed omentum. Subsequent laparotomy and subtotal omentectomy was performed. Material was processed for routine histopathological assessment. Two months after operation the patient is alive and well.
Results: The omentum measured 320x120x10 mm and it was completely replaced by spongiform mass composed of multiple large interconnecting cavities filled by serous fluid. Microscopic examination revealed numerous anastomosing thin-walled cystic structures lined by single layered flat cells. Granular proteinaceous content was present in lumina. Immunohistochemically, the cells showed diffuse expression of CD34 and D2-40 and were negative for mesothelial markers WT1 and calretinin.
Conclusion: Lymphangiomas of the omentum are rare in general. The clinical manifestation as the hydrocele is unique among reported cases. Since they may share some morphological similarities with so called multicystic mesothelioma, this must be excluded in differential diagnosis.

E-PS-20-010
Twelve-month-old twins with facial-limb defects: oral-facial-digital syndrome type 1
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Background & Objective: Oral-facial-digital syndrome (OFDS) has over 160 cases described and the OMIM site refers eighteen variants of the OFDS. An X-linked dominant inheritance is a pathogenic variant in the OFD1 gene, identified in 85% of cases. Patients with Joubert syndrome also have pathogenic variants in the OFD1 gene, reason why this pathology is considered a ciliopathy. OFDS type 1 has poor prognosis and is lethal for the majority of males.
Method: Twelve-month-old female twins, born with 33 weeks; both with abnormal oral frenula accompanied by alveolar and lingual clefting and multiple infracentimetric lesions in the back and tongue's tip; one, with soft palate cleft and syndactyly of the 4th right hand space; the other, with preaxial polydactyly of right hand and foot. Parents have no clinical apparent lesions and normal mental development.
Results: Gross examination of the tongue lesions, from both children, revealed polypoid structures, dimensions between 0.6cm and 0.8cm, whitish and elastic. Microscopic examination showed multiple hamartomatous lesions, containing mature adipose tissue, glandular and neural structures, with disorganized growth. Considering the multiple tongue hamartomatous lesions, the facial and digital malformations known so far, we suspect of OFDS type1. Sequence analysis of OFD1 gene was requested, and at the time of submission was under way.
Conclusion: Several syndromes with oral facial and digital abnormalities have significant overlap with OFDS type 1, which makes difficult to establish a precise diagnosis and proper prognosis. A molecular diagnosis and genetic counseling are crucial to correct management of patients and their families.

E-PS-20-011
Ghrelin– and Tryptase-positive mast cells in lung tissue of newborns with respiratory distress syndrome
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Background & Objective: The presentation reported some peculiarities in ghrelin (Ghr)- and tryptase (Try)-positive mast cells (MCs) distribution in human lung of preterm newborns with respiratory distress syndrome (RDS). According to recent data the peptide hormone ghrelin possessed anti-inflammatory activity and reliable therapeutic properties in some lung diseases. So far, ghrelin expression has been defined predominantly in neuroendocrine cells of bronchial mucosa in fetal and infant lung and occasionally in adult human lung.
Method: Lung tissue from 8 dead newborns with RDS where investigated immunohistochemically with anti- Ghr and anti-Try antibodies. The number of Ghr+ and Try+ MCs was determined in three locations – around bronchi, around bronchiole and in alveolar septa.
Results: MCs were more numerous around main bronchi with diminishing numbers aroun bronhioli and in alveolar septa. The number of MCs in the latter was increased in newborns with pneumonia. The number of Ghr+ MCs in alveolar septa was lower in newborns with RDS as compared to newborns with RDS combined with pneumonia (2.83±1.13 vs 4.81±2.6, $p<0.001$). The amount of Try+ MCs along bronchial wall was significantly more than Ghr+ MCs in RDS newborns (6.97±4.53 vs 3.85±4.31, $p=0.014$).
Conclusion: It could be supposed that pulmonary mast cells increased in newborn lungs in inflammatory process. MCs in human lung contained ghrelin peptide that had immunomodulatory function and participated in hormone regulation of inflammation.

E-PS-20-012
Placental vasculature peculiarities in pregnancies with circulatory hypoxia
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Background & Objective: Adverse influences in the maternal compartment of the 'mother-placenta-fetus' system affect placental morphology and function. It is known that placenta forms the interface between the fetus and its mother. Altered nutrient and oxygen supply of the fetus is associated with growth restriction and other pathologies. Structural response of placental fetal vessels to chronic circulatory hypoxia due congenital heart defect (CHD) was the aim of present study.
Method: We examined 35 term placentas. They were divided into groups: I - 20 cases of CHD and 15 cases of physiological pregnancy (control group). Fetal vessels in chorion villi were studied microscopically and by the computer morphometry. Histopathologic findings were correlated with medical history data and immunohistochemical studies. The standard immunohistochemical staining protocol with monoclonal mouse antibodies to VEGF (RTU, Spring), SMA (Dako, 1:500) for placental tissue samples has been developed. Differences between groups' data were elucidated by non-parametric Wald-Wolfowitz test. Reliability established at $p<0.05$.
Results: The results have shown the increased volume fraction of structural alterations in fetal capillaries, terminal villi syncytiotrophoblast and stroma in cases of CHD. These were accompanied with vessels location at peripheral zone of villi, therefore the length of vascular-syncytial membranes increased. Immunohistochemistry revealed higher VGEF, SMA expression compared with control group.
Conclusion: Histopathological and immunohistochemical peculiarities of the placental fetal capillaries in patients with CHD display a structural adaptation of placenta to hypoxia stress. Knowledge of possible mechanisms of placental respond to lack of oxygen in feto-placental unit may support adequate management of women with a history of CHD.

E-PS-20-013
Children with Crohn's disease morphological features of tunica mucosa of large intestine
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Background & Objective: The activity and severity of children with Crohn's disease pathological process is characterized by a lesser degree of manifestation. It determines the appropriateness of studying the mechanisms of immunopathological reactions involved in the realization of inflammation. Objective: to research the characteristics of the cellular composition of children's tunica mucosa (TM) of large intestine, which determine the favorable and unfavorable clinical course of Crohn's disease.
Method: Histological, immunohistochemical and morphometric analysis of the thick and terminal ileum tunica mucosa biopsy specimens of 35 children aged 1 to 18 years with Crohn's disease. Two groups have been formed: I-favorable clinical course, II-unfavorable clinical course.
Results: It has been found that the group I children has lower cellular density of the infiltrate and smaller lymphoid tissue ($p\leq0,05$) compared with the group II. The group I children has had more structured lymphoid nodules. Group II children have had a proliferating lymphoid tissue without follicles with capillaries with closely spaced swollen endotheliocytes ($p\leq0,003$). Both groups have had high T-lymphocyte CD3+ count, however, a predominance of positive CD8 + cells has been observed in the group II children. Homogeneous distribution of cellular forms with inconsiderable extracellular matrix producer cells changes has been most evident for group I children. A less pronounced response of fibroblasts has been observed in group I children in comparison with the group II children.
Conclusion: The result has shown the differences in the own plate of TM of large intestine distribution, which affect the course of the inflammatory process with a differently directed regeneration character.

E-PS-20-014
CD117 expression in the retina and lens of the human eye in prenatal develepment
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Background & Objective: The aim was to determine CD117 (C-kit; SCF receptor) spatial localization in the retina and lens of human fetal eyes.
Method: The eyes from 9 to 23 weeks of gestation (WG) were taken for autopsy according to ethical approvals. Immunohistochemistry was performed (Ventana Medical System, Roche) on paraffin-embedded slices using CD117 primary monoclonal antibodies (ready to use, Cell Mark).
Results: At 9-11 WG, CD117 localization was detected in the layer of nerve fibers, in the inner and outer neuroblastic layers of the retina from the center to eye cup edge. Beginning from 15 WG, there was no staining both in ora serrata and epithelium of ciliary body. In the center of the retina, staining both in the inner and outer nuclear retinal layers was observed up to 18 WG. From 19 to 23 WG, staining was localized in the layer of nerve fibers and ganglion cells layers. In the lens from 9 to 23 WG, CD117 expression was present in the lens epithelium.
Conclusion: These results indicate the role of CD117 in regulation and differentiation of retinal neurons and epithelial cells of the lens in early stages of prenatal development.

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E-PS-20-015

Congenital malformations at the neonatal resuscitation of a maternity and neonatology center: a year summary

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Background & Objective: About 3% of newborns in the world suffer congenital malformations. In Tunisia there aren't any prior studies that provide an accurate record of these malformations. Some malformations remain a major cause of morbidity and high mortality rates, and they represent a burden to both family and society. Identify the main congenital malformations registered at the CMNT in 2016 to create a preliminary draft of an institutional register of malformation, in anticipation of a regional one.
Method: This is a retrospective descriptive study conducted at the department of neonatology at the CMNT. It's a summary of congenital malformations registered at the CMNT during the year 2016 (from January 1st, 2016 until December 31st, 2016).
Results: 175 new born children had congenital malformations. The malformations found were dominated by poly-malformations (22.29%), followed by chromosomal aberrations (21.14%), cardiovascular malformations (16.00%), and malformations of the nervous system (11.43%). The congenital malformations impacted 11.67‰ of births with 1.23 sex ratio. 53% of the parents were living in unfavourable socioeconomic conditions. The average paternal and maternal ages were respectively 38.70 and 32.20 years. The prenatal ultrasound was positive in two thirds of the cases. A quarter of the pregnancies were accompanied by dysgravidie mainly gestational diabetes.
Conclusion: Congenital malformations are at the basis of morbidity and major mortalities. The early detection of pregnancies prone to develop these anomalies is executed by armed supervision. The best treatment for these malformations is prenatal diagnosis.

E-PS-20-016

A case of ganglioneuroblastoma - nodular type associated with opsoclonus-myoclonus-ataxia syndrome

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Background & Objective: Opsoclonus-myoclonus-ataxia syndrome (OMAS), also called "Kinsbourne syndrome" or "dancing eye syndrome," is a serious, rare, and often chronic neurological disorder. OMAS is generally a paraneoplastic or parainfectious entity, but in children, it is most commonly associated with occult neuroblastoma (NB) in about 50% of cases and between 2% and 3% of children with NB have OMAS.
Method: A 3 year old girl presented with balance disorder for past 3-4 months. Magnetic resonance imaging demonstrated a 31x26x19 cm mass with calcification adjacent to the right adrenal gland. Urine levels of vanillylmandelic acid, adrenalin, noradrenalin, metanephrines, and normetanephrine were all normal in 24 hours. The patient underwent adrenalectomy and mass excision.
Results: Macroscopic examination of the surgical specimen showed a 4.5 cm grey and multilobulated roundish mass with well-defined margins. The cut surface of the solid mass was soft yellow and gray brown with focal areas of hemoragie. Histopathological examinations revealed that the tumour is a ganglioneuroblastoma, nodular type. In addition, lymphocytes infiltration and lymphoid follicles are seen in the tumour. The histology was judged to be unfavorable.
Conclusion: Neuroblastic tumours (NT) with OMAS display characteristic histological features such as lymphocytic infiltration with lymphoid follicles. The pathogenesis was thought to be immune mediated, with a cross-reactive autoimmunity between neuroblastoma cells and the central nervous system. OMAS is a rare disorder, but it affects children more frequently than adults and exhibits an excellent rate of survival. Screening for an occult NB/ GNB is necessary in all children with this syndrome.

E-PS-20-018

Immunohistochemical expression of Napsin A in normal human foetal lungs and congenital and acquired pathologic conditions

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Background & Objective: Surfactant protein B (SP-B) is a key component of pulmonary surfactant. SP-B is processed to mature surface-active protein from a pro-peptide by two distinct cleavages at its N-terminal and C-terminal portions. Napsin A is the protease, expressed in type-II pneumocytes, involved in the N-terminal cleavage of this pro-peptide. In this paper, for the first time, we evaluate the immunohistochemical expression of Napsin A in normal human fetal lungs at different gestational ages, and in examples of congenital and acquired pulmonary pathological conditions.
Method: Samples of lungs were collected at the Department of Medicine and Surgery of Parma University, (Italy) from fetal and neonatal autopsies. The immunohistochemical study was performed using primary monoclonal antibody anti-Napsin A (clone MRQ-60). A section of lung adenocarcinoma was used as an external positive control.
Results: The results reveal that Napsin A is expressed early in normal fetal lungs and in the entire epithelium of distal pseudoglandular tracts. At 30 weeks' gestation and in the newborn at term of pregnancy, immunoreactivity to Napsin A already presents the same distribution as that in adult subjects, affecting isolated cells of the alveolar epithelium. In pathological conditions, such as inflammatory diseases and pulmonary hypoplasia, both in the fetus and in the newborn, this study demonstrates an increase in the expression of Napsin A compared to a control group.
Conclusion: In conclusion, this study demonstrates that Napsin A is produced early during fetal life and its production increases in many diseases in the effort to resolve a functional pulmonary deficiency.

E-PS-20-019

Listeriosis: a case report of a preterm stillborn

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Background & Objective: Listeriosis of fetal and perinatal life is a bacterial infection acquired transplacentally or intrapartum. Maternal infection is caused by consumption of fresh farm products, unpasteurized milk or contaminated food. If not properly treated the outcome can be fatal especially for the fetus. We report a 360-g. female stillborn at 20+ weeks of gestation born to a 33-year-old gravida 1, nullipara mother. The mother's pregnancy was uncomplicated until the onset of fever and abdominal pain 3 days before delivery. On admission she was found to have fever of 40 Celsius and fetal demise. After laparotomy and hysterotomy she was delivered of the stillborn. After being treated with antibiotics she had a full recovery. Placenta tissue culture grew Listeria monocytogenes.
Method: We received the placenta for histological examination and the stillborn for aytopsy. Tissue sections from the fetal organs were also examined.
Results: The placenta had multiple microabscesses in the chorionic villi and acute chorioamnionitis. The postmortem examination showed numerous small yellow-white skin pustules. Microabscesses were found in lungs, kidneys and skin of the stillborn.
Conclusion: Listeriosis is a relatively rare disease. In Greece 139 cases were registered during the period 2004-2016. These included 4 pregnant women and 3 neonates. In our case that occurred in 2017 the histological findings of placenta and fetal organs were typical for listeriosis. The source and the nature of the food responsible for the infection of the mother could not be identified. The fetal and neonatal mortality is high. Prompt antimicrobial treatment of the adult patients is usually curative.

E-PS-20-020

"Outburst" of embryonal rhabdomyosarcoma – series of 5 cases

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Background & Objective: Embryonal rhabdomyosarcoma (E-RMS) is a malignant soft tissue sarcoma with morphologic and immunophenotypic characteristics of embryonic skeletal muscle.
Method: We report a series of 5 cases from a total of 9 cases of rhabdomyosarcomas diagnosed in our department in the last 15 years.
Results: All the E-RMS cases occurred in paediatric patients (median 9 years; range 10 months - 9 years), mainly boys (M:F=3:2), all in head&neck area; the other rhabdomyosarcomas were alveolar type (3 cases, adults >60 years) and mixed alveolar-embryonal (one patient 18 years). Interestingly, the alveolar RMSs were almost evenly distributed in time while all E-RMS cases occurred in the last 17 months; no similar variation of lymphoid malignancies was identified. All E-RMSs presented as blue cell tumours with specific cambium layer in one case; mild pleomorphism was present in 4 cases; minute necrotic areas in 3/5 cases. All the tumours showed diffuse positivity for vimentin and at least focal positivity for SMA, HHF35, desmin, MYOD1 and negativity for lymphoid markers, CD99, S100 protein, GFAP and cytokeratins. Ki67 index: 60-75%.
Conclusion: Our data show an increase of E-RMS incidence in the last year. Since small biopsies are frequently provided, specific architecture (cambium layer) may not be present; differential diagnosis of a blue cell tumour relies on immunophenotype.

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E-PS-20-021

Differential expression of microRNAs in mesenchymal hamartoma and undifferentiated embryonal sarcoma

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Background & Objective: Hepatic mesenchymal hamartoma (HMH) is a benign tumour that occurs in children. In contrast, undifferentiated embryonal sarcoma (UES) of the liver is highly malignant and aggressive tumour. In some cases, the HMH can evolve to UES. Translocations have been described in the HMH, which involve the band of chromosome 19q13.4, in this region a cluster of 46 miRNAs is located, denominated C19MC (chromosome 19 microRNA cluster). This suggests that the alteration in the microRNAs may contribute to the tumourigenesis of HMH. The objective of this study was to characterize the expression of the microRNAs in the HMH and the UES.
Method: Formalin-fixed and paraffin-embedded biopsies from 2 cases of HAM, 2 from SEI and 2 from HAM with transition zones towards sarcoma were included; as control was used liver without neoplastic disease. We used miRNA PCR Array for Human Cancer PathwayFinder. In this arrays we evaluated 84 microRNAs. For the analysis we used the software Significance Analysis of Microarrays.
Results: In the UES and in HAM with transition tumour, a group of microRNAs (17%) showed significantly lower expression in comparison with benign HAM and controls, among which miR-143-3p, miR-193a-5p, several members of let-7.
Conclusion: In the UES and tumour in transition, there was less expression of microRNAs with tumour suppressor activity involved in functions of inhibition of proliferation, migration because they target c-Myc, MAPK among others. These microRNAs have not been reported in these tumours.

E-PS-21 | Pulmonary Pathology

E-PS-21-001

PD-L1 differential expression among non-small cell lung cancer histologic subtypes and association with EGFR mutational status and ALK/ROS1 rearrangements

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Background & Objective: The association of PD-L1 immunoexpression and oncogenic drivers in non-small cell lung cancer (NSCLC) is controversial. We aim to assess PD-L1 immunoexpression in a series of NSCLC, mostly including adenocarcinoma (ADC) and squamous cell carcinoma (SCC), and to establish associations with clinicopathological and molecular features (EGFR mutational status, ALK and ROS1 rearrangements).
Method: Methods: We selected a consecutive cohort of NSCLC patients diagnosed and treated at IPO Porto (November 2016-December 2017). Relevant clinicopathological data were retrieved. PD-L1 expression (immunohistochemistry, 22C3), EGFR mutational status (real-time PCR) and ALK/ROS1 rearrangements (FISH) were assessed in lung/pleural biopsies/resections of the primary tumour (n=327) and metastatic sites (n=18), when appropriate.
Results: Results: A total of 345 NSCLC patients were selected, including 235 ADC, 92 SCC and 18 NSCLC NOS. Median age at diagnosis was 66 years and 262 (76%) were male. PD-L1 positivity (>=1%) was observed in 150 (44%) cases, showing similar proportions in ADC (105/234, 45%) and SCC (35/91, 39%). PDL-1 expression was positive in 18/49 (37%) EGFR-mutant cases, 5/9 (56%) cases showing ALK rearrangements and in 1/2 cases showing ROS1 rearrangement. We found no significant association between molecular features and PD-L1 positivity.
Conclusion: Conclusion: In our NSCLC series, PD-L1 immunoexpression was not associated with EGFR mutational status or ALK/ROS rearrangements, neither it was significantly different among major tumour histological subtypes. Further investigations in larger series are warranted to elucidate the regulation of PD-L1 expression in NSCLC and its relation to tumour driver gene alterations.

E-PS-21-002

Plasma EGFR liquid biopsy test in the assessment of exon 20 T790M mutation in lung cancer patients

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Background & Objective: Plasma EGFR liquid biopsy test is a useful tool in the follow up of lung cancer patients, as it is easier and faster than analysis of formalin fixed paraffin embedded tissues and rebiopsy during TKI (thyrosine kinase inhibitor) therapy is not always feasible. Exon 20 T790M mutation results in resistance to first generation TKIs. In our laboratory we started to identify these mutations using plasma liquid biopsy technique in 2017. Our objective was to analyse our results and compare with literature data.
Method: The EGFR mutation status of 100 lung cancer patients was evaluated using blood plasma liquid biopsy technique with a cf Cobas 4800 EGFR Mutation Test Kit. After review of the medical history the ratio of the different mutations was calculated in the different patient groups that were formed based on progression and therapy.

Results: 68 of the 100 patients showed progression. 16/68 were positive for EGFR mutations, of which 7 were positive for T790M (43,7%), and also for a primary mutation. The ratio of EGFR mutations were: L858R - 37,5%; G719X-12,5%; S768I-6,2%; exon 19 deletion-43,7%. Two patients were positive for plasma EGFR mutation without signs of clinical progression; one of these patients showed an exon 19 delition, the other a coexistant exon 18 G719X and an exon 21 L861Q.
Conclusion: Our results show that the method we used is reliable for plasma testing but rebiopsy is important in negative cases. Further investigations are needed to determine the exact clinical relevance of detection of EGFR mutation without progression during TKI therapy.

E-PS-21-003
Exhaustive histological, immunohistochemical and molecular study of an unusual case: adenocarcinoma of lung associated with osteoclastic-like giant cells
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Background & Objective: Osteoclast-like giant cells (OLGCs) are extremly rare in lung carcinoma, generally they are found within lesions that have an osteogenic component. There are only nine reported cases, and just one with molecular study. We present a case with clinicopathological, histological and immunohistochemical features of lung carcinoma with OLGCs and its molecular study.
Method: A 74-year old woman presented with an 8 cm mass in the right lung, from which an endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was performed. In the cytological study, multinucleated giant cells without presence of epithelial cells were observed. Therefore a lobectomy was performed.
Results: Histologically, an OLGCs tumour with mononuclear cells intermingled with a poorly differentiated adenocarcinoma was observed. An electron microscopic examination was completed, as well as an immunohistochemical and molecular study. Mononuclear cells were positive at variable immunointensity for epithelial markers and both adenocarcinoma and mononuclear cells had same k-ras mutation. These findings support the origin of mononuclear cells was neoplastic epithelium rather than reactive mesenchymal component. However, OGCs were considered non-neoplastic origin, due to its benign histological appearance, lack of epithelial markers and immunoreaction for histiocytic markers.
Conclusion: Although the prognostic implication of this extremely rare condition largely unknown and further studies are required for clarification, there may be the potential for good prognosis according to the cases reported. Likewise, our patient is free of disease almost 2 years after surgery. Therefore, it is important not to misdiagnose this entity as a high grade malignant tumour such as pleomorphic carcinoma, giant cell carcinoma or carcinosarcoma.

E-PS-21-004
Metastatic hepatocellular carcinoma to the lung: EBUS-TBNA cytologic diagnosis of two consecutive cases
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Background & Objective: Hepatocellular carcinoma (HCC) is the most common primary tumour of the liver and a major public health problem worldwide. Amongst Western populations, liver cirrhosis constitutes the most important HCC risk factor. HCC metastatic sites include lungs, lymph nodes, bone and adrenal gland followed by others.
Method: We present two cases of patients with HCC, with metastases to the lungs, diagnosed by cytology. Serum alpha-fetoprotein was within normal limits in both cases. They were associated with cirrhosis, one owing to Hepatitis C Virus and the other related to alcohol abuse. In the first case, imaging studies showed a hepatic mass (9cm), suprahepatic veins invasion and prominent lymph nodes in the paratracheal nodal region. The second one coexisted with severe portal hypertension at the moment of diagnosis, so he had been treated with radiofrequency ablation. Two years later, CT revealed two suspicious lesions in the right lung.
Results: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was performed in both cases, which showed large polyhedral cells with a granular cytoplasm, round vesicular nuclei with prominent nucleoli and sometimes nuclear inclusions, highly suggestive of metastatic HCC. Immunohistochemical studies in the cellblocks, along with the morphology, favoured the diagnosis of metastatic HCC over primary lung hepatoid adenocarcinoma.
Conclusion: In conclusion, cytological features are very important as they may orientate the diagnosis. The lack of undoubtful morphological criteria makes the cellblock sections study, which allow immunohistochemical staining essential to confirm the suspected diagnosis. The usefulness of EBUS-TBNA in the diagnosis of lung lesions is well illustrated by these cases.

E-PS-21-005
PD-L1 expression in NSCLC and the comparison with the other types of cancer
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Background & Objective: Expression of programmed death-ligand 1 (PD-L1) either in tumour or in infiltrating immune cells has been verified predominantly by immunohistochemistry (IHC) in a variety of tumours, suggesting a role for the PD-1/ PD-L1 axis as a prognostic trait and therapeutic target across multiple histotypes. Our aim in this study was to evaluate the positivity rates of cases in which we studied PD-L1 immunohistochemically in terms of tumour primer and tumour type.
Method: Retrospectively, positivity fractions, tumour primers and tumour histological types of cases with PD-L1 studied immunohistochemically in Gazi University Medical Faculty Pathology Department within 17 months period were investigated. Protein expression of PD-L1 was examined by immunohistochemistry method using the VENTANA PD-L1 (SP263) rabbit monoclonal antibody.
Results: Of the 298 cases studied, 84.3% were lung carcinoma, while the remaining 15.7% were colon, bladder, breast and pancreatic adenocarcinomas. Of the lung carcinomas, 54.9% are adenocarcinomas and 31% are SCC; PD-L1 positivity was 26.8% in adenocarcinomas and 45.5% in SCCs. The expression of PD-L1 was equal or higher than 75% in 6 cases (7.5%) of SCC and 4 cases (2.8%) of the adenocarcinomas.
Conclusion: PD-L1 has been studied most frequently in lung carcinoma. Our results suggest a significantly higher PD-L1 expression in tumour cells of squamous-cell lung cancer compared to adenocarcinoma.

E-PS-21-006
Expect the unexpected - late recurrence of a "benign pleural fibroma"
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Background & Objective: Low grade fibromyxoid sarcoma (LGFMS) is a rare low grade fibroblastic soft tissue tumour, in particular as primary manifestation in the pleura. Surgical resection remains the gold standard in treatment. Rare cases of local chest wall recurrence or metastasis to the pleura have been reported.
Method: We investigated a case of a 36-year- old female, who presented with a painless chest mass at the site of previous surgery. The patient had

no pulmonary symptoms and an unremarkable medical history except for a 16 years previously surgically resected pleural fibroma at the level of the newly formed lesion.
Results: On preoperative PET-CT scan, an large inhomogeneous process was seen, infiltrating the chest wall between the ribs. Core needle biopsy of the 11cm large tumour showed of a spindle cell proliferation, set in a relatively scarcely vascularized, alternatingly dense fibrous and myxoid stroma. Immunohistochemistry did not reveal any line of differentiation. FiSH-analysis showed 35 of 100 cells to be rearranged for FUS. The case of the previously diagnosed pleural fibroma was reviewed. Histological and molecular features of both lesions were in keeping with LGFMS. The patient was treated with wide surgical resection and chemotherapy. Less than 10% of evaluated area of the widely excised tumour showed fibrosarcoma-like morphology.
Conclusion: To the best of our knowledge, we report the first case of late recurrence of a primary pleura-based LGFMS more than 15 years after primary presentation, showing areas of de-differentiation. The presented case highlights the fact that this neoplasm is underdiagnosed and that long-term follow-up of this neoplasm is required, even after presumed adequate surgical resection.

E-PS-21-007
Clinical significance of E-Cadherin and Vimentine in a metastatic model of lung adenocarcinomas to the brain
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Background & Objective: E-cadherin and vimentin are now regarded as major and conventional canonical markers of epithelial-to-mesenchymal transition in metastatic pathways of cancer. To study the expression of E-cadherin and vimentin in samples of lung adenocarcinoma and their respective brain metastases and to study their clinical relevance with survival rates.
Method: Twenty-three consecutive patients with lung cancer and subsequent brain metastasis surgically removed between 2007 and 2017 were studied. Tissue arrays were produced using a 2 mm diameter needle. Immunohistochemical studies were conducted, where the positivity was classified from 1 to 3 degrees and the extension was graded between 0 and 100%. A global score was obtained by multiplying both values. Statistical analysis of these findings was carried out using the SPSSv23; $p<0.05$ program.
Results: Positive immunoexpression was noted in 92% of lung adenocarcinoma samples for E-cadherin and 45% for vimentin. In comparison, about 82% of their respective metastatic tumours showed positivity for E-cadherin and up to 59% for vimentin. No significant differences for both molecules were noted between primary tumours and their metastatic samples (232.5 vs 242.7; p=0.478 for E-cadherin. 90.6 vs 110.6; p=0.752 vimentin). However, samples with more than 50 points for E-cadherin immunoexpression reveals a group of patients with better prognosis ($p<0.05$). Finally, samples with positive immunoexpression for vimentin reveals a group of patients with worse ($p<0.05$).
Conclusion: No significant differences for E-cadherin and vimentin were noted. An opposite clinical significance for E-cadherin and vimentin has been observed in lung adenocarcinoma samples.

E-PS-21-008
Immunohistochemical expression of STAT6 in model of lung adenocarcinoma with brain metastasis
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Background & Objective: The protein encoded by this gene is a member of the STAT family of transcription factors produced in response to cytokines and growth factors, the role of non-phosphorylated STAT6 in the pathogenesis of lung cancer. To study the expression of STAT6 in samples of lung adenocarcinoma and their respective brain metastases and to study their clinical relevance with survival rates.
Method: Twenty-three consecutive patients with lung cancer and subsequent brain metastasis surgically removed between 2007 and 2017 were studied. Tissue arrays were produced using a 2 mm diameter needle. Immunohistochemical studies were conducted, where the positivity was classified from 1 to 3 degrees and the extension was graded between 0 and 100%. A global score was obtained by multiplying both values. Statistical analysis of these findings was carried out using the SPSSv23; $p<0.05$ program.
Results: Almost 69% of lung adenocarcinoma samples and up to 55% their respective metastatic tumours showed different degrees of STAT6 immunoexpression. No significant differences in STAT6 immunoexpression were noted between primary tumours and their metastatic samples (74.2 vs 76. p=0.88). Interestingly, metastatic samples of LUNG adenocarcinomas in the brain with more than 50 points of STAT6 immunoexpression classify a group of patients with better overall survival, disease-free time and post metastasic survival ($p= 0.004$, $p = 0.002$, $p = 0.005$ respectively).
Conclusion: No significant differences for STAT6 were found between primary and metastatic adenocarcinoma samples. Considering metastatic adenocarcinoma samples, those with more than 50 points of immunoexpression for STAT6 reveals a group of patients with better prognosis.

E-PS-21-009
Pulmonary micropapillary adenocarcinoma and BRAF mutations – case report
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Background & Objective: Micropapillary bronchial-pulmonary adenocarcinoma is well recognized as the most aggressive subtype. Emphasis is now demanded to apply stromal scoring to understand its importance in tumoural outcome. Both epithelial malignant subtyping and stroma morphology scoring might together contribute to recognize and preview tumoural biopathological behaviour.
Method: A seventy-year-old woman, smoker, presented with RUL and LUL tumoural nodules, hepatic metastasis and highly-dimensioned mediastinal lymph nodes. RUL main bronchus biopsy indicated a micropapillary adenocarcinoma (CK7/TTF1 3+; Vim 2+; CK5.6 / CD56 -; Ki67 30%) with predominant fusiform-celled stroma (α- actin +). EGFR and ALK were both wild type indicating therapy with carboplatin/ pemetrexed and cranial radio-surgery; Nivolumab was prescribed latter due to more and enlarged liver nodules.
Results: The patient had progressively poorer OS with pleura/ peritoneum metastization and more brain nodules; liquid biopsy was performed and Idylla EGFR/ KRAS/ NRAS-BRAF determinations pointed BRAF codon 600 mutations.
Conclusion: Few studies are available to understand correlation between morphology, therapeutical biomarkers and tumoural stromal subtypes. Although staging at the moment of the diagnosis keeps the best survival parameter, micropapillary subtype (independently of its tumoural percentage) together with α-actin/ fusiform-celled stroma should indicate the determination of the available targeted biomarkers. BRAF mutations keep MEK and RTKs activated and might be "protected" by stromal barrier with α-actin and together may support the poor outcome of the present case, indicating the need to include BRAF in first- line biomarker determinations (Yan Ankersmitt 2015; Hiromichi Ebi 2017; Baohni Han 2017; Yasushi Yatabe 2018).

E-PS-21-010

Combined trimolecular (EGFR, ALK and PD-L1) and clinicopathological approach to lung adenocarcinoma

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Background & Objective: Testing lung adenocarcinomas for EGFR mutation, ALK translocation and PD-L1 expression is currently recommended. Nevertheless, their joint correlation with clinical data is rarely reported in the literature.
Method: We examined clinicopathological characteristics (gender, age, smoking habits, localization, predominant microscopic pattern and disease stage) of 48 lung adenocarcinoma patients routinely tested for EGFR, ALK and PD-L1.
Results: Nine patients (18.8%) had an EGFR mutation. Six patients (12,5%) had a positive ALK immunohistochemistry score (2+ or 3+). No patient showed both molecular alterations. Mean tumour cells PD-L1 expression was 28.8%. A third of cases was strongly positive (>50%), and 37.5% mildly positive (1-50%). Most of the patients were known current smokers (59.4%) and their mean consumption reached 60,5 pack-years. Interestingly, a higher pack-years consumption for current smokers was associated with higher qualitative (p=0.014) and quantitative (p=0.007) PD-L1 expression. Regarding localization, most known primary tumours were right-sided (66.7%). EGFR-mutated tumours were however often left-sided (Odds-Ratio=13.6, p=0.032). Acinar pattern was predominant in operated adenocarcinomas (58.4%). Those predominantly acinar tumours were all either PD-L1 negative or strongly positive. The remaining non-acinar-predominant tumours were all mildly positive. Finally, PD-L1 expression (qualitative or quantitative) wasn't associated with either ALK or EGFR profile.
Conclusion: Recommended routine trimolecular approach to lung cancer allows deeper investigations. Higher tobacco consumption is strongly associated with higher PD-L1 expression in current smokers. Curiously, left-sided tumours are more often EGFR-mutated. Finally, no significant association is found between EGFR, ALK and PD-L1 profiles, according to our series.

E-PS-21-011

Pulmonary chondroid hamartomas – rare, benign and unexpected

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Background & Objective: 179 pulmonary chondroid hamartomas were resected from 175 patients. The patients were in average 60 years old and slightly more males (57 %).
Method: Most patients had no pulmonary symptoms (65/175). The nodule was detected incidentally during a diagnostic work-up. Primary diagnosis of lung cancer (25/175), other cancer types (22/175) and tumour follow-up (9/175) led to discovery. In 40 patients with pulmonary symptoms further nodules were identified, most likely not being the cause. Only in 3 patients the symptoms were caused by an endobronchially located chondroid hamartoma.
Results: In more than half of all cases (94/179) imaging revealed an unspecific nodule. 36 were suspected to malignancy or metastasis and 10 to a growing size. A chondroid hamartoma was assumed only in 14 cases and a benign tumour in 9 further cases. 14 were not detected preoperatively. Frozen sections were performed in most cases (154/179, 86 %). In all but one case the histopathological diagnosis revealed a chondroid hamartoma. The average tumour size was 1,4 cm. Well-demarcated boarders with deep clefts are typical features of pulmonary chondroid hamartomas. Within the tumour, cartilage represented the predominant tissue component, partly with immature appearance. Degenerative changes, calcifications, and ossification and even bone marrow were often found. All tumours consisted of more than one and up to seven different tissue components.
Conclusion: Chondroid hamartomas represent the most frequent benign lung tumour. They are build up from cartilage and other mature tissue components. In contrast to the non-specific preoperative imaging results, histopathological diagnosis was prompt and valid, even on frozen sections.

E-PS-21-012

Relationship between histological type and PD-L1 expression in non-small cell lung cancer (NSCLC)

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Background & Objective: Immunotherapy with checkpoint inhibitors is becoming a brand-new standard of treatment for patients with advanced or metastatic NSCLC. PD-L1 expression is reported to be the predictor of clinical response in NSCLC. Our objective was to investigate the relation between PD-L1 expression level and tumour histological type.
Method: PD-L1 expression level was evaluated via immunohistochemistry using the monoclonal antibody (22C3, DAKO). Clinicopathological characteristics were acquired from the laboratory registry database. Histological types and subtypes were determined according to WHO 2015 classification. PD-L1 expression levels in tumour cells (TC) were analyzed according to recommended cut-off values of < 1%, 1-49% and > 50%.
Results: Our study included 236 cases of NSCLC: 183 lung adenocarcinomas (AC) and 53 squamous cell carcinomas (SCC). There were 156 (66.1%) male and 80 (33,9%) female. The median (Q1; Q3) age at diagnosis was 62 (54; 68) years. In TC, the PD-L1 expression level was negative in 82 (34.7%), 1% - 49% in 85 (36%) and >50% in 69 cases (29.3%). The PD-L1 expression level in SCC was higher than AC (43,8 (20; 70)% vs. 5 (0; 40)%; p=0,000002). The PDL-expression levels in solid AC [55 (1; 75)%] was higher than in lepidic [0 (0; 2,5)%], micropapillary [0 (0; 0)%], papillary [0 (0; 5)%] and mucinous [0 (0; 10)%] AC (p=0,001).
Conclusion: The PD-L1 expression level in SCC was higher compared to AC. The PDL-expression levels in solid AC was higher compared to lepidic, micropapillary, papillary and mucinous AC.

E-PS-21-013

Sarcomatoid carcinomas of the lung: review of cases at a university hospital over the last 20 years

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Background & Objective: The aim of this review is to study and classify the cases of sarcomatoid carcinomas of the lung, on the basis of the current histological tumour classification (TNM 8th edition).
Method: Retrospective study of the medical records and archival tissue sections of all cases with a diagnosis of sarcomatoid carcinoma at the Cruces University Hospital (Barakaldo, Spain) between January 1998 and January 2018.
Results: We found 25 cases, with a mean age of 62,7 years (range 39-81). A striking male predominance was noted (22 cases, 88%). On average, most of the tumours underwent lobectomy (14 cases, 56%), or pneumonectomy (3 cases, 12%), with 3 cases associating partial chest wall resection. Pleomorphic carcinoma was the most frequent tumour, accounting for 60% of the specimens (15 cases). Despite the fact that nearly all the specimens were completely

extirpated, some cases were diagnosed on advanced stages (9 tumours on stage III/IV, 36%).
Conclusion: The WHO classification of lung tumours defines sarcomatoid carcinomas as a group of poorly differentiated non-small cell lung carcinomas that contain a component of sarcoma or sarcoma-like (spindle and/or giant cells) differentiation. They are very rare, comprising no more than 2% of all lung cancers. The prognosis of these lesions is significantly worse than that of the typical non-small cell lung cancer.

E-PS-21-014
SATB2 reveals a group of patients with better prognosis in a metastatic model of lung adenocarcinomas to the brain
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Background & Objective: SATB2 plays an important role in transcriptional regulation and chromatin recombinant and is involved in progression of several carcinomas is related to the progression and the and poor prognosis in lung cancer patients and their metastases acting as like as a tumour suppressor gene To study the expression of SATB2 in samples of lung adenocarcinoma and their respective brain metastases and to study their clinical relevance with survival rates.
Method: Twenty-three consecutive patients with lung cancer and subsequent brain metastasis surgically removed between 2007 and 2017 were studied. Tissue arrays were produced using a 2 mm diameter needle. Immunohistochemical studies were conducted, where the positivity was classified from 1 to 3 degrees and the extension was graded between 0 and 100%. A global score was obtained by multiplying both values. Statistical analysis of these findings was carried out using the SPSSv23; p<0.05 program.
Results: Almost 65% of lung adenocarcinoma samples and up to 26% their respective metastatic tumours showed different degrees of SATB2 immunoexpression. A significant overexpression of SATB2 in the lung adenocarcinomas compared to their brain metastases was found (23.00 vs 7.66; p=0,029). Finally, samples with more than 50 points classify a group of patients with better overall survival, disease-free time and post metastasic survival (p = 0.012, p = 0.016, p = 0.024 respectively).
Conclusion: Significant differences for SATB2 were noted between primary and metastatic adenocarcinoma samples. Lung adenocarcinomas with more than 50 points classify a group of patients with better prognosis.

E-PS-21-015
Syndecan-1 reveals a group of patients with better prognosis in a metastatic model of lung adenocarcinomas to the brain
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Background & Objective: The syndecan family has five isotypes. Syndecan-1 (CD138) has been found in various cells such as epithelial cells and is critically involved in the differentiation and prognosis of various tumours. To study the expression of syndecan-1 in samples of lung adenocarcinoma and their respective brain metastases and to study their clinical relevance with survival rates.
Method: Twenty-three consecutive patients with lung cancer and subsequent brain metastasis surgically removed between 2007 and 2017 were studied. Tissue arrays were produced using a 2 mm diameter needle. Immunohistochemical studies were conducted, where the positivity was classified from 1 to 3 degrees and the extension was graded between 0 and 100%. A global score was obtained by multiplying both values. Statistical analysis of these findings was carried out using the SPSSv23; p<0.05 program.
Results: Almost 70% of lung adenocarcinoma samples and up to 85% their respective metastatic tumours showed different degrees of syndecan-1 immunoexpression. A significant overexpression of syndecan-1 in the metastatic lung adenocarcinomas to the brain was found (80.5 vs 155.5; p=0,004). Finally, samples with more than 50 points sorts a group of patients with better overall survival, disease-free time and post metastasic survival (p=0,024; p=0,041; p=0,023 respectively).
Conclusion: Significant differences for syndecan-1 were noted between primary and metastatic adenocarcinoma samples. Lung adenocarcinomas with more than 50 points reveals a group of patients with better prognosis.

E-PS-21-016
A young non-smoker male with clinical diagnosis of idiopathic pulmonary fibrosis: the pathologist discovered the true diagnosis
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Background & Objective: Idiopathic pulmonary fibrosis (IPF) is a progressive, life-threatening, interstitial lung disease with the histologic appearance of usual interstitial pneumonia (UIP). Two-thirds of patients with IPF are over the age of 60 years at the time of presentation, exceedingly rare in younger adults. Genetic testing is recommended if familial fibrosis is suspected or IPF occurs at a younger age.
Method: Here we report an intriguing case of a 46-year-old non-smoker male, professional trombone player suffering for persistent, non-productive cough diagnosed by clinicians and radiologists as UIP/IPF. Given young age the genetic screening revealed a heterozygote mutation of surfactant protein C, thus the final diagnosis was a genetic related IPF. Due to progressive respiratory failure, the patient underwent bilateral lung transplantation. The pathologist performed a careful microscopic evaluation of several fragments sampled from both lungs.
Results: UIP pattern was detected in association to several other histological features suggesting an alternate diagnosis of UIP/IPF: centrolobular chronic inflammation, small granulomas, bridging fibrosis and diffuse peri-bronchial metaplasia. The case was finally diagnosed as chronic hypersensitivity pneumonitis (HP) with UIP pattern. Bacterial analysis of the micro-film inside the trombone was positive for Fusarium Oxysporum.
Conclusion: UIP pattern can be detected in several interstitial lung diseases; a careful pathological analysis is mandatory. HP caused by fungi and bacteria in wind instruments has been seldom reported, probably due to underdiagnoses. The association of genetic disorder in surfactant protein could explain the susceptibility to potential trigger of HP. Larger cases series are required to investigate this last intriguing feature.

E-PS-21-018
Primary pulmonary follicular dendritic cell neoplasm
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Background & Objective: Follicular Dendritic Cell Tumour (FDCT) is an extremely rare neoplasm with only few reports in the current literature describing primary pulmonary cases
Method: A sixty-one year-old lady has started with back pain complaint. After falling on the floor, she decided to look for a doctor. At CT image it was identified multiple nodules in both lungs and pleura. At microscopic analysis there was an epithelioid tumour with conspicuous nucleoli, oval nuclei, eosinophilic and indistinct cytoplasm. At immunohistochemistry it was negative to cytokeratins (AE1/AE3, CK7, CK20, CK5/6), CD45, CD30, WT1. It was positive to CD23 and podoplanin. The diagnosis of primary pulmonary follicular dendritic cell neoplasm was performed. She

has been treated with chemotherapy (gemcitabine and docetaxel) for two months.
Results: FDCT represents less than 1% of all lymphoid neoplasm. Lymph nodes are the most common affected sites. Primary pulmonary cases are extremely rare. Since multiples lesions were found in the image exam, metastasis and primary epithelial lung cancer were the first hypotheses. Immunohistochemistry study is requisite to perform that diagnosis.
Conclusion: Since recurrence is frequent and the treatment is completely different from malignant epithelial neoplasm, the precise pathology diagnosis, despite it is challenging, it is necessary for an adequate follow-up.

E-PS-21-019
Genetic instability and recurrent MYC amplification in ALK-translocated NSCLC; a central role of TP53 mutations
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Background & Objective: The Anaplastic lymphoma kinase (ALK) rearrangement defines a distinct molecular subtype of non-small cell lung cancer (NSCLC). Despite the excellent initial efficacy of ALK inhibitors in patients with ALK+-lung cancer, resistance occurs almost inevitably. To date, there is no reliable biomarker allowing the identification of patients at higher risk of relapse. Here, we aimed to investigate if TP53 mutations in ALK+-NSCLC lead to genetic instability at the chromosomal level, and if the co-occurrence of TP53 mutations in ALK+-tumours describes a specific subtype of ALK+-NSCLCs.
Method: We analysed a subset of 53 ALK+-tumours with and without TP53 mutation and ALK+-NSCLC cell lines by NanoString nCounter technology.
Results: We found that the co-occurrence of early TP53 mutations in ALK+-NSCLC can lead to chromosomal instability: 24% of TP53-mutated patients showed amplifications of known cancer genes such as MYC (14%), CCND1 (10%), TERT (5%), BIRC2 (5%), ORAOV1 (5%), YAP1 (5%). MYC-overexpressing ALK+/TP53-mutated cells had a proliferative advantage compared to wildtype cells. ChIP-Seq data revealed MYC-binding sites within the promoter region of EML4 and MYC-overexpression in ALK+/TP53-mutated cells resulted in an upregulation of EML4-ALK, assuming a potential MYC-dependent resistance mechanism in patients with increased MYC copy numbers.
Conclusion: Our study reveals for the first time that ALK+-NSCLC represents a more heterogeneous subgroup of tumours than initially thought and that TP53 mutations in that particular cancer type define a subset of tumours that harbour chromosomal instability leading to the co-occurrence of pathogenic aberrations.

E-PS-21-020
EGFR L858R and T790M coexistence before first line therapy in pulmonary adenocarcinoma – case report
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Background & Objective: Somatic activating mutations in tyrosine kinase (TK) domain of EGFR confer tumour sensitivity to tyrosine kinase inhibitors (TKIs). Currently exon 20 T790M mutation appears after treatment with EGFR TKIs as consequence of tumoural acquired resistance. Osimertinib targets EGFR sensitizing mutations (exon 21 L858R, exon 19 deletions and exon 20 T790M resistance mutation) inhibiting EGFR T790M-positive tumours/metastasis growth (and crosses SNC blood barrier). TKIs EGFR resistance mutations may precede therapy with approved first/second-generation drugs.
Method: A 54-year-old man former eight years' smoker presented clinical staged T2aN2M1c (bone/brain) adenocarcinoma, diagnosed in brain metastasis; applied immunochemistry panel revelead CK7/TTF1/Vimentine positivity; CK5.6/CD56 negativity in unique solid pattern representation. Formalin-fixed paraffin-embedded microdissected tumoural tissue of the metastasis with over 50% represented tumoural cells was analyzed for EGFR mutations by IdyllaTM EGFR Mutation Test (exons 18/19/20/21). Similar procedure was applied to adjacent brain normal tissue (100% normal looking cells).
Results: EGFR mutational pattern was: exon 18 - wild-type, exon 19 - wild-type, exon 20 -T790M, exon 21 - L858R; normal brain tissue presented with wild-type for EGFR four exons.
Conclusion: EGFR exon 21 L858R mutation confers tumour sensitivity to TKIs while exon 20 T790M acts as resistance to TKIs and is rarely detected in untreated tumours. In this case it was not of germline origin, by testing neighbour tissue normal DNA, confirming the somatic origin of EGFR exon 20 T790M. The patient is under Osimertinib as first-line treatment. This type of cases is showing up together with germline EGFR mutated families where lung cancer risk becomes higher.

E-PS-21-021
Trends in lung cancer by immunohistochemistry markers from a specific region between January to September 2017
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Background & Objective: The introduction of molecular testing in lung cancer is key to improving therapeutic results and in low- and middle-income countries like Brazil since the access and incorporation strategies remain a significant challenge. Identify the main markers present in the studied group and understand the relation between the positivity of the markers and the prognosis of the patients
Method: They were retrospectively evaluated patients, between January and September 2017, diagnosed with pulmonary non-small cell carcinomas. Sixty-six (40 women and 26 men; 35 - 88 years old) patients were investigated immunohistochemistry with antibodies against ALK, EGFR, PDL-1 and ROS-1.
Results: The sample is comprised of 40 women and 26 men, ranging in age from 35 to 88 years old, the most frequent histological type being adenocarcinoma In 63 patients, EGFR mutational analyses were performed. In 10 EGFR mutations were not identified (wild type). The main types of EGFR mutations were: deletion in exon 19 (5); L858R point mutation in exon 21 (3), and mutations in exon 20 (3). ALK protein expression was considered positive in 4,7% (3 cases) in a total of 63 cases analyzed. PD-L1 expression was analyzed in 21 of the tumour samples. Of these, 14 (66%) were negative for PD-L1 expression and 7 (33%) showed some degree of positivity. The marker ROS-1 expression was analyzed in 7 and only one showed positivity.
Conclusion: No important associations among those biomarkers were found. The EGFR status mutation was smaller than the frequency reported in Brazil. Further studies are encouraged in order to understand how these biomarkers are distributed along this heterogeneous population.

E-PS-21-022
Morphological and morphometrical diagnostics of pulmonary tuberculosis and sarcoidosis
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Background & Objective: Morphological verification of granulomatous pulmonary disease remains a relevant problem. A major place is given to differential diagnostics of pulmonary tuberculosis and sarcoidosis due to absence of pathognomonic morphological signs. To take a morphological and morphometrical assessment of granulomatous process in pulmonary tuberculosis and sarcoidosis.
Method: Implemented analysis of medical history of in-patients, lung CT, thoraco-biopsy material during the period 2011 to 2016. Carried out 89 patients, among them 68 cases with pulmonary disseminated tuberculosis and 27 patients with pulmonary sarcoidosis.
Results: For pulmonary sarcoidosis there is peculiar formation of epithelioid-lymphoid and giant-cell granuloma, circularly divided with collagen fibers, placed perivascularly, no caseation necrosis area; morphometrical signs: increased number of plasmatic cells 44 (37;50) p=0,003*, lymphocytes 161 (154;174,5) p=0,057 – evidence of immunological injury, number of granulocytes 30 (26,5;40) p=0,011*, epithelioid cells decrease to 52 (40,5; 58) p=0,012*; number of stroma structural elements increases to 165 (155;178,5) p=0,016*, which points to predominance of fibroplastic processes; vessels number increase 21 (17;23) p=0,00*, there is noted remodeling of lung tissue with active angiogenesis. In case of pulmonary tuberculosis granuloma are at different formation stages, in the middle – with caseation necrosis area; morphometrically – increase of granulocytes number 102 (98;106,5) p=0,011*, and epithelioid cells 89 (82;95) p=0,012*, and multinucleate giant cells 9 (8;10) p=0,000*.
Conclusion: Developed morphological and morphometrical criteria can serve for differential diagnostics of pulmonary tuberculosis and sarcoidosis aimed to verification of clinical diagnosis.

E-PS-21-023
The value of sperm-associated antigen 9 in lung cancer progression
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Background & Objective: Sperm-associated antigen 9 (SPAG9) is a member of cancer testis antigen family and is highly expressed in some cancer types like kidney, breast, thyroid and colon. The aim of this study is to evaluate the SPAG 9 expression in non-small cell lung carcinomas (NSCLC) and analyze its effects on tumour progression.
Method: We reviewed 80 NSCLC who underwent surgical resection at Baskent University, Department of Thoracic Surgery between 2011 and 2016. SPAG 9 immunohistochemistry were performed to all cases. SPAG 9 expression was scored as low or high, according to both the density and intense of expression.
Results: The expression of SPAG 9 was low in 64 (80%) and high in 16 (20%) patients. In all squamous cell carcinoma cases, SPAG 9 expression was low, while in adenocarcinoma, 23 cases (63.9%) had low expression and 13 (36.1%) had high expression. Statistically significant association was detected between the density of SPAG 9 expression and the histological type (p=0.001), pT stage (p=0.05), TNM stage (p=0.001), the presence of lymph node metastasis (p=0.001) and the presence of metastases (p=0.03). The SPAG 9 expression was significantly higher in adenocarcinoma, compared with other histological types. By increasing pT and TNM stage, SPAG 9 expression was found to be increased. Also, SPAG 9 expression was increased in the patients who had metastasis,
Conclusion: We concluded that, SPAG 9 expression was increased in NSCLC and the density of SPAG 9 expression is correlated with tumour progression. Therefore, the inhibition of SPAG 9 expression could positively effect the patient's prognosis.

E-PS-21-024
Pleural desmoid-type fibromatosis: a case report
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Background & Objective: Desmoid-type fibromatosis is a benign tumour composed of fascicles of fibroblasts or myofibroblasts interlacing dense collagen bundles. Although the metastatic potential is low, fibromatosis has an infiltrative growth pattern and relatively high recurrence rate (25-60% at 5 years). It is located at body anywhere but pleural-based lesion is rarely reported.
Method: The Author reports a case of pleural desmoid-type fibromatosis.
Results: A 70- year-old man presented with a pleural mass on medical check-up. Chest computed tomography (CT) demonstrated a 9cm-sized mass of pleura attached to the right anterior chest wall. Percutaneous needle aspiration was performed. On biopsy slide, a low cellular fibrotic lesion was identified. Video-assisted thoracoscopic surgery (VATS) excision was performed. According to operation findings, the mass was well separated from lung, and ovoid, whitish and solid. Received specimen showed a whitish, resilient mass with an uneven surface. On cut section, the mass was homogeneous in consistency. No necrosis or hemorrhage was identified. Histologically the mass was a low cellular fibrous lesion. It consisted of dense collagen bundles and interlacing spindle cells. There were some areas with increased spindle cell cellularity. The spindle cells looked like fibroblasts or myofibroblasts and showed no cytologic atypia. No mitosis was identified. Differential diagnosis included solitary fibrous tumour, fibromatosis, and desmoplastic mesothelioma. Immunohistochemically, the spindle cells showed nuclear staining for b-catenin but negative for calretinin, D2-40, and pan-cytokeratin. The final diagnosis was Desmoid-type fibromatosis.
Conclusion: When diagnosing a pleural-based fibrous tumour, fibromatosis is rare but should be considered as a differential diagnosis.

E-PS-21-025
Epitheloid hemangioendothelioma diagnosed on lung biopsy: case report
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Background & Objective: Epitheloid hemangioendothelioma (EHE) is a rare neoplasm of vascular origin known to arise in soft tissue, liver and lung. Here we describe a case which was diagnosed on lung wedge biopsy whose prior lesions in liver and distal phalangial soft tissue were reported as indetermine vascular lesion 15 years ago.
Method: A 35-year-old women presented with multipl non-regressing lung nodules that have been detected 10 mounts ago. In the wedge resection specimen, there was multiple nodules measuring between 0.2 to 1 cm.
Results: The biggest nodule was well-circumscribed, showing a intraalveolar growth pattern and containing collagenised myxoid stroma. Scattered microscopic areas of necrosis were noted. Tumour cells are mostly epitheloid and some have intracytoplasmic vacuolisations and intranuclear inclusions. There was mild nuclear atypia and pleomorphism. Mitotic activity was 5 per 10 HPF. In the surrounding lung paranchyma and pleural surfaces, there was small microscopic nodules with similar histolojic features. Immunohistochemical studies showed that tumour cells diffusely stained positive for CD34, CD31, FLI-1, ERG, Factor-8 and TFE-3. Ki-67 proliferation index was 9 %. Considering the clinical findings and patient's history, the case was diagnosed as EHE. The former hepatic and soft tissue biopsies were re-evaluated and those vascular lesions were considered as EHE.
Conclusion: We report a rare case of multinodular pulmonary EHE in lung which was presented more than 10 years after primary liver and soft tissue involvement.

E-PS-21-026
Pleural diffuse malign mesothelioma with a specific pattern: adenomatoid (microcystic) form
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Background & Objective: Diffuse malignant mesothelioma (DMM) is a rare malignant tumour originating from mesothelial cells lining serosal membranes. Distinct histologic subtypes of epithelioid, sarcomatoid and biphasic mesothelioma according to WHO 2015 classification (1,2) are determined. Diffuse malignant mesothelioma with adenomatoid pattern (APMM) is a rare pattern of epithelioid type, accounting for 6% of malignant mesotheliomas.
Method: An 80 years old male farmer admitted to our chest surgery department with recurrent pleural effusions and dyspnea complaints. At CT scan of the thorax revealed pleural thickening with multiple calcifications in the right hemithorax and diaphragmatic pleural surface. Multiple biopsies were obtained and send for pathological examination. Histologic examination revealed microcystic structures with lace-like or signet ring appearances accompanied by focally micropapillary architecture. Immunohistochemical studies showed calretinin, WT-1, D2-40, CK7 positivity, and TTF-1, CK5/6, CK20 negativity.
Results: The case was defined as malign mesothelioma, epitheloid type (adenomatoid form) and was sent for chemotherapy options to the oncology department. After three sessions of single agent therapy with pemetrexed and two sessions with pemetrexed + carboplatin, the patient is followed-up without progression for six months.
Conclusion: Epithelioid mesothelioma shows mostly a solid, tubulopapillary and trabecular pattern. Differential diagnosis is difficult in rare cases with micropapillary, mixoid, adenomatoid, clear cell, transitional, deciduoid and small cell pattern. Adenomatoid form may show similar morphological features with pulmoner/metastatic adenacarcinoma and therefore, may be misdiagnosed. We present her a very rare case of APMM located in pleural space and try to discuss its clinicopathological features and differential diagnosis in light of literature.

E-PS-21-028
Cyclin D1 uniformly positive in pure lepidic lung adenocarcinoma suggesting tumour homogeneity
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Background & Objective: Cyclin D1 is a protein normally found in replicative cells. It plays a key role in p16 - cyclin D1- CDK4 - RB pathway of cell-cycle G1-S transition. In neoplastic cells, cyclin D1 is abnormal by quantity, not by quality. This was proven by authors [1,2,3] in this field through genetic studies which revealed that in lung adenocarcinoma, exccess of cyclin D1occur due to overexpression or due to increased copy number of the gene.
Method: We investigated by immunohistochemistry 27 cases of lung adenocarcinoma regarding positivity for cyclin D1 and the presence of intratumoural CD3+ T lymphocytes.
Results: We have observed that in four out of five cases of pure lepidic type lung adenocarcinoma, cyclin D1 was uniformly positive in tumour cells. In contrast, all other 22 cases, acinary, solid, papillary and mixed types of lung adenocarcinoma showed patchy positivity for cyclin D1. CD3+ T lymphocytes were rarely seen in lepidic type, while in other histological types they infiltrate peritumoural and in tumoural stroma in variable amount.
Conclusion: In lepidic type of lung adenocarcinoma, cell-cycle deregulation that imply p16 - cyclin D1- CDK4 - RB pathway may be a collateral event supporting alveolar cell neoplasia before the invasive potential. Lymphocytic inflammation in tumoural milieu is reduced. Aditional studies are needed.

E-PS-21-029
Resistance L747S mutation in an epidermal growth factor receptor tyrosine kinase inhibitor naïve patient and squamous cell carcinoma transformation after osimertinib treatment: a case report
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Background & Objective: The purpose of the present study was to report a case of epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI)-naïve patient carrying a mutation associated with acquired resistance to the drug and the histological change after EGFR-TKI treatment.
Method: A 55-year-old woman presented to our hospital with dyspnea. Her computed tomography (CT) showed a well-defined nodule in left upper lobe and multiple enlarged lymph-nodes around neck, hilar and mediastinum. The first biopsy was obtained from supraclavicular lymph node. At disease progression, the second and third lung biopsies were performed.
Results: The first biopsy was diagnosed metastatic adenocarcinoma from lung (TTF-1 positive) with EGFR exon19 deletion using a PNA-clamping assay. After gefitinib treatment, the second biopsy revealed few atypical cells and these are positive for TTF-1. The PNA clamping test with second biopsy showed T790M mutations without E19del mutation. Thereafter, osimertinib was administered. Third biopsy reveled immunohistochemically proven squamous cell carcinoma transformation with no mutation. We retrospectively assessed targeted next-generation sequencing (NGS) with her initial, second and third biopsy samples. The OncoChase Cancer Panel identified a p.749_754del mutation and a p.L747S mutation of EGFR exon19 in initial biopsy sample. In second biopsy tissue, two L747S and T709M mutations were identified. In third biopsy sample, a L747S mutation was only found.
Conclusion: The early detection of rare resistance EGFR mutation may be beneficial in making treatment decisions for lung carcinoma patients. When TKI resistance develops, we recommend that patients undergo a second biopsy to guide the next treatment and predict the prognosis.

E-PS-21-030
Choriocarcinoma: rare case
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Background & Objective: Gestational trophoblastic neoplasia (GTN) is a spectrum of diseases including partial and complete hydatidiform moles, placental site trophoblastic tumour, and choriocarcinoma. One of the most important considerations is recognition of the possibility of GTN after molar pregnancy or even normal pregnancy. This disease has an unpredictable biological behavior, whereas approximately 10-15% have clinically malignant evolution.
Method: A 28-years old female patient presented with ectopic pregnancy three years ago. The examination of the ectopic pregnancy material was diagnosed as hydatidiform mole diagnose at another institute. At 2018, she admits to our hospital for right shoulder pain. The chest X-ray evaluation revealed a mass on right and left lung. PET-CT revealed multiple noduler lesions. Incisional biopsy was performed for lung mass.
Results: On microscopic examination; focal necrotic and hemorrhagic areas were observed. A small number of cytotrophoblasts and syncytiotrophoblasts were seen in these areas. Immunostaining with β-hCG and hPL were applied and were both positive.
Conclusion: A very rare entity of multiple hemorrhagic metastases of choriocarcinoma to lung is very rare.

E-PS-21-031
Sclerosing pneumocytoma: two case reports and review of the literature
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Background & Objective: Pneumocytoma is very rare benign tumour of the lung with a predilection for middle-aged females. This tumour is derived from primitive respiratory epithelial cells.

Method: The first case is a 52 years old woman presented with a nodule in the lung. Chest CT revealed a 2.5 cm well-circumscribed nodule in the left upper lobe. The second case is a 28-year-old woman presented 3 cm nodule in the right upper lobe.
Results: The circumscribed mass was composed predominately of papillary structures, with the surface cuboidal cells located on the surface of the papillae and round cells in the stroma of papillae. There was hyalinized collagen in papillae, in solid areas, and in hemorrhagic areas at the periphery. Immunohistochemical staining demonstrated nuclear reactivity for TTF-1 and EMA in both cell types. Pan CK was positive in the surface cuboidal cells and was negative in the round cells. Surfactant protein B, HMB-45, CD56 were negative.
Conclusion: We report these extremely uncommon cases to assist in avoiding a misdiagnosis.

E-PS-21-032
New fusion gene PURA-ALK in patient with non-small cell lung cancer: case report
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Background & Objective: Alterations of gene ALK (anaplastic lymphoma kinase) have been described in many neoplastic processes, even in about in 1- 7 % of non-small cell lung cancer (NSCLC). The most frequent fusion partner in NSCLC is gene EML4, but other fusion partners have also been found (including KIF5B, TFG, KLC1, PTPN3, HIP1, TPR, STRN and A2M).
Method: 149 NSCLCs in the University Hospital Plzen (in the period 1/2017-12/2017) were tested by FISH and NGS (Archer FusionPlex CTL kit) to detected ALK gene alterations.
Results: One case of PURA-ALK fusion gene adenocarcinoma was detected. The fusion transcript consists of part of exon 1 of PURA gene followed by 124 bp long terminal part of intron 19 of ALK gene and then of exon 20 of ALK gene resulting in productive in-frame transcript with preserved ALK kinase domain. No other alteration of gene covered with CTL kit were detected (including mutations of EGFR, KRAS, and MET). The presence of PURA and ALK genes rearrangement as well as PURA-ALK fusion transcript was confirmed by FISH and by RT -PCR followed by Sanger sequencing, respectively. Histologically, tumour was adenocarcinoma with predominantly solid grown pattern, only focally with tubular architecture (CK7, TTF1 and ALK positive).
Conclusion: We described new fusion gene PURA-ALK in NSCLC. To the best of our knowledge, this is the first report about PURA-ALK fusion gene in NSCLC.

E-PS-21-033
Immunoglobulin G4 related disease in thorax: four cases report
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Background & Objective: Immunoglobulin G4 related disease is sclerosing fibroinflammatory disorder characterized by peculiar symptoms and lesions. It can be mistaken for malignancy. We describe 4 cases of thoracic IgG4 related disease.
Method: Case 1, a 70-year-old male was noted pulmonary parenchimal consolidation and mediastinal lymphadenopathy. Case 2, a 31-year-old male, computed tomography demonstrated left hilar and mediastinal lymphadenopathy. Case 3, a 35-year-old male who was being evaluated for tracheal tumour. Case 4, a71-year-old female, had anterior mediastinal mass and lymphadenopathy.
Results: Histopathology of all cases featured dense lymphoplasmacytic infiltrates, stromal storiform fibrosis and obliterative vasculitis and minimal eosinophilia.
Conclusion: Immunoglobulin G4 related disease can possess a broad spectrum of thoracic variety including lung, trachea, mediastinum.

E-PS-21-034
Adenocarcinoma of foetal lung type: report of a case
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Background & Objective: Adenocarcinoma of fetal lung type is a rare variant of pulmonary adenocarcinoma of endodermal origin, that exhibits architectural and cellular characteristics that resemble fetal lung tissue. It is considered a variant of solid adenocarcinoma with mucin production. The diagnosis of high grade fetal adenocarcinoma is rendered only for tumours that present at least 50% of fetal morphology. It is estimated to be 0.5% of all lung carcinomas.
Method: We report the case of a 75-year old male with a 11,5 cm mass located in his upper left lung lobe. A left standard pneunonectomy was performed and sent to our laboratory.
Results: Gross pathology revealed a well demarcated whitish tumour with extensive necrosis located in the upper lobe without any pleural involvement. Histological examination revealed an adenocarcinoma composed of glygogen-rich, complex neoplastic glands formations that resembled fetal lung at the 3rd month of gestation. The neoplastic cells displayed prominent nuclear atypia and high proliferation index (Ki67=80%). The scent interstitial stroma lacked morule formations. Immunohstochemical examination revealed that tumour cells expressed TTF1 and CK7 but not SMA, βCatenin, Chromogranin, Synaptophysin and Thyreoglobulin. The diagnosis was Adenocarcinoma of Fetal Lung Type, high grade.
Conclusion: These rare carcinomas occur predominately in the elderly with a long standing heavy smoking history. It is important to distinguish this type of lung carcinoma as its prognosis is considered to be more favorable than that of other forms of NSCLC.

E-PS-21-035
Spontaneous recurrent pneumothorax in a patient with pneumocystis pneumonia
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Background & Objective: We present a case of 35-year-old female complaining of progressive dyspnea, high fevers, diarrhea, diagnosed with ulcerous colitis 4 months ago (treatment with Mesalazine).
Method: Because of chest pain a radiography was administered and showed bilateral pneumonia with a left pneumothorax, treated with chest tube drainage, thoracotomy and excision.
Results: The material of lung is 63/12/10mm with reddish color, bullous emphysema, multiple whitish areas 1mm in diameter. Histologically the structure of the pulmonary parenchyma is significantly altered - alveolar spaces with fibrinous exudate, Giant cells "foreign body" type in the alveolar spaces and in the interstitium, focal deposition of calcium salts, fibrin microthrombi, foci of interstitial alveolitis - infiltration with lymphocytes, histiocytes, eosinophils, multiple zones with interstitial granulation tissue, fibrinous exudate in the interstitium, bronchiolar lumens filled with fibrinous materials, areas with hyperplasia of type 2 pneumocytes; cystic spaces, areas with fibro-cystic remodeling of the pulmonary parenchyma. PAS and Grocott staining showed multiple circular and elliptical structures diagnosed as Pneumocystis jirovecii. One month later the patient presented with pneumothorax on the right side treated with thoracotomy and excision. The material of lung is 43/16/12mm, with bulla and multiple whitish areas 1mm. The final

diagnosis was interstitial lung disease - diffuse alveolar damage in a patient with ulcerative colitis, Mesalazine treatment; partial fibro-cystic remodeling of pulmonary parenchyma; Pneumocystis jirovecii bilateral pneumonia. The patient was diagnosed with HIV.
Conclusion: Pneumocystis jirovecii can cause diffuse alveolar damage, fibro-cystic remodeling and recurrent spontaneous pneumothorax and should be considered in immunosupressed patients.

E-PS-21-036
Primary lung adenocarcinoma with morule-like components: clinicopathological study of 4 cases
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Background & Objective: The presence of morules has been detected in several tumours. In lung tumours, morule formation has been reported in pulmonary blastoma and low-grade adenocarcinoma of fetal lung type. Lung adenocarcinoma with morule-like components (MLC) is a very unusual variant.
Method: We present 4 cases of lung adenocarcinoma with MLC. We examined their clinico-pathological, and immunohistochemical features.
Results: 3 male/1 woman. Mean age: 55 years (range: 29-72). All but one tumours were peripheral: 3 right upper lobe, and 1 lower left lobe. Three tumours were acinar-predominant, and 1 was solid-predominant; size: 1,7 to 5 cm (mean: 2,9 cm). MLC: small solid nested uniform, spindle or polygonal cells, budding in the lumen of the neoplastic glands. MLC occupied 5-40% of total tumour. All cases stained positive for CK7, TTF-1, and Napsin-A. In 1 case: focal positive with neuroendocrine markers in both morule-like components and the adjacent tumour. All cases showed membranous staining of beta-catenin, and 2 cases focal aberrant expression. No difference in Ki-67 index between the MLC and the adjacent tumour. Metastatic adenocarcinoma was not found in lymph nodes. Three carcinomas were at stage I, and one at II. Three patients were alive 1-225 months after surgery, and one died of disease 21,8 months.
Conclusion: Adenocarcinoma with MLC was identified as a rare variant of pulmonary adenocarcinoma. We consider tumours with MLC a distinct morphological variant without prognostic significance. MLC should be discriminated from micropapillary and true sarcomatous spindle cells components, which are associated with aggressive behavior.

E-PS-21-037
Expression of p63 in adenocarcinoma of the lung as a factor of poor prognosis
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Background & Objective: Investigation of the effect of various markers of adenocarcinoma (ACL) of the lungs as prognostic factors.
Method: For 3-year period (2014 - 2017), adenocarcinoma of the lung was diagnosed in 104 patients (average age 59.8 years, women 54, men 50). The differential diagnostic panel of markers was used for diagnostic ACL: cytokeratins 7, 5/6 and 20, TTF-1, napsin A and p63. The analysis of the expression characteristic of these markers in the ACL as possible factors for the prognosis of the clinical course was carried out.
Results: In ACL cells, expression of CK7 was observed in 53/55 (96.4%) cases, CK20 - 5/27 (18.5%), TTF-1 - 50/55 (90.9%), napsine A-54 / 57 (90.7%), p63 - 14/33 (42.4%) cases, respectively. According to preliminary data, an important prognostic value of the expression of a markers was found only one marker - p63, and it is statistically significant ($p < 0.005$). Cytoplasmic and/or nuclear expression of p63 in different proportions of tumour cells is observed in ACL in 14 patients, in 5 (38.5%) of them progression and aggressiveness of the course of the disease were greater than in cases of the absence of expression of this marker. In the same patients, the status of the EGFR gene was determined. A mutation in this gene was detected in 4 patients, and in 3 patients (del19ex-2 cases and L858R-1 case) of them p63 expression was observed in the tumour. At present, this work continues.
Conclusion: p63 expression in adenocarcinoma of the lung is a factor of poor prognosis and faster progression.

E-PS-22 | Soft Tissue and Bone Pathology

E-PS-22-002
Low-grade fibromyxoid sarcoma in a young female – a case report and review of the literature
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Background & Objective: Low-grade fibromixoid sarcoma is a rare fibroblastic soft tissue neoplasm with bland morphologic features, but with possible aggressive course.
Method: We report the case of a 37-year-old female presenting with an 11-month history of increasing pain and slow growing swelling in the left popliteal area. Magnetic resonance imaging demonstrated the presence of a popliteal fossa soft tissue tumour, eliciting a mass effect in the nearby vascular-nerve sheet. The lesion was initially submitted to biopsy and was later surgically resected.
Results: The small biopsy fragments showed a fusocellular neoplasia, of variable cellularity (low/moderate), comprising areas of whorled architecture with myxoid stroma intermingled with areas of fibrous stroma. The neoplastic cells had ill-defined cytoplasm, elongated and hyperchromatic nucleus without cytological atypia. The immunohistochemistry study showed EMA focal expression and MUC4 diffuse expression. A diagnosis of low-grade fibromyxoid sarcoma was made. The surgical specimen was a 92g nodule of 8x5x4,5cm, with smooth and white external surface, partially involved by adipose tissue. The curt surface showed a well-defined multinodular neoplasia, with blue mucoid nodules, haemorrhagic foci, without necrosis. The histologic analysis confirmed the previous diagnosis. The neoplastic cells were positive for MUC4 and EMA, but were negative for CD34, S100 protein, MDM2 and Desmin.
Conclusion: This case illustrates the main features of these rare lesions, which display benign histologic characteristics, however, they might have aggressive behavior with recurrence and metastases rates that can go up to 60% at 15 years post-surgical removal. Therefore, a long term follow-up of the patients is mandatory.

E-PS-22-003
Alveolar soft part sarcoma from soft tissue and bone. A single reference hospital experience
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Background & Objective: Alveolar soft part sarcoma is a rare tumour, accounting for less than 1% of sarcomas. It usually arises between the second and the third decade without a clear sex preponderance. The most common location is the thigh. Primary bone location is extremely rare. The ASPSCR1-TFE3 translocation has been described as the most characteristic molecular alteration. Our objective is to review the cases diagnosed in our hospital.
Method: Seven cases between the years 1966-2017 were collected from our archives and clinical data was retrieved. Histological slides, including the immunohistochemical stainings available, were reviewed. Electron

microscopy was used in three cases and FISH probe for TFE3 translocation was used in one case.
Results: Ages ranged from 20 to 34 years (mean: 27). Three patients were females and four males. Five tumours arised from the soft tissues while two were primary bone tumours (femur and ulna). All cases showed organoid nests of cells with an alveolar pattern and irregular nuclei with prominent central nucleoli. Six cases presented PAS-positive diastase-resistant cytoplasmic crystals. We found no demonstrable crystals in the case located in the femur, but TFE3 translocation was confirmed by FISH. Immunohistochemistry for a wide panel of markers (S100, Cytokeratin AE1/AE3, alpha-actin, desmin, CD34) was consistently negative.
Conclusion: Our series is consistent with known epidemiological data. Interestingly, we found two primary osseous tumours. To our knowledge, ulnar location has not been described before.

E-PS-22-004
Primary angiosarcoma of the spleen: a case report
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Background & Objective: Case of a primary angiosarcoma of the spleen with hepatic metastasis in a patient presenting with a one-week lumbar pain.
Method: A 69-year-old female presented to our emergency department with a one week left lumbar/iliac pain and a not quantified weight loss in the previous year. Upon Abdominal examination it was found a tender, firm, palpable mass on the left upper quadrant. The analytical evaluation was unremarkable. The abdominal CT-scan showed a markedly enlarged spleen with ill-defined heterogeneous areas enhanced after contrast infusion. There were also hepatic and osteoblastic lesions. The patient was submitted to splenectomy and metastatic hepatectomy.
Results: Macroscopically, the spleen weighted 1385g and measured 22,5x13,5x7,5 cm with a smooth, red dark surface and a nodular appearance. In transverse section it presented ill-defined lesions with areas of hemorrhage and geographical necrosis. Microscopically the tumour was mainly composed of epithelioid cells, arranged in a solid pattern or lining disorganized vascular channels with extravased erythrocytes. There were smaller populations of fusiform or bizarre cells with marked atypia, anisokaryosis, hyperchromatic nuclei, irregular nuclear membrane and a high mitotic index (10/10 HFP). The immunohistochemistry study revealed positive expression for endothelial markers (CD31, CD34, FVIII) but was negative for CKAE1/AE3, S100, CD45 and HHV8. The hepatic lesion presented the same histological and histochemical characteristics.
Conclusion: Primary angiosarcoma of the spleen is a rare and aggressive neoplasm. It should be distinguished from other splenic vascular lesions, namely hemangioma, hemangioendothelioma, littoral cell angioma and Kaposi sarcoma.

E-PS-22-005
Spinal osteochondroma with malignant transformation and pushing border kidney infiltration in a patient with multiple osteochondromas
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Background & Objective: The most important complication of multiple osteochondromas (MO) is malignant transformation, which is estimated to occur in 0,5-5% of patients and leads to a secondary peripheral chondrosarcoma in 94% of the cases. We present a case of a malignantly transformed spinal osteochondroma in a 64-year old man with MO and pushing border infiltration in the kidney.
Method: Radiology revealed MOs through the whole skeleton. The largest osteochondroma suspected for malignization, located at the spine from the 11th thoracic vertebrae to the 2nd lumbar fulfilled the whole retroperitoneum and left lower abdomen. Two of the vertebrae were incompletely destroyed. A tumour was also seen in the upper pole of the kidney with radiological signs of malignancy. Nephrectomy and cytoreduction of the osteochondroma was performed. The operative material was composed of numerous bony and cartilaginous fragments (1600gr) and a kidney with a well-demarcated tumour located on the upper pole measuring 16,5x15x7,5cm, with a torn capsule. A standard procedure of paraffin embedded section routinely stained with H&E was performed.
Results: On naked eye, the kidney tumour was well–demarcated, having a firmly attached pseudocapsule which separated it from the kidney. On cut surface the tumour was determined as a cartilaginous malignant neoplasm. Microscopically it was diagnosed as a high grade conventional chondrosarcoma. The reminder material was diagnosed as osteochondroma with malignant transformation.
Conclusion: Patients with MO should be permanently followed up for early detection of malignancy even in older adults. Pushing border infiltration is an unusual example of a chondrosarcoma infiltrating into a visceral organ.

E-PS-22-006
Soft tissue liposarcoma: a very unusual tumour in the setting of Muir-Torre syndrome
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Background & Objective: Muir-Torre Syndrome (MTS) is a rare autosomal dominant genodermatosis, associated with loss of expression of DNA reparatory proteins (hMSH2, hMSH6, hMLH1 and hPMS2 genes), and is therefore considered by some a subtype of the Lynch Syndrome. It is characterized by the coexistence of sebaceous neoplasms with one or more visceral tumours, mainly gastrointestinal and genitourinary. Soft tissue sarcomas are exceptional in this context.
Method: We present a case of a 68 years old patient, with history of multiple neoplasms (cutaneous squamous cell carcinoma, ampulloma and lower limb soft tissue liposarcoma), who presents a cutaneous lesion in the left eyelid
Results: Histological examination of the eyelid lesion revealed a sebaceous adenoma. Given the history of this individual, once this diagnosis was made, we considered the possibility of a case of MTS. Thus, immunohistochemical studies were performed in all previous tumours. Loss of expression of MSH2 and MSH6 proteins was demonstrated in all of them, surprisingly, including the liposarcoma. Given this exceptional result in this tumour, diagnosed 14 years ago, a revision of new slides and up to date immunohistochemical studies were performed, confirming this diagnosis.
Conclusion: Small numbers of Lynch Syndrome-associated soft tissue sarcomas have been reported, but there is only one documented case of soft tissue liposarcoma in MTS, related to previous radiotherapy. To our knowledge, our case represents the second example of this association and the first one not arising in a previous radiation field. There is also a reported case of a retroperitoneal undifferentiated pleomorphic sarcoma not related with radiation therapy

E-PS-22-007
Metastatic vena cava leiomyoma of Mullerian origin: an unusual presentation of a histologically benign smooth muscle tumour
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Background & Objective: Leiomyoma is a benign smooth muscle tumour. In rare occasions, nevertheless, metastasis of leiomyomas may occur, and a high degree of suspicion is required for the correct diagnosis of such lesions.
Method: Herein we report a case of metastatic leiomyoma of Mullerian origin to the vena cava.
Results: A 31-year-old female with history of extensive uterine leiomyomatosis developed a vascularized lesion in the inferior vena cava measuring 16.0cm. Microscopy demonstrated a spindle cell proliferation with subtle cytologic atypia, alternating cellularity and concentric perivascular growth pattern in a richly vascularized hyaline background. There was no necrosis or mitotic activity. The patient also presented a pulmonary nodule with similar morphological characteristics. Immunohistochemistry demonstrated the myogenic nature of the lesion, and the diagnostic hypothesis of primary leiomyoma originating from vasa vasorum and metastatic leiomyoma of Mullerian origin were investigated. The tumour cells were strongly positive for estrogen receptor and WT1, and in situ hybridization for EBV was negative. Considering the histological characteristics and clinical data, the patient was diagnosed with a metastatic leiomyoma of Mullerian origin non-related to EBV-infection.
Conclusion: Metastasic leiomyomas are rare, and are usually derived of Mullerian leiomyomatosis with evidence of clonality between the metastatic lesions and their uterine counterparts. The expression of common immunohistochemical markers of a gynaecologic origin may aid the diagnosis. As EBV has been associated with multifocal and heterogeneous smooth muscle tumours with a perivascular growth, the exclusion of this infection is recommended. In conclusion, a thorough clinical history and complementary immunohistochemistry are key elements for the definitive diagnosis of metastatic leiomyomas.

E-PS-22-008
Post-radiation epithelioid angiosarcoma of the neck soft tissue: report of two cases
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Background & Objective: Epithelioid angiosarcoma is a rare variant of angiosarcoma composed of large rounded epithelioid endothelial cells. A minority of cases is associated with radiotherapy. High level of MYC amplification is the hallmark of most radiation-induced AS that does not occur in other radiation-related sarcomas.
Method: We present two cases of epithelioid angiosarcoma developed secondary to previous radiotherapy in the neck soft tissue.
Results: First patient – a 65-year-old man was treated in 2007 with radiotherapy for laryngeal squamous cell carcinoma. Second patient – a 72-year-old woman had received radiotherapy for synonasal carcinoma in 2009. In 2017 and 2018, incidental mass measured 2,0 and 1,5 cm developed at neck soft tissue in both patients, which subsequently was resected. Microscopically, both neoplasms are composed of round to epithelioid cells with abundant eosinophilic cytoplasm. There were poorly formed vascular channels with erythrocytes. Vasoformative pattern of usual angiosarcoma was found focally in the first case. Immunohistochemical study revealed expression of CD31, ERG, focal and dot-like AE1/3 and c-myc. Analysis of MYC by fluorescence in situ hybridization have identified high level of gene amplification in both samples what supports the diagnosis of post-radiation epithelioid angiosarcoma.
Conclusion: Post-radiation epithelioid angiosarcoma is extremely rare tumour with specific morphology that may lead to erroneous diagnosis of poorly differentiated carcinoma metastasis in patients with previous cancer. Careful clinico-morphological examination and evidence of MYC amplification, as seen in the current case, is crucial to establish a correct diagnosis.

E-PS-22-009
Glomus tumour of uncertain malignant potential. A case report
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Background & Objective: Glomus tumours are a group of uncommon tumours accounting 1-2% of soft tissue tumours. They arise from the muscle cells of glomus body, which is involved in thermoregulation. These tumours usually occur in the distal extremities of younger adults and very rarely in the deep soft tissue.
Method: We present a case of a 38 year old female with a long lasting mass located in her dorsal forearm. CT imaging revealed an 45mm tumour ill defined mass located in deep soft tissue of the patient's forearm. Tumour was excised and sent to our laboratory for histological examination.
Results: Histological examination revealed a neoplasm consisting of small homogeneous round and spindle cells, located around dilated blood vessels and infiltrating the co-excised striated muscle fibers. Tumour cells displayed very low mitotic activity (1/50HpF with Ki67 <1%) while no necrotic areas were observed. Immunohistochemical stains revealed that the tumour cells expressed SMA, Vimentin but not CD34. After taking into account the size, the deep location and the absence of atypical mitotic figures the final diagnosis was Glomus Tumour of Uncertain Malignant Potential (GTUMP/Atypical Glomus Tumour).
Conclusion: GTUMP are rare tumours diagnosed incidentally. Although several genetic alterations have been identified (like Mir143-NOTCH fusion) the exact cause is yet unknown. Complete excision with negative margins is the treatment of choice, however it is difficult to predict the outcome of these tumours as follow-up for soft tissue Glomus Tumours is scarce in literature. Our patient is free of disease for over 24 months.

E-PS-22-011
Extraskeletal chondrosarcomas: a retrospective study of 8 cases
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Background & Objective: Extraskeletal chondrosarcomas (ECS)are rare tumours, far less common than their intraosseous counterparts, representing approximately 2% of all soft tissue sarcomas. Soft tissue chondrosarcomas are typically divided into myxoid, mesenchymal, and well-differentiated type, which are very rare. The aim of the study was to evaluate the histopathologic characteristics of this rare tumour and to highlight its diagnostic difficulty.
Method: We retrospectively analyzed the clinical and pathologic data of 8 patients, initially diagnosed with ECS at our institution from 2000 to 2016. The size, location and histological type of the tumours were analyzed.
Results: There were 5 men and 3 women with a mean age of 42 years (16-61 years). The average tumour size was 10.75 cm (6 to 21 cm). The tumour was located at the proximal extremities of the lower limbs in 50% of the cases (n = 4), in the upper limbs in 25% of the cases (n = 2) and at the chest wall in 25% of the cases (n = 2). Two histological types were found in our series: mesenchymal chondrosarcoma in 5 patients (62.5%) and myxoid chondrosarcoma in 3 patients (37.5%). Local recurrence after excision of the tumour was found in 37.5% (n = 3).
Conclusion: ECS is a rare soft tissue tumour with high rates of recurrence presenting multiple challenges. Diagnostic pitfalls include inadequate

biopsy samples, which may result in sample error. ECS needs to be treated stringently in cooperation with an oncology center. Future cooperative studies may help standardize treatment and improve our understanding of this rare malignancy.

E-PS-22-012

Alternative lengthening of telomeres in soft tissue sarcoma is associated with aggressive clinical prognosis

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Background & Objective: Alternative lengthening of telomeres (ALT) is a telomerase-independent telomere maintenance mechanism. The molecular basis and features of ALT in soft tissue sarcomas have not been clearly established yet. In this study, we assessed clinicopathologic features of various kinds of bone and soft tissue sarcomas, with the ALT phenotype and the possible relationship between ALT and ATRX/DAXX expression.
Method: Tissue microarray (TMA) was constructed using 249 cases of soft tissue sarcoma from 2000 to 2015 at single institute of the Asan Medical Center. FISH for ALT and immunohistochemistry for ATRX/DAXX were performed and the results were compared with clinicopathologic parameters.
Results: ALT and loss of ATRX/DAXX nuclear expression was observed in 19.7% (49/249) and 1.6% (4/249), respectively. ALT-positive sarcomas displayed a significantly shorter recurrence-free survival period (HR=1.65, 95% CI=1.08-2.52; p=0.022). The higher the tumour grade, the shorter overall survival (p=0.018) and recurrence-free survival (p=0.001) period was identified. No correlation is observed between ALT FISH and loss of ATRX/DAXX (p=0.586). No statistical significance is identified another parameters including tumour grade (p=0.285), tumour location (p=0.169), and tumour size (p=0.387). Although no statistical significance is observed between ALT and tumour grade, there is a tendency that the more pleomorphic histology showed the more abnormality of ALT (p=0.002).
Conclusion: We concluded that the ALT phenotype in the bone and soft tissue sarcomas is associated poor clinical behavior. Therefore, ALT status may be used as prognostic markers of soft tissue sarcoma.

E-PS-22-013

A curious case of intravenous lobular capillary haemangioma (pyogenic granuloma) of the ovarian vein: a case report

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Background & Objective: Intravenous capillary haemangioma is a rare benign lesion with minimal plubished reports containing a description of its appearance at medical imaging. It is usually located in the head and neck regions.
Method: 84 years old woman with a history of abdominal discomfort for several weeks. Physical exam showed light abdominal pain at abdominal palpation. Ultrasound examination was performed and showed an 10cm mass with multiple cystic spaces.
Results: The patient underwent surgery. Pathology report showed: Multiple vasclular spaces with capillaries lined with flattened endothelial cells grouped in a lobular pattern. These lobules are separated by an edematous fibromyxoid stroma. There was not necrosis or mitotic figures. Inmunohistochemestry stains showed positive stain for: CD34, CD31 and ERG. Ki65< 2%.
Conclusion: Intravenous lobular capillary haemangioma (pyogenic granuloma) is a common benign lesion, usually found on the skin and mucous membranes. The intravascular variant is a rare lesión. It appers to have been first described in 1967 although Cooper´s series of 18 cases published in 1979 is usually referenced as the initial description. The latter paper used the term "Intravascular Pyogenic Granuloma". Despite the potentially concerning intravascular presentation has an excellent prognosis after excision with the associated vein Wall. Recurrences or more distant disseminated vascular lesions have not been described.

E-PS-22-014

An unusual variant of dermal nerve sheath myxoma with regular highly pleomorphic features: a case study

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Background & Objective: Nerve sheath myxoma (NSM) was first described in 1969 by Harkin and Reed. Later NSM had been regarded as neurothekeoma. But now they are designated as separate distinctive entities. Dermal NSM usually has only mild nuclear atypia. Herein we present an unusual variant of dermal NSM with sarcoma-like cytological pleomorphism.
Method: A 34-year-old woman was presented with a nodular cutaneous lesion 1.5 cm in greatest dimension, located on anterior surface of the thigh, clinically diagnosed as dermatofibroma. It had been existed for two years, remained stable and was excised for cosmetic reasons. Tissue samples were examined histologically and immunohistochemically.
Results: Microscopic examination revealed a circumscribed multinodular tumour bordered by dense fibrous capsule. This tumour was located in dermis superficially extending into subcutis. Nodules consisted of large pleomorphic uni-, bi- and multinuclear cells of variable shape (oval, multipolar, stellate) with variably vacuolated dense eosinophilic granular cytoplasm. Nuclei were large, hyperchromatic and bizarre in shape, some with large cytoplasmic pseudoinclusions and large prominent nucleoli. Tumour cells were set in abundant pale myxoid stroma. Mitoses were absent, Ki67 index was low (2%). Tumour cells were negative for CK, SMA, desmin, MyoD1 and positive for vimentin, S100, NSE, GFAP, SOX10 and EMA. The final diagnosis was "dermal nerve sheath myxoma with marked pleomorphism".
Conclusion: In some rare cases the dermal NSM can be completely composed of pleomorphic atypical cells resembling sarcoma. Long duration, small dimensions, absence of rapid growth, circumscription, low mitotic activity confirm benign nature of this unusual lesion. We propose classify it as pleomorphic variant of dermal NSM.

E-PS-22-015

Radiation-induced pelvic rhabdomyosarcoma following treatment of cervical cancer

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Background & Objective: Post-radiation sarcomas are rare complications of radiotherapy that occur within a previously irradiated field after several years of latency. Undifferentiated pleomorphic sarcoma, Osteosarcoma, and Angiosarcoma are the most common histological subtypes. Herein we present an unusual subtype of radiation induced sarcoma with rhabdomyoblastic differentiation.
Method: A 48-year old female with a history of moderately differentiated squamous cell carcinoma of the cervix diagnosed 12 years ago and was treated with chemo-radiotherapy with complete response and no residual disease. She lost follow-up and then presented incidentally with hip pain after a fall. Pelvic MRI showed an aggressive uterine/cervical mass involving most of the pelvic organs and extending through the right greater sciatic foramen into the gluteal muscles, vaginal wall, and the vulva.
Results: A biopsy from the vulva showed fragments of unremarkable squamous epithelium overlying sheets of malignant high-grade

epithelioid and spindle cells with no specific growth pattern. The neoplastic cells were positive for vimentin, desmin, myogenin, and moyD1; and negative for pan-cytokeratin, CK5/6, EMA, p63, p16, LCA, S-100, caldesmon, and SMA. Based on this immunoprofile, a diagnosis of post-radiation rhabdomyosarcoma was made.
Conclusion: To the best of our knowledge, this case is one of the extremely rare post-radiation sarcoma showing rhabdomyoblastic differentiation. Though it is very unusual, it should be kept in mind whenever a high-grade, locally advanced, malignant neoplasm is encountered in a patient with a previous history of radiation.

E-PS-22-016
Primary monostotic diffuse large B-cell lymphoma (DLBCL): report of a series of 4 cases
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Background & Objective: Primary bone lymphomas are rare. They are usually DLBCL in localized stages and with a better prognosis than its nodal counterpart. We present the clinical-pathological features of four cases diagnosed in our geographical area.
Method: Our series correspond to four patients (male:2, female:2) between 46 and 68 years old, with solitary lesions at ilium (3) and olecranon (1), showing lytic lesions (2) and permeative bone pattern (2) at imaging techniques.
Results: All cases correspond histologically to DLBCL, NOS (WHO 2016), with proliferative index between 50-80%. In three of the cases, their immunophenotype could be classified (2: germinal center, 1: non-germinal center. The extension study showed a localized stage, and no progression was detected in the available follow-up period (6 months to 2 years) after chemotherapy.
Conclusion: Primary bone lymphomas are rare (less than 1% lymphomas, up to 5% of extranodal cases). They are isolated lesions, frequently biopsied under suspicion of metastasis of unknown origin. The most frequent locations are femur and pelvis (as three of our four cases). Most of the reported cases are DLBCL. Prognosis is good compared to their nodal counterpart, with survival between 70-100% at 5 years The immunophenotypic subclassification (in our group of cases at least 50% belongs to the "germinal center" group) does not seem to have a significant prognostic value, being age (less than 60 years, as two the cases in our series) and initial response to treatment (as in all of the current cases) predictors of good prognosis and the presence of pathological fractures indicator of bad behavior

E-PS-22-017
Diagnostic value of synovial biopsy in clinical practice
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Background & Objective: Histopathological study of synovial biopsy is one of the most valuable means for the diagnosis of joint diseases, as clinical diagnosis has its own limitations. Aim: to evaluate the reliability of the synovial biopsy in the etiological diagnosis of mono- and oligo-arthropathies.
Method: Our retrospective study concerned 43 synovial biopsies collected at the department of pathology of the university hospital Mongi Slim La Marsa hospital over a three-year period (March 2015- March 2018).
Results: The average age of our patients was 56.18 years with extremes ranging from 24 to 80 years old. In our series, synovial biopsies were performed exclusively in large joints. They interested in order of frequency the knee (79%), the hip (9%), the elbow (7%) and the ankle (5%). Histopathological examination classified synovial biopsies into septic arthritis (n=23), mechanical arthropathy (n=5), rheumatic synovitis (n=5), reactive synovitis (n =7), chondrocalcinosis (n=1) and metastatic adenocarcinoma of synovium (n=1). The definitive diagnosis was based on a set of arguments including clinical, biology, radiological examination, histology and evolution data. The pathological examination was consistent with the definitive diagnosis in 90% of the cases in our series, in agreement with the data of the literature where this rate varies from 28.7 to 85%.
Conclusion: Synovial biopsy is an important and final tool for definitive diagnosis of joint disorders. Correlation with clinical, radiological, and serological findings helps to arrive at an accurate diagnosis.

E-PS-22-018
Leiomyosarcoma of the inferior vena cava: a case report
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Background & Objective: Leiomyosarcoma (LMS) of the inferior vena cava (IVC) is a rare type of neoplasm, accounting for <0,5 of adult soft tissue sarcoma affecting <1/100.000 of all adult malignancies.
Method: 64 years old female with chief complaint of abdominal pain during the last 4 months. The physical examination revealed pain on mesogastric palpation with no signs of peritoneal irritation and no palpable masses. CT scan showed a 10cm rertoperitoneal mass and multiple hepatic metastases.
Results: The patient underwent surgery post neoadjuvnt. Pathological analysis revealed an 10x7x8,5cm mass with intraluminal growth that showed a hypercellular spindle cell neoplasm, with cells resembling smooth muscle cells but with moderate to sevre pleomorphism. Inmunohistochemestry showed strong positive staining for: vimentin, desmin, smooht muscle a-actina (SMA) and caldesmon and negative staining for: CKAe1-Ae3, S100; Ki67:25%. Clear surgical margins.
Conclusion: Most of the cases of primary leiomyosarcoma of the inferior vena cava occur in women in their 6th decade of life who present with abdominal pain. Due to its retroperitoneal location, the presentation of leimyosarcoma of IVC is usually insidious, the majority of cases in the published literatura were diagnosed at a late atage. Agressive surgical resection is the current treatment of choice. Complete resection with clear margins is feasible in two-thirds of the treated patients.

E-PS-22-019
Omental lipoma-like hibernoma in pregnancy: case report
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Background & Objective: Hibernomas are slow growing, rare benign tumours, which are derived from brown adipose tissue. The lipoma like variant is a rare variant and it can be misdiagnosed as lipoma. In contrast to lipomas, hibernomas are extremely rare, with fewer than 200 overall cases reported in the literature. In this report, we present the clinical and morphological features of a omental lipoma-like variant of hibernoma in a pregnant woman.
Method: In gross examination, the specimen was 2x1,5x1 cm in size, well-circumscribed and encapsulated. Its cut surface was yellow to brown, rich in adipose tissue with focal areas of hemorrhage. Microscopically, the tumour was encapsulated, well-circumscribed and it mostly consisted of mature univacuolar adipocytes. At high power view, tumour cells had generally coarse, granular, eosinophilic and rarely clear multivacuolated cytoplasm with centrally located nucleus and were scattered among the univacuolar adipocytes. Mitotic activity, necrosis, and cellular

atypia were absent. There was a prominent vascularity with extensive hemorrhage. Finally, a histologic diagnosis of lipoma-like variant of hibernoma was made
Results: Lipoma-like hibernoma is a rare variant of hibernomas. Thigh is the most common site and they are rarely identified in the abdominal cavity.
Conclusion: We herein report an incidentally detected omental lipoma-like hibernoma in a pregnant woman

E-PS-22-020
Concordance in the diagnosis of soft tissue / bone pathology cases, reviewed in a reference center
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Background & Objective: Soft tissue and bone sarcomas are infrequent tumours that need to be managed in reference centers by a multidisciplinary team. Our hospital has been designated as such, which has provided us with high numbers of cases to review. Our purpose is to compare the diagnostic concordance between the initial diagnosis from the original report and the reviewed one.
Method: We searched for reviewed soft tissue and bone pathology cases from patients treated in our institution since july 2015 until now. Concordance was scored as follows: Concordance: both diagnosis were the same; minor discordance: variations affecting histological grade or name of a benign or low-grade tumour, with no clinical implications; major discordance: there was a change from benign to malignant, from malignant to benign, or different tumour with clinical implications.
Results: 75 cases were identified, 55 of them with original report available. Concordance was found in 40/55 cases (72,7%), minor discordance in 7/55 cases (12,7%) and major discordance in 8/55 cases (14,5%). Among the last group, 4 cases changed from benign to malignant, 2 cases from malignant to benign and 2 cases to another entity with clinical implications.
Conclusion: Our proportion of discordant cases fits in with that reported in the literature. Most of discrepancies correspond to superficial soft tissue tumours that are easily biopsied or excised in small hospitals and primary care centers. This fact emphasizes the difficulty in managing these rare tumours and why they should be handled in reference centers from the beginning.

E-PS-22-021
A case report of an axillary malignant peripheral nerve sheath tumour
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Background & Objective: Malignant peripheral nerve sheath tumours (MPNSTs) are uncommon biologically aggressive soft tissue sarcomas of neural origin (peripheral nerves or elements of the nerve sheath such as Schwann cells, fibroblasts or peripheral cells). One half of MPNSTs occur with neurofibromatosis 1(NF1). Most common sites of involvement include the nerve roots and bundles in the extremities and pelvis.
Method: A 80-year old woman was presented with a painful, rapidly growing left axillary mass. Tumour's size (7x5x7cm) and anatomical extent (subcutaneous tissue) were evaluated using MRI records. A complete surgical excision was performed.
Results: We received a lobulated, whitish firm in consistency tumour. Histological study showed a masenchymal neoplasm consisting exclusively of dense fascicles of spindled cells localized in close proximity to blood vessels. Several scattered pleomorphic giant elements and areas of nuclear palisading, necrosis and hemorrhage were found. Immunohistochemistry demonstrated positivity for vimentin, S100p, CD34, CD99, CD56, P53, NSE (focally) and Ki67 (60%). SMA, desmin, EMA, CK7, CK19, Factor VIII, TTF1, ER/PR, HMB45 did not expressed. By all these findings histological diagnosis was made as MPNST.
Conclusion: MPNSTs are rare high-grade sarcomas with a high propensity of local reccurence and distance metastasis (usually lung). The 5-year survival rate (ranging between 5-50%) is based on the tumours size, location, grade, stage, status of surgical margins and the NF1-association (poorer prognosis). Treatment of choise is complete tumour's surgical removal. Radiotherapy and adjuvant chemotherapy also may recomented.

E-PS-22-022
Tumoural calcinosis: a case report
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Background & Objective: Tumoural calcinosis is a rare disease characterized by periarticular calcium deposits in soft tissue. It can be seen idiopathically but more often it may result in an imbalance in the calcium-phosphate metabolism. Patients usually are presented in the first or second decade of life with large progressively enlarging juxta-articular calcification.
Method: The surgical specimen was formalin-fixed and paraffin embedded. The sections were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 21-year-old male patient with a Nieman-Pick disease was regularly hemodialysed three times a week for the last six years. He had attended to orthopedics clinic in our hospital with the complaint of painful swelling of the right forearm. On physical examination; a soft, mobile mass approximately 4 cm in diameter was detected. Radiological examination revealed periarticular, intense, soft tissue calcifications in both left and right forearm. Macroscopic examination of the surgical material revealed 4x3x2 cm sized, yellow-cream coloured, soft-grained textures. Histopathological examination revealed hyalinized fibrotic tissues and cystic structures with multinuclear histiocytic cells, fibroblasts and inflammatory cells around in different shapes and sizes.
Conclusion: Tumoural calcinosis is a rare, benign condition, characterised by large calcific periarticular soft tissue masses composed of hydroxyapatite or amorphous calcium phosphate crystals. This case draws attention to soft tissue complications of unbalanced calcium phosphate control in hemodialysis patients and giant cell tumours and histiocytic tumours absolutely should be kept in mind in the differential diagnosis of tumoural calcinosis.

E-PS-23 | Thymic and Mediastinal Pathology

E-PS-23-001
Contribution of a new case of "nut" carcinoma
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Background & Objective: The carcinoma "NUT" is a subtype of clinically very aggressive squamous cell carcinoma that is defined by the mutation of the "NUT" (NUclear protein of the Testis) gene. It was first described in 1991 and usually occurs in young patients. Although initially the cases were described affecting the mediastinum, today approximately

35% of cases occur in other areas, mainly head and neck. We present a diagnosed case of maxillary localization.
Method: A 16-year-old male who came to the hospital due to a sudden appearance of left facial edema. In the radiological study an infiltrating mass was observed in the left maxillary bone that extended to the palate. It was resected by subtotal maxillectomy. Two months later, the tumour recurred extending to soft tissue and periorbital bone ridge, so the patient underwent enucleation. Finally, the patient dies two months after tumour persistence.
Results: The histopathological study showed a poorly differentiated squamous cell carcinoma. Due to the clinicopathological characteristics, it was decided to study a possible mutation of the "NUT" gene by immunohistochemical study, with a positive result in 70% of the tumour cells. An ultrastructural study was also carried out that supported the squamous origin of the neoplasm.
Conclusion: The subtype "NUT" of poorly differentiated squamous cell carcinoma, although infrequent, is likely to be underdiagnosed. On the other hand, despite existing targeted therapies for this rare carcinoma, the prognosis is unfortunate. However, clinical trials are being conducted with different therapeutic options.

E-PS-23-002
A rare case of primary anterior mediastinal yolk sac tumour in an elderly adult male with lung metastasis
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Background & Objective: Primary yolk sac tumour (YST) of the anterior mediastinum is rare and has a poor prognosis. A few cases of gonadal and extragonadal germ cell tumours have been reported in elderly patients. We present an elderly 64-year-old male with primary yolk sac tumour of the mediastinum.
Method: A 64-year-old male was admitted to our hospital with a history of chest pain. Alpha-fetoprotein (AFP) was elevated at 4.569 IU/ml, and lactate dehydrogenase (LDH) was 1038 U/l. Positron emission tomography/computed tomography (PET/CT) showed anterior mediastinal mass, measuring 13x5x7 cm and hypermetabolic metastatic bilateral nodules in lungs.
Results: Histologic evaluation of the mediastinal mass revealed abundant pleomorphic tumour cells with reticular growth pattern. Immunohistochemistry showed reactivity with SALL4, Glypican-3, AFP and focal positivity EMA. The tumour cells were nonreactive with CD117, PLAP, TTF-1, synaptophysin. Considering the unremarkable PET-CT of the scrotum based on the light microscopy, morphology and immune phenotype, our final diagnosis is a primary anterior mediastinal YST.
Conclusion: Extragonadal GCTs (EGGCTs) are rare. The mediastinum is the most common site of EGGCTs. It rarely appears after the age of 30. Elderly patients with germ cell tumour generally have worse clinical outcomes compared to younger patients.

E-PS-23-003
Child with chest pain and dyspnea due to mature teratoma of the thymus: a case report
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Background & Objective: Mediastinal germ cell tumours (MGCT) are rare and represent approximately 1-3% of all germ cell neoplasms. Teratomas are an infrequent observation, accounting for only 7%-11% of extragonadal teratomas, mainly located in the anterior mediastinum arising from the thymus and rare in paediatric age. The most common histologic type of MGCT is mature teratoma (MT) and Computed Tomography (CT) is the modality of choice for diagnostic evaluation. MT is a benign neoplasm that can arise within the thymic parenchyma, more frequently in women in postpuberal age, and asymptomatic in 50% of children with diagnosis as an incidental finding on imaging studies.
Method: A 14-year-old boy presented with chest pain and dyspnea needing emergency observation; Echocardiogram revealed pericardial effusion understood as acute pericarditis. It relapsed 1 month later, and CT revealed an anterior mediastinum mass 77x64x60mm large; β-HCG and α-fetoprotein was not validated in peripheral blood.
Results: A complete surgical excision of the thymus was performed. Grossly it was an encapsulated mass, with cystic cavities filled with hair, keratinaceous debris and cartilage. Mature tissues were visualized representing all three embryonic layers, with predominance of skin and appendages as well as bronchial type mucosa.
Conclusion: MGCT representing approximately 24% of anterior mediastinal tumours in children, may produce symptoms due to compression of mediastinal structures as chest pain and dyspnea mainly when reaching huge dimensions. In these instances, pleural effusion may occur. The treatment of MT consists of complete surgical excision of the mass. MT have an excellent prognosis and 5-year survival rates approach 100%.

E-PS-23-004
Solitary fibrous tumour of the pleura: review of cases in a university hospital over the last twenty years
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Background & Objective: The aim of this review is to study and classify the cases of solitary fibrous tumour of the pleura, on the basis of the histological classification accepted nowadays (WHO 2015)
Method: Retrospective study of the medical records and archival tissue sections of all cases with solitary fibrous pleural tumours that were diagnosed and surgically resected at the Cruces University Hospital between January 1998 and January 2018
Results: We found 23 cases, with a mean age of 61,9 years (range 36-81). A slight male predominance was noted (12 cases, 52%). The tumour size ranged from from 3-38 cm lengthwise. On average, most of the tumours were classified as benign / with low malignant potential, with only 3 lesions with malignant features / high malignant potential (13%). SFT relapse ocurred in two patients despite the original radical extirpation (100% in cases with malignant features (>4 mitosis/2 mm2). Adjuvant treatment was administered to one of this two patients
Conclusion: Solitary fibrous tumours represent a heterogeneous group of primary pleural neoplasms with a low incidence rate and of which the biological origin, which consists of mesenchymal cells, is uncertain. The gold standard of SFT treatment is radical surgical removal. Additionally, patients at risk of recurrence would requiere careful follow-up. The administration of adjuvant therapy is still a subject to discussion

E-PS-23-005
Impact of iron-molybdenum polyoxometalates on the thymus and blood leukocytes in rats
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Background & Objective: A change in blood leukocytes could follow the penetration of nanoparticles into the immunopoietic organs. Iron-molybdenum polyoxometalates (POM) are promising nanoparticles for targeted drug delivery because of their low toxicity, association with biologically active substances and percutaneous transport by electrophoresis. It is unclear whether POM can penetrate a special haemato- thymic

barrier. The aim of the study is to investigate changes in the thymus and blood leukocytes in rats treated with POM.
Method: Male Wistar rats (5 intact, 15 experimental) were used in accordance with the ethical principles of Directive 2010/63 / EU. Experimental rats received 1, 7 and 30 intramuscular injections of an aqueous POM solution (1.5 mg / kg of mass in one injection). Histological, chemical, immunohistochemical and flow cytometry methods were performed.
Results: We revealed an iron and molybdenum accumulation and cortex thickness depletion in the thymus after 7 injections. The heat shock protein (HSP) expression increased in the thymus after a single and multiple POM injections. We observed a decrease in the total number of leukocytes and their fractions with a single and seven-fold administration of POM and an increase in leukocyte apoptosis and histone proteins in leukocytes after 30 injections.
Conclusion: Therefore, the accumulation of iron, molybdenum and HSP in the thymus suggests the penetration of POM through the haemato-thymic barrier. Despite minor and transient changes in the thymus, the accumulation of apoptotic leukocytes and histone proteins after 30 injections raises the question of reducing the number of POM injections for possible therapeutic use.

E-PS-23-006
Nuclear protein in testis midline carcinoma (NUT carcinoma). Report of three cases.
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Background & Objective: Nuclear protein in testis midline carcinoma (NUT carcinoma) is an aggressive epitelial neoplasm with average survival less than 7 months. It is defined by chromosomal rearrangement of the NUT gene. BRD4 is the most common fusion partner. We report three new cases with complete follow up data.
Method: Three patients, two males and one female (aged 18, 43 and 20 years respectively) presented with mediastinal tumours. The tumours were sampled under radiological guidance. Histological examination showed at least focal keratinization in all cases. The two youngest undervent concomitant bone marrow sampling. The final diagnosis were based on histology combined immunohistochemistry against NUT protein (clone C52B1, Cell Signaling Technology, product number 3625).
Results: All patients had metastatic disease at presentation. Affection of adrenal glands, lymph nodes, brain and skeleton were present at the time of diagnosis. The two youngest undervent bone marrow sampling because of B-symptoms and suspicion of lymphoma. All tumours had expression of NUT protein and squamous cell markers. Both bone marrow smears had findings consistent with metastatic disease. The patients were treated with chemo- and radiotherapy, but all had progression of the disease during treatment. Male 18 years died 4 months after diagnosis, male 43 years died after 6 months, while the 20 years old female died after 14 months.
Conclusion: Nuclear protein in testis midline carcinoma is highly aggressive. Awareness of the entity is mandatory due to differential diagnosis and to avoid misdiagnosis. Despite intense treatment with chemoradiotherapy the prognosis is dismal.

E-PS-23-007
Cystic trophoblastic tumour: a rare presentation in the mediastinum in a post-chemotherapy patient with previous germ cell tumour in the testis
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Background & Objective: Cystic trophoblastic tumour (CTT) is a rare lesion, usually seen in post-chemotherapy patients with previous testicular germ cell tumour. Limited data is available in the literature. The lesion appears benign in behaviour, with a clinical significance similar to residual teratoma.
Method: We report a case of cystic trophoblastic tumour (CTT) identified in the mediastinum of a 34 year old male with previous germ cell tumour in the testis. The patient initially presented with stage 3 germ cell tumour in the testis and widespread lymphadenopathy including neck and retroperitoneum. After four cycles of neoadjuvant chemotherapy, a left orchidectomy and a second stage retroperitoneal lymph node dissection was performed. Both revealed residual teratoma.
Results: 22 months later the patient presented with raised LDH and a new enlarging lesion in the posterior mediastinum. At this stage, the left neck node and posterior mediastinal mass were removed. The neck node revealed mature teratoma. The mediastinal mass was a 40mm multilocular cyst examined in its entirity. Histology showed elements of mature teratoma along with large cystic spaces lined by trophoblastic cells with focal papillary tufts. There was no necrosis or increased mitotic activity. The diagnosis of a metastatic teratoma with CTT was made and the patient received no additional chemotherapy.
Conclusion: To our knowledge this represents the first report of a CTT in the mediastinum developing two years following chemotherapy in a patient with primary germ cell tumour of the testis.

E-PS-24 | Uropathology

E-PS-24-001
Large-cell calcifying Sertoli cell tumour with macrocalcification in partially resected testis of a young adult patient
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Background & Objective: There are less than 100 cases of Large-cell calcifying Sertoli cell tumour (LCCSCT) reported in english literature. Most of them are benign, bilateral and affect paediatric population. Malignant cases occur in older patients. LCCSCT is often associated with Carney complex or Peutz-Jaghers syndrome. We present the clinicopathological features of a young adult, with unilateral LCCSCT, without changes in hormonal status and no clinical characteristics of noted genetic disorders.
Method: A 24-year old male presented with painless hardening of the right testis. There was no gynaecomastia, and serum levels of human chorionic gonadotropin and α-fetoprotein were normal. Ultrasound depicted hyperechogenic, clearly demarcated intratesticular lession. Partial orchiectomy was performed.
Results: Macroscopically, tumour appeared as almost entirely calcificated round mass, measuring 10mm. Histopathological evaluation showed well-circumscribed, unencapsulated tumour composed of massive calcificated geographic formations, surrounded with tumour cells. Neoplastic cells were large, polygonal, with abundant eosinophilic cytoplasm, and formed irregular cords, pseudotubular structures, and nests in a fibrous and myxoid stroma, surrounded with lymphocytes. Other forms of calcification were also present: needle-like deposits and lamellar, mulberry-like structures. There was no necrosis, mitotic activity and nuclear pleomorphism. Immunohistochemistry was positive for inhibin α. and negative for Melan-A, EMA, synaptophysin, chromogranin and AFP.
Conclusion: LCCSCT needs to be differentiated from other, more frequent, sex cord stromal tumours. Clinical and genetical evaluation of this patients has to be performed, due to connection of LCCSCT with genetic abnormalities. In evidently benign cases, organ-sparing surgery should be considered for younger patients, followed with long term follow-up.

E-PS-24-002
MCM 6 expression in transitional cell carcinoma of the bladder
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Background & Objective: MCM6 is a protein belonging to a complex involved in the initiation of DNA synthesis and its replication. Its expression during the G1 phase of the cycle is earlier than that of Ki-67. Its prognostic impact as a function of histological grade has been proven in various tumour tissues, such as meningioma, lung cancer or endometrioid carcinoma of the endometrium. To date, no study has evaluated the impact of MCM6 in bladder tumours (BT). The aim of our work is to evaluate the expression of MCM6 in bladder tumours and its correlation with predictive parameters of biological aggressiveness and evolution (recurrence and metastasis).
Method: We carried out a retrospective study of 53 cases of bladder tumours diagnosed following endoscopic resection and radical cystoporostatectomy between 2011 and 2013. Correlation between MCM6 immunoexpression and tumour grade, tumour stage and evolution (recurrence and metastasis) was assessed.
Results: Our results showed that there was not a statistically proven correlation between the rate of MCM6 and these settings with a lack of correlation between MCM6 expression and tumour size, stage, grade, recurrence and progression.
Conclusion: Our study is the first to evaluate MCM6 in urothelial carcinoma of the bladder. In this preliminary study, the lack of correlation of MCM6 with different clinico-endoscopic and pathological parameters suggests that MCM6 could not be a predictive marker assessing the prognosis of these tumours.

E-PS-24-003
Bilateral cystic clear cell papillary renal cell carcinoma in end stage renal disease

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Background & Objective: Clear cell papillary renal cell carcinoma (CCP-RC) is a low grade indolent tumour with relatively distinct clinic-pathological features. It was classified as a new subtype of renal cell carcinoma in the 4th WHO Classification, accounting for untill 4.3% of all renal epithelial neoplasms.
Method: Case report of a bilateral clear cell papillary renal cell carcinoma.
Results: A 65 year-old man with chronic renal disease was referred for the outpatient consultation since 2008. Bilateral multicystic renal lesions were detected in ultrasound exam in 2012. Bilateral nephrectomies were performed in 2016, because of progression of the lesion and evolution to end stage renal disease (ESRD). Macroscopically, the kidneys were diffusely enlarged by multiple cyst and few circumscribed grey solid nodules, with residual atrophic parenchyma. Microscopically, the tumour showed cystic and tubulopapillary architectures, which were lined by a single layer of cubic/columnar cells with clear cytoplasm and small round "low-grade nuclei (Furhman grade 1), characteristically aligned in the apical pole of cells. In immunohistochemical study, tumour cells diffusely and strongly expressed CK7 and 34BE12 and only focally and weakly expressed CD10 in the cystic areas. There were no necrosis, sarcomatoid changes, vascular/perinephric or renal sinus invasion.
Conclusion: We report a rare case of pure bilateral CCP-RCC, with exuberant cystic changes in a patient with ESRD.

E-PS-24-004
Mucinous tubular and spindle cell carcinomas: a series of 3 cases

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Background & Objective: Mucinous Tubular and Spindle Cell Carcinoma (MTSCC) accounts for <1% of all renal neoplasms with female predilection and mean age of 58years old. The objective is to report of a series of three rare cases of MTSCC of the kidney.
Method: Case 1: 49-year-old woman, with a 35mm solid mass on the inferior portion of the left kidney. The lesion was a well circumscribed lesion consisting of a yellowish and elastic tissue. Case 2: 45-year-old woman with a 11mm solid mass on the left kidney that was well circumscribed and consisting of a white and elastic tissue. Case 3: 52-year-old woman, with a 60mm mass of the left kidney. The lesion was well circumscribed, consisting of white and soft tissue with small yellowish areas. All cases underwent total nephrectomy without complications and specimens were sent to the pathology department.
Results: Histologically, all lesions were well circumscribed, and consisting of branching tubular structures, lined by cuboidal cells without atypia, alternating with areas with spindle cells with eosinophilic cytoplasm and elongated and monomorphic nuclei with occasional nucleoli. Stroma had basophilic to eosinophilic mucin (Alcian Blue and Periodic acid–Schiff–diastase stains), with areas of bubbly appearance. The 2nd case showed focal foamy macrophages. Immunohistochemistry showed positivity for CK7 and racemase and negativity for CD10.
Conclusion: MTSCC is a rare tumour, with indolent clinical course and recurrence is rare. All patients are female and tumour was localized on the left kidney. Patients are well, without complaints and with no tumour recurrence on the 3-month follow-up consult.

E-PS-24-005
Malignant Leydig cell tumour of the testis: case report and review of the literature

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Background & Objective: Leydig cell tumour (LCT) of the testis is the most common stromal tumour and account for 1-3% of testicular neoplasms. Approximately 5% are clinically malignant. Metastatic disease is a definitive indicator of malignancy, but there are also histologic findings correlating with malignant behavior. We intent to characterize the pathological features and outcome of malignant LCTs.
Method: Case report of malignant LCT and review of the published cases.
Results: We present a case that describes a 60-year-old patient hospitalized due to a septic shock. LCT of the left testis was an incidental finding in imaging test and already had hepatic metastatic involvement at presentation. Histologically, there were moderate to marked cytological atypia, 5 mitotic figures per 10 high-power fields (HPF) and extensive areas of necrosis. Altogether, 85 cases of malignant LCTs were reported in the literature. They tended to occur at an older age (54.2 years, average) and their mean size was 5.8cm. The most common histologic feature was cytological atypia (74%), followed by mitotic count >3/10 HPF (65%), infiltrative borders (63%), vascular invasion (60%) and necrosis (34%). Metastases were found in 82% of cases involving regional lymph nodes (63%), lung (46%), liver (35%) and bone (17%). The average interval between the initial diagnosis and detection of metastases was 27 months, but there are reports of metastatic spread after 17 years.
Conclusion: Malignant LCTs are aggressive with poor prognosis, however the number of malignant histological features present in each case seems to be fundamental to correlate with survival time.

E-PS-24-006
Urachal mucinous cystadenocarcinoma - a rare entity

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Background & Objective: Urachal carcinoma is an extremely rare entity that develops in the urachal remnant, accounting for <1% of all bladder cancers.

Method: We report a case of a urachal mucinous cystadenocarcinoma and review the literature.
Results: A 51-year-old man presented with haematuria with 3-months duration. A thoracic abdominal and pelvic computed tomographic scan revealed in the midline an exophytic solid-cystic mass extending from the dome of the bladder to the urachal tract. A radical cystoprostatectomy with a bilateral lymphadenectomy was performed and on gross examination a well circumscribed and irregular solid-cystic mass measuring 6cm longer axis centred at the dome of the bladder. The cut surface of the mass was partly solid and partly cystic with a gelatinous surface. The microscopic examination revealed a mucinous cystadenocarcinoma, with extension into the bladder wall. Immunohistochemically, CK20 and CDX2 were diffusely positive, the tumour cells were focally positive for CK7 and revealed a negative nuclear staining for beta-catenin and no expression with 34BE12. Lymph nodes metastasis was absent, and it was IIIA stage in the Sheldon staging system. After 7 months of follow-up, the patient has no evidence of recurrence on laboratory and imaging examinations.
Conclusion: We report a rare case of urachal mucinous cystadenocarcinoma which immunohistostainings do not unequivocally discriminate an urachal from a colorectal carcinoma. Therefore, clinical suspicion and characteristic imaging features, proved to be decisive for establishing the diagnosis of an urachal carcinoma.

E-PS-24-007
Testicular tumour in elderly patient

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Background & Objective: Spermatocytic tumour is a testicular neoplasm derived from post-pubertal germ cells. It represents approximately 1% of testicular tumours and it involves adults over 50 years old as a solid pseudonodular tumour with particular histological and immunohistochemical characteristics. The prognosis is considered excellent.
Method: We report the case of a 62-years-old man with a testicular mass. A radical orchiectomy was per-formed.
Results: The cut surface showed a pseudonodular tumour that occupies most of the testicular parenchyma. Microscopically, there was a solid neoplasm formed by three types of neoplastic cells arranged in solid sheets separated by fibrovascular tracts, forming a multinodular pattern. There was no evi-dence of inflammatory infiltrate in the fibrous septa. There were frequent mitotic figures, areas of hemorrhage and foci of neocrosis. Germinal neoplasia in situ was not observed. A large immunohistochemical panel was performed, in which only SOX-2 and SALL-4 were positive, the rest of the typical markers of germ cell neo-plasms being negative.
Conclusion: Spermatocytic tumour has a series of distinctive characteristics. Macroscopically, its pseudonodular appearance is typical. Histologically, it is characterized by three types of cells, absence of lympho-cytes in the fibrous septa and seminiferous tubules without germinal neoplasia in situ. Immunohisto-chemically, most of the usual markers for germ cell neoplasms are negative. The case presented illustrates that in the presence of a testicular tumour in an elderly patient, the differential diagnosis should include this entity.

E-PS-24-008
Squamous cell carcinoma of the urinary tract: 12-year experience in a single institution

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Background & Objective: Squamous cell carcinoma (SCC) of the urinary tract is a rare entity. We reviewed histopathological features of our data with SCC of the urinary tract.
Method: We performed a retrospective single center analysis of 20 patients with SCC in our department from 2006 to 2017. Patient demographics as well as pathologic factors were analyzed. While tumours with a histologically pure SCC phenotype were included, those with a history of urothelial carcinoma were not taken into study.
Results: While 7 cases (6%) out of 110 tumours in renal pelvis were found to be SCC, only 13 cases (0.7%) out of 1745 tumours in bladder were SCC. However, no cases were found in the ureter. At the time of diagnosis, the mean ages of bladder and renal pelvis SCC were 63 and 50, respectively. The review of TNM staging showed that 5 SCC of the renal pelvis being staged pT3. Four patients with SCC of the renal pelvis were associated with urolithiasis and hydronephrosis. The average follow-up was 17 months and one-year survival rate was 16%. The pathological stage of 10 SCC of the bladder (76%) was pT2 and above. The main symptom was hematuria (61%). No schistosomiasis was found in the background of cases. The average follow-up was 25 months and one-year survival rate was 23%.
Conclusion: In conclusion, our data underline the pure SCC of the urinary tract which is rarely observed and it appears to be aggressive with often poor outcomes.

E-PS-24-009
Urothelial carcinoma of the upper urinary tract: 10-year experience in a single institution

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Background & Objective: Upper urinary tract urothelial carcinoma (UTUC) accounts for approximately 5-10% of urothelial carcinomas. Studies have reported that coexisting bladder neoplasm is present. In this study, we determined the clinicopathologic features of the UTUC.
Method: A retrospective review was performed on pathology reports of UTUC between 2008 and 2017 in our institution. The histopathological, demographic and clinical features were analyzed.
Results: 17% of kidney tumours originated from renal pelvis and 92% of the renal pelvic tumours were UTUC. There were 87 cases, the mean age was 67. Male to female ratio was 2.5:1. Forty of the tumours were located in the renal pelvis and 14 in the ureter. The localization of 33 of them was in both the renal pelvis and the ureter. 42 of patients (48%) had presence of bladder neoplasm. At the time of diagnosis, most of the cases had high pathologic stage (pT2 and above). The average follow-up was 26 months (range, 1-97 months). 40 patients were followed up for 5 years. Five-year survival rates were 36% in renal pelvis localized tumours, 50% in ureter localized tumours, 9% in both renal pelvis and ureter-localized tumours and 40% in with the presence of bladder neoplasm.
Conclusion: In conclusion, coexisting bladder neoplasm was present in nearly half of the patients. This study shows that both renal pelvis and ureter localized tumours have worse prognosis and ureteral tumours have better prognosis than renal pelvic tumours.

E-PS-24-010
HMB-45/Melan-A negative malignant perivascular epitheloid cell tumour of kidney - a case report

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Background & Objective: A case report of an HMB-45 and Melan-A negative, but TFE-3 and MDM2 positive malignant Perivascular Epitheloid Cell tumour (PEComa) in kidney.
Method: A 69-year old male patient presented with a renal mass approximately 62x20x32mm in size. After total nephrectomy, histopathological, immunohistochemical (IHC) and Fluorescence In Situ Hybridization (FISH) testing was performed.
Results: Morphology showed a tumour composed of polygonal epithelioid cells with dense eosinophilic cytoplasm and round nuclei with

prominent nucleoli and multiple multinucleated giant cells. Necrosis was focally present. Mitotic index was high (19/50HPF). Vascular invasion was not detected. Immunohistochemical staining showed focal positivity for CKAE1/AE3, EMA, SMA, CD10 and MITF, and diffuse expression of TFE3, MDM2, CD99 and INI 1. Surprisingly and interestingly melanocytic markers as HMB-45, Melan-A were negative. Additionally, CK7, CK20, RCC, Vimentin, Desmin, MyoD1, Myogenin, S100, STAT6, LCA, ALK-1, TLE-3 were also negative. Diagnosis of malignant PEComa was made. TFE3 break-apart FISH testing showed absence of TFE3 rearrangements, and presence of polyploidy (59% of tumour cells).
Conclusion: According to histopathological analysis the tumour was classified as a malignant PEComa. Immunohistochemical coexpression of melanocytic and muscle markers was expected. However, we found negativity for HMB-45 and Melan A. Moreover, FISH testing showed absence of TFE3 rearrangements, suggesting that polyploidy of TFE3 could result in positive IHC expression.

E-PS-24-011
Basal cell carcinoma of the prostate - report of a case
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Background & Objective: The spectrum of the Basal Cell lesions in the prostate is wide, and the diagnosis of carcinoma may be difficult as there are different patterns of presentation. Some morphologic changes have been described in order to help achieve a diagnosis.
Method: We present a case of a 71-year old man with low urinary tract symptoms and normal PSA values who was submitted to a suprapubic prostatectomy.
Results: At microscopic examination we found lesions of benign prostatic hyperplasia and an incidental basal cell carcinoma. Presented as an expansive, multinodular tumour with infiltrative areas to the adjacent parenchyma, composed of basaloid cells organized in small nests with peripheral palisading or in tubular pattern, surrounded by fibromyxoid stroma and with areas of squamous differentiation.
Conclusion: Basal cell carcinoma found in the prostate is a rare diagnosis with less than 100 cases reported in the literature. It is considered a potentially aggressive neoplasm with some capacity for recurrence and metastases to other organs have been described. In this case, the neoplasm had a clean surgical margin and follow-up after one year of surgery there is still no new clinical findings.

E-PS-24-012
A rare case of a solitary cutaneous metastasis of transitional cell carcinoma with squamous differentiation of urinary bladder
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Background & Objective: Cutaneous metastasis of transitional cell carcinoma (TCC) of urinary bladder is a rare finding, with an incidence of 0,84% of all cutaneous secondary disseminations. There are only 12 similar cases described in the literature. Among these cases, only one was found as a unique metastasis. None of these cases showed squamous differentiation. We present a rare case of a solitary cutaneous metastasis of high-grade TCC with squamous differentiation of urinary bladder.
Method: A 59-year-old female patient presented with a painful, solitary cutaneous nodule in the left scapular region, for which an excisional biopsy was performed. Patient's medical history included a diagnosis of high-grade TCC of urinary bladder (pT3aN2) on a radical cystectomy with pelvic lymphadenectomy surgical specimen. No other metastatic lesions were found at a computed tomography scan.
Results: Gross examination of the cutaneous surgical specimen revealed a well demarcated, unencapsulated, white, firm nodule, measuring 3,5 x 3,5 cm. Microscopic findings showed an intradermic and hipodermic malignant tumour, consisting of urothelial cell nests, trabeculae, with high-grade cytological atypia, and squamous differentiation. Immunohistochemical markers were positive for p63, CK5/6, p53, CK7, GATA 3, uroplakin, and a diagnosis of cutaneous metastasis of TCC with squamous differentiation of urinary bladder was made.
Conclusion: Altough a rare occurrence, cutaneous metastasis of TCC of urinary bladder should always be considered in the differential diagnosis in patients with skin nodules and medical history of bladder carcinoma.

E-PS-24-013
Bilateral testicular masses associated with congenital adrenal hyperplasia. A case report
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Background & Objective: Congenital Adrenal Hyperplasia (CAH), is related to the 21-beta-hydroxylase deficiency. Chronic excessive ACTH stimulation may result in Testicular Adrenal Rest Tumours (TARTs). The main differential diagnosis is the Leydig cell tumours (LCTs).
Method: We present a case of a patient with CAH, who presented with bilateral testicular masses.
Results: A 28-year-old man, with CAH related to 21-beta-hydroxylase deficiency diagnosed by the age of 45 days. He had a precocious puberty. The patient presented with bilateral enlarged testicles. Contrast enhanced CT showed highly enhanced bilateral intra-scrotal tissue masses. Semen analyses revealed azoospermia. Serum hormonal screening showed high levels of 17-OH progesterone and testosterone, normal level of ACTH and low levels of LH and FSH. The patient underwent a testicular biopsy. Microscopic study showed clusters of polygonal cells with abundant eosinophilic cytoplasm. The nuclei were nucleated showing moderate anisocaryosis. Reinke crystals were absent. Immunohistochemical study revealed a reactivity for Inhibin, Calretinin and focally for Synaptophysin. The patient underwent bilateral orchidectomy in two stages because tumour size had not decreased under medical treatment. Pathological findings showed well-circumscribed brownish tumours measuring 8 and 8.5cm. Microscopic study showed a similar appearance to biopsy. The rare residual seminiferous tubules were atrophic. The diagnosis of LCT was discussed but clinic presentation and immunohistological features were suggestive of the diagnosis of TARTs.
Conclusion: It is extremely difficult to distinguish TARTs caused by CAH from LCTs. Although the presentation of these two entities is similar, therapeutic approach is completely different.

E-PS-24-014
Sarcomatoid carcinoma of the urinary bladder - a case report
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Background & Objective: Sarcomatoid Carcinoma of the Urinary Bladder is very rare and acount for only 0.3% of all histologic subtypes. Less than 100 cases have been reported in literature. Here we report a case of Sarcomatoid squamous carcinoma of the Urinary bladder from Syria.
Method: 53 years old female presented with frequency, urgency and gross hematuria. Cystoscopy showed tumour arising from the bladder base. TURBT was carried out.
Results: Biopsy specimen had over all volume of 20cc. The tumour was characterized by biphasic proliferation of malignant epithelial and sarcomatoid elements. The epithelial element consisted of sheets and nests of large atypical, polyglonal cells with irregular chromatin and prominent nucleoli with keratin pearls. The second sarcomatoid element

consisted of spindle, pleomorphic and bizarre cells. Both components contained atypical mitotsis. The epithelial component was positive for EMA, P63, CK and CK 5/6, and negative for CK7 and CK20. The sarcomatoid component was positive for EMA, VIM and Actin, and negative for Desmin and CD34. The histologic features and IHC results confirm the diagnosis of Sarcomatoid squamous carcinoma of the bladder.
Conclusion: Pathologist, Urologist and Oncologist should be encouraged to report cases of Sarcomatoid Carcinoma of the Urinary Bladder in order to contribute to the understanding of biological behavior of this tumour and to arrive at a consensus opinion regarding the best treatment option.

E-PS-24-015
An unusual hybrid renal tumour associating a diffuse large B-cell lymphoma and a clear cell renal cell carcinoma
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Background & Objective: Introduction: Synchronous occurrence of primary renal lymphoma and renal cell carcinoma is an unusual phenomenon, only described once in the English literature.
Method: A 61-year-old Lebanese male patient consulted for recent rapid weight loss. Physical examination and laboratory tests were unremarkable. Abdominopelvic CT and MRI revealed a left kidney 4 cm mass, close to the pelvicalyceal system and renal sinus; no enlarged retroperitoneal lymph node was noted. The patient underwent left radical nephrectomy.
Results: Gross examination showed a main 3.7 x 3.2 cm tan-brown mass with cystic changes. On histology, it was well circumscribed, with papillary and tubular patterns. Resorptive, hemorrhagic, cystic and fibrous modifications were observed. The tumour cells had abundant clear cytoplasm with irregular nuclei (Fuhrman grade 2). They were positive for AE1/AE3, CK7, Vimentin and PAX8. They were negative for CD10 and RCC. The stroma contained diffuse sheets of large lymphoid cells, sometimes with centroblastic features. Karyorrhexia, numerous mitoses and few eosinophils were noted. Lymphoid cells were CD20+, Bcl-2+, Bcl-6+ and MUM1+. They were negative for CD5, CD10, CD23 and c-MYC. Proliferation index was estimated at 90%. An adjacent independent 3.8 cm simple multilocular renal cyst was also found. A clear cell papillary renal cell carcinoma admixed with a diffuse large B-cell lymphoma was diagnosed. EBER FISH was negative.
Conclusion: To the best of our knowledge, this is the second reported case describing a renal tumour associating a diffuse large B cell lymphoma and a clear cell renal cell carcinoma. Any lymphocyte-rich stroma should be carefully inspected for a lymphomatous component.

E-PS-24-016
A case of primary renal synovial sarcoma
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Background & Objective: Synovial cell sarcoma of the kidney is a rare tumour with poor prognosis. Only about 60 cases have been reported till date. We report this case, clinically suspected to be a renal cell carcinoma.
Method: A 25-year-old female presented with a right flank pain. MR imaging revealed a heterogenous, well-marginated, parenchyma confined mass arising in the lower pole of right kidney with solid, haemorragic and necrotic components with no evidence of renal vein thrombosis or lymphadenopathy. Clinico-radiological diagnosis was consistent with renal cell carcinoma. The patient underwent right radical nephrectomy without complications.
Results: The specimen weighed 678 g and measured 19×11×10 cm. Cut surface showed a partly cystic tumour of yellow-brown / tan color and firm consistency, measuring 10,5x9,5x9 cm. Hemorrhage and necrosis were evident. Tumour macroscopically infiltrated renal parenchyma and renal sinüs with near complete filling of the renal pelvis. The neoplasm consisted of homomorphic spindle cells with scant cytoplasm, arranged in nondescript solid, or intersecting fascicles. Mitoses were ten per ten high-power fields and necrosis was noted. Immunoprofile: vimentin+/ Bcl2 +/ nuclear TLE1+, focal EMA, patchy cytokeratin (AE1/AE3+ and CK8/18+). CD99, S-100, CD34, CD117, desmin, WT-1, FLI-1, CD10, chromogranin and synaptophysin were negative. Diagnosed – Monophasic spindle cell type of primary renal synovial sarcoma (PR-SS).
Conclusion: PR-SS should always be included in the differential of renal sarcomas. It is diagnostically challenging, and also needs to be distinguished from sarcomatoid RCC and metastatic / secondary involvement by non-renal sarcoma

E-PS-24-017
Brain choriocarcinoma after postpuberal testicular teratoma diagnosis
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Background & Objective: Brain choriocarcinoma is a very rare tumour and it is typically related to metastasis from a malignant germ cell tumour of the gonad. We herein report the case of a postpuberal testicular teratoma with an unfavourable outcome.
Method: We reviewed the relevant clinical data and pathology samples from the testis, retroperitoneal lymph node and brain mass. Routine haematoxylin-Eosin staining as well as a panel of antibodies that variably included anti-CK, EMA, desmin, vimentin, S100 protein, CD-34, HCG, SOX-2 and D2-40.
Results: 37-year-old patient with ultrasound diagnosis of a multicystic tumour of 3.3x2.5cm on the left testicle. After orchiectomy, the pathologic diagnosis was "Teratoma, postpuberal type". Seven months later, the patient undergoes surgical removal of retroperitoneal lymph nodes, which revealed metastases with teratoma pathological pattern. Two months later, after neurologic symptoms developed, brain imaging studies were performed and a brain biopsy revealed a 2.5x1.8cm metastasis from a cell germ tumour with choriocarcinoma pattern.
Conclusion: -Chroriocarcinoma as a primary brain tumour is possible but a very rare situation. Clinicopathologycal correlations in our case make it more likely that we are dealing with a brain metastasis from a testicular tumour. -The discordance between the composition of testicular germ cell primary tumours and their metastases is well known. -Postpuberal testicular teratomas, such as the one presented herein, must be considered as neoplasms of malignant biological behaviour and they can be associated with metastases of the full spectrum of germ cell neoplasms. Our case included lymph node metastases as teratoma while the brain metastasis was a choriocarcinoma.

E-PS-24-018
Paratesticular fibrous pseudotumour and the importance of immunohistochemical evaluation of IgG4/IgG ratio
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Background & Objective: In this report, we will discuss the importance of systematic immunohistochemical evaluation of IgG4/IgG whilst the investigation of testicular fibrous pseudotumours, as to emphasize the importance of this systemic disease diagnose.
Method: A 38-year-old male was subjected to urology consultation due to a right-sided painless scrotal mass, with noted increased size in the last

six months. On physical examination, a chord-like rigid, mobile, structure was palpated in right paratesticular area. No elevated serum marker was noted, as ultrasound denoted a benign mass. Consequently, surgical resection was proposed.
Results: On excision, a glistening hardened mass, irregularly shaped, was evidenced, with homogenous cut surface. Histology revealed a densely fibrotic tissue, vascularized in a homogenously sparse fashion, with a background lymphoplasmocytoid infiltrate, CD138 positive, with a higher than 50% IgG4/IgG ratio, characterizing as an IgG4-mediated disease.
Conclusion: Paratesticular fibrous pseudotumours are benign, self-limited entities, usually confined to intraescrotal structures. Recent evidence has been pointing the importance of exclusion of IgG4-sclerotic mediated disease, once, as a systemic disease, it has been associated with other autoimmune events, as retroperitoneal fibrosis, sclerosing pancreatitis, cholangitis, Riedel's thyroiditis and sclerosing sialadenitis. Once characterized as an IgG4-mediated disease, further workout and follow-up may ensure better healthcare assistance.

E-PS-24-022
Large nest variant urothelial carcinoma: clinico-pathological and immunohistochemical profile of three cases
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Background & Objective: Large nested urothelial carcinoma is characterized by an unusual bland morphology, nevertheless this has a clinical behaviour of high-grade conventional urothelial carcinomas (CUC). The nested component (large or not) demonstrated a basic immunoprofile like CUC. The goal of our study is to describe the histopathological and clinical behavior of a series of cases of large nested urothelial carcinoma and analyze if an immunohistochemical profile could help us to predict a worst clinical progression.
Method: Retrospective review of CUC diagnosis, only three cases fulfilled the morphological criteria for pure large nest variant of urothelial carcinoma. Tissue sections for staining with ck5-6, CD44, ck20, P63, ck 14 and P53 were evaluated
Results: All cases were male, over 60 years old suffering hematuria. One patient presented as nonfiltrative tumour and two with distant metastases at diagnosis. Basal-like subtype (positive expression of CD44) was demonstrated in all three cases. Expression of CK20 and p53 was observed in all of them. The stain was diffuse and intense in the patients with metastases. CK 5-6 was only present in one case, as for CK14.
Conclusion: Pathologist must be aware to recognize this variant in routine diagnosis. We validated the malignant potential of this histological variant as two of the patients presented an advanced stage of the disease. Inmunohistochemical results suggest a subtype of tumour with an aggressive phenotype that can help in the differential diagnosis of superficial cases. More cases are in need to determine the prognostic value of immunohistochemistry markers.

E-PS-24-023
Osteoclast-rich undifferentiated carcinoma of urinary bladder. A unique occurrence in a bladder diverticulum
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Background & Objective: Osteoclast-rich giant cell tumours of the urinary tract are an exceptionally rare malignancy. They were first described by Kimura et al. in 1983 and subsequently reported infrequently in the literature. Terminology, histogenesis and cancer biology behaviour of these tumours remains controversial.
Method: We present a case of osteoclast-rich undifferentiated carcinoma arising in a bladder diverticulum.
Results: A 65-year-old male, with no history of bladder cancer, but a long-standing bladder diverticulum (8 years) underwent diverticulectomy for frank haematuria. Grossly, the diverticulum contained haemorrhage, assumed clinically to represent blood clot. However, microscopically, the haemorrhagic mass consisted of pleomorphic epithelioid mononuclear cells and multinucleated giant cells. The urothelial origin of the neoplasm was supported by focal staining of the mononuclear cells with CK7, CEA and the occurrence of adjacent urothelial carcinoma in-situ. Positive markers included: vimentin, p63, p53, CD68. The following stains were negative: BerEP4, S100, Caldesmon, Actin, CK20. These findings were consistent with osteoclast-rich undifferentiated carcinoma of bladder. The tumour involved the muscular wall of the diverticulum, but not peridiverticular fat. The patient developed a pelvic recurrence unresponsive to chemotherapy and died of disease, 8 months following the initial diagnosis.
Conclusion: 18 patients with this bladder tumour have been previously reported in the English literature. Osteoclast-rich undifferentiated carcinoma of bladder has aggressive behaviour and poor prognosis, in contrast to the favourable outcome in giant cell tumours of bone and other sites. Our case is unique in its occurrence in a bladder diverticulum and confirms the aggressive clinical behaviour of this tumour.

E-PS-24-024
Metastatic colorectal carcinoma in a 76-year old male: a pitfall in the diagnosis of unclassified renal cell carcinoma
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Background & Objective: The kidney is the most common site of metastasis to the urinary tract. However, tumour characteristics are deceptive, and the diagnosis of metastasis to the kidney may be challenging.
Method: Herein we report the differential diagnosis of a poorly differentiated carcinoma in the kidney.
Results: A 76- year old male was admitted with pyonephrosis for a total nephrectomy. At gross examination, the kidney presented an extensive lesion occupying the pyelo-calix and ureter. Microscopy demonstrated a high-grade carcinoma with rare areas of tubular differentiation. The tumour infiltrated the renal sinus and perirenal fat. Considering the tumour location, high grade and infiltrative growth, the diagnostic hypothesis of collecting duct carcinoma and urothelial carcinoma were investigated. However, a thorough investigation of the patient's chart revealed a history of colorectal carcinoma. Immunohistochemistry demonstrated expression of CK20 and CDX-2 and negativity for CK7, CK5, PAX-8, Vimentin, CD117, GATA3 and p63; therefore, the patient was diagnosed with a poorly differentiated metastatic colorectal carcinoma to the left kidney.
Conclusion: Metastasis to the kidney has unspecific clinical findings and usually occurs in the setting of widespread disease. Most metastasis present as a solid renal mass, but up to 77.5% are solitary lesions, and the most common histological presentation is high grade carcinoma. Therefore, metastatic tumours to the kidney may mimic primary neoplasms in clinical, gross and histological findings. A high degree of suspicion is necessary for the diagnosis of metastatic disease to the kidney, which should ruled out before the final diagnosis of an unclassified renal cell carcinoma.

E-PS-24-026
Histologic characterization and subtyping of 374 small renal masses (smaller than 4 cm) in adult patients over a period of 18 years.
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Background & Objective: The aim of this study is to characterize the proportion of benign and subtypes of malignant renal tumours smaller than 4 cm with special focus on low and intermediate malignant potential variants of renal cell carcinoma (RRC).

Method: We searched in the database of Pathology Archives of La Paz University hospital to identify all adult kidney tumour cases diagnosed in 2000 - 2017. We excluded urothelial carcinoma and simple cysts. Then we selected for histologic subtyping evaluation tumours smaller than 4 cm.
Results: Out of 829 tumours (792 patients), 374 tumours (353 patients) measured 4 cm or less (44%). In this series 70% were male. Age 20-84 years (mean 61 y). Tumours removed by nephron-sparing surgery were 54% and by radical nephrectomy 46 %. Benign tumours represented 12,6% (47 cases), tumours of low malignant potential 5,9% (22 cases), tumours of intermediate malignant potential 10,6% (40 cases), tumours of high malignant potential 68% (254 cases) (Table 1). Eight cases were unclassified carcinoma and 3 secondary tumours. Intrarrenal pT1a tumours represented 63,4%, pT3a 11%, pT3b 0,8% and 24,5% of non-staging tumourectomies.
Conclusion: In the present series, small renal masses were 44% of all renal tumours and more frequent in males. Benign and low malignant potential tumours represented 18,5% and up to one third if tumours of intermediate malignant potential are included. These results suggest the convenience of including morphologic diagnosis and RCC subtyping in management algorisms of patients with renal masses smaller the 4 cm.

E-PS-24-027
A rare and unusual histological variant of prostatic carcinoma: a case report
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Background & Objective: Primary squamous cell carcinoma (SCC) of the prostate is a very rare entity with fewer than 100 cases reported in the literature. It is typically described as an aggressive cancer, deemed rather more malignant than the ordinary adenocarcinoma and resistant to the usual therapy for prostate cancer.
Method: We report a new case of primary SCC involving the prostate diagnosed in our pathology department.
Results: A 65-year-old man was admitted for acute urinary retention. Physical examination was unremarkable, except for an unevenly swollen and stony hard prostate. Serum prostate specific antigen (PSA) concentration was at 4 ng/mL. Sextant transrectal ultrasound-guided needle biopsy of the prostate was subsequently performed. Histological examination demonstrated nests and sheets of moderately differentiated squamous carcinomatous cells characterised by intercellular bridges. Focal areas presented with evidence of keratin pearl formation. No transitional cell or adenocarcinomatous components could be observed. Immunohistochemically, tumour cells were non reactive for PSA, but stained positive for high molecular weight cytokeratin. Primary or metastatic lesions in the respiratory organs and the alimentary tract were excluded by thorough investigation.
Conclusion: Primary SCC is a rare but distinct clinico-pathological entity with rather aggressive natural course. Its histogenesis has long been a topic for debate. Some have thought the origin to be of prostatic urethral urothelium, although others believe it arises from the transitional epithelium of periurethral ducts or the basal cells of prostatic acini. There are well defined histologic criteria for diagnosis of primary SCC of the prostate. Surgical treatment and multimodal approaches are most commonly used with varying degrees of success.

E-PS-24-028
Melanoma in the genitourinary tract. 3 cases in the last 10 years
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Background & Objective: To review cases of melanoma in the genitourinary tract in our hospital in the last ten years.
Method: We completed the search using Patwin computer program and reviewing tissue and cytological samples and the medical history of the patients.
Results: Case 1: 62-year old male with lesion in urethra and therefore partial urethrectomy was performed (amelanotic melanoma). No suspicious lesions were found on skin nor in other locations, so partial penectomy was performed (multifocal in-situ amelanotic melanoma). The patient is alive and disease-free. Case 2: 21-year old female with pigmented lesion on thigh (superficial spreading melanoma). Fourteen years later an inguinal lymph node was removed (metastatic melanoma) and a year later lesions were discovered on the bladder (metastatic melanoma). The patient is alive and relapse-free. Case 3: 31-year old male with incidental hepatic lesions by ultrasonography, so fine needle aspiration puncture was performed (poorly differentiated malignant tumour). A computed tomography revealed masses in mediastinum, different organs and nodules in right testis, so radical orchiectomy was performed (melanoma). No suspicious lesions were found on skin and the origin of the tumour could never be assessed. Patient died two months after.
Conclusion: When melanoma is diagnosed in the genitourinary tract, it is mandatory to look for lesions on skin. We recommend to include an inmunohistochemical marker of melanocytic differentiation when we encounter a solid neoplasm that doesn't meet typical morphology or inmunophenotype.

E-PS-24-029
Collecting duct renal carcinoma: a series of four rare cases
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Background & Objective: Collecting duct carcinoma (CDC) is a very rare neoplasm, counting of < 1% of kidney malignancies. It arises from the distal collecting ducts, affects a wide range of ages and is slightly more common in males. There are well defined criteria for diagnosis.
Method: Retrospective study of CDC diagnosed over a period of 12years (2004-2016): 4 patients, median age of 68years (42months-87years), 2M:2F. CDC had a median size of 11.5cm (7-15), equally common in both kidneys. All 4 patients were submitted to radical nephrectomy. Patients were staged using AJJC 8th edition (2017).
Results: The median follow-up was only 6.5 months, and none of the 4 cases survived for over 10 months. None of the patients were submitted to adjuvant therapy. 3 tumours extended into perinephric tissue and 1 had extension into to the liver. Regarding grade WHO/ ISUP: 2 tumours were G3 and 2 were G4, sarcomatoid features were present in 3 cases, and all 4 cases had necrosis and lymphovascular Invasion. 2 cases had perinephric fat positive margins, 1 had renal vein positive margin and the remaining showed negative margins. 3 patients were at stage III and 1 at stage IV.
Conclusion: CDC is a very aggressive neoplasm, with 2/3 of patients dying within 2years after diagnosis, owing to its infiltrative borders and large size, commonly with incomplete resection and frequent metastasis. None of our patients had known distant metastasis, probably because of the low follow-up period achieved.

E-PS-24-030
Idiopathic scrotal calcinosis – mini review of five cases
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Background & Objective: The aim of this study to report our 5 cases of Idiopathic Scrotal Calcinosis (ISC) and revise the clinical and histological findings.
Method: Histopathological slides of the 5 patients diagnosed with ISC for last 2 years were reviewed. The clinical details was recorded from the electronic medical records.

Results: The mean age at diagnosis was 44,6 (range 30-62 years). Two of the patients had moderate painfull and icthy lesions but other three patients were asympthomatic. All of cases were presented with multiple, yellowish white, chalky nodules and size of nodule range was 0,2-1 cm. One of cases had scrotal epidermoid cyst with intact epithelial walls. One of the case had intra/undermural calcification with mild chronic inflamation and foreign body giant cell reaxion.
Conclusion: ISC is a rare and benign condition presented with multiple nodules and lumps within scrotal skin. The lesions have been attributed clinically as sebaceous cysts, fibroma, and xanthoma. Numerous theories about the pathogenesis of ISC have been proposed. There is considerable debate as to whether "idiopathic" term accurately applies, as some investigators suggest that ISC is truly a late presentation of epidermal inclusion cysts that have undergone dystrophic calcification. Recently, it has been suggested that ISC is the result of dartos muscle necrosis and degeneration with resulting dystrophic calcification of the dartos muscle as well as the calcification process of uterine leiomyoma.

E-PS-24-032
Malignant mesothelioma of paratesticular region of testis: a case report
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Background & Objective: Paratesticular malignant mesothelioma is a very rare type of mesothelioma, although it is the most common malignant tumour in paratesticular region. Here we report a malignant epithelioid mesothelioma case in paratesticular region.
Method: A 39-year old male patient admitted to urology department with recurrent hydrocele and pain. CT scan displayed 33x35 mm cystic mass along to the left spermatic cord. In gross examination there was a 3.5x1.5 cm cystic mass. The Wall of cyst was thickened and the surface was irregular. Histologically, a malignant tumour infiltrating the spermatic cord and growing in micropapillary and papillary patterns. Atypical mesothelial tumour cells were eosinophilic with vesicular nuclei, prominent nucleolus and scattered multinuclear giant cells. There were various mitosis, but no necrosis. In immunochemical panels, mesothelial markers were positive (CK5/6, D2 40, WT1).
Results: Malignant mesothelioma of paratesticular region has similar features with pleural and peritoneal ones. The main risk factor is asbestos exposure. The malignant behavior of our case was infiltrating pattern, increase in mitosis, atypical pleomorphic mesothelial cells and hypercellularity.
Conclusion: Malignant mesotheliomas should be distinguished from mesothelial hyperplasia, well differentiated papillary mesothelioma, paratesticular mullerian type tumours, adenomatoid tumour and metastatic carcinomas. Malignant mesotheliomas are different from benign tumours in terms of their stromal invasion, atypical mesothelial cells, high mitotic activity, and necrosis. Moreover, they distinguish from metastasis with their histologic feature and specific immunohistochemical stainings.

E-PS-24-033
Adult type granulosa cell tumour of the testis: case report of an exceptional histological type
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Background & Objective: Granulosa cell tumours of the testis are classified as sex cord-stromal tumours that are divided into juvenile and adult subtypes. The juvenile type commonly occurs in the first 6 months of life. Compared to the juvenile type, adult testicular granulosa cell tumour are extremely rare and can occur at any time after puberty with a mean age at diagnosis of 47 years. Only 49 cases of adult granulosa cell tumour of the testis are described to date.
Method: We report an exceptional case of this rare tumour which was predominantly cystic, causing a diagnostic dilemma clinically and ultimately diagnosed on histopathology.
Results: It's about a 63-years-old man with adult type granulosa cell tumour with sarcomatous component. The only case of sarcomatous component associated with this tumour was described by Schubert and Al in 2014. To the best of our knowledge, this would be the second case.
Conclusion: Meticulous histological examination and immunohistochemistry helped in the diagnosis and the patient underwent an orchiectomy.

E-PS-24-034
Multiple myeloma with testicular involvement
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Background & Objective: Testicular multiple myeloma is a rare entity. The incidence of extramedullary lesions in myeloma ranges from %11 to %73, but the incidence of clinical testicular multiple myeloma is assumed to be %0.03 to %0.1 of all primary and secondary tumours of the testis. We report a rare case of multiple myeloma with testicular localization. A 65-year-old man with known multiple myeloma history, attended to the urology clinic with the complaint of bilateral testicular mass. Right orchiectomy was performed.
Method: The surgical specimen was formalin-fixed and paraffin embedded. The sections were stained with routinary H&E. Immunohistochemistry was performed.
Results: Right orchiectomy specimen was macroscopically 14,5x5,5x4 cm in diameter; multiple, solid nodules were observed filling the parenchyma of the testis and the largest nodule was 2 cm in diameter. Histopathological examination showed extensive infiltration by kappa-restricted CD 138 and CD 38 positive plasma cells. In our patient, the systemic myeloma progression was associated with the development of extramedullary testicular involvement.
Conclusion: Advanced extramedullary multiple myeloma is not a rare occurrence. However, the testis is a rare site of localization for multiple myeloma. The prognosis of multiple myeloma patients with testicular involvement is generally poor. As a result of the testicular blood barrier, the testes serve as a sanctuary site for haematological malignancies. By the way testicular localization of multiple myeloma is a rare entity, it should be kept in mind in routine pathology practice of metastatic testicular tumours.

E-PS-24-035
Renal malignant epithelioid angiomyolipoma with pelvic and paraaortic lymph node metastasis
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Background & Objective: Epithelioid angiomyolipoma (PEComa) is a rare variant of angiomyolipomas, which is composed of epithelioid cells at least 80%. It displays a wide spectrum of biological behavior varying from benign to malignant potential.
Method: A 43-years old female patient underwent radical nephrectomy due to mass lesion in left kidney in another center in 2015. She was diagnosed as epithelioid angiomyolipoma. As intra-abdominal lesions suggestive for multiple malignancies were observed on PET-CT scan during follow-up, the patient underwent diagnostic laparotomy in our hospital. Intraoperatively a mass lesion over left psoas muscle and enlarged uterus were seen. On gross examination, mass lesion (8x4x2 cm)

was multi-lobulated with creamy white section with hemorrhagic foci. Uterus and adenexa were unremarkable.
Results: Tumour cells were polygonal with enlarged nuclei and marked nucleoli. Diffuse necrotic areas were observed. Three mitoses were counted in 10 high power fields. On immunohistochemistry, panCk, PAX 8, TFE 3 and S100 were found to be negative while HMB 45 and Melan A were found to be positive. The metastasis was detected in 5 pelvic and 2 para-aortic lymph nodes. Histopathological and immunohistochemical findings were compatible with recurrence of PEComa with lymph node metastasis.
Conclusion: Primary Malignant PEComa of kidney with pelvic and paraaortic lymph node metastasis are rare.

E-PS-24-036
Atypical presentation of prostate carcinoma
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Background & Objective: Prostatic carcinoma is one of the most common tumours in males. The diagnosis is usually established during the pathological analysis of prostatic tissue fragments. A prostatic tumour is rarely diagnosed while searching for the primary site of a non-osseous metastatic tumour or during the assessment of a recto-sigmoid tumour.
Method: The clinical and pathological data were collected for patients with prostate cancer with unusual presentation from our institution.
Results: 4 patients were identified, with ages between 51 and 82 years. The diagnosis of prostatic adenocarcinoma was established after the examination of the perirectal lymph node (1 case) and of the extension of a primary colo-rectal tumour (1 case) or after the immunohistochemical assessment of a renal/perirenal tumour in two patients with clinical suspicion of renal tuberculosis and perirenal sarcoma/lymphoma respectively. In 3 of the 4 cases presented, there was no suspicion of a prostatic tumour after the clinical and imagistic evaluation. The correct diagnosis was suspected after the examination of H&E stained slides, but in one case the initial diagnosis was wrong. Immunohistochemistry confirmed the diagnosis.
Conclusion: The multiple clinical presentations of prostatic cancer and the different ages at which it can occur in advanced, metastatic stage, can be misleading to urologists, radiologists and oncologists. The unusual clinical aspects and/or the lack of imaging and lab information can cause errors in the pathological diagnosis.

E-PS-24-037
Aggressive angiomyxoma of spermatic cord: a case report of a rare entity
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Background & Objective: Aggressive angiomyxoma (AA) was first reported by Steeper and Rosai in 1983. It is an uncommon myxoid soft tissue of the genital, perineul and pelvic region of adult females. Occurence in males is extremely rare and involves scrotum, spermatic cord, ingumal region and perineum.
Method: We report a rare case of AA of spermatic cord of a 55 years old male who presented with a painless inguinal swelling. There was no history of trauma or any genitourinary disease or previous surgery. CT/scan and MRI images revealed and ill-defined gelatinous mass measured 4,5x4cm adherent to the spermatic cord. An excition was performed.
Results: We received a witish tumour with elastic and gelatinous cut surface. Histological examination revealed a neoplasm composed of scattered spindle cells in a myxocollagenus stroma with numerous variable sized vessels and extravasation of red blood cells. Mitoses are absent. Immunohistochemical study positive stain of tumour cells for vimentin, CD34 focally, SMA and ER. On the other hand negative stain was observed with the use of Pankeratin, S100p, Desmin and PR, Ki67 $\leq$3%. The tumours microscopic features and immunohistochemical profile favored the diagnosis of aggressive angiomyxoma.
Conclusion: AA is a benign myxoid soft tissue neoplasm seen rarely to involve spermatic cord. Because off its locally infiltrative course and frequent reccurrences it has been termed "aggressive". Differential diagnosis includes other benign tumour with low reccurense propensity such us intramuscular myxoma neurofibroma, myxoid lipoma and tumours with metastatic potential such as myxoid liposarcoma, low grade myxoid fibrasarcoma. The definitive diagnosis is made by histological examination of the excisional spesiment.

E-PS-24-038
Xanthogranulomatous pyelonephritis with Liesegang rings: a case report
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Background & Objective: Xanthogranulomatous pyelonephritis is a rare form of chronic pyelonephritis in which the involved areas of the kidneys are destroyed and replaced by granulomatous tissues containing lipid-laden macrophages. It accounts for approximately 1% of pyelonephritis cases reported worldwide. Affected patients are usually females in their fifth or sixth decade of life, with a background of destructive uropathy, nephrolithiasis or recurrent urinary tract infections.
Method: A 77-year-old female patient presented to our hospital with acute renal failure. U/S and CT scan showed three cystic lesions with focal solid elements in the left kidney and the patient underwent a nephrectomy. Macroscopic examination revealed two irregular yellowish-whitish tumour-like lesions, in the lower and upper pole, with maximum diameter 2cm and 4cm respectively. Smaller, similar areas were observed in the remaining parenchyma, as well cysts measuring 0,3-1,5cm.
Results: Microscopic examination revealed abundant histiocytes, foamy macrophages, chronic inflammatory infiltrate and areas of fibroblastic reaction with lobular architecture or diffusely infiltrating the perinephric and peripyelic fat. Multiple multinucleated giant cells were also observed, focally in association with concentric acellular PAS+ ring-like structures (Liesegang rings).
Conclusion: Xanthogranulomatous pyelonephritis can mimick on clinical or gross examination, and sometimes even at the microscopic level, renal cell carcinoma. Liesegang rings are concentric noncellular lamellar structures, due to accumulation of insoluble products in colloidal matrix. A rare histological finding with unclear pathogenesis and should not be mistaken for parasites, calcifications, psammoma bodies, amyloid or lithiasis.

E-PS-24-039
Renal small cell oncocytoma with pseudorosettes, rare case
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Background & Objective: Renal oncocytoma (RO) is a benign tumour of the kidney and small cell "oncoblastic" variant of RO is a very rare subtype described by Hes et al in 2001. Small cell RO may display variegated growth patterns including solid and organoid areas and varying number of pseudorosettes.
Method: A 49 years old women's physical examination was unremarkable. Computed tomography disclosed that the mass was located at the upper pole of right kidney, was 4.2×4.0×3.4 cm in size and well circumscribed with contrast enhancement. Right partial nephrectomy was carried out. Macroscopical examination revealed 4.5x4x3.5 cm well-circumscribed

solid lesion in the renal parenchyma, yellowish/tan in color with white stellate scar in the center. Light microscopy showed classic oncocytoma and scattered small nodules, comprasing 20% of total tumour volume, thightly packed small tubules and pseudorosettes consisted of small cells having scant cytoplasm, high nucleus:cytoplasmic ratio.
Results: Immunohistochemically, small cell areas was positively stained with EMA, CD117, E-cad, CK7 (focally positive), and negatively with vimentin, WT-1, CD10, CgA and Synaptophysin. The tumour was diagnosed as renal oncocytoma including small cell oncocytoma with pseudorosettes
Conclusion: Because of the rarity and diagnostic difficulty, we presented our case.

E-PS-24-040
Prognostic relevance of Ki-67 immunohistochemical expression in transitional cellcarcinoma of the urinary bladder
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Background & Objective: Urothelial carcinoma of the urinary bladder is the ninth most common cancer worldwide, accounting for 3% of the global cancer incidence. Several studies have identified Ki-67 as an independent prognostic marker of bladder cancer, and a large multicenter study has confirmed that Ki-67 is independently associated with disease recurrence and overall survival in patients treated with radicalcystectomy. The purpose of our work was to determine the association of the cell proliferative marker Ki-67 with pathologic features and disease prognosis in patients with transitional cell carcinoma (TCC) of the urinary bladder.
Method: We carried out a retrospective study of 53 cases of bladder tumours diagnosed following endoscopicresection and radical cystoporostatectomy between 2011 and 2013. Correlation between Ki-67 immunoexpression and tumour grade, tumour stage and evolution (recurrence and metastasis) was assessed.
Results: Our resultsshowedthat the immunohistochemical expression of Ki-67 wasstatisticallycorrelatedwith grade (high grade = 34% and low grade = 6%), stage (pTa = 8%, pT1 = 28%, pT2 = 41%), and tumour size ($p = 0.009$). However, thereis no correlationwith the number of tumours, reccurence and progression.
Conclusion: Our study confirmed the correlation between Ki-67 and prognostic factores. These results were predictable given the aggressive and proliferative potential of these tumours.

E-PS-24-041
Cyst of the canal of Nuck
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Background & Objective: The cyst of the canal of Nuck is an infrequent entity, consisting in a persistent processus vaginalis that usually becomes apparent in young women. During embryonic development, parietal peritoneum folds in the inguinal canal forming the canal of Nuck. Near birth or during the first year of life, this canal is usually obliterated, developing the round ligament. Rarely, closure may not occur, resulting in a persistent canal or fold walled by parietal peritoneum. It presents as an inguinal mass, asymptomatic or mildly painful, translucent, unchanged with Valsalva maneuver, usually without accompanying inflammatory signs. It can be complicated by infection, bleeding or enlargement with protrusion of intraabdominal organs.
Method: We present the case of a 39-year-old woman with a non-painful mass in the right inguinal fossa, which she had noticed for the last months, without accompanying symptoms.
Results: An ultrasound study was performed, finding an anechoic, well-defined lesion, thin walls with no septations, suggestive of a cyst. This lesion was extirpated, macroscopically consisted of a fragment of fibroadipotic tissue with a well-delimitated, thin-walled cyst, with serous content. In the microscopic study, this cyst was covered by a flat-cuboid mesothelium, with inmmunoexpresion for calretinin; surrounded by fibroadipotic tissue without atypia, with siderophages and multiple activated fibroblasts.
Conclusion: It is important to recognize this congenital anomaly to differentiate it from usual inguinal lesions, such as hernias, lymph nodes, abscesses or neoplasms. Elective treatment is surgical removal with posterior mesh implantation.

E-PS-24-042
Chromophobe renal cell carcinoma combined with neuroendocrine carcinoma and extensive sarcomatoid component
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Background & Objective: Chromophobe renal cell carcinoma (chRCC) is characterized by large cells with prominent membranes and wrinkled nuclei. Primary renal neuroendocrine carcinoma (NEC) is rarely diagnosed with similarity in morphology between NEC at other sites. Coexistence of these 2 neoplasms within the same tumour mass is exceedingly rare. Even our case contains extensive high grade sarcomatous component.
Method: A 52-year-old man presented with a 5-month history of gross hematuria. Computed tomography (CT) revealed a 10 cm lobulated mass in the interpolar area of the left kidney. Radical nephrectomy was done.
Results: Gross examination revealed heterogeneous, multinodular tumour, measuring 9.1 x 8.9 x 7.7cm. Representative tissue sections of the specimen were fixed in 10% buffered formalin and embedded in paraffin. Haematoxylin and eosin stained slides were reviewed. Microscopically, the mass showed coexistence of the distinctive three (chRCC, NEC and sarcoma) components with no overlapping features. The immunohistochemical stain including pancytokeratin (CK), C-Kit, vimentin, CD56, synaptophysin and chromogranin was performed. The chRCC component showed C-Kit and CK positivity. The NEC component expressed CD56 and synaptophysin. The sarcomatoid component was positive for vimentin and focal weak positive for CK.
Conclusion: We demonstrated an interesting case of chRCC combined with NEC and extensive sarcomatous component. NEC element combined with RCC is important because the neuroendocrine element may show aggressive clinical outcome and should suggest the use of a modified adjuvant therapy.

E-PS-24-043
Morphological features and prognosis of non-clear cell renal cell carcinoma types
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Background & Objective: The prognosis and therapy individualization are an actual problem for patients with renal cell carcinoma (RCC). Objective: to establish morphological features and prognosis of non-clear cell RCC types.
Method: The data of 897 patients of Belarus Cancer Registry (2011-2015) and specimens of 75 patients with non-clear cell RCC (NCCRCC) were analyzed. IHC panel: EMA, vimentin, CD10, CK7, AMACR, PAX8, CD117, CK20, HMB45 was performed.
Results: NCCRCC types were diagnosed in 1/4 cases in the structure of kidney tumours and were represented by papillary (PRCC-4.9%), chromophobe (ChRCC-3.5%) and unclassified (16.1%) RCC, clear cell papillary RCC and MTSC (<0.5%). The most favorable RCC with 95.4% 5-year survival was ChRCC, which was represented by localized forms

(pT1a/pT2a-87%). PRCC was also diagnosed at the stage of localized tumours (pT1a-pT2a-84%) with a fraction of locally advanced (pT3a) and metastatic (pT3bM1) RCC 13% and 3%, respectively, and 78.6% 5-year survival. The significantly better survival of patients with PRCC was observed in cases of low-grade tumours ≤4cm (5-year survival: G1/G3=90.9%/48.7%; pT1a/pT2a-90.9%/37.5%, p=0.02). pTNM and G were independent predictors of non-clear cell RCC types (p<0.006).
Conclusion: The most favorable course was observed for ChRCC compared to papillary with a 5-year survival rate of 95.4% and 78.6%, respectively. Significantly better survival was noted in cases of low-grade PRCC ≤4cm. pTNM and G were independent prognostic factors.

E-PS-24-045
Recurrence and upstaging rates of urothelial carcinoma diagnosed on transurethral resection of bladder specimens
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Background & Objective: Urothelial carcinoma (UC) has a high recurrence rate, 36 to 60 % of patients with UC having a tumour recurrence. The aim of our study was to evaluate the recurrence and upstaging rates of UC diagnosed on transurethral resection of bladder specimens (TURB) in our Pathology Department.
Method: We reviewed all the TURB performed in the Urology Department and examined in the Pathology Department of the Tîrgu Mureş Emergency County Hospital between 2011 and 2017. We selected only the patients with tumour recurrence and we analyzed the evolution of tumour grade and stage on the repeat TURB specimens.
Results: From a total of 1133 UC, 210 had tumour recurrence (179 men and 31 women), with a mean age of 68.29, ranging from 38 to 88. The recurrences occurred after a mean period of 13.64 months. The patients with noninvasive pTa papillary UC (95 cases) had the most frequent recurrence rate (45,23%). Of these, 18 cases (19%) were upstaged on repeat resection (pT1 - 7, pT2 - 4, "at least" pT1 - 7) and grade progression was reported in 19 cases. Of the 36 patients with pT1 and 33 patients with "at least" pT1 initial stage, 16 were upstaged to pT2. Two patients from the 28 with pT2 stage, developed a pT4 stage tumour.
Conclusion: The non-invasive papillary UC had the most frequent recurrence rate, but usually the tumour recurrence had the same grade and stage, in contrast to infiltrative UC, which presented more frequent a stage progression on the repeat resection.

E-PS-24-047
Plasmacytoid variant of urothelial carcinoma: two rare case reports
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Background & Objective: Plasmacytoid urothelial carcinoma is an extremely rare variant of urothelial carcinoma with aggressive behavior and poor survival rate. The differential diagnosis include plasma cell-derived neoplasms, such as lymphoma and plasmacytoma, lymphoepithelioma-like carcinoma and metastatic carcinomas.
Method: We report the case of a 83-year-old and 80-year-old males who both presented with recent macroscopic hematuria. Subsequent cystoscopy revealed a solid tumour involving the dome and the left lateral wall of the urinary bladder respectively. Trans-urethral resection of the bladder tumours was performed.
Results: Histological examination of the tumours showed a high-grade malignant neoplasm arranged in discohesive cords and sheet with plasmacytoid features, penetrating the deeper mucosa and the muscularis propria respectively. Immunohistochemical examination was diffusely positive for CD138, cytokeratins 7 and 20 and p63 protein and patchy for c-erb-B2. Accordingly, the diagnosis of plasmacytoid urothelial carcinoma was made. The first patient is receiving BCG treatment and the second was advised to undergo palliative cystectomy, however he died one month later due to heart failure.
Conclusion: In conclusion, we present two rare casew of plasmacytoid urothelial carcinoma. It is an aggressive variant of urothelial carcinoma and may be confused with plasmacytoma and lymphoma, as long as metastatic carcinomas, so a high index of suspicion is essential to avoid a misdiagnosis. Morphologic distinction of the plasmocytoid phenotype and immunohistochemical confirmation is critical for correct diagnosis and early treatment of this highly aggressive disease.

E-PS-24-048
Small cell neuroendocrine carcinoma of the prostate after androgen deprivation therapy for low-risk prostatic adenocarcinoma
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Background & Objective: Small cell neuroendocrine carcinoma of the prostate is an aggressive form of cancer and accounts for only 1% of all prostate cancers. Approximately 50% are mixed with conventional adenocarcinoma. We present a rare case of a 83-year-old patient who developed prostatic small cell carcinoma following androgen deprivation therapy for low-risk prostatic adenocarcinoma.
Method: The patient was diagnosed with a low-grade adenocarcinoma of the prostate with Gleason score 6(3+3) by transrectal prostate needle biopsy. CT-scan and a bone-scan scintigraphy revealed the clinical stage to be organ confined. The patient received androgen deprivation therapy and two years later he complained of difficulty in urinating. Clinical examination revealed an enlargement of the prostate with low-rate of PSA, so he underwent a prostate needle biopsy.
Results: Histologically, the tumour cells have scant cytoplasm and hyperchromatic nuclei and showed a solid growth pattern. Immunohistochemically, the tumour cells were positive for AE1/AE3, CD56, chromogranin and synaptophysin and focally positive for TTF-1 and they were negative for PSA and PSAP. There was no component of conventional prostatic adenocarcinoma noted. These findings are consistent with small cell neuroendocrine carcinoma of the prostate. A metastatic work-up revealed lymph node and bone metastasis. The patient died 3 months later due to heart failure.
Conclusion: In conclusion, we report an extremely rare case of small cell neuroendocrine carcinoma of the prostate. Although rare, it should kept in mind this possibility in patients who are rebiopsied soon after therapy for conventional prostatic adenocarcinoma, and apply the proper immunohistochemistry to prompt the correct diagnosis.

E-PS-24-049
Urothelial carcinoma with rhabdoid features: a rare case report
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Background & Objective: Urothelial carcinoma with rhabdoid features which has recently been described as a primary tumour of urinary bladder, is an extremely rare neoplasm and constitutes a diagnosis of exclusion.
Method: We present the case of a 65-year-old man who presented with macroscopic hematuria and lower abdominal pain. On cystoscopy a large ulcerative mass was found and an emergency cystoprostatectomy followed.
Results: Microscopically, a low-differentiated carcinoma with rhabdoid features was identified with focal squamous differentiation. Conventional urothelial morphology was not found. The immunohistochemical profile (positivity for p63, cytokeratin 7, cytokeratin 20 and 3412) suggests an

urothelial origin, with INI1 expression maintenance, whereas the analysis was negative for actin, desmin, S100 protein, AFP as well as Myogenin. The patient died one month later due to cardiorespiratory failure.
Conclusion: The exact proportion of rhabdoid-shaped cells required for the diagnosis of urothelial carcinoma with rhabdoid features is not clearly defined, as the urothelial component can be totally absent, as in our case. In such instances, it can be discriminated from extrarenal malignant rhabdoid tumour safely only by applying molecular analysis. Differential diagnosis from both extrarenal malignant tumour and rhabdomyosarcoma is extremely essential for the accurate and timely treatment, taking into consideration the aggressive character of these neoplasms.

E-PS-24-050
Primart Ewing's sarcoma of the seminal vesicles. A case report
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Background & Objective: Primary Ewing's Sarcoma of the male genital track is rare and in the seminal vesicles even rarer, with only a handful of cases been reported. We present a case of Ewing's sarcoma arising from the left seminal vesicle of a young man. The right vesicle was also involved.
Method: A 39-year-old male presented in our hospital with a history of haematospermia and painful defecation. CT and MRI scanning revealed a large mass between the bladder and the rectum, with no other pathologic processes. Intraoperative frozen section showed a small round cell tumour. The patient underwent total cystoprostatectomy with reimplantation of the ureters into the abdominal wall.
Results: Macroscopic examination confirmed a 9cm tumour, totally repalcing the left seminal vesicle with extention to the bladder wall. The right seminal vesicle was present, but distorted. Microscopically the tumour was composed of uniform small round cells. Immunohistochemical stains for CD99, Fli-1, and ERG were positive. Tumour cells were present in the right seminal vesicle and into the bladder wall. Fluorescent In Situ Hibridization confirmed the translocation of the EWSR1 gene. The patient received chemotherapy. Two years on follow up he is free of disease.
Conclusion: Primary Ewing's Sarcoma of the seminal vesicle is rare. Exclusion of extention from other sites should be considered before the diagnosis is made.

E-PS-24-051
Clear cell urothelial carcinoma. Report of a case
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Background & Objective: More than 90% of urothelial carcinomas arise in the urinary bladder, with 5-10% developing in the upper urinary tract. Clear cell variants of transitional cell carcinomas of the bladder are extremely rare tumours, with only a handful of cases reported in modern literature. Carcinomas with clear cell features may arise in almost any site including prostate, kidneys, uterus, ovary, vagina, lung and breast. The histogenesis of it is not certain and Müllerian origin and urothelial origin have been postulated. It usually affects women.
Method: We present a case a 65-year-old man, presented to our hospital with painless gross haematuria. Cysteoscopy was performed and a polypoid mass protruding from bladder's dome was identified. Transurethal resection of the entire mass has been performed. Tumour specimens were sent to our laboratory for histopathological assessment.
Results: Histologically the tumour consisted predominantly of malignant cells with severe nuclear atypia and abundant clear cytoplasma. Tumour cells were PAS positive and PAS-D negative thus proving the presence of intracellular glycogen. Positive immunohistochemical stains for CK7 and GATA3 ruled out the possibility of metastasis. The definitive diagnosis was High grade Clear Cell (glycogen-rich) urothelial carcinoma.
Conclusion: One should be aware of this variant of urothelial carcinoma as it has very similar histologic features with other clear cells neoplasms including clear cell adenocarcinoma of the urinary bladder and metastatic clear cell renal or prostatic carcinomas. Furthermore, in female patients, metastasis of cervical or vaginal clear cell adenocarcinoma should also be considered. In ambiguous cases the utilization of immunohistochemical stains is recommended.

E-PS-24-052
Prognostic impact of RKIP expression in clear cell renal cell carcinoma. An immunohistochemical study of 100 cases with long term follow up
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Background & Objective: Clear cell renal cell carcinoma (CCRCC) is a complex disease in which inactivation of VHL gene and loss of VHL protein are critical events. Raf kinase inhibitory protein (RKIP) is known to be a suppressor of multiple oncogenic pathways in several solid tumours.
Method: A series of 100 CCRCC with at least 15 years of follow-up was retrospectively collected in a single institution (Pathology Department, University Hospital). A representative and well preserved tumour area in each case has been selected and included in a tissue microarray (TMA). A commercially available anti-RKIP antibody (Abcam, ab 76582, working dilution: 1:250, Dako Envision) was used in the study.
Results: RKIP immunostaining was negatively correlated with tumour diameter (Spearman Rho, p=0.012). RKIP expression was higher in low grade (G1/2) than in high grade (G3/4) tumours (Chi-square test, p=0.018). In addition, RKIP expression was higher in pT1a than in pT3/4 CCRCCs (Chi-square test, p=0.002).
Conclusion: 1) RKIP expression is correlated with classic histological parameters of low tumour aggressiveness, which suggests a tumour suppressor role of this protein in this disease. 2) RKIP expression could be considered as a potential marker to define prognosis of CCRCC patients.

E-PS-24-053
Idiopathic scrotal calcinosis: a rare case report
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Background & Objective: Idiopathic scrotal calcinosis is a rare and benign disorder characterized by presence of multiple calcified nodules in scrotal skin. Its distinct features are slow growing, painless masses appearing in childhood or early adulthood. Clinically it can manifest by multiple palpable dark yellow and brown subcutaneous nodules on the scrotum.
Method: Demographic, clinical and pathological findings of the patient were investigated retrospectively.
Results: 39-year-old male patient was admitted to the hospital with asymptomatic multiple calcified scrotal skin nodules. The scrotal skin was excised, and the nodules removed. Macroscopically, three part of skin excision material were received. At the cut sections the lesions appeared as cystic lesions contained by white, hard and dry material. The largest diameter of nodules was measured between 5-11 mm. The histological examination revealed presence of globules of basophilic calcified material within the dermis of scrotum surrounded by pseudocapsule and histiocytic inflammation. There was no atypia or any mitotic activity, and no remnants of epidermal cysts. Because of the features listed above the diagnosis of idiopathic scrotal calcinosis was made. The serum calcium level was normal.

Conclusion: Idiopathic scrotal calcinosis can be found accidentally as asymptomatic scrotal lesion regardless of the serum calcium level.

E-PS-24-056

Urothelial carcinoma with myxoid/mucinous stroma and chordoid features - a case report

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Background & Objective: Although invasive urothelial carcinoma is the most common type of bladder carcinoma, urothelial carcinoma with myxoid/mucinous stroma and chordoid features is very rare. The English literature has only a few cases.
Method: 12The surgical specimens were formalin-fixed and paraffin embedded. The section was stained with routinary H&E. Immunohistochemistry was performed.
Results: A 79-year-old woman suffering from hematuria and burning with urination. The urography with computed tomography showed 1,9 cm diffuse wall thickening of the left posteroinferior wall of the urinary bladder with perivesical fat tissue and left ureteral orifices involvement. During cystoscopy, a solid tumoural mass of 10 cm in diameter was detected and resected by transurethral resection. Microscopic examination revealed atypical urothelial cells in small groups and chords on the H&E sections and represents muscle involvement in the myxoid/mucinous stroma. Histopathological and immunohistochemical results were compatible with invasive urothelial carcinoma with myxoid/mucinous and chordoid features.
Conclusion: Because of the rarity of invasive urothelial carcinoma with myxoid/mucinous and chordoid features, pathologists should keep in mind this entity and also exclude the diagnosis of chordoma, adenocarcinoma and metastatic carcinoma of the urinary bladder.

E-PS-24-057

Sarcomatoid carcinoma of the urinary bladder with heterologous elements: report of two cases

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Background & Objective: Sarcomatoid urothelial carcinoma, originally termed carcinosarcoma, is a rare, aggressive malignant neoplasm, accounting for less than 1% of all bladder carcinomas. It is defined according to the WHO classification as a biphasic tumour consisting of malignant epithelial and mesenchymal elements, with abrupt or gradual transition from one to the other. Heterologous elements may be present. We report two cases of sarcomatoid carcinoma of the urinary bladder, with heterologous elements
Method: Both patients were males, aged 67 and 81 years, presented with painless gross haematuria and bulky tumour masses and underwent transurethral resection. (TURBT).
Results: Histological and immunohistochemical features of both tumours were consistent with sarcomatoid urothelial carcinoma of the urinary bladder. Heterologous elements were present and included leiomyosarcoma in the first case and chondrosarcoma in the second case. The first patient received chemotherapy, followed by radical cystectomy, whereas the second patient received radiotherapy and chemotherapy. They both remain alive, 4 years and 3 months after initial diagnosis respectively.
Conclusion: Sarcomatoid urothelial carcinoma is a rare entity, which usually presents at advanced stage and behaves more aggressively than conventional urothelial carcinoma. Heterologous elements, including osteosarcoma, chondrosarcoma, rhabdomyosarcoma, leiomyosarcoma, liposarcoma and angiosarcoma may be present and appear to be associated with reduced survival in some studies. It has been proposed that sarcomatoid urothelial carcinomas represent either multiclonal collision tumours or monoclonal carcinomas with divergent differentiation, with recent molecular studies favoring the latter theory. Sarcomatoid urothelial carcinoma must be differentiated from true mesenchymal neoplasms, especially on small biopsies or when the mesenchymal component is extensive.

E-PS-24-059

A renal tumour in a patient with prostatic acinar adenocarcinoma

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Background & Objective: We present a case of renal metastasis of prostatic origin.
Method: A 79 year old man was submitted to our hospital with left flank pain and hematuria. He had a previous history of prostatic acinar adenocarcinoma Gleason score 9 (4+5), pT3b, diagnosed 5 years ago and treated with radical prostatectomy. The patient was examined thoroughly and the only findings were an elevated PSA level of 21ng/ml and a left renal mass on Pet Scan. A left nephrectomy was performed. We received a kidney with its perinephric fat measuring 19x10x9 cm, having a nodular solid whitish to yellow tumour with maximun diameter 7.5 cm, in the hilar region.
Results: Microscopically the tumour was composed of solid nests or sheets of monomorphic atypical cells, with prominent nucleoli and scant cytoplasm. The tumour was located in the hilar region infiltrating the ureteral wall. Immunohistochemistry stained positive for CKAE1/AE3, CK8, AMACR, PSA(weakly), CD57 and negative for RCC, CD10, CK7, CK20, CK34bE12, S100, SYP, LCA, p63, TTF1, CDX2, CD5, compatible with prostatic adenocarcinoma
Conclusion: Prostate cancer is frequent and usually spreads to regional lymph nodes and bones but metastasis to the kidney is extremely rare.

E-PS-24-061

A rare neoplasm of kidney: cystic nephroma

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Background & Objective: Cystic nephroma is a rare benign neoplasm that is often regarded as mixed epithelial and stromal tumour usually occurs in premenopausal women.
Method: The patient was 63-year-old female. While the patient was being investigated because of hypertension, abdominal CT revealed a type 3 renal cortical cyst located in the left kidney. Then left nephrectomy was performed. Macroscopically, the cystic structure of the kidney is exophytic, well-defined and 8x7x6 cm in size. Whole cortex, medulla and pelvis were involved and multiple septa were seen. Calcification and orange colored areas were observed in the septa and solid stromal component was not seen. Specimen was formalin-fixed and paraffin embedded. The sections were stained with routinary H&E. Immunohistochemistry was performed.
Results: Histopathologic examination revealed multilocular cystic lesion lined by cuboidal, focally flattened and hobnail epithelium. The stroma of septa consisted of spindle cells and there were focally cholesterol-loaded histiocytes. Immunohistochemically ER, PR nuclear expresions were detected in the stroma.
Conclusion: Cystic nephroma is a rare benign neoplasm. Premenopausal women are often affected because of their hormonal imbalance, but studies are limited because of tumour's rare occurrence. Our patient was undergone histerectomy 7 years ago due to ovarian cyst. There was no hormonal drug used in the history. Cystic nephroma should be kept in mind during routine pathology practice because it can't be distinguished from multicystic renal cell carcinoma without microscopic examination. Our case will contribute to the diagnosis and differential diagnosis of cystic nephroma during routine microscopic examination.

E-PS-24-062

A case report of a congenital mesoblasticnephroma

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Background & Objective: Congenital mesoblasticnephroma (CMN) is a mesenchymal renal tumour. It is the most frequent type of renal tumours in the neonatal and early infantile period. It's subclassified into classic and cellular types. After surgical resection, prognosis is generally excellent and only 5% develop recurrences.
Method: We report a case of a cellular CMN in a one-year old female, treated with bothsurgery and chemotherapy with multiple recurrences.
Results: A 9,5 cm tumour mass was excised. It was adherent to the spleen and the pancreatic parenchyma. The cut surface was whitish, multinodular with cystic changes and hemorrhage. On histological examination, this tumour was made of a heterogeneous mesenchymal proliferationwith dense areas arranged in intersecting bundles. The cells in these areas were medium sized with scant eosinophilic cytoplasm and ovoid monomorphic nuclei. Mitoses were numerous. Haemangiopericytoma-like vascular pattern were observed. Necroses with cystic changes were extensive. Elswhere, there was less cellular areas made of fibroblastic and myofibroblastic cells with a low mitotic rate. The tumour was adherent to the splenic and pancreatic tissue without invasion. Immunohistochemical study showed a focal expression of vimentin. EMA, CD99, CD34, desminand smooth muscle actin were negative.
Conclusion: Classic CMN has a good overall prognosis, but cellular CMN can be associated with a potential for malignancy with possible recurrence and metastasis. Prognosis depends on the stage. Complete surgical resection is the adequate treatment.

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A use of chromogranin A, IGF-1, EGFR, and AR immunohistochemical markers in atypical small acinar proliferation and adenocarcinoma of the prostate

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Background & Objective: Preneoplastic lesion, such as atypical small acinar proliferation (ASAP) play an important role in prostate cancer development. We aimed to compare chromogranin A, IGF-1, EGFR, and AR markers expression levels in preneoplastic lesions and carcinoma of the prostate, and to discuss its predictive value in prostate cancer early diagnosing.
Method: We used prostate biopsy samples, obtained from 90 patients with clinical diagnosis of prostate hyperplasia and prostate cancer and divided them into 6 groups, according to the morphological diagnosis: ASAP and carcinoma Grade Groups 1, 2, 3, 4, and 5. Group of samples without prostate lesions served as control one. We used monoclonal antibody to chromogranin A, IGF-1, EGFR, and AR in immunohistochemical assay.
Results: Chromogranin A expression was positive in neuroendocrine cells of all research groups, except ASAP. The highest level of Chromogranin A expression was detected in carcinoma Grade Group 5. The highest expression level of androgen receptors was registered in carcinoma Grade Group 2. The lowest expression level of androgen receptors was observed in ASAP. The lowest levels of IGF-1 and EGFR markers expression were found in carcinoma Grade Group 2. The highest level of EGFR marker expression was found in carcinoma Grade Group 1.
Conclusion: The greatest similarity in markers expression was observed in ASAP and carcinoma of Grade Groups 1, 2. The obtained data can supplement the pathways of prostate carcinoma morphogenesis and prostate tumour growth regulation by neuroendocrine cells through paracrine and autocrine secretory mechanisms.

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Cell renewal markers and D2-40 expression level in atypical small proliferation and prostate carcinoma of different grades

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Background & Objective: Small acinar proliferation (ASAP), an exception phenomenon, is believed to play an important role in prostate cancer development. Early differential diagnosis of those still lacks proper methodic. We aimed to compare Ki-67, caspase-3, and D2-40 markers expression levels in preneoplastic lesions and carcinoma of the prostate, and to discuss their predictive value in prostate cancer early diagnosing.
Method: We used prostate biopsy samples, obtained from 90 patients with clinical diagnosis of ASAP and prostate cancer and divided them into 6 groups, according to morphological diagnosis (ASAP and carcinoma Grade Groups 1, 2, 3, 4, and 5). Group of samples without prostate lesions served as control one.
Results: The highest mitotic activity of epithelial cells was found in patients with carcinoma Grade Group 5 (Me = 15% [9-31]). The lowest mitotic activity was observed in patients with ASAP (Me = 3% [1-6]). The lowest caspase-3 expression level was detected in patients with ASAP and carcinoma Grade Groups 1, 2. The lowest caspase-3 expression level was observed in patients with carcinoma Grade Group 5 (Me = 3% [1-12]). There was no D2-40 expression in the cytoplasm of the basal epithelial cells, both adenocarcinoma and ASAP. D2-40 expression was positive in the control group (Me = 37,5% [14-47]).
Conclusion: The greatest similarity in the direction of cellular renewal processes was observed in ASAP and carcinoma Grade Groups 1 and 2. D2-40 marker can be used in complex differential diagnostic algorithm of prostate preneoplastic and neoplastic lesions.

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Malignant rhabdoid tumour of the kidney: a case report

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Background & Objective: Malignant rhabdoid tumours most commonly occur in children with extrarenal variants seen in the CNS, liver, female genital tract, and soft tissues. Here we present a case of a 2-year-old male child with a primary malignant rhabdoid tumour of the kidney with metastasis to the liver and right adrenal gland.
Method: Surgical specimens were formalin-fixed and paraffin-embedded. Sections were stained with routinary H&E.
Results: A 2-year-old male child with no significant past medical history presented to an outside hospital with a history of abdominal pain. He was noted to have right upper quadrant tenderness and underwent an abdominal ultrasound that showed an intra-abdominal mass. Physical examination showed abdominal distension and hepatomegaly. The patient underwent right radical nephrectomy, hepatectomy, cholecystectomy and also retroperitoneal lymph node dissection was performed. Microscopic examination revealed variable necrosis and diffuse sheets of neoplastic cells which have pink cytoplasm with eccentric nuclei due to intracytoplasmic inclusions of the eosinophilic hyaline globule. Immunohistochemically, diffuse vimentin staining and loss of INI1 expression were observed. Histopathological and immunohistochemical results were compatible with a primary malignant rhabdoid tumour of the kidney with metastasis to liver and right adrenal gland.
Conclusion: Because of the rarity of a primary malignant rhabdoid tumour of the kidney, pathologists should keep in mind this entity and also exclude the diagnosis of Wilms tumour, clear cell sarcoma, and Ewing sarcoma.

E-PS-24-066

A rare case report of testicular lesion - paratesticular fibrous pseudotumour

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Background & Objective: Paratesticular fibrous pseudotumour also known as chronic proliferative periorchitis, is a rare benign lesion of unknown etiology. Usually located between testicular tunica layers and involves epididymis and spermatic cord. Sometimes is difficult to distinguish this pseudotumour from malignant lesion. That's why intraoperative rapid diagnosis its helpful method to preserve the organ from unnecessary orchiectomies. We presented a case of 44 years old man with painless, solid, palpable structures in the left testicle.
Method: Demographic, clinical, radiological and pathological findings of the patient were investigated retrospectively.
Results: The ultrasonography revealed hyperechoic lesions adjacent to the left testis. The surgeon decided to undergo local excision, with intraoperative evaluation of tumour mass. During the frozen section the diagnosis couldn't be established, and lesion was completely removed. The mass was excised in five parts, largest tissue measured about 1,5x2,5 cm. The gross appearance of lesion presented as homogeneous thickened mass of firm white tissue surrounded with dense capsule, with some small hemorrhagic zones. The histological evaluation revealed dense fibrous tissue, with thick collagen bundles, sparse fibroblasts and inflammatory cells and dystrophic calcification in some areas. There were no atypical cells and necrosis.
Conclusion: Immunohistochemistry with Ki67 showed low proliferation index, and beta catenin show negative reaction. The lesion was reported as a fibrous pseudotumour.

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Ewing sarcoma of the kidney. Report of a case

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Background & Objective: Ewing Sarcoma (ES) is a malignant tumour usually located in bones. ES of the kidney is extremely rare, with fewer than 100 cases reported in the English literature. We present a case of ES of the kidney.
Method: A 62-year-old patient with history of squamous cell lung carcinoma was admitted to the urology department due to hematuria. Imaging studies revealed a 17 cm mass involving the right kidney. CT guided FN biopsy was performed which was positive for malignant mesenchymal neoplasm with neuroectodermal differentiation. Immunohistochemical study was positive for Vimentin, CD-99, Fli-1 and negative for CK-8/18, p63, RCCma, GATA-3, CEA, CK-7, Oct3/4, 3412, EMA, CD-34 and Melan-A, Chromogranin and Synaptophysin. Ki-67 stained 90% of tumour nuclei. A right nephrectomy was performed. On gross examination the tumour was solid and had gray–white color. On microscopic examination the kidney was extensively infiltrated by a tumour consisting of small round cells devoid of prominent nucleolus. Mitotic count was high. Immunohistochemical investigation was identical to FNB investigation.
Results: The diagnosis of malignant mesenchymal neoplasm morphologically and immunohistochemically consistent with ES of the right kidney was made. The patient died a month after surgery.
Conclusion: ES of the kidney is a very aggressive neoplasm that predominantly affects young adults, with a slight male predominance. It exhibits aggressive clinical behavior showing early metastasis and high recurrence rate.